LITERATURE-RELATED DISCOVERY: COMMON FACTORS FOR PARKINSON'S DISEASE AND CROHN'S DISEASE

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ABSTRACT

Literature-related discovery (LRD) is the linking of two or more literature concepts that have heretofore not been linked (i.e., disjoint), in order to produce novel, interesting, and intelligible knowledge (i.e., potential discovery). The mainstream software for assisting LRD is Arrowsmith, and it generates intermediate linking literatures by matching title phrases from two disjoint literatures (literatures that do not share common records). Arrowsmith then prioritizes these linking phrases through a series of text-based filters.

The present study examines another route to linking disjoint literatures (shared references) through a process called bibliographic coupling. Two disjoint literatures were selected: Parkinson's Disease (PD) (neurodegeneration) and Crohn's Disease (CD)(autoimmune). Three cases were examined: matching phrases in records with no shared references; shared references in records with no matching phrases; matching phrases in records with shared references. In addition, the main themes in the body of shared references were examined through grouping techniques to identify the myriad linkages between the two literatures.

No concepts were identified in the matching phrases/no shared references records that could not be found in the matching phrases/shared references records. Some new concepts (at the sub-set level of the main themes) not found in the matching phrases/shared references records were identified in the shared references/no matching phrases records. The synergy of matching phrases and shared references provides a strong prioritization to the selection of promising matching phrases as discovery mechanisms.

There were three major themes that unified the PD and CD literatures: Genetics; Neuroimmunology; Cell Death. However, these themes are not completely independent. For example, there are genetic determinants of the inflammatory response. Naturally occurring genetic variants in important inflammatory mediators such as TNF-alpha appear to alter inflammatory responses in numerous experimental and a few clinical models of inflammation. Additionally, there is a strong link between neuroimmunology and cell death. In PD, for example, neuroinflammatory processes that are mediated by activated glial and peripheral immune cells might eventually lead to dopaminergic cell death and subsequent disease progression.

1. INTRODUCTION

Discovery in science is the generation of novel, interesting, and intelligible knowledge about the objects of study. Literature-related discovery (LRD) is the linking of two or more literature concepts that have heretofore not been linked (i.e., disjoint), in order to produce novel, interesting, plausible, and intelligible knowledge (i.e., potential discovery). Two major variants of LRD are: 1) open discovery systems (ODS), where one starts with a problem and generates a potential solution (or vice versa); and closed discovery systems (CDS), where one starts with a problem and a potential solution (or starts with two problems), and generates linking mechanism(s). (Kostoff, 2008).

A 2008 study surveyed the literature on ODS LRD (Kostoff et al, 2008a), and included some CDS techniques peripherally. Perhaps the most widely known and used CDS approach is expressed by the Arrowsmith software (Smalheiser, 2005), where the mechanisms that link two literatures are identified/discovered through common phrases shared by document titles in each of the literatures. These common phrases can be viewed as reflections of intermediate literatures that link the two primary literatures of interest. The author has used Arrowsmith for discovery experiments related to potential treatments and preventative measures in an ODS mode, and has found it a useful supplement to the author's variant of LRD (Kostoff et al, 2008b,c).

One operational problem with Arrowsmith and similar text-based linking techniques is that thousands, or tens of thousands, of shared phrases may be identified. There is no guarantee that each shared phrase represents a relevant concept linking the two disparate literatures. To check for relevancy of a given phrase, each article in the two literatures (or a representative sample of articles if the number is large) must be examined by experts, and a judgment made as to whether there is a relevant linkage. Checking out each phrase for relevancy can be a very time consuming process. Therefore, for feasibility, some method of prioritizing phrases for relevancy is required.

In the MS and PD LRD studies published by the author (Kostoff et al, 2008b,c), Arrowsmith was used sporadically to compare with the author's approach. Because the author's approach used abstracts, while Arrowsmith used titles, the author's LRD variant generated far more voluminous potential discovery. However, in using Arrowsmith, the author found the most efficient ranking approach for potential discovery purposes to be matching of the shared title phrases with dominant medical terms obtained from clustering the MS and PD

abstracts. The clustering algorithm used TF-IDF term weighting, and the highest weighted biomedical terms in each cluster were selected for comparison with the matching phrases.

The developers of Arrowsmith have generated their own method for prioritizing/filtering the matching phrases (Torvik and Smalheiser, 2007; Smalheiser, 2005). They identified eight features that could be incorporated into a filtering model, which the user could select optionally. These include: features that capture various aspects of absolute and relative frequencies of the terms within each literature; recency of the term when first appearing in MEDLINE; cohesion (roughly, whether the term refers to a highly specific or a general concept); conceptthood (i.e. whether the term maps to any UMLS semantic categories or not); shared MeSH headings between the two disjoint literatures, and presence on a stoplist of common words. All of these features focused on filtering of the text linkages.

However, there are many ways in which intermediate literature linkages between two or more primary disjoint literatures can be established. One could search for common authors, common institutions, common journals, common citing papers, common MeSH terms, common keywords, etc. One promising alternative, or supplement, to matching title phrases is matching references. A reference in an article reflects one or more concepts upon which the article draws. Two articles that share a common reference (bibliographic coupling) would therefore have some linkage through the shared concept(s), even though the articles themselves might have vastly different terminology. So, searching for linkages among two or more articles through shared references offers a way to identify linking mechanisms or underlying joint themes that might not be accessible through text linking alone.

The main objective of this paper is to demonstrate proof-of-principle that shared references between two disjoint literatures provide a strong prioritization mechanism for selecting shared title phrases for potential CSD. A secondary objective is to demonstrate that some mechanisms linking the two literatures through shared references were not identifiable through phrase matching alone. The demonstration testbed is the Parkinson's Disease literature (neurodegeneration) and the Crohn's Disease literature (autoimmunity). What are the common medical/biological themes that link/underlay these two seemingly disparate diseases?

2. BACKGROUND

2.1. Text Mining

2.1.1. Closed Discovery Systems

Over the past two decades, there have been numerous attempts to identify indirect linkages among two or more disjoint literatures. Starting in the mid-late 1980s, Swanson and colleagues (e.g., Swanson, 1987; Swanson, 1988; Swanson, 1990; Smalheiser and Swanson, 1996; Swanson et al, 2001) published a series of papers on mechanisms connecting two essentially disjoint literatures. The concepts linking the two disjoint literatures were obtained by identifying phrases common to titles in both literatures. For example, in Swanson's article linking magnesium to migraine, he found that the phrase "spreading depression" occurred in the titles of papers in both the magnesium and migraine literatures. He then read the papers in each literature containing "spreading depression" in their titles to ascertain whether a physiologically defendable linking mechanism existed. During this evolutionary process, Swanson and Smalheiser developed a software package (Arrowsmith) that would import the two disjoint literatures and identify all the common title phrases (Smalheiser, 2005).

Wren et al (2004) also used a linking methodology based on phrase co-occurrences. They constructed "a network of tentative relationships between „objects' of biomedical research interest (e.g. genes, diseases, phenotypes, chemicals) by identifying their co-occurrences within all electronically available MEDLINE records. Relationships shared by two unrelated objects are then ranked against a random network model to estimate the statistical significance of any given grouping."

Srinivasan (2004) used a linking methodology based on weighted vectors of MeSH terms of the two starting disjoint literatures. The linking terms are those shared by the MeSH profiles (weighted vectors) of the two starting literatures, limited by semantic type. There are other linking processes based on text linking variants, such as linking MeSH terms, other types of keywords, and latent semantic analysis.

Almost all the CDS approaches (samples of which are shown above) have focused on medical topics, and have used primarily the Medline database. While Medline is very comprehensive in terms of laboratory research and clinical practices, it does not contain citation data. Thus, all the linking approaches above have focused on textual link variants.

2.1.2. Citation Connections

Another pathway for linking articles is through citation connections. Thus, articles could be linked through shared references, shared citing papers, and many other variants that are sub-sets of a comprehensive citation network. Two linking mechanisms have been described extensively in the literature. Bibliographic coupling and co-citation. Co-citation is defined as the edge between two documents cited by the same paper(s). Bibliographic coupling is defined as the edge between two documents citing the same paper(s). If both paper A and B are cited by C, there is co-citation between A and B. And, if both D and E cite F, there is bibliographic coupling between D and E. The more shared references, the stronger their relationship. Co-citation analysis was not used in the present study, and will not be discussed further.

2.1.2.1. Bibliographic Coupling

Bibliographic coupling appears to have originated in a series of papers by MM Kessler in the early 1960s (Kessler, 1963). Martyn (1964) observed that there is no guarantee that two bibliographically coupled documents cite the same piece of information in the shared reference. He also observed that even if the same unit of information in the shared reference is cited, the degree of alignment is unknown. Martyn concluded that a bibliographic coupling denotes some indication of a relationship of unknown strength between two documents.

Schiminovich (1971) classified academic publications automatically with recursive bibliographic coupling. Jarneving (2007) combined bibliographic coupling with complete link clustering to map the field of organic chemistry. Shibata et al (2009) compared the performance of methods for detecting emerging research fronts. Three types of citation network, co-citation, bibliographic coupling, and direct citation, were tested. Direct citation, which could detect large and young emerging clusters earlier, showed the best performance in detecting a research front, and co-citation showed the worst (a time lag is inescapably needed in order for papers to build up a co-citation record.).

Glanzel and Czerwon (1996) showed that bibliographic coupling techniques can be used to identify 'hot' research topics. The methodology is based on appropriate thresholds for both number of related documents and the strength of bibliographic links. These „core' documents have more than 9 links of at least the strength 0.25 according to Salton's measure. The measure of normalized coupling strength

applied had previously been suggested by Sen and Gan (1983) as the "coupling angle" (C.A.) between documents, analogous to Salton's cosine measure.

Most relevant to the present paper are approaches that combine bibliographic coupling with textual linkages. Calado et al (2006) evaluated how the link structure of the Web can be used to determine a measure of similarity appropriate for document classification. They experimented with five different similarity measures, and showed that link information alone allows classifying documents with an average precision of 86%. Further, when combined with a traditional text-based classifier, precision increased to values of up to 90%, representing gains that range from 63 to 132% over the use of text-based classification alone.

The combination of text and citations for classification purposes was shown to be superior in Cao and Gao (2005), Couto et al (2006), and Zhu et al (2007). Janssens et al (2006) examined hybrid clustering methods that exploited both text and citations to map the bioinformatics field. In general, text was more powerful than cited references, and dimensionality reduction by single value decomposition further improved results. However, the best outcome was obtained by integration.

2.2. Medical

2.2.1. Parkinson's Disease

PD is a progressive neurodegenerative disorder, affecting approximately 1% of individuals older than 60 years, and is characterized by resting tremor, rigidity, bradykinesia, and postural instability. PD develops when a part of the brain known as the substantia nigra degenerates. In healthy people, the substantia nigra contains nigral nerve cells that produce the chemical dopamine. Dopamine travels along nerve cell pathways from the substantia nigra to the striatum. In the striatum, dopamine activates nerve cells that coordinate normal muscle activity. In people with PD, nigral cells deteriorate and die at an accelerated rate, and the loss of these cells reduces the supply of dopamine to the striatum.Without adequate dopamine, nerve cells of the striatum activate improperly, impairing a person's ability to control movement. Additionally, collections of proteins (Lewy bodies, a sign of nerve cell death) form in the nerve cells (See the background in Kostoff et al, 2008b, for a more extensive summary of PD). There have been many reviews and books about PD, and the interested reader should refer to these for further medical details (Schapira et al, 2009; Poewe, 2009; Lees et al, 2009; Olanow et al, 2009; Lang, 2007; Lang, 2009; Ahlskog, 2005).

2.2.2. Crohn's Disease

CD and ulcerative colitis are chronic inflammatory diseases resulting from an inappropriate immune response (in genetically susceptible individuals) to microbial antigens of commensal microorganisms. CD is an inflammatory autoimmune disease where the body's immune system attacks the gastrointestinal tract. It primarily causes abdominal pain, diarrhea, vomiting, or weight loss, but may also cause complications outside of the gastrointestinal tract (e.g., arthritis).

Males and females are equally affected. Smokers are three times more likely to develop CD. It affects between 400,000 and 600,000 people in North America, and in the range of 30-50 per 100,000 for Northern Europe. CD tends to present initially in the teens and twenties, with another peak incidence in the fifties to seventies, although the disease can occur at any age. There have been many reviews and books about CD, and the interested reader should refer to these for further medical details (McBrewster et al, 2009; Cadwallader et al, 2008; Baumgart, 2009; Caprilli et al, 2008; Akobeng, 2008; Panes et al, 2007).

3. METHODOLOGY

3.1. Database

The Science Citation Index/Social Science Citation Index (SCI/SSCI) was selected as the source database, due both to its strong medical component and its use and linking of references. In August 2009, a search of these databases limited to Articles and Reviews yielded ~23,500 records for PD and ~11,000 records for CD. There were five records common to the two databases. Four of the five included both diseases in lists of chronic diseases, and there were no linking mechanisms discussed. To ensure disjointness of the two literatures, the PD query negated any records containing CD. The most recent 5,000 records from each retrieval were downloaded, resulting in the PD literature from ~mid-2007-2009 and the CD literature from ~2004-2009.

3.2. Software

These records were imported into the Vantage Point software, and its Natural Language Processing feature generated the title and Abstract phrases (in the present context, a phrase is one or more adjacent words contained in the text). Its bibliometrics feature also generated various field lists (authors, journals, institutions, etc), especially all the references cited in the downloaded records. Vantage Point also allows common field items between two data files to be determined. This feature was exploited to identify title and Abstract phrases shared between the PD and CD records and references shared between the two databases' records.

3.3. Approach

3.3.1. Overview

The major objective of this study can be summarized as:

demonstrate proof-of-principle that shared references between two disjoint literatures provide a strong prioritization mechanism for selecting shared phrases for potential CDS;

a. identify those mechanisms linking the two literatures through shared references that were not identifiable through phrase matching alone.

There are myriad ways that linking mechanisms between two disjoint literatures can be identified through shared references and/or phrase matching. The most complete is to read all the records in each literature, identify related records, and extract the linking mechanisms. In the present case, with 5000 records in each literature, 10000 records would have to be read (at least the Abstract, preferably full text for completeness), and 12,500,000 potential binary linkages considered. This is clearly infeasible.

A simpler approach is to search for records in each literature that have common features, and read only those records. While some linkages may be lost depending on differences in expressing the features of interest, this approach becomes feasible. If the common features are matching phrases in the titles, this is equivalent to the Arrowsmith approach. Even with this approach, many records must be read. In the present case, there were 1066 shared title phrases. In the Parkinson's literature, there were 2872 records that contained these 1066 title phrases, and in the Crohn's case, there were 3329 records. This is still a large number of records to read, and a larger number of combinations to consider, although only the records in both literatures associated with each phrase need to be read for the purpose of binary combinations. Some method of prioritizing phrases is necessary, since in nominal usage only a few phrases and their associated records will be examined due to time limitations. As has been shown, Arrowsmith has a number of prioritization approaches; as will be shown later, the present paper has one as well. Phrase matching in the titles with prioritization based on shared references will be demonstrated in the present study. For purposes of analysis, it will be assumed that only the matching title phrases are the linking mechanisms.

If the common features are matching phrases in the Abstracts, the approach is similar to the one above based on titles, but there will be far more phrases that have to be prioritized, and the potential for more linking mechanisms to be identified. In the present case, there are 13267 matching Abstract phrases, an order of magnitude more than the matching phrases in the titles. In the PD literature, there were 4928 records that contained these 13267 title phrases, and in the CD case, there were 4738 records. Essentially, all the records in the databases contain matching phrases in the Abstracts. If Abstracts are to be used as the phrase matching medium, a strong prioritization technique for phrase selection is required. To limit the scope of the present study, Abstracts from the citing papers will not be considered as linking mechanisms here, but will be left for future efforts. Abstracts from the references will be used for document clustering/factor analysis, which will identify the main underlying themes.

If the common features are shared references, then 2284 PD records and 2427 CD records must be read, but the only combinations for each reference will be all the records in each literature that include the reference. The linking mechanisms could be represented by all the technical phrases in the shared references, or by the sub-set of matching phrases (title or Abstract) contained in the references. For those records that contain both matching phrases and shared references, the linking mechanisms will be assumed to be represented by the matching phrases. This will be validated by grouping (factor analysis and/or document clustering) the shared references, and comparing the themes of the groups/clusters with those of the matching phrases.

For those records that contain matching phrases but not shared references, the linking mechanisms will be assumed to be represented by the matching phrases. For those records that contain shared references but not matching phrases, the linking mechanisms will be assumed to be represented by the title phrases of the shared references.

In all cases above, because of time and other resource limitations, only the highest prioritized phrases (matching or total) will be validated as mechanisms by reading the associated records from both literatures.

3.3.2. Records with matching phrases and shared references

To identify linking mechanisms between two disjoint literatures through shared references, two approaches were used. In the first approach, the shared title phrases (1066) were matrixed with the shared references (3254) for each literature. Initially, all the items in the shared phrases list (1066) were matrixed against all the items in the shared references list (3254). Later, all the items in either the shared phrases list (1066) or shared references list (3254) were matrixed against all the items in the corresponding list treated as a group (1).

This two-step approach effectively integrated over all the items on the axis of interest. In the first matrix (item x item), phrases that appeared frequently with one of the shared references being analyzed were identified. These phrases were then examined in the second matrix (phrase item x ref group) to select those phrases whose appearance in records that shared common references between the two literatures was a substantial fraction of their appearance in the total database. Or, if preferred, one could start with the second matrix, and select those phrases whose appearance in records that shared common references between the two literatures was a substantial fraction of their appearance in the total database. For phrases whose fractions were identical, prioritization was ordered by total frequency of appearance.

The reason for the second-step (integration) can be shown by the following example. In the total CD literature, the title word ‚apoptosis' appeared 22 times. In the sub-set of the CD literature that shared references with the PD literature, ‚apoptosis' appeared 17 times. Thus, using this integrated approach, one can obtain a measure of the relative appearance of a phrase in those records with shared references to total literature appearance, which might provide some

indication of concept commonality across the two literatures. The combination of reading the shared reference, reading some of the citing papers from each literature, and identifying the phrases in the citing literature that appear most of the time in the records with shared references should provide the links between the citing literatures and the shared reference, the underlying common theme, and the common features of the actual disease.

Each underlying common theme can be viewed as a piece of a much larger puzzle. If all the themes common between the two diseases could be identified, then they might be integrated to identify a more complete picture of the underlying common biological problems driving both diseases. Then, a more eclectic medical approach could be devised to address the underlying problems in parallel. One could see the natural expansion of this process to searching for commonality among multiple diseases, allowing more comprehensive eclectic approaches to be pursued. While this approach is most directly applicable to specific people who experience all the multiple diseases examined, there would be useful applications to people who perhaps exhibit symptoms of only one of the diseases studied.

3.3.3. Records with matching phrases and no shared references

To identify mechanisms linking the two literatures through matching phrases whose associated records in the two literatures did not share references, two approaches were taken. First, a list of the matching title phrases in the PD/CD literatures (1066) and a list of title phrases of the shared references (8005) were generated. The lists were combined, and the matching title phrases that had no counterpart in shared references titles were identified. Those matching title phrases that had biomedical significance were used to query the Abstracts of the shared references, to see whether the biomedical concepts reflected in the matching phrases could be found in the body of the shared references' Abstracts. The final step consisted of reading the PD/CD Abstracts of the articles whose title matching phrases could not be found in the titles or the Abstracts of the shared references. The purpose of the final step was to ascertain whether the matching title phrases formed a credible link to an underlying mechanism of PD/CD, or whether the

phrases led to no credible link. For an example of the latter, a very general phrase like „blood tests' could occur as a matching phrase in the titles of PD and CD papers, but have no discernable relation to any underlying mechanism.

Second, a matching phrase-shared reference matrix (phrase item (1066) x reference group (1)) was generated, and those records identified that had matching phrases and no shared references. The matching phrases were assumed to be the linking mechanisms. These matching phrases were priority ordered by the numbers of record titles in which they appeared in both databases. Those matching title phrases that had biomedical significance were used to query the Abstracts of the shared references, to see whether the biomedical concepts reflected in the matching phrases could be found in the body of the shared references'. The final step, same as in the first approach above, consisted of reading the PD/CD Abstracts of the articles whose title matching phrases could not be found in the titles or the Abstracts of the shared references.

3.3.4. Records with shared references and no matching phrases

To identify mechanisms linking the two literatures through shared references whose associated records in the two literatures did not contain matching phrases, the following steps were taken. A matching phrase-shared reference matrix (phrase group (1) x reference item (3254)) was generated, and those records that had shared references and no matching phrases were identified. These records were downloaded into a sub-database.

Phrases from the records in the titles of the sub-database were extracted as potential linking mechanisms. Those that were identical to any of the 1066 title matching phrases were eliminated. The remainder of the extracted phrases was then compared to phrases in the Abstracts of the articles with the 1066 matching phrases, and any that were identical were excluded as well. Finally, the remaining extracted phrases were then compared with the phrases in the Abstracts of the shared referencesto articles that had matching phrases as well, and any identical

phrases were removed. What remained were title phrases from shared references that could not be found in the other shared references associated with matching title phrases, or the Abstracts or titles of the citing records that contained the matching phrases. These title phrases were potential linking mechanisms not obtainable by the matching phrases approach.

4. RESULTS

4.1. Bibliometrics

Table 1 presents the resulting bibliometric numbers for the two databases examined. Most of the downloaded records had Abstracts. For both the Title and Abstract phrases, about ten percent were shared between the two databases. The PD records had, on average, noticeably more references than the CD records (~40%). About 2-3% of these references were shared. This is in contrast to a precursor study (unpublished) comparing the cataract and tinnitus literatures. In that study, 2500 records from each database were downloaded, there were ~54500 references in the cataracts records and ~42500 references in the tinnitus records, and only 315 references were shared. This is less than 1% of total references, and is about 1/3 the fraction shared in the PD/CD databases.

TABLE 1 – PARKINSON'S/CROHN'S BIBLIOMETRICS

METRIC	PARK	CROHN
# RECORDS	5000	5000
# RECORDS W/ABSTRACTS	4928	4733
# ABSTRACT PHRASES	117105	109520
# ABSTRACT PHRASES-SHARED	13267	13267
# CITED REFERENCES	156031	111165
# CITED REFERENCES-SHARED	3254	3254
# TITLE PHRASES	12630	10859
# TITLE PHRASES-SHARED	1066	1066

4.2 Themes of shared references

This section presents the major biomedical themes that /underly/link the PD and CD literatures, from the perspectives of document clustering and factor analysis. This section will serve as background for the more detailed phrase-level linking mechanisms that follow. In particular, linking mechanisms reflected by one or two papers may not appear in these aggregation approaches, but will surface in the phrase-level analyses.

4.2.1. Document clustering results

The 3254 references from the SCI/SSCI consisted of one line of information each, containing first author, publication year, abbreviated journal title, volume, and page (for journal references). To extract the text (title/abstract) from these references, the articles were located in the Medline database, and the titles and Abstracts extracted. Of the total articles searched, 169 could not be found in Medline, and 246 had no Abstracts. For the latter, the title and MeSH terms were used as proxy Abstracts. Thus, 3085 records with Abstracts were imported into the CLUTO clustering package, and a 64 cluster run was made.

The CLUTO output has a hierarchical structure. The highest level is the root node, containing all 3085 records. The next level, termed Level 1, is a bifurcation of the root node into two clusters. Level 2 is a bifurcation of each Level 1 cluster into two clusters for a total of four clusters, and so on down the hierarchy until the lowest level of 64 clusters. In the following presentation, Levels 1 and 2 will be discussed, followed by the lowest levels. The detailed contents of each cluster are contained in Appendix 1. The cluster heading numbers are taken from the CLUTO output.

In the outputs shown for each cluster in Appendix 1, there are either four or five phrase groupings (those clusters in the higher hierarchical levels have four groupings; those in the lowest level have five groupings), and for the clusters in the lowest level, sample titles of records in the cluster are shown. In the phrase groupings, Descriptive Terms are TF-IDF-weighted phrases whose weighting reflects their contribution to the cluster's theme, Discriminating Terms are TF-IDF-weighted phrases whose weighting reflects their contribution to the cluster's uniqueness, Single Word Terms are single words ranked in order of unweighted record frequency (numbers of cluster records in which the terms appear), Double Word Terms are double words ranked in order of unweighted record frequency,

and Triple Word Terms are triple words ranked in order of unweighted record frequency.

4.2.1.1. Levels 1 and 2

The first two hierarchical levels of the cluster taxonomy are shown on Table 2. The two clusters in Level 1 are Clusters 124 and 125. Cluster 124 (1131 records) focuses on patient genetics and the associated disease risk, while Cluster 125 (1954 records) focuses on laboratory research on the immune and central nervous systems at the cellular level. For Level 2, Cluster 124 sub-divides into Clusters 119 and 116, while Cluster 125 sub-divides into Clusters 121 and 123. Cluster 119 (661 records) focuses on genetics and disease association, while Cluster 116 (470 records) focuses on myriad aspects of patients' risk factors for disease. Cluster 121 (909 records) focuses on neuroimmunology, while Cluster 123 (1045 records) focuses on cell death.

TABLE 2 – HIERARCHICAL TAXONOMY

LEVEL 1	**LEVEL 2**
CL 124: Patients genetics; associated disease risk (1131)	CL 119: Genetics/disease assoc (661)
	CL 116: Disease risk factors (470)
CL 125: Laboratory research, immune/CNS, cellular level (1954)	CL 121: Neuroimmunology (909)
	CL 123: Cell death (1045)

4.2.1.2. Lowest Level Clusters

The lowest level clusters under each of the Level 2 clusters will now be summarized. The format is as follows: Column 1-cluster number (corresponds to cluster number in Appendix 1); Column 2-number of records in cluster; Column 3-abbreviated cluster theme (unabbreviated theme in Appendix 1); Column 4-sample record titles (more sample titles in Appendix 1).

Cluster 119: Genetics and disease association

CL #	**# REC**	**CLUSTER THEME**	**SAMPLE RECORD TITLES**
51	43	Gene mutations and relation to disease	Mutation in the alpha-synuclein gene identified in families with Parkinson's disease. APC mutations occur early during colorectal tumorigenesis.

33	32	Regulation of gene expression, emphasizing gene silencing	Expression profiling reveals off-target gene regulation by RNAi. Therapeutic silencing of an endogenous gene by systemic administration of modified siRNAs.
41	44	Microarrays to monitor gene expression levels	Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Evaluation of gene expression measurements from commercial microarray platforms.
15	25	Real-time PCR to study low abundance gene expression	Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Guideline to reference gene selection for quantitative real-time PCR.
50	46	Multiple sequence alignment of proteins and DNA for protein structure and function	Mass spectrometric sequencing of proteins silver-stained polyacrylamide gels. Genome sequencing in microfabricated high-density picolitre reactors.
26	56	Segment duplication in the human genome architecture; DNA re-arrangements for disease	Causal relation between alpha-synuclein gene duplication and familial Parkinson's disease. Detection of large-scale variation in the human genome.
3	30	Copy number variations within the human genome associated with disease	Genomic rearrangements and gene copy-number alterations as a cause of nervous system disorders. Copy-number variation and association studies of human disease.
45	76	Multilocus genetic linkage maps of the full genome	Construction of multilocus genetic linkage maps in humans. Genome-wide strategies for detecting multiple loci that influence complex diseases.
27	53	Statistical issues associated with genetic association tests	Family-based tests of association in the presence of linkage. An efficient Monte Carlo approach to assessing statistical significance in genomic studies.
14	44	SNP and haplotype analyses; haplotype/trait associations	Family-based tests for associating haplotypes with general phenotype data: application to asthma genetics. Score tests for association between traits and haplotypes when linkage phase is ambiguous.
31	68	Genome-wide SNP genotyping for whole genome association studies of diseases	Whole-genome patterns of common DNA variation in three human populations. Candidate single-nucleotide polymorphisms from a genomewide association study of Alzheimer disease.
38	48	Genetic predisposition to disease	Genetic determinants of the inflammatory response. The genetic epidemiology of neurodegenerative disease.
54	58	Genotype frequencies of polymorphisms;association with diseases	Molecular genetics and epidemiology of the NAT1 and NAT2 acetylation polymorphisms. A proinflammatory genetic profile increases the risk for chronic atrophic gastritis and gastric carcinoma.
34	38	Disease risk based on polymorphism analysis for allelic association	Complement factor H polymorphism in age-related macular degeneration. A common allele on chromosome 9 associated with coronary heart disease

Cluster 116: Patient risk

CL #	# REC	CLUSTER THEME	SAMPLE RECORD TITLES
4	38	Risk of hip fracture, and how it is affected by vitamin supplementation	Risk of hip fracture derived from relative risks: an analysis applied to the population of Sweden. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials.

60	72	Risk factors for diseases, especially cancer, and the impact of nutrition	Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. Cancer risk of heterocyclic amines in cooked foods: an analysis and implications for research.
58	61	Neurodegenerative diseases diagnosis	Progression of symptoms in the early and middle stages of Huntington disease. Autoantibodies as predictors of disease.
18	27	Risk factors for cardiovascular disease	Is the apoE4 allele an independent predictor of coronary events? C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women.
10	26	Myocardial infarction, especially risk factors	A common variant on chromosome 9p21 affects the risk of myocardial infarction. Smoking and risk of myocardial infarction. Statistical and biological interactions should not be confused.
32	40	Placebos in research and clinical trials	The placebo effect in irritable bowel syndrome trials: a meta-analysis. Understanding the placebo effect: contributions from neuroimaging.
52	53	Treatment for neurodegenerative and autoimmune diseases, emphasizing stem cell transplantation	Hematopoietic stem cell transplantation for multiple sclerosis. A retrospective multicenter study A phase I clinical trial of the treatment of Crohn's fistula by adipose mesenchymal stem cell transplantation.
21	31	Diagnosis, rating, treatment, and epidemiology of depressive disorders	The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). Hospital Anxiety and Depression Scale (HAD): some psychometric data for a Swedish sample.
39	45	Items and rating scales in health and quality-of-life surveys/questionnaires	Clinical impact versus factor analysis for quality of life questionnaire construction. Work losses related to inflammatory bowel disease in the United States: results from the National Health Interview Survey.
37	37	Meta-analyses and reviews, especially controlled clinical trials	Assessing the quality of reports of randomized clinical trials: is blinding necessary? Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses.
42	40	Drug development, interactions, adverse effects, and testing	Proposal for a new tool to evaluate drug interaction cases. Potential role of pharmacogenomics in reducing adverse drug reactions: a systematic review.

Cluster 121: Neuroimmunology

CL #	# REC	CLUSTER THEME	SAMPLE RECORD TITLES
17	80	The role of pro-inflammatory cytokine tnf-alpha in promoting inflammation	Tumor necrosis factor-alpha and FMLP receptors are functionally linked during FMLP-stimulated activation of adherent human neutrophils. The role of glial reaction and inflammation in Parkinson's disease.
25	67	The role of tnf in signal transduction/ induction of nf-kappa B responses	Failure to regulate TNF-induced NF-kappaB and cell death responses in A20-deficient mice. TNF receptor subtype signalling: differences and cellular consequences.
8	37	Transcription factor nf-kappa B and its role in	NF-kappaB: linking inflammation and immunity to cancer development and progression.

		inflammatory and innate immune responses	NF-kappaB regulation in the immune system.
55	66	Neurons, minocycline, nerve growth factor, and microglia in CNS protection	Minocycline slows disease progression in a mouse model of amyotrophic lateral sclerosis. Granulocyte-colony stimulating factor is neuroprotective in a model of Parkinson's disease.
36	57	enteric nervous system role in controlling gastrointestinal system	Choline acetyltransferase immunoreactivity of putative intrinsic primary afferent neurons in the rat ileum. Changes in chemical coding of myenteric neurones in ulcerative colitis.
9	29	Peroxisome proliferator-activated receptors; role in the regulation of inflammation	PPAR-gamma agonists inhibit production of monocyte inflammatory cytokines. The peroxisome proliferator-activated receptor-gamma is a negative regulator of macrophage activation.
6	26	Cannabinoids and endocannabinoids; effects on the immune and neural systems	The endogenous cannabinoid system controls extinction of aversive memories. Targeting endocannabinoid degradation protects against experimental colitis in mice: involvement of CB1 and CB2 receptors.
59	72	Receptors, especially histamine, dopamine, and opoid; impact on immune and neural functions	Histamine H4 receptor expression in human synovial cells obtained from patients suffering from rheumatoid arthritis. Molecular analysis of nicotinic receptor expression in autism.
7	30	Adenosine, especially adenosine receptors; impact on immune system and CNS	Activation of A2A adenosine receptor attenuates intestinal inflammation in animal models of inflammatory bowel disease. Grafts of adenosine-releasing cells suppress seizures in kindling epilepsy.
24	32	Matrix metalloproteinases /ghrelin in modulating inflammatory and immune responses	Membrane-type 1 matrix metalloproteinase cleaves CD44 and promotes cell migration. Ghrelin and des-acyl ghrelin inhibit cell death in cardiomyocytes and endothelial cells through ERK1/2 and PI 3-kinase/AKT.
35	35	Osteopontin, CD44, and CD200 in immune function mediation and regulation.	Soluble osteopontin inhibits apoptosis of adherent endothelial cells deprived of growth factors. Down-regulation of the macrophage lineage through interaction with OX2 (CD200).
47	71	Cytokines in regulating host immune response, especially inflammation, emphasing the interferons	IL-23 drives a pathogenic T cell population that induces autoimmune inflammation. The flavonoid baicalin exhibits anti-inflammatory activity by binding to chemokines.
30	47	Host inflammatory response, emphasizing toll-like receptors in activating inflammation	Toll-like receptor 4: the missing link of the cerebral innate immune response triggered by circulating gram-negative bacterial cell wall components. Role of Toll-like receptors in pathogen recognition.
61	56	Role of NO/nicotine in neural and immune diseases	Nitric oxide in inflammatory bowel disease: a universal messenger in an unsolved puzzle. RJR-2403: a nicotinic agonist with CNS selectivity II. In vivo characterization.
48	53	Causes and treatments for inflammation	Apoptosis and caspases regulate death and inflammation in sepsis. A cytokine-mediated link between innate immunity, inflammation, and cancer.
57	60	Role of blood-brain barrier dysfunction in central nervous system disease	Human TH17 lymphocytes promote blood-brain barrier disruption and central nervous system inflammation. Delivery of peptides and proteins through the blood-brain barrier.
46	48	Immunity, autoimmunity, and the response of the immune system	Immune cell migration in inflammation: present and future therapeutic targets. Recognition of microorganisms and activation of the immune response.

44	43	Role of Copolymer 1 in EAE; role of Th1/Th2 cytokines in relation to autoimmunity and allergy.	Copolymer 1 induces T cells of the T helper type 2 that crossreact with myelin basic protein and suppress experimental autoimmune encephalomyelitis. The paradigm of Th1 and Th2 cytokines: its relevance to autoimmunity and allergy.

Cluster 123: Cell Death

CL #	# REC	CLUSTER THEME	SAMPLE RECORD TITLES
1	24	Melatonin as a broad spectrum antioxidant, free radical scavenger, and anti-inflammatory agent.	Anti-inflammatory effect of melatonin on A beta vaccination in mice. Potent protective effect of melatonin on in vivo paraquat-induced oxidative damage in rats.
29	37	Signalling pathways necessary for inducing key immune and inflammatory responses	From calcium to NF-kappa B signaling pathways in neurons. Recent advances in the protein kinase B signaling pathway.
40	75	The role of mitogen activated protein kinases in signal transduction and regulation pathways	Mitogen-activated protein kinase pathways mediated by ERK, JNK, and p38 protein kinases. MAPK signalling pathways as molecular targets for anti-inflammatory therapy--from molecular mechanisms to therapeutic benefits.
22	43	The role of c-Jun amino-terminal kinases in JNK-mediated degenerative/ inflammatory processes	The c-Jun N-terminal kinases in cerebral microglia: immunological functions in the brain. Signal transduction by the c-Jun N-terminal kinase (JNK)--from inflammation to development.
0	28	Mesenchymal stem cells, as cardiac therapeutics and immunomodulation agents.	Comparative analysis of mesenchymal stem cells from bone marrow, umbilical cord blood, or adipose tissue. HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells.
43	70	Bone marrow-derived stem cells, especially for therapeutic purposes	Bone marrow as a source of endothelial cells and NeuN-expressing cells After stroke. Transplanted bone marrow generates new neurons in human brains.
12	42	Caspases, especially their central role in apoptosis	Caspases 3 and 7: key mediators of mitochondrial events of apoptosis. Caspases: pharmacological manipulation of cell death.
13	72	Autophagy, its physiological and pathophysiological roles, and the role of Beclin	Tor-mediated induction of autophagy via an Apg1 protein kinase complex. Loss of autophagy in the central nervous system causes neurodegeneration in mice.
53	86	Apoptosis-programmed cell death	Review of current evidence for apoptosis after spinal cord injury. Death receptors: signaling and modulation.
28	48	Role of autophagosomes in autophagy, and LC3 as a specific marker to monitor autophagy	LC3, a mammalian homologue of yeast Apg8p, is localized in autophagosome membranes after processing. LC3, GABARAP and GATE16 localize to autophagosomal membrane depending on form-II formation.
16	50	Regulatory T cells and their role in autoimmune disease, and Foxp3, a key regulatory gene	Control of regulatory T cell development by the transcription factor Foxp3. Defective regulatory and effector T cell functions in patients with FOXP3 mutations.
56	79	Oxidative stress and oxidative injury/damage	Reactive oxygen species, cell signaling, and cell injury. Oxidative damage and Alzheimer's disease: are antioxidant therapies useful?
49	72	The role of oxides in tissue injury and disease,	Bright and dark sides of nitric oxide in ischemic brain injury. Oxidative DNA damage induced by simultaneous generation of nitric

			oxide and superoxide.
20	40	Ubiquitin system in diverse cellular processes: neurodegenerative and immunological disorders.	Ubiquitin ligases and the immune response. Proteasome-independent functions of ubiquitin in endocytosis and signaling.
19	38	Unfolded protein response signaling pathway; impact of unfolded or malfolded proteins on cell survival	The presence of malfolded proteins in the endoplasmic reticulum signals the induction of glucose-regulated proteins. Parkinsonian mimetics induce aspects of unfolded protein response in death of dopaminergic neurons.
62	72	Proteins/ protein binding and its role in the activation of transcription factor NF-kappa B	The P-loop--a common motif in ATP- and GTP-binding proteins. Regulation of signaling protein function and trafficking by the hsp90/hsp70-based chaperone machinery.
63	79	The role of zinc in neurodegenerative disease/antioxidant;amino acid as zinc transporter	Zinc and disease of the brain. Effects of amino acids on zinc transport in rat erythrocytes.
2	17	Prion protein (PrP) in neuronal dysfunction; Poly(ADP-ribosyl)ation in inflammation,	Role of poly(ADP-ribose) synthetase in inflammation and ischaemia-reperfusion. Eight prion strains have PrP(Sc) molecules with different conformations.
11	23	The role of infection in gastric diseases, especially helicobacter pylori	Effect of diet and Helicobacter pylori infection to the risk of early gastric cancer. Cell wall-deficient (CWD) bacterial pathogens: could amylotrophic lateral sclerosis (ALS) be due to one?
5	22	Childhood development disorders, especially autism	Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey.
23	28	Iron regulation: relation to neural disorders, inflammation, and nitric-oxide mediated apoptosis;	Balancing acts: molecular control of mammalian iron metabolism. Cellular non-heme iron content is a determinant of nitric oxide-mediated apoptosis, necrosis, and caspase inhibition.

4.2.2. Factor matrix results

There were approximately 72,000 phrases in the Abstracts of the shared references extracted by NLP. The 2,000 phrases of highest frequency (frequency >=seven records) were inspected visually, and 984 phrases were identified as having biomedical significance. Different numbers of factors for a factor matrix were examined, and the default number (31, square root of the number of phrases) seemed to give good results. The 31 factors are highlighted in dark red in the matrix in Figure 1.

The format of Figure 1 is interpreted as follows. The top row is the number of each of the 31 factors, where each factor is viewed as a theme. The horizontal rectangles in blue are the themes of each factor, and the phrases listed below each Blue horizontal rectangle are the main phrases that determined the theme. The criterion for phrase selection was absolute value of loading (the matrix cell value) greater than or equal to 0.3. The main red vertical rectangle for each factor denotes loading values (matrix entries-not shown) in the selection range. Discrete red cells denote phrases that were in the selection range for multiple factors, but were listed only in one place. Thus, ‚degradation' is listed under Factor 2, but is also in the selection range for Factor 14.

The rightmost column lists the clusters associated with each factor. The clusters were selected (by visual inspection) on the basis that the factor theme was an important component of the cluster theme. In some cases, like Factor 7, the factor and cluster themes were essentially aligned. In other cases, like Factor 1, the factor theme was an important component of many clusters. Those cases in which the factor theme was mentioned in the cluster description or cluster record titles, but was not judged to play a major role in the cluster theme, are not listed in the rightmost column.

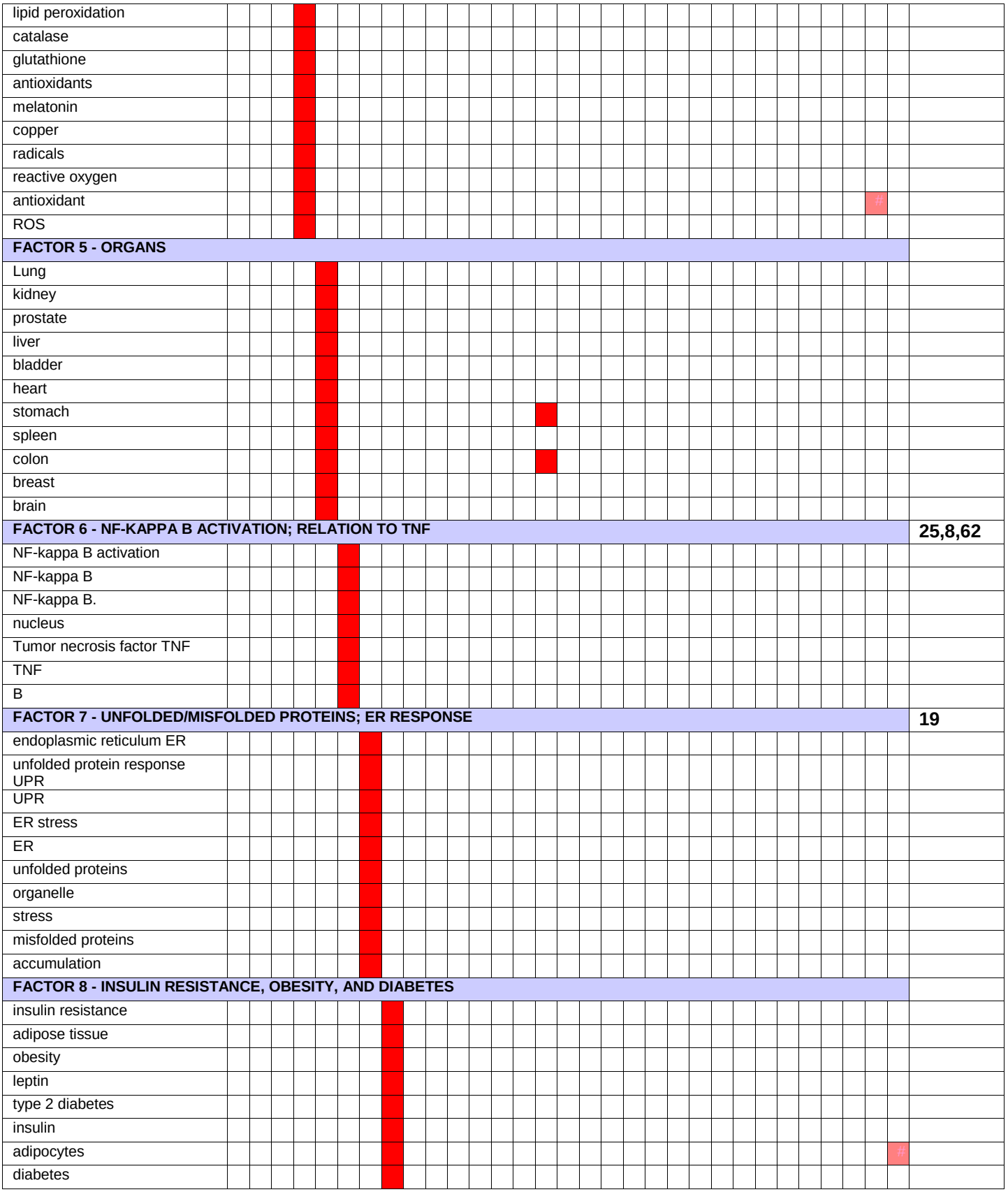
There were three factors listed that had no cluster mapping. Factor 5 was a listing of various body organs. While these were mentioned in many clusters, they were not the dominant theme in any. Factor 8 dealt with diabetes, and while it also was mentioned in a few clusters, it did not dominate any. The same was true for Factor 23.

There were twenty clusters that had no factor mapping. The cluster-factor mapping was done mainly by exact phrase matching. Unfortunately, the clustering software uses TF-IDF weighting to identify key phrases, while the factor matrix software uses NLP to generate phrases that were selected by visual inspection. It

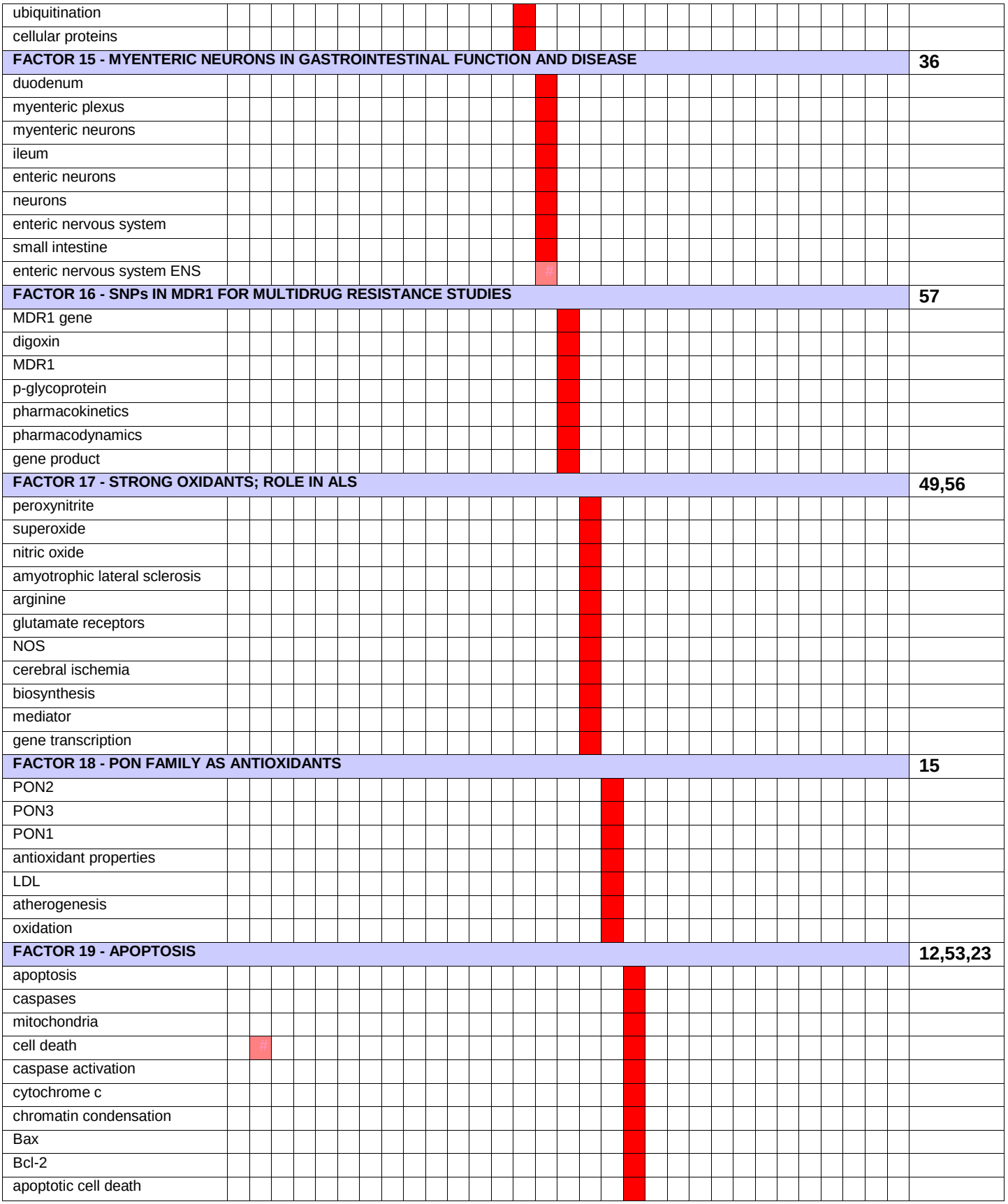
was the exact phrase mismatch more than thematic differences that generated most of the cluster non-mappings.

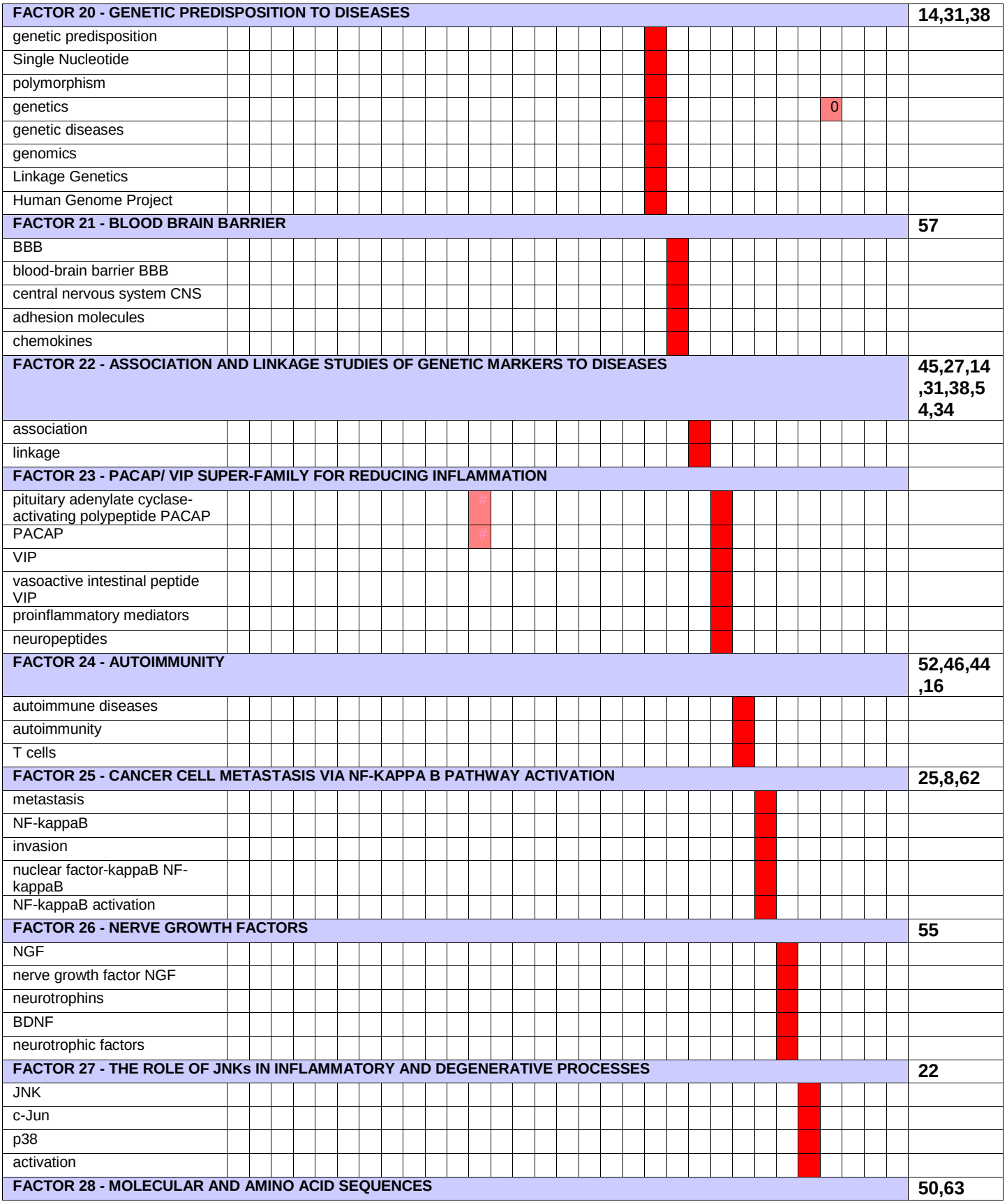
FIGURE 1 – FACTOR MATRIX OF SHARED REFERENCES ABSTRACT PHRASES

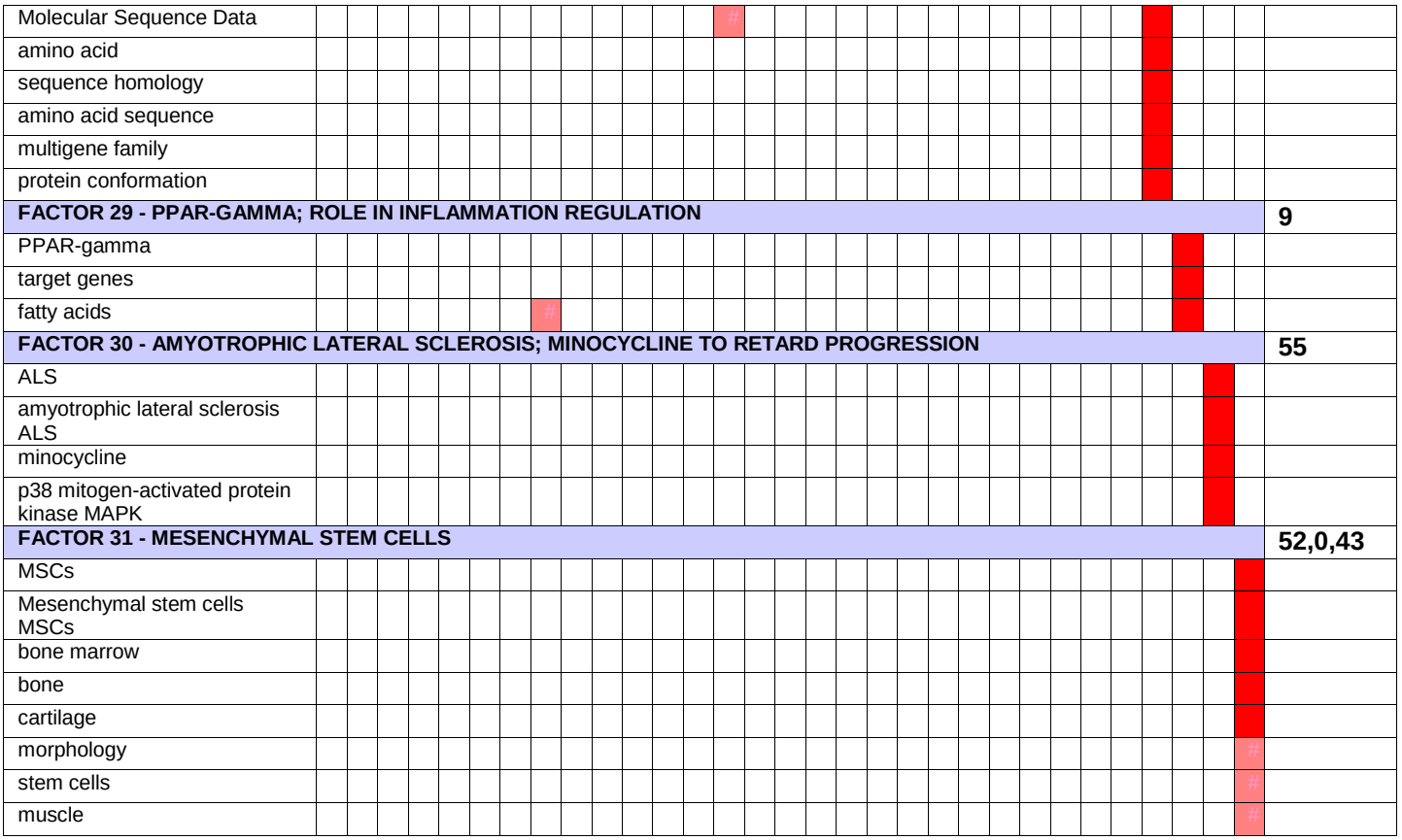
Factor	1	2	3	4	5	6	7	8	9	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	REL CL
FACTOR 1 - CYTOKINES; FOR PROMOTING AND REDUCING INFLAMMATION																															**17,47,48,46,44**
IL-1 beta																															
human monocytes																															
IL-4																															
IL-10																															
IL-8																															
IL-6																															
monocytes																															
LPS																															
TNF alpha																															
IFN-gamma																															
proinflammatory cytokines																															
FACTOR 2 - AUTOPHAGY																															**13,28**
autophagosomes																															
autophagy																															
lysosomes																															
organelles																															
macroautophagy																															
LC3																															
fusion																															
starvation																															
lysosome																															
autophagosome																															
long-lived proteins																															
autophagosome formation																															
degradation														#																	
eukaryotic cells																															
FACTOR 3 - MICROGLIA ACTIVATION AND PD																															**55**
microglia																															
microglial activation																															
dopaminergic neurons																															
Parkinson's disease PD																															
PD																															
degeneration																															
substantia nigra																															
neurodegeneration																															
neuronal degeneration																															
FACTOR 4 - OXIDATIVE STRESS																															**1,56,49,63,2**
oxidative stress																															
free radicals																															
iron																															
hydrogen peroxide																															



FACTOR 9 - EXPERIMENTAL AUTOIMMUNE ENCEPHALITIS ANIMAL MODELS FOR MULTIPLE SCLEROSIS	**44**
EAE	
MBP	
experimental autoimmune encephalomyelitis EAE	
myelin basic protein MBP	
multiple sclerosis	
multiple sclerosis MS	
MS	
FACTOR 10 - ROLE OF TOLL-LIKE RECEPTORS IN INNATE IMMUNE RESPONSE	**30**
TLRs	
Toll-like receptors TLRs	
TLR4	
innate immune system	
TLR2	
recognition	
TLR	
pathogens	
MyD88	
FACTOR 11 - DUPLICATION/COPY NUMBER VARIATION IN HUMAN GENOME AND DISEASE SUSCEPTIBILITY	**3**
inversions	
deletions	
insertions	
human genome	
duplications	
CNVs	
structural variation	
genetic variation	
genome	
genomes	
disease susceptibility	
SNPs	
FACTOR 12 - RELATION OF FRACTURE RISK TO BONE MINERAL DENSITY	**4**
fractures	
bone mineral density	
fracture	
hip	
hip fractures	
hip fracture	
osteoporosis	
FACTOR 13 - INFLAMMATORY BOWEL DISEASE	**61,32**
ulcerative colitis UC	
UC	
CD	
Crohn's disease CD	
inflammatory bowel disease IBD	
IBD	
ulcerative colitis	
nicotine	
FACTOR 14 - UBIQUITIN DYSFUNCTION IN NEURODEGEN-IMMUNOLOGICAL DISORDERS	**20**
ubiquitin	







4.2.3 Classes of shared references

The main objective of the present study was to identify common biomedical themes/mechanisms that underlay the two medical literatures. The main focus was on shared references. However, these references covered myriad themes, well beyond biomedical. This sub-section identifies some of the different classes into which these records could be categorized. The approach is to show the class/category title, and provide a few examples of reference titles in the category.

a. Disease economics

   The burden and costs of chronic diseases in low-income and middle-income countries.

Unemployment and disability in patients with moderately to severely active Crohn's disease.
Measuring the value of pharmacogenomics.

b. Relevant mechanisms from non-Parkinson's non-Crohn's literatures
The utilization of recombinant prostanoid receptors to determine the affinities and selectivities of prostaglandins and related analogs.
Innate immunity and toll-like receptors: clinical implications of basic science research.
Ways of dying: multiple pathways to apoptosis.
Oxidative stress and gene regulation.

c. Analytic methodology papers; software packages
Direct power comparisons between simple LOD scores and NPL scores for linkage analysis in complex diseases.
Transmission-disequilibrium tests for quantitative traits.
Genetic mapping in human disease.

d. Analytic software packages
PHENIX: building new software for automated crystallographic structure determination.
Basic local alignment search tool.
Gapped BLAST and PSI-BLAST: a new generation of protein database search programs.

e. Statistical methodologies
A tutorial on statistical methods for population association studies.
Statistical methods for assessing agreement between two methods of clinical measurement.
Estimating the population attributable risk for multiple risk factors using case-control data.

f. Data gathering
Mode of questionnaire administration can have serious effects on data quality.
Validating the SF-36 health survey questionnaire: new outcome measure for primary care.
Bowel patterns among subjects not seeking health care. Use of a questionnaire to identify a population with bowel dysfunction.

g. Alternative therapies

Pilot study of a moderate dose multivitamin/mineral supplement for children with autistic spectrum disorder.
Curcumin (diferuloylmethane) down-regulates expression of cell proliferation and antiapoptotic and metastatic gene products through suppression of IkappaBalpha kinase and Akt activation.
Green tea epigallocatechin-3-gallate mediates T cellular NF-kappa B inhibition and exerts neuroprotection in autoimmune encephalomyelitis.

h. Risk factor studies
A prospective study of diet and the risk of symptomatic diverticular disease in men.
Heterogeneity at the HLA-DRB1 locus and risk for multiple sclerosis.
The role of cigarettes and nicotine in the onset and treatment of ulcerative colitis.

i. Clinical trial methodologies
The revised CONSORT statement for reporting randomized trials: explanation and elaboration.
Assessing the quality of reports of randomized clinical trials: is blinding necessary?
Evidence-based decision making on micronutrients and chronic disease: long-term randomized controlled trials are not enough.

j. Psychological problems
Dreams of depressed patients. Characteristic themes in manifest content.
Depression: influence on time estimation and time experiments.
Discontinuation of use and switching of antidepressants: influence of patient-physician communication.

k. General laboratory techniques
Rapid and simple method for purification of nucleic acids.
A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding.
A rapid method of total lipid extraction and purification.

4.3 Phrase-level linking mechanisms

4.3.1 Matching phrases, no shared references

The following steps result in matching title phrases (not associated with shared references) that could not be found in the PD and CD records with shared references, or in the shared references associated with those records. In the first approach, the 1066 matching title phrases in the PD and CD literatures were reduced by eliminating the overlaps with the 8005 phrases in the titles of the shared references, and of the remainder, 84 were judged to be biomedically relevant. The Abstracts of the shared references were then queried for each of the 84 phrases, and 67 were located in the Abstracts. These 67 were excluded from further consideration. The Abstracts of the records in the PD and CD literatures that contained these 17 remaining matching phrases in their titles were read, to identify whether these phrases were serving as linking mechanisms. The judgment was made that none of these phrases were serving as linking mechanisms; they tended to be general phrases that happened to occur in titles in both literatures.

In the second approach, the process was initiated with the 302 matching phrases from records that had no shared references, and the above process (starting from those judged to be biomedically relevant) was repeated. There were no new linking mechanisms identified from the matching phrases in records with no shared references that could not be found in the shared references.

4.3.2 Shared references, no matching phrases

The following steps result in title phrases from the shared references (not associated with matching title phrases) that could not be found in the PD and CD records with matching phrases, or in the shared references associated with those records. There were 694 shared references whose citing papers did not have matching title phrases. These references were downloaded into a separate database, and 2223 title phrases were extracted. These 2223 phrases were reduced by eliminating overlaps with the 1066 title matching phrases. The remainder was reduced further by eliminating overlaps with the 13267 Abstract matching phrases, and the remainder from this process was reduced further by eliminating overlaps with 57,252 shared reference Abstract phrases (associated with the matching title

phrases). The resultant 1226 phrases may contain potential new concepts from shared references that could not be found from matching phrases in titles or Abstracts of the PD/CD literatures, or shared references associated with these matching phrase documents.

A note of caution. The phrases were generated by a Natural Language Processor in the Vantage Point software. Phrases representing the same concept in different records could be extracted differently by the NLP, so each candidate phrase needs to be inserted in the shared reference from which it came, and the reference evaluated for originality.

Appendix 2 presents some illustrative examples of linkages provided by seven of the 1226 phrases identified above. In general, the concepts tend to be novel sub-sets of the major themes identified by the document clustering and factor matrix, rather than radically new concepts completely disjoint from the clustering and factor themes.

4.3.3 Matching phrases, shared references

There were 764 matching phrases in records with shared references. In general, the higher the ratio of the appearance of these phrases in records with shared references to their appearance in the total database, the more they reflected a biomedically linking concept (e.g., macrophage activation). Additionally, the higher the value of their combined frequency of appearance, the more they reflected a major biomedically linking concept, based on the document clustering and factor matrix results (e.g., autophagy, microglia, melatonin).

Table 3 contains a sub-set of the matching phrases using the following selection criteria (ratio of the appearance of these phrases in records with shared references to their appearance in the total database **>.**8, sum of phrase frequencies in records with shared references >5. It should be emphasized these numbers apply strictly to

the phrases generated by the specific NLP used. The numbers would be different for phrases generated by other parsers, and any specific software implementation that combined phrase matching with shared references would have to be optimized based on the parser employed.

Three of the phrases are general (interactions, suppression, susceptibility), and the remainder are specific and biomedically relevant based on the document clustering and factor analysis results. The general phrases tended to be components of concepts that were biomedically relevant.

TABLE 3 – MATCHING PHRASES FOUND MAINLY IN PD/CD RECORDS WITH SHARED REFERENCES

SOURCE	PHR_FRE TOTAL_DB	MATCH PHRASE	PHR_FRE SHR_REF	RATIO SHR/TOT
CROHN	11	autophagy	11	1.00
PARK	8	autophagy	8	1.00
CROHN	10	chronic inflammation	9	0.90
PARK	3	chronic inflammation	3	1.00
CROHN	13	Cytokines	11	0.85
PARK	2	cytokines	2	1.00
CROHN	1	embryonic stem cells	1	1.00
PARK	6	Embryonic Stem Cells	5	0.83
CROHN	2	endoplasmic reticulum stress	2	1.00
PARK	5	endoplasmic reticulum stress	5	1.00
CROHN	4	enteric nervous system	4	1.00
PARK	2	enteric nervous system	2	1.00
CROHN	5	gene expression	5	1.00
PARK	6	gene expression	6	1.00
CROHN	6	genome-wide association studies	6	1.00
PARK	3	Genome-Wide Association Studies	3	1.00
CROHN	6	interactions	5	0.83
PARK	7	interactions	6	0.86
CROHN	8	melatonin	7	0.88
PARK	15	melatonin	14	0.93
CROHN	1	Microglia	1	1.00
PARK	17	microglia	15	0.88
CROHN	1	minocycline	1	1.00
PARK	14	minocycline	14	1.00
CROHN	11	Multiple Sclerosis	10	0.91
PARK	14	multiple sclerosis	12	0.86
CROHN	9	NF-kappa B	9	1.00
PARK	3	NF-kappa B	3	1.00

CROHN	5	suppression	5	1.00
PARK	7	suppression	6	0.86
CROHN	24	Susceptibility	21	0.88
PARK	3	susceptibility	3	1.00

SUMMARY AND CONCLUSIONS

The main objective of this paper is to demonstrate proof-of-principle that shared references between two disjoint literatures provide a strong prioritization mechanism for selecting shared phrases for potential CSD. A secondary objective is to demonstrate that some mechanisms linking the two literatures through shared references were not identifiable through phrase matching alone. The demonstration testbed is the PD (neurodegeneration) and CD literatures (autoimmunity).

The results showed that:

- There were no new linking mechanisms identified from the matching phrases in records with no shared references that could not be found in the shared references.
- There were 1226 phrases in the titles of the shared references that could contain potential new concepts from shared references that could not be found from matching phrases in titles or Abstracts of the PD/CD literatures, or shared references associated with these matching phrase documents. Analysis of seven of these phrases showed that, in general, the concepts tend to be novel sub-sets of the major themes identified by the document clustering and factor matrix approaches, rather than radically new concepts completely disjoint from the clustering and factor themes.
- There were 764 matching phrases in records with shared references. In general, the higher the ratio of the appearance of these phrases in records with shared references to their appearance in the total database, the more they reflected a biomedically linking concept (e.g., macrophage activation). Additionally, the higher the value of their combined frequency of appearance, the more they reflected a major biomedically linking concept, based on the document clustering and factor matrix results (e.g., autophagy, microglia, melatonin). The particular numbers used to classify phrases into these different groups are parser-specific, and would be different for phrases generated by other parsers. Any specific software implementation that combined phrase matching with shared references would have to be optimized based on the parser employed.

The highly positive results from this study suggest a number of follow-on efforts:

- Extend the phrase sources to Abstracts; there were about an order of magnitude more matching phrases in the Abstracts as compared to the titles,

and an order of magnitude more phrases in the shared references' Abstracts compared to their titles; additional linking mechanisms (at least at the fine-structure level) may be possible.
- Explore the synergy between the text-based prioritization filters of Arrowsmith and the bibliographic coupling based filters of the present approach, using an Arrowsmith-like platform (or Arrowsmith itself) with myriad common parsers.
- Examine myriad disjoint literature combinations to understand the breadth of applicability of the present approach, including both medical and non-medical literatures.
- Apply literature-based discovery techniques to the underlying mechanisms for PD/CD to identify novel preventative and treatment options applicable to both diseases.

There were three major themes that unified the PD and CD literatures: Genetics; Neuroimmunology; Cell Death. However, these themes are not completely independent. For example, there are genetic determinants of the inflammatory response. Naturally occurring genetic variants in important inflammatory mediators such as TNF-alpha appear to alter inflammatory responses in numerous experimental and a few clinical models of inflammation. Additionally, there is a strong link between neuroimmunology and cell death. In PD, for example, neuroinflammatory processes that are mediated by activated glial and peripheral immune cells might eventually lead to dopaminergic cell death and subsequent disease progression.

Much of the research effort in genetics is targeted at identifying genetic „signatures' unique to each individual, and diseases associated with those „signatures'. In genome-wide genetic studies with a large number of markers, error-rate reduction is essential to arrive at well-defined linkages.

The neuroimmunology component focuses on the role of myriad signaling pathways in regulating the interplay between the immune and neural systems. Especially important are the role of inflammation in destroying components of the neural system and the role of the neural system in controlling and regulating gastrointestinal functions.

Finally, the cell death component focuses on the different types of cell death (e.g., necrosis, apoptosis, pyroptosis, autophagy), the role of signaling pathways in enhancing and retarding these different cell death mechanisms, the impact of endogeneous and exogenous substances on promoting and delaying cell death, and

the potential for stem cells to serve as replacements in excessive cell death environments.

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APPENDICES

APPENDIX 1 – CLUSTER ANALYSIS OF SHARED REFERENCES – 64 CLUSTERS

CLUSTER 126

(3085 Records)

Cluster Syntax Features

Descriptive Terms

cell 2.8%, gene 1.6%, protein 1.5%, diseas 1.5%, activ 1.5%, receptor 1.2%, patient 1.1%, tnf 0.9%, genet 0.9%, express 0.9%, human 0.8%, genom 0.7%, kinas 0.7%, neuron 0.7%, function 0.7%, factor 0.7%, signal 0.7%, induc 0.6%, respons 0.6%, alpha 0.6%, system 0.6%, autophagi 0.6%, control 0.6%, risk 0.5%, (23.49%)

Single Word Terms

cell 1360, activ 1137, protein 1096, diseas 1077, gene 862, function 845, factor 818, express 802, human 763, role 748, induc 728, respons 660, regul 647, control 622, receptor 595, data 586, mechan 585, mediat 571, two 567, system 566, level 565, signal 557, inhibit 498, genet 486, pathwai 482

Double Word Terms

necrosis.factor 199, cell.death 190, tumor.necrosis 172, gene.expression 172, nervous.system 156, tnf.alpha 126, nitric.oxide 123, protein.kinase 122, single.nucleotide 117, anti.inflammatory 108, alzheimer.disease 105, transcription.factor 103, amino.acid 102, multiple.sclerosis 99, central.nervous 99, factor.alpha 99, growth.factor 96, wild.type 95, immune.system 92, genome.wide 91, activated.protein 88, oxidative.stress 86, parkinson.disease 84, bone.marrow 82, signal.transduction 81

Triple Word Terms

tumor.necrosis.factor 169, necrosis.factor.alpha 99, central.nervous.system 96, mitogen.activated.protein 78, single.nucleotide.polymorphisms 76, necrosis.factor.tnf 69, reactive.oxygen.species 68, nucleotide.polymorphisms.snps 58, alpha.tnf.alpha 58, activated.protein.kinase 58, factor.alpha.tnf 55, nitric.oxide.synthase 53, programmed.cell.death 41, inflammatory.bowel.disease 41, nuclear.factor.kappab 41, polymerase.chain.reaction 40, transforming.growth.factor 37, oxygen.species.ros 34, blood.brain.barrier 33, nervous.system.cns 33, single.nucleotide.polymorphism 33, apoptotic.cell.death 31, major.histocompatibility.complex 30, inducible.nitric.oxide 30, mesenchymal.stem.cells 30

CLUSTER 124

(1131 Records)

*Genetics and disease risk

Cluster Syntax Features

Descriptive Terms

gene 3.4%, genom 3.2%, patient 3.1%, genet 2.9%, risk 2.4%, diseas 2.2%, snp 2.0%, polymorph 1.5%, test 1.4%, data 1.4%, allel 1.4%, genotyp 1.3%, popul 1.1%, linkag 1.0%, haplotyp 1.0%, sequenc 0.9%, sampl 0.8%, control 0.8%, human 0.8%, chromosom 0.7%, marker 0.7%, region 0.7%, statist 0.7%, clinic 0.7%, (36.70%)

Single Word Terms

diseas 505, gene 449, genet 359, data 338, patient 299, control 285, risk 276, human 275, genom 266, two 255, polymorph 249, popul 239, function 228, on 226, clinic 215, singl 215, genotyp 211, number 205, sampl 203, factor 200, allel 198, high 196, region 188, test 182, new 170

Double Word Terms

single.nucleotide 116, genome.wide 90, case.control 78, nucleotide.polymorphisms 76, confidence.interval 68, gene.expression 65, linkage.disequilibrium 64, polymorphisms.snps 58, human.genome 51, odds.ratio 49, copy.number 44, risk.factors 42, alzheimer.disease 41, multiple.sclerosis 38, parkinson.disease 36, high.density 36, relative.risk 35, heart.disease 34, sample.size 32, clinical.trials 32, nucleotide.polymorphism 32, type.diabetes 31, myocardial.infarction 31, whole.genome 30, risk.factor 30

Triple Word Terms

single.nucleotide.polymorphisms 76, nucleotide.polymorphisms.snps 58, single.nucleotide.polymorphism 32, ratio.confidence.interval 26, odds.ratio.confidence 20, nucleotide.polymorphism.snp 20, polymerase.chain.reaction 20, coronary.heart.disease 20, transmission.disequilibrium.test 18, genetic.predisposition.disease 18, bone.mineral.density 18, copy.number.cnvs 16, magnetic.resonance.imaging 15, inflammatory.bowel.disease 14, high.density.lipoprotein 12, major.histocompatibility.complex 12, low.density.lipoprotein 12, coronary.artery.disease 12, risk.confidence.interval 11, positron.emission.tomography 10, age.macular.degeneration 10, population.attributable.risk 10, body.mass.index 10, randomized.controlled.trials 10, array.genomic.hybridization 10

CLUSTER 125

(1954 Records)

*Immune and Central Nervous Systems

Cluster Syntax Features

Descriptive Terms

cell 4.7%, activ 2.3%, receptor 2.1%, protein 2.1%, tnf 1.7%, kinas 1.3%, neuron 1.2%, induc 1.1%, signal 1.1%, autophagi 1.0%, inhibit 0.9%, express 0.9%, alpha 0.9%, regul 0.9%, immun 0.9%, mice 0.9%, apoptosi 0.9%, pathwai 0.8%, respons 0.8%, cytokin 0.8%, inflammatori 0.8%, system 0.7%, death 0.7%, factor 0.7%, (30.72%)

Single Word Terms

cell 1229, activ 1016, protein 927, induc 694, express 650, factor 618, function 617, role 615, regul 593, diseas 572, respons 563, receptor 551, mediat 531, signal 513, mechan 509, human 488, inhibit 478, system 473, pathwai 430, gene 413, level 395, inflammatori 389, depend 359, tissu 355, product 337

Double Word Terms

necrosis.factor 192, cell.death 186, tumor.necrosis 165, nervous.system 142, tnf.alpha 122, protein.kinase 118, nitric.oxide 115, gene.expression 107, anti.inflammatory 102, factor.alpha 95, transcription.factor 95, growth.factor 93, central.nervous 91, wild.type 87, oxidative.stress 86, activated.protein 86, immune.system 84, reactive.oxygen 81, signal.transduction 78, mitogen.activated 76, amino.acid 75, stem.cells 73, bone.marrow 71, transcription.factors 69, oxygen.species 68

Triple Word Terms

tumor.necrosis.factor 162, necrosis.factor.alpha 95, central.nervous.system 88, mitogen.activated.protein 76, reactive.oxygen.species 68, necrosis.factor.tnf 67, activated.protein.kinase 56, alpha.tnf.alpha 54, factor.alpha.tnf 52, nitric.oxide.synthase 49, nuclear.factor.kappab 41, programmed.cell.death 38, transforming.growth.factor 37, oxygen.species.ros 34, nervous.system.cns 32, apoptotic.cell.death 31, mesenchymal.stem.cells 30, blood.brain.barrier 29, tumour.necrosis.factor 29, wild.type.mice 28, inducible.nitric.oxide 27, inflammatory.bowel.disease 27, peroxisome.proliferator.activated 26, experimental.autoimmune.encephalomyelitis 26, extracellular.signal.regulated 25

CLUSTER 119 (124)

(661 Records)

*Genetics and disease association

Cluster Syntax Features

Descriptive Terms

gene 5.8%, genom 5.5%, genet 4.6%, snp 3.7%, polymorph 2.5%, allel 2.2%, genotyp 2.0%, linkag 1.8%, haplotyp 1.8%, sequenc 1.5%, diseas 1.4%, test 1.3%, data 1.2%, chromosom 1.2%, popul 1.2%, region 1.1%, human 1.0%, marker 1.0%, sampl 1.0%, risk 0.9%, map 0.8%, power 0.8%, loci 0.8%, singl 0.8%, (46.51%)

Single Word Terms

gene 417, genet 320, diseas 300, genom 256, polymorph 235, human 216, data 212, genotyp 190, singl 188, two 184, allel 180, region 164, control 159, popul 154, number 153, function 152, linkag 147, sampl 146, chromosom 139, snp 139, risk 138, complex 137, nucleotid 136, on 135, express 134

Double Word Terms

single.nucleotide 116, genome.wide 87, nucleotide.polymorphisms 76, linkage.disequilibrium 64, case.control 63, gene.expression 62, polymorphisms.snps 58, human.genome 50, copy.number 44, nucleotide.polymorphism 32, high.density 31, whole.genome 29, odds.ratio 29, type.diabetes 27, parkinson.disease 26, data.sets 26, large.scale 25, amino.acid 25, sample.size 25, data.set 24, candidate.genes 22, disequilibrium.test 22, allele.frequency 22, candidate.gene 21, genotype.data 21

Triple Word Terms

single.nucleotide.polymorphisms 76, nucleotide.polymorphisms.snps 58, single.nucleotide.polymorphism 32, nucleotide.polymorphism.snp 20, transmission.disequilibrium.test 18, genetic.predisposition.disease 18, polymerase.chain.reaction 17, copy.number.cnvs 16, major.histocompatibility.complex 12, ratio.confidence.interval 11, histocompatibility.complex.mhc 10, array.genomic.hybridization 10, coronary.heart.disease 10, odds.ratio.confidence 10, quantitative.trait.loci 9, age.macular.degeneration 9, hardy.weinberg.equilibrium 9, high.density.lipoprotein 9, population.attributable.risk 8, human.genome.project 8, real.time.pcr 8, disequilibrium.test.tdt 8, low.density.lipoprotein 7, case.control.data 7, high.density.snp 7

CLUSTER 116 (124)

(470 Records)

*Pateint risk

Cluster Syntax Features

Descriptive Terms

patient 10.9%, risk 3.3%, clinic 2.0%, fractur 2.0%, drug 1.9%, diseas 1.8%, health 1.8%, placebo 1.6%, trial 1.5%, ag 1.2%, medic 1.2%, women 1.1%, treatment 1.1%, depress 1.0%, measur 0.9%, rate 0.9%, vitamin 0.8%, disord 0.7%, item 0.7%, data 0.7%, cancer 0.7%, therapi 0.6%, scale 0.6%, test 0.6%, (40.11%)

Single Word Terms

patient 233, diseas 205, clinic 168, risk 138, data 126, control 126, treatment 120, ag 112, background 94, measur 92, on 91, factor 91, rate 87, health 86, popul 85, therapi 79, high 78, function 76, drug 75, new 74, reduc 72, two 71, activ 70, gener 70, design 69

Double Word Terms

confidence.interval 48, clinical.trials 30, risk.factors 27, relative.risk 26, myocardial.infarction 26, alzheimer.disease 23, heart.disease 21, multiple.sclerosis 21, double.blind 20, odds.ratio 20, main.measures 20, patients.treated 20, crohn.disease 19, bone.mineral 19, controlled.trials 19, magnetic.resonance 19, health.care 18, men.women 17, mineral.density 17, disease.patients 16, randomized.controlled 16, ratio.confidence 15, case.control 15, inflammatory.bowel 14, placebo.controlled 14

Triple Word Terms

bone.mineral.density 17, ratio.confidence.interval 15, magnetic.resonance.imaging 13, risk.confidence.interval 11, inflammatory.bowel.disease 11, coronary.heart.disease 10, odds.ratio.confidence 10, randomized.controlled.trials 10, risk.hip.fracture 10, positron.emission.tomography 10, relative.risk.confidence 9, acute.myocardial.infarction 8, selective.serotonin.reuptake 8, patients.alzheimer.disease 7, patients.crohn.disease 6, primary.end.point 6, randomized.double.blind 6, adverse.drug.reactions 6, serotonin.reuptake.inhibitors 6, crohn.disease.patients 6, blind.placebo.controlled 6, double.blind.placebo 6, creutzfeldt.jakob.disease 6, visual.analogue.scale 5, risk.myocardial.infarction 5

CLUSTER 121 (125)

(909 Records)

*Neuroimmunology

Cluster Syntax Features

Descriptive Terms

tnf 5.1%, receptor 4.8%, neuron 2.2%, cell 2.2%, alpha 2.0%, cytokin 1.8%, inflammatori 1.8%, immun 1.7%, activ 1.6%, tnf.alpha 1.3%, mice 1.3%, kappab 1.3%, express 1.1%, macrophag 1.1%, lp 1.0%, induc 1.0%, respons 1.0%, inhibit 0.9%, inflamm 0.9%, system 0.8%, factor 0.8%, brain 0.8%, anti 0.8%, signal 0.6%, (38.36%)

Single Word Terms

cell 549, activ 481, receptor 421, induc 365, express 364, factor 360, respons 341, protein 322, inflammatori 308, mediat 301, function 300, role 294, diseas 294, regul 283, system 270, human 268, inhibit 258, cytokin 255, mechan 234, immun 231, signal 227, level 214, alpha 194, stimul 194, gene 190

Double Word Terms

necrosis.factor 171, tumor.necrosis 147, nervous.system 121, tnf.alpha 112, anti.inflammatory 91, factor.alpha 90, central.nervous 81, nitric.oxide 62, factor.tnf 60, gene.expression 59, alpha.tnf 58, immune.system 56, ifn.gamma 54, nuclear.factor 53, multiple.sclerosis 50, lipopolysaccharide.lps 49, growth.factor 47, wild.type 46, immune.response 45, immune.responses 44, factor.kappab 43, innate.immune 42, interferon.gamma 40, inflammatory.cytokines 39, transcription.factor 39

Triple Word Terms

tumor.necrosis.factor 145, necrosis.factor.alpha 90, central.nervous.system 79, necrosis.factor.tnf 60, alpha.tnf.alpha 53, factor.alpha.tnf 51, nitric.oxide.synthase 36, nuclear.factor.kappab 34, nervous.system.cns 30, blood.brain.barrier 26, tumour.necrosis.factor 25, wild.type.mice 25, peroxisome.proliferator.activated 23, inducible.nitric.oxide 23, experimental.autoimmune.encephalomyelitis 23, enteric.nervous.system 22, inflammatory.bowel.disease 22, gamma.ifn.gamma 20, factor.kappab.kappab 20, proliferator.activated.receptor 19, interferon.gamma.ifn 19, mitogen.activated.protein 18, dose.dependent.manner 18, nuclear.factor.kappa 16, autoimmune.encephalomyelitis.eae 16

CLUSTER 123 (125)

(1045 Records)

*Cell death

Cluster Syntax Features

Descriptive Terms

cell 5.6%, protein 3.7%, autophagi 3.1%, kinas 2.7%, activ 2.0%, apoptosi 1.8%, stress 1.6%, death 1.6%, oxid 1.4%, signal 1.1%, cell.death 1.0%, caspas 1.0%, pathwai 1.0%, msc 0.9%, regul 0.8%, induc 0.8%, ubiquitin 0.7%, membran 0.7%, cellular 0.6%, bind 0.6%, melatonin 0.6%, degrad 0.6%, inhibit 0.6%, phosphoryl 0.6%, (35.91%)

Single Word Terms

cell 680, protein 605, activ 535, induc 329, role 321, function 317, regul 310, signal 286, express 286, diseas 278, mechan 275, factor 258, pathwai 253, mediat 230, gene 223, respons 222, inhibit 220, human 220, kinas 213, death 208, cellular 208, system 203, apoptosi 201, stress 200, depend 199

Double Word Terms

cell.death 156, protein.kinase 90, oxidative.stress 81, stem.cells 66, activated.protein 66, reactive.oxygen 63, mitogen.activated 58, transcription.factor 56, oxygen.species 55, signal.transduction 54, nitric.oxide 53, bone.marrow 52, amino.acid 50, endoplasmic.reticulum 49, gene.expression 48, growth.factor 46, wild.type 41, cell.lines 39, programmed.cell 38, protein.kinases 37, transcription.factors 36, cell.proliferation 34, superoxide.dismutase 34, alzheimer.disease 32, mesenchymal.stem 31

Triple Word Terms

mitogen.activated.protein 58, reactive.oxygen.species 55, activated.protein.kinase 42, programmed.cell.death 35, mesenchymal.stem.cells 30, oxygen.species.ros 29, apoptotic.cell.death 26, induced.cell.death 21, unfolded.protein.response 21, terminal.kinase.jnk 21, transforming.growth.factor 21, stem.cells.mscs 20, endoplasmic.reticulum.stress 20, extracellular.signal.regulated 19, activated.protein.kinases 17, poly.adp.ribose 17, tumor.necrosis.factor 17, amino.acid.sequence 15, protein.kinase.mapk 15, superoxide.dismutase.sod 15, protein.response.upr 14, p38.mitogen.activated 14, cd4.cd25.regulatory 14, serine.threonine.kinase 13, signal.transduction.pathways 13

CLUSTER 51 (124-119)

(43 Records)

*Gene mutations and relation to disease, especially cancer and neural disorders

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Cluster Syntax Features

Descriptive Terms

mutat 13.2%, gene 10.9%, zebrafish 3.4%, cancer 2.6%, phenotyp 2.4%, genet 1.9%, colorect 1.7%, epilepsi 1.3%, disease.genes 1.2%, function 1.2%, diseas 1.1%, inherit 1.0%, mutant 1.0%, splice 0.8%, loci 0.7%, chromosom 0.7%, human 0.7%, morpholino 0.7%, famili 0.7%, hereditari 0.7%, meganucleas 0.6%, transposon 0.6%, librari 0.6%, scei 0.6%, disord 0.6%

Discriminating Terms

mutat 8.4%, gene 3.6%, zebrafish 2.6%, cell 1.9%, colorect 1.2%, phenotyp 1.1%, activ 1.0%, epilepsi 1.0%, disease.genes 0.9%, receptor 0.9%, cancer 0.8%, tnf 0.8%, inherit 0.6%, kinas 0.6%, morpholino 0.5%, induc 0.5%, hereditari 0.5%, splice 0.5%, factor 0.5%, meganucleas 0.5%, transposon 0.5%, signal 0.5%, mutant 0.5%, scei 0.5%, autophagi 0.5%

Single Word Terms

gene 38, genet 23, mutat 23, function 22, diseas 19, phenotyp 19, human 18, protein 14, two 12, cancer 12, model 12, famili 12, number 12, genom 11, chromosom 11, sequenc 11, disord 11, inherit 11, express 10, mechan 9, gener 9, role 9, defect 9, cell 9, organ 9

Double Word Terms

gene.function 6, human.disease 5, disease.genes 4, disease.gene 4, candidate.genes 4, gene.expression 3, parkinson.disease 3, loss.function 3, central.role 3, amino.acid 3, autosomal.dominant 3, tumor.suppressor 3, suppressor.genes 3, colorectal.cancers 3, mutations.genes 3, mutations.gene 3, suppressor.gene 3, large.scale 3, colorectal.cancer 3, gain.function 2, data.set 2, human.chromosome 2, four.mutations 2, human.genes 2, rna.interference 2

Triple Word Terms

adenomatous.polyposis.coli 2, tumor.suppressor.genes 2, online.mendelian.inheritance 2, transposon.insertion.mutants 2, inheritance.man.database 2, mendelian.inheritance.man 2, tumor.suppressor.gene 2, subunits.voltage.gated 2, dna.methylation.gene 2, premature.stop.codon 2, genetic.basis.complex 1, patients.mouse.model 1, play.role.gene 1, structure.gene.expression 1, dna.methylation.histone 1, regulation.gene.expression 1, mutations.gene.encoding 1, mutation.premature.stop 1, autosomal.recessive.disorder 1, human.mouse.gene 1, proton.nuclear.magnetic 1, nicotinic.acetylcholine.receptors 1, magnetic.resonance.nmr 1, region.single.nucleotide 1, colorectal.cancer.colorectal 1

Genetics of idiopathic epilepsies.
Human disease genes.
Epigenetic changes in colorectal cancer.
Most rare missense alleles are deleterious in humans: implications for complex disease and association studies.
A human phenome-interactome network of protein complexes implicated in genetic disorders.
Mutations of mitotic checkpoint genes in human cancers.
Mitochondrial disease--its impact, etiology, and pathology.
Identifying autism Loci and genes by tracing recent shared ancestry.
Effective targeted gene 'knockdown' in zebrafish.
Mutations in LRRK2 other than G2019S are rare in a north American-based sample of familial Parkinson's disease.
Identification of the familial cylindromatosis tumour-suppressor gene.
Mutation in the alpha-synuclein gene identified in families with Parkinson's disease.
APC mutations occur early during colorectal tumorigenesis.
The genetics of human epilepsy.
A genomic screen for genes upregulated by demethylation and histone deacetylase inhibition in human colorectal cancer.
I-SceI meganuclease mediates highly efficient transgenesis in fish.

CLUSTER 33 (124-119)

(32 Records)

* Regulation of gene expression, emphasizing gene silencing, by short-interfering RNA and HDAC

Cluster Syntax Features

Descriptive Terms

sirna 12.0%, rna 8.6%, histon 6.7%, mirna 3.4%, hdac 3.1%, gene 3.0%, chromatin 2.6%, silenc 2.5%, transcript 1.8%, rnai 1.6%, express 1.6%, dsrna 1.4%, gene.expression 0.9%, interf 0.8%, small.interfering 0.8%, target 0.7%, acetyl 0.7%, methyl 0.7%, rna.interference 0.5%, mrna 0.5%, protein 0.5%, faah 0.5%, circadian 0.5%, promot 0.5%, direct 0.4%

Discriminating Terms

sirna 8.4%, rna 5.3%, histon 4.6%, mirna 2.3%, hdac 2.2%, chromatin 1.7%, silenc 1.7%, rnai 1.1%, cell 1.0%, dsrna 1.0%, receptor 0.9%, patient 0.8%, diseas 0.7%, tnf 0.7%, small.interfering 0.5%, genom 0.5%, interf 0.5%, neuron 0.5%, signal 0.5%, kinas 0.5%, transcript 0.4%, genet 0.4%, alpha 0.4%, activ 0.4%, autophagi 0.4%

Single Word Terms

gene 26, express 22, rna 19, cell 19, protein 17, activ 15, function 15, target 14, transcript 14, small 11, interf 11, human 11, regul 11, mediat 10, sirna 10, interfer 9, histon 9, mechan 8, encod 8, depend 8, mrna 8, interact 8, silenc 8, complex 8, vivo 8

Double Word Terms

gene.expression 11, rna.interference 9, small.interfering 9, interfering.rnas 7, interference.rnai 6, gene.silencing 6, rnas.sirnas 6, interfering.rna 4, mammalian.cells 4, histone.deacetylases 4, regulation.gene 3, micrornas.mirnas 3, transcriptional.gene 3, animals.plants 3, hdac.inhibitors 3, target.cleavage 3, post.transcriptional 3, post.translational 3, vitro.vivo 3, gene.function 3, double.stranded 3, messenger.rnas 3, protein.activity 3, rna.sirna 3, function.mammalian 2

Triple Word Terms

rna.interference.rnai 6, interfering.rnas.sirnas 6, small.interfering.rnas 5, small.interfering.rna 4, regulation.gene.expression 3, post.transcriptional.gene 3, transcriptional.gene.silencing 3, interfering.rna.sirna 3, interference.rnai.sequence 2, double.stranded.rnas 2, down.regulation.gene 2, gene.silencing.animals 2, silencing.animals.plants 2, sequence.post.transcriptional 2, rnas.sirnas.generated 2, induced.silencing.complex 2, rnai.sequence.post 2, rna.induced.silencing 2, cancer.hdac.inhibitors 2, short.interfering.rnas 2, expression.small.interfering 2, histone.deacetylases.hdacs 2, gene.function.mammalian 2, 100.fold.potent 1, tumor.suppressor.gene 1

Expression profiling reveals off-target gene regulation by RNAi.
Translating the histone code.
Histone-deacetylase inhibitors: novel drugs for the treatment of cancer.
Short hairpin type of dsRNAs that are controlled by tRNA(Val) promoter significantly induce RNAi-mediated gene silencing in the cytoplasm of human cells.
Synthetic dsRNA Dicer substrates enhance RNAi potency and efficacy.
MicroRNAs: genomics, biogenesis, mechanism, and function.
Rational siRNA design for RNA interference.
Chromatin modifier enzymes, the histone code and cancer.
Therapeutic silencing of an endogenous gene by systemic administration of modified siRNAs.
Histone deacetylases: unique players in shaping the epigenetic histone code.
siRNA-mediated gene silencing in vitro and in vivo.
A system for stable expression of short interfering RNAs in mammalian cells.
Histone deacetylases and SAP18, a novel polypeptide, are components of a human Sin3 complex.
Co-expression of anti-NFkappaB RNA aptamers and siRNAs leads to maximal suppression of NFkappaB activity in mammalian cells.

CLUSTER 41 (124-119)

(44 Records)

*Use of arrays and microarrays to monitor the expression levels of thousands of genes

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Cluster Syntax Features

Descriptive Terms

gene 13.5%, gene.expression 7.8%, express 7.5%, microarrai 6.7%, arrai 3.4%, data 2.0%, rna 1.5%, probe 1.4%, oligonucleotid 1.3%, human 1.1%, hybrid 1.0%, normal 1.0%, biolog 1.0%, measur 0.7%, platform 0.7%, profil 0.6%, set 0.6%, genom 0.6%, pattern 0.6%, chimpanze 0.5%, oligonucleotide.array 0.5%, expression.profiling 0.5%, brain 0.5%, tool 0.5%, microarray.data 0.5%

Discriminating Terms

gene.expression 5.0%, gene 5.0%, microarrai 4.8%, express 2.8%, arrai 2.2%, cell 1.8%, activ 1.1%, receptor 1.0%, protein 0.9%, oligonucleotid 0.9%, probe 0.8%, patient 0.8%, tnf 0.7%, rna 0.7%, diseas 0.7%, hybrid 0.6%, kinas 0.6%, induc 0.5%, platform 0.5%, alpha 0.5%, autophagi 0.4%, risk 0.4%, inhibit 0.4%, data 0.4%, signal 0.4%

Single Word Terms

gene 40, express 37, data 21, microarrai 20, human 18, two 16, arrai 15, high 14, genom 14, oligonucleotid 13, biolog 13, function 13, genet 12, dna 12, set 11, profil 11, level 11, on 11, transcript 11, cell 11, pattern 11, diseas 11, sequenc 10, normal 10, rna 10

Double Word Terms

gene.expression 34, expression.patterns 7, high.density 7, number.genes 6, density.oligonucleotide 6, genome.wide 6, differentially.expressed 5, microarray.data 5, expression.profiling 5, oligonucleotide.array 5, data.sets 5, oligonucleotide.arrays 4, expressed.genes 4, genes.expression 4, thousands.genes 4, human.brain 4, expression.data 4, differential.expression 3, microarray.platforms 3, real.time 3, affymetrix.genechip 3, rna.samples 3, expression.gene 3, genes.genes 3, level.data 3

Triple Word Terms

high.density.oligonucleotide 6, gene.expression.patterns 4, gene.expression.profiling 4, density.oligonucleotide.arrays 4, gene.expression.data 3, oligonucleotide.array.sequence 3, probe.level.data 3, biological.interpretation.gene 2, isolation.rna.cells 2, genes.differentially.expressed 2, one.gene.expression 2, real.time.pcr 2, density.oligonucleotide.array 2, one.region.brain 2, gene.expression.brain 2, high.throughput.genomic 2, expression.patterns.human 2, basis.gene.expression 2, expression.thousands.genes 2, brain.gene.expression 2, microarray.gene.expression 2,

patterns.gene.expression 2, diseases.microarray.gene 2, genes.genes.expression 2, gene.set.enrichment 2

Exploration, normalization, and summaries of high density oligonucleotide array probe level data.
Summaries of Affymetrix GeneChip probe level data.
The efficiency of pooling mRNA in microarray experiments.
Regional patterns of gene expression in human and chimpanzee brains.
Critical appraisal of DNA microarrays in psychiatric genomics.
Model-based analysis of oligonucleotide arrays: expression index computation and outlier detection.
Microarray analysis and organization of circadian gene expression in Drosophila.
Microarray reality checks in the context of a complex disease.
A survey of genetic human cortical gene expression.
Regional and strain-specific gene expression mapping in the adult mouse brain.
Quantitative monitoring of gene expression patterns with a complementary DNA microarray.
The MicroArray Quality Control (MAQC) project shows inter- and intraplatform reproducibility of gene expression measurements.
Normalization of cDNA microarray data.
Evaluation of gene expression measurements from commercial microarray platforms.
Significance analysis of microarrays applied to the ionizing radiation response.
Use of a three-color cDNA microarray platform to measure and control support-bound probe for improved data quality and reproducibility.
GoMiner: a resource for biological interpretation of genomic and proteomic data.
Chipping away at the chip bias: RNA degradation in microarray analysis.

CLUSTER 15 (124-119)

(25 Records)

* Use of the real-time polymerase chain reaction (PCR) to amplify cDNA products reverse transcribed from mRNA to study low abundance gene expression, especially the three members of the paraoxonase gene family (PON1, PON2, PON3)

Cluster Syntax Features

Descriptive Terms

pcr 11.8%, pon1 6.6%, real.time 4.7%, real 3.9%, dna 3.1%, probe 1.8%, polymeras 1.7%, pon3 1.6%, time 1.6%, pon 1.5%, effici 1.3%, dna.polymerase 1.3%, time.pcr 1.2%, quantif 1.2%, paraoxonas 1.0%, real.time.pcr 1.0%, sequenc 0.9%, assai 0.8%, amplif 0.8%, reaction 0.7%, substitut 0.7%, base 0.6%, sampl 0.6%, singl 0.6%, protocol 0.6%

Discriminating Terms

pcr 7.4%, pon1 4.3%, real.time 3.1%, real 2.4%, cell 1.6%, pon3 1.0%, protein 1.0%, dna 1.0%, polymeras 0.9%, pon 0.9%, probe 0.9%, diseas 0.9%, receptor 0.8%, dna.polymerase 0.8%, patient 0.8%, time.pcr 0.8%, quantif 0.7%, activ 0.7%, paraoxonas 0.6%, tnf 0.6%, real.time.pcr 0.6%, effici 0.6%, time 0.5%, kinas 0.5%, neuron 0.5%

Single Word Terms

pcr 13, gene 13, high 12, polymeras 11, reaction 11, time 11, real 10, dna 10, sampl 10, sequenc 9, product 9, level 8, two 8, express 8, rna 8, singl 8, mrna 7, oxid 7, human 7, transcript 7, chain 7, detect 7, fluoresc 6, target 6, probe 6

Double Word Terms

real.time 10, polymerase.chain 7, reaction.pcr 6, chain.reaction 6, high.density 5, density.lipoprotein 5, time.pcr 5, pcr.amplification 4, low.density 4, paraoxonase.pon1 4, dna.polymerase 4, pon2.pon3 3, pon1.pon2 3, single.nucleotide 3, gene.expression 3, nerve.agents 3, single.stranded 3, nucleotide.polymorphism 3, reference.gene 3, expression.real 3, pcr.efficiencies 3, polymorphism.snp 3, sequence.dna 2, time.polymerase 2, nucleic.acids 2

Triple Word Terms

chain.reaction.pcr 6, polymerase.chain.reaction 6, real.time.pcr 5, high.density.lipoprotein 5, low.density.lipoprotein 4, single.nucleotide.polymorphism 3, nucleotide.polymorphism.snp 3, expression.real.time 3, pon1.pon2.pon3 3, relative.expression.ratio 2, gene.family.three 2, reporter.fluorescent.emission 2, transcription.polymerase.chain 2, family.three.members 2, time.polymerase.chain 2, three.members.pon1 2, gene.expression.real 2, insecticides.nerve.agents 2, dna.polymerase.reaction 2, real.time.quantitative 2, time.quantitative.pcr 2, real.time.polymerase 2, density.lipoprotein.hdl 2, single.stranded.dna 2, reverse.transcription.polymerase 2

A novel method for real time quantitative RT-PCR.
Promoter polymorphisms of human paraoxonase PON1 gene and serum paraoxonase activities and concentrations.
Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method.
A new mathematical model for relative quantification in real-time RT-PCR.
Relative expression software tool (REST) for group-wise comparison and statistical analysis of relative expression results in real-time PCR.
The human serum paraoxonase/arylesterase gene (PON1) is one member of a multigene family.
Guideline to reference gene selection for quantitative real-time PCR.
Assumption-free analysis of quantitative real-time polymerase chain reaction (PCR) data.
Development and validation of real-time quantitative reverse transcriptase-polymerase chain reaction for monitoring gene expression in cardiac myocytes in vitro.
Polymorphisms in the human paraoxonase (PON1) promoter.
Quantitative real-time RT-PCR--a perspective.
Modulation of paraoxonase (PON1) activity.
Rabbit serum paraoxonase 3 (PON3) is a high density lipoprotein-associated lactonase and protects low density lipoprotein against oxidation.
Pharmacogenetics of paraoxonases: a brief review.

CLUSTER 50 (124-119)

(46 Records)

*Multiple sequence alignment of proteins and DNA for protein structure and function prediction and phylogeny inferencing, and analysis of databases of sequences

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Cluster Syntax Features

Descriptive Terms

sequenc 17.7%, align 3.1%, databas 2.8%, dna 2.1%, protein 1.8%, tree 1.4%, genom 1.3%, comput 1.1%, structur 1.1%, evolutionari 0.9%, map 0.9%, tool 0.9%, code 0.8%, blast 0.8%, exon 0.8%, amino 0.8%, amino.acid 0.8%, clone 0.8%, gel 0.7%, acid 0.7%, search 0.7%, project 0.6%, http 0.6%, gene 0.6%, pair 0.6%

Discriminating Terms

sequenc 10.4%, align 2.3%, cell 1.9%, databas 1.8%, activ 1.1%, tree 1.0%, patient 0.9%, diseas 0.7%, tnf 0.7%, receptor 0.6%, blast 0.6%, evolutionari 0.6%, dna 0.6%, comput 0.6%, express 0.6%, kinas 0.5%, neuron 0.5%, respons 0.5%, factor 0.5%, code 0.5%, exon 0.5%, induc 0.5%, gel 0.4%, alpha 0.4%, autophagi 0.4%

Single Word Terms

sequenc 32, protein 23, genom 20, data 18, human 17, two 16, dna 16, gene 16, databas 15, new 14, comput 14, gener 14, function 14, structur 14, set 12, map 12, region 11, acid 11, molecular 11, high 11, http 11, complex 11, align 10, tool 10, clone 9

Double Word Terms

amino.acid 6, sequence.data 5, protein.sequence 5, large.scale 5, dna.protein 5, http.www 4, sequences.human 4, single.nucleotide 4, dna.sequence 4, dna.sequences 4, sequence.alignment 4, high.throughput 4, phylogenetic.trees 4, protein.dna 3, chromosome.mapping 3, computer.programs 3, evolutionary.distances 3, full.length 3, cpg.islands 3, mass.spectrometry 3, two.dimensional 3, data.set 3, protein.coding 3, protein.sequences 3, open.reading 3

Triple Word Terms

dna.protein.sequence 3, yeast.two.hybrid 2, throughput.yeast.two 2, high.throughput.yeast 2, amino.acid.sequence 2, testing.evolutionary.hypotheses 2, mapping.chromosomes.pair 2, chromosome.mapping.chromosomes 2, protein.protein.interactions 2, manual.sequence.alignment 2, nucleic.acid.protein 2, open.reading.frames 2, automatic.manual.sequence 2, http.www.genome 2, multiple.sequence.alignment 2, acidic.basic.proteins 2, complex.protein.mixtures 2, single.nucleotide.polymorphisms 2,

chem.1975.250 2, tandem.mass.spectrometry 2, 1975.250.4007 2, biol.chem.1975 2, multiple.regions.similarity 2, 250.4007.4021 2, farrell.biol.chem 2

Aindex: amino acid index database.
Two-dimensional electrophoresis of proteins: an updated protocol and implications for a functional analysis of the genome.
MEGA3: Integrated software for Molecular Evolutionary Genetics Analysis and sequence alignment.
IMGT unique numbering for MHC groove G-DOMAIN and MHC superfamily (MhcSF) G-LIKE-DOMAIN.
Use of mass spectrometric molecular weight information to identify proteins in sequence databases.
Genome sequencing in microfabricated high-density picolitre reactors.
Prediction of the coding sequences of unidentified human genes. XV. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro.
SIFT: Predicting amino acid changes that affect protein function.
PolyPhred: automating the detection and genotyping of single nucleotide substitutions using fluorescence-based resequencing.
Analysis of the mouse transcriptome based on functional annotation of 60,770 full-length cDNAs.
Improved tools for biological sequence comparison.
An integrated epigenetic and genetic approach to common human disease.
Towards a proteome-scale map of the human protein-protein interaction network.
The neighbor-joining method: a new method for reconstructing phylogenetic trees.
Mass spectrometric sequencing of proteins silver-stained polyacrylamide gels.
Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences.

CLUSTER 26 (124-119)

(56 Records)

*Segment duplication in the human genome architecture allowing DNA re-arrangements for disease; sequencing of structural variation in human genomes

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Cluster Syntax Features

Descriptive Terms

genom 29.9%, duplic 7.2%, sequenc 4.0%, human.genome 3.9%, rearrang 2.4%, delet 1.9%, chromosom 1.9%, human 1.6%, structur 1.5%, genet 1.3%, segment 1.2%, imbal 0.9%, region 0.9%, breakpoint 0.9%, project 0.8%, map 0.8%, gene 0.7%, snp 0.6%, human.genome.project 0.6%, genome.project 0.6%, dna 0.6%, diseas 0.5%, arrai 0.5%, cytogenet 0.5%, segmental.duplications 0.5%

Discriminating Terms

genom 17.3%, duplic 4.9%, human.genome 2.5%, cell 1.9%, rearrang 1.6%, sequenc 1.5%, delet 1.1%, activ 1.0%, protein 1.0%, receptor 0.9%, chromosom 0.8%, segment 0.7%, tnf 0.7%, breakpoint 0.7%, imbal 0.6%, express 0.5%, kinas 0.5%, neuron 0.5%, induc 0.5%, signal 0.4%, respons 0.4%, project 0.4%, genome.project 0.4%, human.genome.project 0.4%, autophagi 0.4%

Single Word Terms

genom 53, human 33, diseas 29, gene 28, sequenc 25, genet 25, duplic 24, chromosom 24, region 22, number 19, dna 18, delet 18, polymorph 17, copi 17, structur 17, segment 16, high 16, rearrang 16, larg 15, map 15, phenotyp 14, data 14, singl 13, inform 13, arrai 13

Double Word Terms

human.genome 25, copy.number 12, segmental.duplications 9, single.nucleotide 9, genomic.hybridization 9, genome.wide 8, array.genomic 8, whole.genome 7, genome.project 7, high.resolution 6, large.scale 6, genome.sequence 5, nucleotide.polymorphisms 5, genomics.human 4, base.pair 4, array.cgh 4, genetic.diseases 4, polymorphisms.snps 4, high.density 4, fluorescence.situ 4, genomic.dna 4, genome.sequencing 3, genome.data 3, homologous.recombination 3, sequence.human 3

Triple Word Terms

human.genome.project 7, array.genomic.hybridization 7, single.nucleotide.polymorphisms 5, nucleotide.polymorphisms.snps 4, fluorescence.situ.hybridization 3, genomics.human.genome 3, copy.number.polymorphism 3, low.copy.repeats 3, genetic.predisposition.disease 3, high.density.snp 3, reflect.constitutional.copy 2, mapped.segmentally.duplicated 2, tumors.cell.lines 2, duplicated.regions.reflect 2, mapped.intervals.ranging 2, intervals.ranging.size 2, median.probe.spacing 2, recurrent.chromosomal.rearrangement 2, neuroblastoma.tumors.cell 2, million.base.pairs 2, regions.reflect.constitutional 2,

first.high.resolution 2, snp.genotype.data 2, segmentally.duplicated.regions 2, exon.level.resolution 2

Human SULT1A3 pharmacogenetics: gene duplication and functional genomic studies.

The functional impact of structural variation in humans.

Detection of large-scale variation in the human genome.

Causal relation between alpha-synuclein gene duplication and familial Parkinson's disease.

Recent segmental duplications in the human genome.

Mapping and sequencing of structural variation from eight human genomes.

Paired-end mapping reveals extensive structural variation in the human genome.

Initial sequencing and analysis of the human genome.

The diploid genome sequence of an individual human.

Genome sequence, comparative analysis and haplotype structure of the domestic dog.

DNA duplication associated with Charcot-Marie-Tooth disease type 1A.

Genomic disorders: structural features of the genome can lead to DNA rearrangements and human disease traits.

Genomic disorders: molecular mechanisms for rearrangements and conveyed phenotypes.

CLUSTER 3 (124-119)

(30 Records)

*Copy number variations within the human genome associated with disease

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Cluster Syntax Features

Descriptive Terms

cnv 24.9%, copi 15.6%, copy.number 15.6%, number 5.0%, genom 4.4%, duplic 1.2%, cnp 1.1%, human 1.1%, gene 1.1%, copy.number.cnvs 0.8%, number.cnvs 0.8%, snp 0.8%, genet 0.7%, human.genome 0.5%, ccl3l1 0.5%, arrai 0.5%, phenotyp 0.4%, polymorph 0.4%, nucleotid 0.4%, region 0.4%, asd 0.3%, gene.copy.number 0.3%, gene.copy 0.3%, delet 0.3%, disord 0.3%

Discriminating Terms

cnv 16.0%, copy.number 9.9%, copi 9.7%, number 2.0%, cell 1.8%, genom 1.1%, activ 1.0%, protein 1.0%, receptor 0.8%, cnp 0.7%, tnf 0.6%, patient 0.6%, duplic 0.6%, copy.number.cnvs 0.5%, number.cnvs 0.5%, neuron 0.5%, kinas 0.4%, induc 0.4%, express 0.4%, autophagi 0.4%, factor 0.4%, respons 0.4%, signal 0.4%, inhibit 0.3%, alpha 0.3%

Single Word Terms

number 30, copi 29, genom 24, gene 22, genet 22, human 22, diseas 19, polymorph 16, cnv 16, complex 13, duplic 12, phenotyp 11, arrai 11, region 10, snp 10, disord 10, nucleotid 9, two 9, suscept 9, variabl 9, structur 8, control 7, popul 7, delet 7, genotyp 7

Double Word Terms

copy.number 29, number.cnvs 13, human.genome 10, genomic.hybridization 6, gene.copy 6, single.nucleotide 6, number.polymorphisms 5, polymorphisms.snps 4, nucleotide.polymorphisms 4, genomic.regions 4, disease.susceptibility 4, polymorphisms.cnps 4, cnvs.copy 3, human.genetic 3, dna.copy 3, structural.copy 3, genomic.disorders 3, segmental.duplications 3, segmental.duplication 3, genome.sequence 3, genetic.basis 3, odds.ratio 3, number.cnv 3, number.recognized 3, contribution.cnvs 3

Triple Word Terms

copy.number.cnvs 13, gene.copy.number 6, copy.number.polymorphisms 5, number.polymorphisms.cnps 4, single.nucleotide.polymorphisms 4, nucleotide.polymorphisms.snps 4, number.cnvs.human 3, dna.copy.number 3, copy.number.recognized 3, cnvs.copy.number 3, structural.copy.number 3,

array.genomic.hybridization 3, copy.number.cnv 3, number.copy.number 3, copy.number.copy 3, number.cnvs.copy 2, odds.ratio.confidence 2, number.recognized.source 2, disease.susceptibility.one 2, contribution.cnvs.complex 2, systemic.lupus.erythematosus 2, copy.number.variable 2, autism.spectrum.disorders 2, copy.number.fcgr3b 2, large.scale.copy 2

Genome assembly comparison identifies structural variants in the human genome.

Genome-wide detection of human copy number variations using high-density DNA oligonucleotide arrays.

Increase in GSK3beta gene copy number variation in bipolar disorder.

Genomic rearrangements and gene copy-number alterations as a cause of nervous system disorders.

Linkage disequilibrium and heritability of copy-number polymorphisms within duplicated regions of the human genome.

Copy-number variation and association studies of human disease.

Evidence for an influence of chemokine ligand 3-like 1 (CCL3L1) gene copy number on susceptibility to rheumatoid arthritis.

Copy number variants and genetic traits: closer to the resolution of phenotypic to genotypic variability.

Diet and the evolution of human amylase gene copy number variation.

Global variation in copy number in the human genome.

Challenges and standards in integrating surveys of structural variation.

Large-scale copy number polymorphism in the human genome.

Strong association of de novo copy number mutations with autism.

Relative impact of nucleotide and copy number variation on gene expression phenotypes.

Mapping autism risk loci using genetic linkage and chromosomal rearrangements.

A comprehensive analysis of common copy-number variations in the human genome.

Copy number polymorphism in Fcgr3 predisposes to glomerulonephritis in rats and humans.

Copy number polymorphism and expression level variation of the human alpha-defensin genes DEFA1 and DEFA3.

CLUSTER 45 (124-119)

(76 Records)

* Multilocus genetic linkage maps of the full genome, examining myriad genetic markers

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Cluster Syntax Features

Descriptive Terms

linkag 9.9%, marker 5.3%, loci 5.0%, map 2.9%, genom 2.4%, lod 2.3%, genotyp 2.1%, chromosom 2.0%, data 1.9%, genet 1.9%, trait 1.7%, locu 1.5%, genome.wide 1.4%, qtl 1.4%, allel 1.4%, pedigre 1.3%, model 1.2%, popul 1.1%, set 1.1%, multipoint 1.1%, score 1.0%, wide 1.0%, comput 0.8%, famili 0.8%, power 0.8%

Discriminating Terms

linkag 6.2%, loci 3.2%, marker 2.9%, cell 2.2%, lod 1.7%, map 1.4%, activ 1.1%, qtl 1.0%, protein 1.0%, receptor 0.9%, pedigre 0.9%, trait 0.9%, chromosom 0.9%, multipoint 0.8%, genome.wide 0.8%, genotyp 0.8%, locu 0.8%, patient 0.8%, tnf 0.7%, kinas 0.6%, express 0.6%, neuron 0.5%, induc 0.5%, lod.scores 0.5%, score 0.5%

Single Word Terms

genet 50, linkag 49, marker 43, data 43, loci 38, genom 38, genotyp 35, diseas 33, gene 33, map 30, model 28, famili 27, set 27, locu 26, allel 26, wide 26, popul 25, chromosom 25, statist 23, region 23, detect 22, trait 22, complex 21, power 20, phenotyp 20

Double Word Terms

genome.wide 26, data.sets 13, quantitative.trait 13, lod.scores 11, linkage.disequilibrium 11, lod.score 10, data.set 9, maximum.lod 8, trait.loci 8, maximum.likelihood 7, sample.size 7, software.package 6, genetic.markers 6, allele.sharing 6, allele.frequencies 6, genotype.data 6, case.control 6, hundreds.thousands 6, type.diabetes 6, population.stratification 6, sib.pair 6, linkage.chromosome 6, complex.traits 6, mapping.complex 5, complex.disease 5

Triple Word Terms

quantitative.trait.loci 8, maximum.lod.scores 6, transmission.disequilibrium.test 4, genome.wide.gwa 4, trait.loci.qtls 3, large.data.sets 3, linkage.allele.sharing 3,

mapping.complex.disease 3, single.nucleotide.polymorphism 3, hundreds.thousands.markers 3, real.data.sets 2, allele.sharing.one 2, variance.components.linkage 2, conducted.genome.wide 2, dissection.complex.traits 2, gene.gene.interactions 2, loci.maximum.lod 2, genome.wide.scans 2, allele.sharing.identical 2, genome.wide.large 2, sharing.identical.descent 2, identical.descent.ibd 2, multipoint.identity.descent 2, nucleotide.polymorphism.snp 2, sib.pair.multipoint 2

Linkage of familial amyotrophic lateral sclerosis with frontotemporal dementia to chromosome 9q21-q22.

Genomewide linkage analysis of body mass index across 28 years of the Framingham Heart Study.

Heterogeneity in meta-analyses of genome-wide association investigations.

NIMH Genetics Initiative Millenium Schizophrenia Consortium: linkage analysis of African-American pedigrees.

Allele-sharing models: LOD scores and accurate linkage tests.

Construction of multilocus genetic linkage maps in humans.

Direct power comparisons between simple LOD scores and NPL scores for linkage analysis in complex diseases.

Assessing whether an allele can account in part for a linkage signal: the Genotype-IBD Sharing Test (GIST).

Haploview: analysis and visualization of LD and haplotype maps.

Exhaustive allelic transmission disequilibrium tests as a new approach to genome-wide association studies.

Genome-wide strategies for detecting multiple loci that influence complex diseases.

A new multipoint method for genome-wide association studies by imputation of genotypes.

Mapping a disease locus by allelic association.

A combinatorial partitioning method to identify multilocus genotypic partitions that predict quantitative trait variation.

CLUSTER 27 (124-119)

(53 Records)

*Statistical issues associated with genetic association tests, especially linkage disequilibrium tests, and the resultant trade-off between power to detect meaningful associations and the chance of making false discoveries.

Cluster Syntax Features

Descriptive Terms

test 20.7%, power 7.2%, fals 3.1%, statist 2.8%, tdt 2.5%, linkag 2.4%, marker 2.0%, sampl 1.9%, parent 1.7%, disequilibrium 1.4%, size 1.2%, true 1.1%, error 1.0%, data 0.9%, genotyp 0.8%, famili 0.8%, quot 0.7%, sample.size 0.7%, sibl 0.7%, simul 0.7%, hypothes 0.7%, posit 0.6%, allel 0.6%, case 0.6%, measur 0.6%

Discriminating Terms

test 11.8%, power 4.1%, fals 2.0%, cell 1.9%, tdt 1.7%, statist 1.2%, protein 1.1%, activ 1.0%, parent 1.0%, linkag 0.9%, receptor 0.9%, patient 0.8%, disequilibrium 0.7%, true 0.7%, marker 0.7%, tnf 0.7%, sampl 0.6%, error 0.6%, express 0.6%, size 0.5%, kinas 0.5%, human 0.5%, neuron 0.5%, gene 0.5%, induc 0.4%

Single Word Terms

test 40, power 32, statist 27, sampl 24, data 23, diseas 23, multipl 21, marker 20, control 19, genotyp 18, disequilibrium 18, linkag 18, genet 18, famili 18, gene 17, size 17, number 17, fals 16, simul 16, detect 16, popul 15, larg 15, posit 15, on 15, parent 14

Double Word Terms

disequilibrium.test 13, transmission.disequilibrium 10, linkage.disequilibrium 10, sample.size 9, multiple.testing 8, case.control 8, false.positive 8, family.tests 7, power.detect 7, test.statistic 7, test.tdt 7, complex.diseases 5, false.rate 5, nuclear.families 5, tests.linkage 5, type.error 5, test.statistics 5, loss.power 4, late.onset 4, genetic.models 4, weinberg.equilibrium 4, error.rates 4, test.linkage 4, candidate.gene 4, population.stratification 4

Triple Word Terms

transmission.disequilibrium.test 10, disequilibrium.test.tdt 7, hardy.weinberg.equilibrium 4, tests.linkage.disequilibrium 3, case.control.design 3, linkage.disequilibrium.test 2, test.linkage.disequilibrium 2, family.tests.linkage 2, disequilibrium.test.pdt 2,

disequilibrium.general.pedigrees 2, flood.false.positive 2, loss.power.test 2, matched.case.control 2, late.onset.diseases 2, distribution.test.statistics 2, joint.distribution.test 2, complex.disease.genes 2, single.nucleotide.polymorphism 2, nucleotide.polymorphism.snp 2, beta.level.alpha 2, testing.large.number 2, multilocus.haplotype.tests 2, power.sample.size 2, sample.size.power 2, false.positive.rate 2

Gametic disequilibrium measures: proceed with caution.

Genome-wide significance for dense SNP and resequencing data.

A tutorial on statistical methods for population association studies.

Using exact P values to compare the power between the reconstruction-combined transmission/disequilibrium test and the sib transmission/disequilibrium test.

Implementing a unified approach to family-based tests of association.

Family-based tests of association in the presence of linkage.

Genetic dissection of complex traits: guidelines for interpreting and reporting linkage results.

Univariate and multivariate family-based association analysis of the IL-13 ARG130GLN polymorphism in the Childhood Asthma Management Program.

An efficient Monte Carlo approach to assessing statistical significance in genomic studies.

A test for linkage and association in general pedigrees: the pedigree disequilibrium test.

Correcting for a potential bias in the pedigree disequilibrium test.

Operating characteristics of a rank correlation test for publication bias.

A comparative study of sibship tests of linkage and/or association.

Power dressing and meta-analysis: incorporating power analysis into meta-analysis.

Effect of two- and three-locus linkage disequilibrium on the power to detect marker/phenotype associations.

Comparison of statistical power between 2 * 2 allele frequency and allele positivity tables in case-control studies of complex disease genes.

Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker.

A transmission disequilibrium test for quantitative trait loci.

CLUSTER 14 (124-119)

(44 Records)

* single-nucleotide polymorphism (SNP) and haplotype analyses; association between haplotypes and traits

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Cluster Syntax Features

Descriptive Terms

haplotyp 39.4%, snp 6.6%, frequenc 2.1%, gene 2.1%, polymorph 2.0%, hla 2.0%, allel 1.7%, drb1 1.5%, marker 1.1%, mdr1 1.0%, singl 1.0%, nucleotid 0.9%, single.nucleotide 0.9%, region 0.8%, genotyp 0.8%, tag 0.8%, popul 0.7%, suscept 0.7%, test 0.7%, disequilibrium 0.6%, linkag 0.6%, linkage.disequilibrium 0.5%, power 0.5%, chromosom 0.5%, risk 0.5%

Discriminating Terms

haplotyp 26.4%, snp 2.9%, cell 2.0%, hla 1.3%, activ 1.0%, drb1 1.0%, frequenc 1.0%, protein 0.8%, receptor 0.7%, tnf 0.6%, polymorph 0.6%, mdr1 0.6%, express 0.5%, kinas 0.5%, neuron 0.5%, diseas 0.5%, patient 0.5%, allel 0.5%, induc 0.4%, signal 0.4%, tag 0.4%, autophagi 0.4%, single.nucleotide 0.4%, inhibit 0.4%, mice 0.4%

Single Word Terms

haplotyp 43, gene 37, polymorph 32, singl 29, snp 27, nucleotid 25, allel 24, diseas 23, genet 21, frequenc 21, linkag 20, multipl 18, genotyp 18, popul 18, suscept 17, disequilibrium 17, chromosom 16, data 16, region 15, detect 14, control 14, marker 13, risk 13, two 13, locu 12

Double Word Terms

single.nucleotide 25, nucleotide.polymorphisms 17, linkage.disequilibrium 16, polymorphisms.snps 14, nucleotide.polymorphism 7, case.control 7, statistical.power 6, major.histocompatibility 6, leukocyte.antigen 5, risk.haplotype 5, candidate.gene 5, histocompatibility.complex 5, haplotype.frequencies 5, human.leukocyte 5, haplotype.tagging 4, antigen.hla 4, complex.mhc 4, multiple.sclerosis 4, power.detect 4, haplotype.block 4, genotype.data 4, susceptibility.genes 4, haplotype.information 3, hla.loci 3, frequencies.haplotype 3

Triple Word Terms

single.nucleotide.polymorphisms 17, nucleotide.polymorphisms.snps 14, single.nucleotide.polymorphism 7, human.leukocyte.antigen 5, major.histocompatibility.complex

5, leukocyte.antigen.hla 4, histocompatibility.complex.mhc 4, nucleotide.polymorphism.snp 3, strong.linkage.disequilibrium 3, susceptibility.multiple.sclerosis 3, mhc.susceptibility.multiple 2, haplotype.tagging.snps 2, 1501.dqb1.0602 2, gene.susceptibility.multiple 2, expectation.maximization.algorithm 2, snp.markers.two 2, haplotype.frequencies.haplotype 2, two.genes.one 2, drb1.1501.dqb1 2, susceptibility.alleles.linkage 2, statistical.power.detect 2, polymorphism.snp.haplotype 2, polymorphisms.snps.haplotypes 2, genes.major.histocompatibility 2, single.marker.tests 2

The gene encoding 5-lipoxygenase activating protein confers risk of myocardial infarction and stroke.

Significant association of a single nucleotide polymorphism in the tumor necrosis factor-alpha (TNF-alpha) gene promoter with human narcolepsy.

Family-based tests for associating haplotypes with general phenotype data: application to asthma genetics.

Large-scale single-nucleotide polymorphism (SNP) and haplotype analyses, using dense SNP Maps, of 199 drug-related genes in 752 subjects: the analysis of the association between uncommon SNPs within haplotype blocks and the haplotypes constructed with haplotype-tagging SNPs.

Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide.

A "silent" polymorphism in the MDR1 gene changes substrate specificity.

Characterization of a common susceptibility locus for asthma-related traits.

Heterogeneity at the HLA-DRB1 locus and risk for multiple sclerosis.

Worldwide human relationships inferred from genome-wide patterns of variation.

Association analysis in an evolutionary context: cladistic analysis of the DRD2 locus to test for association with alcoholism.

Polymorphisms in human MDR1 (P-glycoprotein): recent advances and clinical relevance.

Identification of a novel risk locus for progressive supranuclear palsy by a pooled genomewide scan of 500,288 single-nucleotide polymorphisms.

On the advantage of haplotype analysis in the presence of multiple disease susceptibility alleles.

Score tests for association between traits and haplotypes when linkage phase is ambiguous.

Haplotype variation and linkage disequilibrium in 313 human genes.

CLUSTER 31 (124-119)

(68 Records)

* Genome-wide single-nucleotide-polymorphism (SNP) genotyping for whole genome association studies of diseases

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Cluster Syntax Features

Descriptive Terms

snp 35.1%, genotyp 3.2%, genom 2.2%, control 1.9%, genet 1.3%, popul 1.1%, sampl 1.1%, case 1.0%, single.nucleotide 1.0%, genome.wide 1.0%, allel 1.0%, nucleotid 1.0%, suscept 1.0%, polymorphisms.snps 0.9%, nucleotide.polymorphisms.snps 0.9%, nucleotide.polymorphisms 0.9%, single.nucleotide.polymorphisms 0.9%, risk 0.8%, singl 0.8%, polymorph 0.8%, case.control 0.8%, gene 0.7%, replic 0.7%, wide 0.7%, locu 0.7%

Discriminating Terms

snp 24.0%, cell 2.1%, genotyp 1.4%, activ 1.1%, protein 1.1%, receptor 0.8%, tnf 0.7%, nucleotide.polymorphisms.snps 0.6%, polymorphisms.snps 0.6%, express 0.6%, single.nucleotide.polymorphisms 0.6%, nucleotide.polymorphisms 0.6%, single.nucleotide 0.6%, kinas 0.5%, neuron 0.5%, genome.wide 0.5%, induc 0.5%, t2d 0.5%, respons 0.5%, case 0.5%, nucleotid 0.4%, system 0.4%, case.control 0.4%, signal 0.4%, inhibit 0.4%

Single Word Terms

snp 64, genom 46, genotyp 45, singl 44, control 41, gene 40, genet 39, polymorph 39, nucleotid 39, diseas 37, data 32, allel 31, two 30, wide 28, sampl 28, risk 27, popul 25, region 25, replic 24, suscept 24, case 24, human 22, independ 22, linkag 20, locu 20

Double Word Terms

single.nucleotide 39, nucleotide.polymorphisms 34, polymorphisms.snps 33, genome.wide 27, case.control 20, linkage.disequilibrium 15, whole.genome 10, odds.ratio 9, independent.replication 7, minor.allele 7, odds.ratios 6, coronary.artery 6, parkinson.disease 6, hapmap.project 6, type.diabetes 6, confidence.interval 6, dna.samples 6, allele.frequency 6, snp.genotyping 5, risk.factors 5, high.density 5, 000.snps 5, genotype.data 5, data.set 5, snps.minor 5

Triple Word Terms

single.nucleotide.polymorphisms 34, nucleotide.polymorphisms.snps 33, snps.minor.allele 5,

nucleotide.polymorphism.snp 4, single.nucleotide.polymorphism 4, minor.allele.frequency 4, coronary.artery.disease 4, population.attributable.risk 3, type.diabetes.t2d 3, neurologically.normal.controls 3, structure.linkage.disequilibrium 3, odds.ratio.confidence 3, ratio.confidence.interval 3, onset.alzheimer.disease 3, patients.sporadic.als 3, major.histocompatibility.complex 3, conducted.genome.wide 3, histocompatibility.complex.mhc 3, million.single.nucleotide 3, data.genome.wide 3, lateral.sclerosis.als 3, amyotrophic.lateral.sclerosis 3, case.control.sample 3, control.united.kingdom 2, 000.single.nucleotide 2

The same sequence variant on 9p21 associates with myocardial infarction, abdominal aortic aneurysm and intracranial aneurysm.

Whole-genome patterns of common DNA variation in three human populations.

A comprehensive review of genetic association studies.

A genome-wide association study identifies alleles in FGFR2 associated with risk of sporadic postmenopausal breast cancer.

Susceptibility genes for age-related maculopathy on chromosome 10q26.

Genotype, haplotype and copy-number variation in worldwide human populations.

Prospects for whole-genome linkage disequilibrium mapping of common disease genes.

Candidate single-nucleotide polymorphisms from a genomewide association study of Alzheimer disease.

A case-control association study of the 12 single-nucleotide polymorphisms implicated in Parkinson disease by a recent genome scan.

Candidate lung tumor susceptibility genes identified through whole-genome association analyses in inbred mice.

The association of a SNP upstream of INSIG2 with body mass index is reproduced in several but not all cohorts.

High-resolution whole-genome association study of Parkinson disease.

A genome-wide genotyping study in patients with ischaemic stroke: initial analysis and data release.

Genotyping over 100,000 SNPs on a pair of oligonucleotide arrays.

Association between SORL1 and Alzheimer's disease in a genome-wide study.

CLUSTER 38 (124-119)

(48 Records)

*Genetic predisposition to disease

Cluster Syntax Features

Descriptive Terms

genet 28.6%, predisposition.disease 3.8%, genetic.predisposition.disease 3.5%, predisposit 3.5%, genetic.predisposition 3.3%, diseas 3.1%, epidemiolog 2.5%, genom 1.6%, gene 1.4%, polymorphism.single 0.9%, popul 0.9%, suscept 0.8%, polymorph 0.8%, trait 0.8%, heterogen 0.7%, linkag 0.7%, associ 0.7%, genetics.genetic 0.6%, twin 0.6%, allel 0.6%, risk 0.6%, predisposition.disease.genome 0.6%, genetic.associations 0.5%, disease.genome 0.5%, complex.traits 0.5%

Discriminating Terms

genet 15.4%, predisposition.disease 2.7%, genetic.predisposition.disease 2.5%, predisposit 2.4%, genetic.predisposition 2.3%, cell 2.0%, epidemiolog 1.5%, activ 1.1%, protein 1.0%, patient 0.8%, receptor 0.7%, polymorphism.single 0.6%, tnf 0.6%, express 0.6%, kinas 0.5%, neuron 0.5%, signal 0.5%, induc 0.4%, genetics.genetic 0.4%, autophagi 0.4%, regul 0.4%, predisposition.disease.genome 0.4%, function 0.4%, genetic.associations 0.4%, twin 0.4%

Single Word Terms

genet 46, diseas 41, gene 23, genom 21, complex 18, predisposit 16, factor 15, polymorph 15, human 14, risk 14, popul 14, allel 13, linkag 12, suscept 12, epidemiolog 12, singl 12, heterogen 10, statist 10, interact 10, model 9, multipl 9, associ 9, number 8, nucleotid 7, mechan 7

Double Word Terms

predisposition.disease 15, genetic.predisposition 14, polymorphism.single 7, genetics.genetic 6, genome.wide 6, multiple.sclerosis 6, disease.genome 5, complex.traits 5, genetic.factors 5, alleles.genetic 4, genetic.markers 4, nervous.system 4, gene.environment 4, disease.risk 4, genetic.associations 4, genetic.epidemiology 4, genetic.diseases 4, genetic.complex 4, complex.diseases 4, sample.size 4, general.population 3, genes.susceptibility 3, linkage.genetics 3, genome.genotype 3, gene.gene 3

Triple Word Terms

genetic.predisposition.disease 14, genetics.genetic.predisposition 5,

predisposition.disease.genome 5, gene.environment.interactions 3, predisposition.disease.genetic 3, gene.disease.associations 3, linkage.genetics.polymorphism 2, genotype.heterozygote.linkage 2, complex.human.diseases 2, susceptibility.multiple.sclerosis 2, diseases.genetics.genetic 2, genetic.diseases.genetics 2, disequilibrium.polymorphism.single 2, gene.gene.gene 2, gene.gene.environment 2, genetic.risk.factors 2, mellitus.type.genetics 2, type.genetics.genetic 2, diabetes.mellitus.type 2, genetic.complex.human 2, immunoglobulin.heavy.chain 2, genetics.multiple.sclerosis 2, design.sample.size 2, genetic.environmental.factors 2, heterozygote.linkage.genetics 2

Genome-wide association studies for common diseases and complex traits.

Gene-environment interactions in human diseases.

What can genome-wide association studies tell us about the genetics of common disease?

Genetic determinants of the inflammatory response.

Assessment of cumulative evidence on genetic associations: interim guidelines.

Replication validity of genetic association studies.

'Racial' differences in genetic effects for complex diseases.

Implications of small effect sizes of individual genetic variants on the design and interpretation of genetic association studies of complex diseases.

Genetic basis for clinical expression in multiple sclerosis.

Genetic dissection of complex traits.

Genome-wide association studies for complex traits: consensus, uncertainty and challenges.

Schizophrenia: a common disease caused by multiple rare alleles.

Meta-analysis of genetic association studies.

Multiple sclerosis: genomic rewards.

A genetic profile of contemporary Jewish populations.

The genetic epidemiology of neurodegenerative disease.

CLUSTER 54 (124-119)

(58 Records)

*Genotype and allele frequencies of polymorphisms; polymorphism association with diseases

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Cluster Syntax Features

Descriptive Terms

polymorph 14.1%, allel 9.4%, genotyp 3.6%, frequenc 2.1%, gene 2.1%, apo 1.8%, mdr1 1.7%, exon 1.5%, risk 1.2%, hnmt 1.2%, genet 1.2%, mutat 0.9%, htt 0.8%, nos2a 0.8%, methyltransferas 0.8%, epsilon 0.7%, 1beta 0.7%, repeat 0.6%, histamin 0.6%, homozyg 0.6%, drug 0.6%, serotonin 0.6%, patient 0.6%, onset 0.6%, ib 0.6%

Discriminating Terms

polymorph 9.0%, allel 5.6%, cell 2.2%, genotyp 1.7%, frequenc 1.2%, mdr1 1.2%, apo 1.1%, exon 1.0%, receptor 1.0%, protein 0.9%, hnmt 0.9%, activ 0.9%, nos2a 0.6%, htt 0.6%, kinas 0.6%, methyltransferas 0.5%, genom 0.5%, signal 0.5%, autophagi 0.5%, epsilon 0.5%, immun 0.4%, homozyg 0.4%, ib 0.4%, mice 0.4%, neuron 0.4%

Single Word Terms

gene 53, polymorph 51, allel 38, diseas 31, genet 30, genotyp 29, risk 28, function 24, frequenc 22, control 22, patient 21, express 19, two 18, region 18, factor 17, role 17, singl 15, promot 14, exon 14, mutat 14, human 14, drug 14, enzym 13, popul 13, sampl 13

Double Word Terms

case.control 10, single.nucleotide 9, parkinson.disease 9, polymerase.chain 8, promoter.region 8, amino.acid 7, odds.ratio 7, allele.frequency 7, polymorphisms.genes 7, serotonin.transporter 7, chain.reaction 7, genetic.polymorphisms 6, expression.function 6, risk.factor 6, play.role 5, histamine.methyltransferase 5, mdr1.gene 5, short.allele 4, interleukin.1beta 4, alzheimer.disease 4, gene.risk 4, nucleotide.polymorphisms 4, nucleotide.polymorphism 4, irritable.bowel 4, functional.polymorphisms 4

Triple Word Terms

polymerase.chain.reaction 7, single.nucleotide.polymorphism 4, single.nucleotide.polymorphisms 4, irritable.bowel.syndrome 4, acid.amide.hydrolase 3, amide.hydrolase.faah 3, bowel.syndrome.ibs 3, fatty.acid.amide 3, serotonin.transporter.gene 3,

one.two.copies 3, histamine.methyltransferase.hnmt 3, tumor.necrosis.factor 3, onset.familial.sporadic 2, patients.irritable.bowel 2, amine.oxidase.copper 2, endogenous.cannabinoid.system 2, polymorphisms.genes.encoding 2, polymorphisms.mdr1.gene 2, ratio.confidence.interval 2, odds.ratio.confidence 2, 122.japanese.patients 2, pgp.expression.function 2, glycoprotein.expression.function 2, tnf.alpha.308 2, polymorphism.gene.encoding 2

Molecular genetics and epidemiology of the NAT1 and NAT2 acetylation polymorphisms.

Functional polymorphisms of the human multidrug-resistance gene: multiple sequence variations and correlation of one allele with P-glycoprotein expression and activity in vivo.

Parkinson's disease is not associated with the combined alpha-synuclein/apolipoprotein E susceptibility genotype.

Sequence diversity in CYP3A promoters and characterization of the genetic basis of polymorphic CYP3A5 expression.

Linkage and association with the NOS2A locus on chromosome 17q11 in multiple sclerosis.

Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region.

Association between Parkinson's disease and polymorphisms in the nNOS and iNOS genes in a community-based case-control study.

Ethnic distribution of slow acetylator mutations in the polymorphic N-acetyltransferase (NAT2) gene.

A proinflammatory genetic profile increases the risk for chronic atrophic gastritis and gastric carcinoma.

The association between polymorphisms in the cytochrome P-450 2D6 gene and Parkinson's disease: a case-control study and meta-analysis.

The T393C polymorphism of the GNAS1 gene is associated with deficit schizophrenia in an Italian population sample.

A nonsynonymous polymorphism in the human fatty acid amide hydrolase gene did not associate with either methamphetamine dependence or schizophrenia.

Early experience and serotonin transporter gene variation interact to influence primate CNS function.

Influence of interleukin-1beta gene polymorphisms on age-at-onset of sporadic Parkinson's disease.

CLUSTER 34 (124-119)

(38 Records)

* Disease risk based on analysis of polymorphisms for allelic association, especially AMD and diabetes

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Cluster Syntax Features

Descriptive Terms

amd 8.9%, risk 8.5%, ac 4.3%, diabet 4.1%, polymorph 3.2%, type.diabetes 2.9%, chd 2.8%, obes 2.6%, allel 2.4%, gene 2.0%, cfh 1.5%, type 0.9%, genotyp 0.8%, popul 0.8%, paraoxonas 0.7%, caucasian 0.7%, suscept 0.7%, diseas 0.7%, haplotyp 0.6%, pon1 0.6%, pon2 0.6%, macular.degeneration 0.5%, age.macular 0.5%, macular 0.5%, age.macular.degeneration 0.5%

Discriminating Terms

amd 6.3%, risk 3.6%, ac 3.1%, diabet 2.2%, chd 2.0%, cell 1.9%, type.diabetes 1.8%, obes 1.5%, polymorph 1.2%, cfh 1.1%, protein 0.9%, activ 0.9%, receptor 0.9%, allel 0.8%, patient 0.8%, tnf 0.7%, express 0.5%, paraoxonas 0.5%, kinas 0.5%, neuron 0.5%, caucasian 0.5%, induc 0.5%, respons 0.5%, alpha 0.4%, autophagi 0.4%

Single Word Terms

gene 31, risk 28, polymorph 25, diseas 21, genet 19, control 19, popul 19, allel 18, factor 18, genotyp 17, region 14, type 13, ag 13, chromosom 13, singl 13, two 12, diabet 12, linkag 11, suscept 11, case 11, genom 10, nucleotid 10, interv 10, sampl 9, interact 9

Double Word Terms

type.diabetes 11, case.control 10, single.nucleotide 10, age.macular 9, macular.degeneration 9, heart.disease 8, genome.wide 8, complement.factor 7, degeneration.amd 7, nucleotide.polymorphisms 7, risk.allele 6, confidence.interval 6, risk.factors 6, coronary.heart 6, linkage.disequilibrium 6, attributable.risk 6, two.independent 5, insertion.deletion 5, deletion.polymorphism 5, factor.gene 5, odds.ratio 4, angiotensin.converting 4, disease.risk 4, gene.environment 4, insig2.gene 4

Triple Word Terms

age.macular.degeneration 9, macular.degeneration.amd 7, single.nucleotide.polymorphisms 7, coronary.heart.disease 6, insertion.deletion.polymorphism 5, angiotensin.converting.enzyme 4, heart.disease.chd 4, population.attributable.risk 4, complement.factor.gene 4,

type.diabetes.mellitus 4, converting.enzyme.ace 3, single.nucleotide.polymorphism 3, ratio.confidence.interval 3, gene.environment.interaction 3, histidine.amino.acid 2, factor.gene.cfh 2, homozygous.risk.allele 2, strong.linkage.disequilibrium 2, coronary.artery.disease 2, disease.odds.ratio 2, beta.cell.function 2, two.independent.case 2, type.diabetes.controls 2, promoter.region.htra1 2, amd.irreversible.vision 2

A common genetic variant is associated with adult and childhood obesity.

Measured haplotype analysis of the angiotensin-I converting enzyme gene.

Complement factor H polymorphism in age-related macular degeneration.

Large meta-analysis establishes the ACE insertion-deletion polymorphism as a marker of Alzheimer's disease.

CFH haplotypes without the Y402H coding variant show strong association with susceptibility to age-related macular degeneration.

A common allele on chromosome 9 associated with coronary heart disease.

Prediction of coronary heart disease risk using a genetic risk score: the Atherosclerosis Risk in Communities Study.

Angiotensin-I converting enzyme insertion/deletion polymorphism and its association with diabetic nephropathy: a meta-analysis of studies reported between 1994 and 2004 and comprising 14,727 subjects.

An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels.

Hypothetical LOC387715 is a second major susceptibility gene for age-related macular degeneration, contributing independently of complement factor H to disease risk.

DNA polymorphisms in two paraoxonase genes (PON1 and PON2) are associated with the risk of coronary heart disease.

Cigarette smoking strongly modifies the association of LOC387715 and age-related macular degeneration.

CLUSTER 4 (124-116)

(38 Records)

*Risk of hip fracture, and how it is affected by vitamin supplementation

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Cluster Syntax Features

Descriptive Terms

fractur 31.6%, vitamin 10.8%, hip 5.0%, bone 4.7%, risk 4.3%, women 4.0%, hip.fracture 1.6%, risedron 1.3%, miner 1.2%, bone.mineral 1.1%, bone.mineral.density 1.0%, mineral.density 1.0%, risk.hip 0.9%, densiti 0.9%, supplement 0.9%, intak 0.7%, bmd 0.7%, calcium 0.7%, osteoporosi 0.7%, placebo 0.7%, oral 0.5%, serum 0.5%, fracture.risk 0.5%, vertebr 0.5%, rct 0.5%

Discriminating Terms

fractur 18.6%, vitamin 6.0%, hip 2.9%, bone 2.1%, women 2.0%, cell 1.6%, risk 1.2%, gene 1.0%, hip.fracture 0.9%, protein 0.8%, activ 0.8%, diseas 0.7%, risedron 0.7%, receptor 0.7%, bone.mineral 0.7%, miner 0.6%, bone.mineral.density 0.6%, mineral.density 0.6%, tnf 0.6%, risk.hip 0.5%, express 0.5%, genet 0.5%, supplement 0.5%, genom 0.4%, kinas 0.4%

Single Word Terms

fractur 30, risk 29, bone 27, vitamin 22, densiti 20, women 20, ag 20, hip 20, miner 20, low 17, control 17, incid 17, interv 15, reduc 14, confid 14, popul 14, osteoporosi 14, patient 13, rel 13, background 12, dose 12, supplement 12, calcium 12, treatment 12, data 12

Double Word Terms

bone.mineral 19, mineral.density 17, confidence.interval 14, risk.hip 13, fracture.risk 11, relative.risk 11, hip.fracture 11, hip.fractures 9, postmenopausal.women 8, vertebral.fractures 8, risk.fracture 7, nonvertebral.fractures 7, bone.density 7, calcium.vitamin 6, risk.factors 6, randomized.controlled 5, controlled.trials 5, reduce.risk 5, risedronate.placebo 5, bone.mass 5, fracture.women 5, density.bmd 5, women.osteoporosis 5, vitamin.bone 5, vertebral.fracture 5

Triple Word Terms

bone.mineral.density 17, risk.hip.fracture 10, mineral.density.bmd 5, relative.risk.confidence 4, relative.risk.hip 4, risk.confidence.interval 4, ratio.confidence.interval 4, randomized.controlled.trials 4, hip.fracture.women 4, energy.ray.absorptiometry 3, postmenopausal.women.osteoporosis 3, vitamin.supplementation.reduce 3, dual.energy.ray 3,

mineral.density.dual 3, fractures.postmenopausal.women 3, odds.ratio.confidence 3, mineral.density.risk 3, vitamin.bone.mineral 3, oral.glucocorticoids.gcs 3, vertebral.fractures.postmenopausal 3, bone.density.women 3, hip.fractures.nonvertebral 2, women.age.older 2, new.vertebral.fractures 2, fractures.risedronate.placebo 2

Japanese fermented soybean food as the major determinant of the large geographic difference in circulating levels of vitamin K2: possible implications for hip-fracture risk.

Risk of hip fracture derived from relative risks: an analysis applied to the population of Sweden.

Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures.

Evidence-based decision making on micronutrients and chronic disease: long-term randomized controlled trials are not enough.

Effect of risedronate on the risk of hip fracture in elderly women. Hip Intervention Program Study Group.

Safety of vitamin A.

Efficacy of risedronate administration in osteoporotic postmenopausal women affected by inflammatory bowel disease.

Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y.

Effect of Vitamin D on falls: a meta-analysis.

Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials.

Psychotropic drug use and the risk of hip fracture.

Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes.

Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Vertebral Efficacy with Risedronate Therapy (VERT) Study Group.

Vitamin K2 (menatetrenone) effectively prevents fractures and sustains lumbar bone mineral density in osteoporosis.

Oral glucocorticoid use is associated with an increased risk of fracture.

CLUSTER 60 (124-116)

(72 Records)

*Risk factors for diseases, especially cancer, and the impact of nutrition

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Cluster Syntax Features

Descriptive Terms

risk 8.5%, cancer 6.5%, ag 6.0%, nutrit 2.6%, women 2.4%, intak 2.4%, glaucoma 1.5%, sleep 1.3%, epidemiolog 1.1%, men 1.1%, phytoestrogen 1.0%, diseas 1.0%, mortal 0.9%, incid 0.9%, peopl 0.9%, diet 0.9%, colorect 0.9%, white 0.8%, dietari 0.8%, breast 0.7%, veget 0.7%, fruit 0.7%, angl 0.6%, intervent 0.6%, popul 0.6%

Discriminating Terms

risk 4.0%, ag 3.2%, cancer 3.1%, cell 1.9%, nutrit 1.8%, intak 1.6%, women 1.4%, gene 1.2%, glaucoma 1.1%, protein 1.1%, receptor 1.0%, sleep 0.9%, activ 0.9%, phytoestrogen 0.8%, tnf 0.7%, men 0.7%, express 0.6%, epidemiolog 0.6%, mortal 0.6%, peopl 0.6%, diet 0.5%, neuron 0.5%, incid 0.5%, kinas 0.5%, colorect 0.5%

Single Word Terms

risk 42, ag 39, diseas 36, popul 26, data 24, cancer 23, high 21, women 20, control 19, factor 17, interv 17, confid 16, patient 16, incid 15, ratio 15, reduc 15, measur 15, rate 14, men 14, design 13, health 13, epidemiolog 13, cardiovascular 13, low 13, total 12

Double Word Terms

confidence.interval 13, men.women 8, risk.factors 8, alzheimer.disease 8, heart.disease 7, sex.age 6, age.sex 6, cardiovascular.disease 6, colorectal.cancer 5, relative.risk 5, open.angle 5, reduce.risk 5, main.measures 5, mass.index 4, intake.risk 4, risk.risk 4, odds.ratio 4, cardiovascular.diseases 4, aged.older 4, body.mass 4, case.control 4, risk.confidence 4, death.rates 4, cancer.incidence 4, racial.ethnic 4

Triple Word Terms

ratio.confidence.interval 4, risk.confidence.interval 4, body.mass.index 4, risk.colorectal.cancer 3, cerebral.amyloid.angiopathy 3, selective.serotonin.reuptake 3, incidence.mortality.survival 3, serotonin.reuptake.inhibitors 3, anti.inflammatory.drugs 3, disease.design.prospective 2, body.weight.body 2, cardiovascular.diseases.cancer 2, apolipoprotein.apoe.gene 2, angle.closure.glaucoma 2, data.center.health 2, population.case.control 2,

glaucoma.second.leading 2, age.race.ethnicity 2, risk.upper.gastrointestinal 2, cancer.incidence.rates 2, mortality.data.center 2, center.health.statistics 2, incidence.death.rates 2, data.cancer.incidence 2, cancer.incidence.mortality 2

Trends in breast cancer by race and ethnicity.

Cancer statistics, 2005.

Prevalence of glaucoma. The Beaver Dam Eye Study.

Sclerosis of the internal anal sphincter--a process of aging.

Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.

Association of dietary intake of soy, beans, and isoflavones with risk of cerebral and myocardial infarctions in Japanese populations: the Japan Public Health Center-based (JPHC) study cohort I.

Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes.

Improvement of weight and fat-free mass with oral nutritional supplementation in patients with Alzheimer's disease at risk of malnutrition: a prospective randomized study.

Cancer risk of heterocyclic amines in cooked foods: an analysis and implications for research.

The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies.

Methylenetetrahydrofolate reductase polymorphism, dietary interactions, and risk of colorectal cancer.

Environmental risk factors in multiple sclerosis aetiology.

The apolipoprotein E epsilon2 allele and the pathological features in cerebral amyloid angiopathy-related hemorrhage.

Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease.

Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study.

Phytoestrogens: a review of the present state of research.

Lessons learned from gene expression profile studies of aging and caloric restriction.

Cancer statistics, 1996.

Use of proteomic patterns in serum to identify ovarian cancer

CLUSTER 58 (124-116)

(61 Records)

*Diagnosis of neurodegenerative diseases

Cluster Syntax Features

Descriptive Terms

patient 12.9%, diagnosi 3.3%, dementia 3.2%, diseas 3.2%, cjd 2.0%, csf 1.8%, parkinson 1.5%, clinic 1.4%, alzheim 1.3%, pet 1.3%, disord 1.2%, schizophrenia 1.1%, rbd 0.9%, dlb 0.9%, syndrom 0.8%, encephalopathi 0.8%, quot 0.8%, symptom 0.7%, progress 0.7%, patholog 0.7%, korsakoff 0.7%, alzheimer.disease 0.7%, fdg 0.7%, criteria 0.6%, imag 0.6%

Discriminating Terms

patient 5.5%, dementia 2.3%, diagnosi 2.2%, cell 2.0%, cjd 1.5%, gene 1.1%, csf 1.1%, activ 0.9%, receptor 0.9%, pet 0.9%, parkinson 0.7%, tnf 0.7%, protein 0.7%, rbd 0.7%, alzheim 0.7%, dlb 0.7%, express 0.6%, schizophrenia 0.6%, kinas 0.6%, genet 0.6%, encephalopathi 0.5%, genom 0.5%, korsakoff 0.5%, fdg 0.5%, signal 0.5%

Single Word Terms

patient 49, diseas 43, clinic 26, diagnosi 25, control 24, on 19, ag 19, brain 17, disord 16, dementia 15, alzheim 14, data 14, normal 13, featur 13, two 13, imag 13, protein 13, progress 13, background 12, patholog 12, function 12, test 12, onset 12, parkinson 11, match 11

Double Word Terms

alzheimer.disease 13, magnetic.resonance 8, parkinson.disease 8, multiple.sclerosis 7, patients.alzheimer 7, creutzfeldt.jakob 6, jakob.disease 6, resonance.imaging 6, positron.emission 5, emission.tomography 5, cerebrospinal.fluid 5, korsakoff.syndrome 4, fdg.pet 4, pet.imaging 4, disease.cjd 4, disease.progression 4, diagnostic.criteria 4, age.matched 4, clinical.diagnosis 4, lewy.bodies 4, patients.clinical 4, features.patients 4, patients.patients 3, one.patient 3, dlb.patients 3

Triple Word Terms

creutzfeldt.jakob.disease 6, magnetic.resonance.imaging 6, patients.alzheimer.disease 6, positron.emission.tomography 5, jakob.disease.cjd 4, onset.alzheimer.disease 3, fdg.pet.imaging 3, emission.tomography.pet 3, lewy.bodies.dlb 3, dementia.lewy.bodies 3, cerebrospinal.fluid.csf 3, serum.copper.zinc 2, standardized.uptake.suv 2, systemic.lupus.erythematosus 2,

herpes.simplex.encephalitis 2, diagnostic.criteria.multiple 2, dissemination.lesions.time 2, ratio.confidence.interval 2, odds.ratio.confidence 2, criteria.multiple.sclerosis 2, clinical.criteria.diagnosis 2, sleep.behavior.disorder 2, resonance.imaging.mri 2, behavior.disorder.rbd 2, diagnosis.creutzfeldt.jakob 2

The sensitivity of 18-fluorodopa positron emission tomography and magnetic resonance imaging in Parkinson's disease.

Metabolic profiling of CSF: evidence that early intervention may impact on disease progression and outcome in schizophrenia.

The 14-3-3 brain protein in cerebrospinal fluid as a marker for transmissible spongiform encephalopathies.

Progression of symptoms in the early and middle stages of Huntington disease.

Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis.

Reactive microglia are positive for HLA-DR in the substantia nigra of Parkinson's and Alzheimer's disease brains.

Cerebrospinal fluid levels of non-neurotransmitter amino acids in patients with Alzheimer's disease.

Abnormal activity patterns in premotor cortex during sequence learning in autistic patients.

Amyloidosis.

Neurology and the gastrointestinal system.

Encephalitogenic potential of the myelin basic protein peptide (amino acids 83-99) in multiple sclerosis: results of a phase II clinical trial with an altered peptide ligand.

Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria".

FDG-PET findings in the Wernicke-Korsakoff syndrome.

Association between nonpsychotic psychiatric diagnoses in adolescent males and subsequent onset of schizophrenia.

Therapeutic strategies for human amyloid diseases.

The MPTP model: versatile contributions to the treatment of idiopathic Parkinson's disease.

Autoantibodies as predictors of disease.

CLUSTER 18 (124-116)

(27 Records)

*Risk factors for cardiovascular disease, especially plasma homocysteine, cholesterol, and genetic factors, and nutritional approaches to reduce these risks

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Cluster Syntax Features

Descriptive Terms

homocystein 8.7%, cholesterol 8.2%, risk 4.0%, coronari 3.9%, cardiovascular 3.7%, mthfr 3.5%, ldl 3.1%, folic 2.5%, folic.acid 2.5%, folat 1.7%, thrombosi 1.3%, level 1.1%, reactive.protein 1.1%, plasma 1.0%, ldl.cholesterol 1.0%, heart.disease 1.0%, lipoprotein 1.0%, coronary.heart 1.0%, coronary.heart.disease 1.0%, diseas 0.9%, heart 0.8%, serum 0.6%, cardiovascular.disease 0.6%, venous.thrombosis 0.6%, vascular.disease 0.6%

Discriminating Terms

homocystein 5.6%, cholesterol 5.0%, mthfr 2.2%, coronari 2.2%, cardiovascular 2.0%, ldl 1.8%, cell 1.7%, folic.acid 1.6%, folic 1.6%, risk 1.1%, folat 1.0%, receptor 0.8%, gene 0.8%, thrombosi 0.8%, activ 0.8%, reactive.protein 0.7%, ldl.cholesterol 0.7%, protein 0.6%, tnf 0.6%, heart.disease 0.6%, coronary.heart 0.6%, coronary.heart.disease 0.6%, express 0.5%, lipoprotein 0.5%, genom 0.5%

Single Word Terms

risk 21, diseas 18, level 15, factor 14, coronari 12, reduc 12, cholesterol 12, high 11, homocystein 11, cardiovascular 10, total 10, plasma 10, serum 9, control 9, heart 8, elev 8, lipoprotein 8, acid 8, patient 7, mean 7, densiti 7, clinic 7, low 7, blood 7, ldl 7

Double Word Terms

risk.factors 8, heart.disease 7, folic.acid 6, density.lipoprotein 6, low.density 6, coronary.heart 6, risk.factor 5, confidence.interval 5, mutation.mthfr 5, cardiovascular.disease 5, reactive.protein 5, myocardial.infarction 5, plasma.homocysteine 4, cholesterol.levels 4, risk.cardiovascular 4, reductase.mthfr 4, mthfr.gene 4, artery.disease 4, methylenetetrahydrofolate.reductase 4, men.women 4, homocysteine.levels 4, women.mean 3, lipoprotein.cholesterol 3, clinical.trials 3, total.homocysteine 3

Triple Word Terms

coronary.heart.disease 6, low.density.lipoprotein 5, mutation.mthfr.gene 4,

methylenetetrahydrofolate.reductase.mthfr 4, density.lipoprotein.cholesterol 3, coronary.artery.disease 3, deciliter.mmol.liter 3, ldl.cholesterol.levels 3, plasma.homocysteine.levels 3, cholesterol.levels.130 2, plasma.homocyst.ine 2, base.line.levels 2, ratio.confidence.interval 2, disease.folic.acid 2, high.density.lipoprotein 2, reduce.thrombotic.tendency 2, risk.factor.coronary 2, total.plasma.homocysteine 2, nested.case.control 2, 130.deciliter.mmol 2, homocyst.ine.levels 2, vascular.disease.folic 2, normal.coronary.arteries 2, reactive.protein.crp 2, risk.factors.coronary 2

Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study.

Procyanidin dimer B2 [epicatechin-(4beta-8)-epicatechin] in human plasma after the consumption of a flavanol-rich cocoa.

Intermediate hyperhomocysteinemia resulting from compound heterozygosity of methylenetetrahydrofolate reductase mutations.

Molecular genetic analysis in mild hyperhomocysteinemia: a common mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for cardiovascular disease.

Reduction of plasma homocyst(e)ine levels by breakfast cereal fortified with folic acid in patients with coronary heart disease.

C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women.

Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events.

C-reactive protein levels and outcomes after statin therapy.

Is the apoE4 allele an independent predictor of coronary events?

A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes.

Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis.

Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans.

Adult family members and their resemblance of coronary heart disease risk factors: the Cardiovascular Disease Study in Finnmark.

Rapid and noninvasive diagnosis of the presence and severity of coronary heart disease using 1H-NMR-based metabonomics.

CLUSTER 10 (124-116)

(26 Records)

*Myocardial infarction, especially risk factors

Cluster Syntax Features

Descriptive Terms

infarct 14.0%, myocardi 9.0%, myocardial.infarction 5.2%, patient 4.7%, risk 2.3%, ami 2.1%, bmc 2.0%, heart 2.0%, ventricular 1.9%, left 1.5%, left.ventricular 1.4%, intracoronari 1.4%, infus 1.2%, rofecoxib 1.0%, risk.myocardial 1.0%, risk.myocardial.infarction 1.0%, progenitor 0.9%, stroke 0.9%, gvhd 0.8%, heart.rate 0.8%, smoke 0.8%, bone.marrow 0.8%, intracoronary.infusion 0.7%, acut 0.7%, marrow 0.7%

Discriminating Terms

infarct 8.1%, myocardi 5.2%, myocardial.infarction 3.1%, ami 1.3%, bmc 1.2%, ventricular 1.1%, gene 1.0%, protein 0.9%, heart 0.9%, intracoronari 0.9%, left.ventricular 0.8%, patient 0.8%, left 0.8%, activ 0.8%, cell 0.8%, receptor 0.8%, infus 0.7%, rofecoxib 0.6%, tnf 0.6%, risk.myocardial 0.6%, risk.myocardial.infarction 0.6%, genet 0.6%, diseas 0.5%, express 0.5%, gvhd 0.5%

Single Word Terms

infarct 23, myocardi 22, patient 20, risk 16, control 14, cell 13, background 12, acut 11, coronari 11, treatment 11, heart 11, function 10, ventricular 10, left 10, diseas 10, arteri 9, transplant 9, factor 9, global 8, marrow 8, bone 8, clinic 8, safe 8, cardiovascular 7, intracoronari 7

Double Word Terms

myocardial.infarction 20, left.ventricular 10, bone.marrow 8, acute.myocardial 8, patients.acute 6, progenitor.cells 6, intracoronary.infusion 6, ejection.fraction 6, relative.risk 6, infarction.ami 5, infarct.artery 5, global.left 5, end.systolic 5, risk.myocardial 5, heart.disease 5, patients.ami 5, coronary.artery 4, ventricular.function 4, progenitor.cell 4, two.patients 4, ventricular.ejection 4, confidence.interval 4, coronary.heart 3, systolic.volume 3, transplantation.progenitor 3

Triple Word Terms

acute.myocardial.infarction 8, risk.myocardial.infarction 5, myocardial.infarction.ami 5, patients.acute.myocardial 5, global.left.ventricular 5, left.ventricular.ejection 4, ventricular.ejection.fraction 4, left.ventricular.function 4, end.systolic.volume 3,

marrow.derived.progenitor 3, derived.bone.marrow 3, bone.marrow.derived 3, derived.progenitor.cells 3, coronary.heart.disease 3, transplantation.progenitor.cells 3, stimulating.factor.csf 2, peripheral.blood.stem 2, progenitor.cells.derived 2, cells.derived.bone 2, heart.rate.variability 2, granulocyte.colony.stimulating 2, patients.myocardial.infarction 2, left.ventricular.systolic 2, ejection.fraction.lvef 2, myocardial.infarction.stroke 2

A common variant on chromosome 9p21 affects the risk of myocardial infarction.

Visualisation of cell death in vivo in patients with acute myocardial infarction.

Risk factors for chronic graft-versus-host disease after HLA-identical sibling bone marrow transplantation.

Transplantation of Progenitor Cells and Regeneration Enhancement in Acute Myocardial Infarction (TOPCARE-AMI).

Transcoronary transplantation of progenitor cells after myocardial infarction.

Differential effect of intracoronary infusion of mobilized peripheral blood stem cells by granulocyte colony-stimulating factor on left ventricular function and remodeling in patients with acute myocardial infarction versus old myocardial infarction: the MAGIC Cell-3-DES randomized, controlled trial.

Noninvasive detection of programmed cell loss with 99mTc-labeled annexin A5 in heart failure.

The clinical study of autologous peripheral blood stem cell transplantation by intracoronary infusion in patients with acute myocardial infarction (AMI).

Increased circulating hematopoietic and endothelial progenitor cells in the early phase of acute myocardial infarction.

Autologous bone marrow-derived progenitor cell transplantation for myocardial regeneration after acute infarction.

Smoking and risk of myocardial infarction. Statistical and biological interactions should not be confused.

Transplantation of progenitor cells and regeneration enhancement in acute myocardial infarction: final one-year results of the TOPCARE-AMI Trial.

Cardiovascular morbidity and mortality in women diagnosed with rheumatoid arthritis.

Autologous bone-marrow stem-cell transplantation for myocardial regeneration.

Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial.

CLUSTER 32 (124-116)

(40 Records)

*Placebos in research and clinical trials, especially Crohn’s and other inflammatory bowel diseases

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Cluster Syntax Features

Descriptive Terms

placebo 23.7%, patient 6.6%, crohn 4.9%, crohn.disease 4.0%, pain 2.7%, ib 2.3%, bowel 1.7%, treatment 1.4%, diseas 1.2%, coliti 1.0%, nocebo 0.9%, ulcerative.colitis 0.8%, ulcer 0.8%, psoriasi 0.8%, symptom 0.7%, abt 0.7%, placebo.response 0.7%, trial 0.7%, clinic 0.7%, rate 0.6%, expect 0.6%, remiss 0.6%, abdomin 0.5%, respons 0.5%, nicotin 0.5%

Discriminating Terms

placebo 15.3%, crohn 3.0%, crohn.disease 2.5%, cell 1.8%, patient 1.7%, pain 1.5%, ib 1.5%, gene 1.0%, bowel 0.9%, protein 0.9%, receptor 0.8%, nocebo 0.6%, express 0.6%, tnf 0.5%, neuron 0.5%, psoriasi 0.5%, coliti 0.5%, kinas 0.5%, abt 0.5%, ulcerative.colitis 0.5%, placebo.response 0.5%, genom 0.5%, genet 0.5%, signal 0.4%, ulcer 0.4%

Single Word Terms

patient 32, diseas 23, treatment 23, placebo 22, clinic 20, activ 19, crohn 16, pain 16, bowel 15, background 15, therapi 14, control 12, respons 12, treat 12, rate 11, random 10, advers 10, score 10, area 10, index 9, safeti 9, human 9, baselin 9, inflammatori 9, symptom 8

Double Word Terms

crohn.disease 16, placebo.controlled 8, inflammatory.bowel 8, treatment.placebo 7, ulcerative.colitis 7, double.blind 7, patients.active 7, disease.patients 7, bowel.disease 6, abdominal.pain 6, response.rates 5, active.crohn 5, placebo.response 5, patients.treated 5, clinical.trials 5, activity.index 5, disease.activity 5, irritable.bowel 5, patients.placebo 5, treated.patients 5, area.index 4, placebo.patients 4, psoriasis.area 4, monoclonal.antibody 4, randomized.placebo 4

Triple Word Terms

inflammatory.bowel.disease 6, crohn.disease.patients 6, active.crohn.disease 5, patients.active.crohn 5, irritable.bowel.syndrome 4, crohn.disease.activity 4, disease.activity.index 4, blind.placebo.controlled 4, double.blind.placebo 4, psoriasis.area.index

4, bowel.disease.questionnaire 3, randomized.placebo.controlled 3, primary.end.point 3, disease.ulcerative.colitis 3, crohn.disease.ulcerative 3, patients.crohn.disease 3, abdominal.pain.diarrhea 3, background.amp.aims 3, positron.emission.tomography 3, bowel.syndrome.ibs 3, placebo.response.rates 3, human.monoclonal.antibody 2, body.surface.area 2, activity.brain.regions 2, ibs.symptoms.abdominal 2

Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment.

Escherichia coli O157:H7 infection mimicking Crohn's disease.

Review article: smoking cessation as primary therapy to modify the course of Crohn's disease.

Placebo theory and its implications for research and clinical practice: a review of the recent literature.

Cognitive therapy for irritable bowel syndrome is associated with reduced limbic activity, GI symptoms, and anxiety.

Infliximab improves quality of life in patients with Crohn's disease.

Understanding the placebo effect: contributions from neuroimaging.

Anti-interleukin-12 antibody for active Crohn's disease.

Mind does really matter: evidence from neuroimaging studies of emotional self-regulation, psychotherapy, and placebo effect.

Placebo and nocebo in cardiovascular health: implications for healthcare, research, and the doctor-patient relationship.

The irritable bowel syndrome: long-term prognosis and the physician-patient interaction.

The placebo effect in irritable bowel syndrome trials: a meta-analysis.

The role of cigarettes and nicotine in the onset and treatment of ulcerative colitis.

Transdermal nicotine for active ulcerative colitis.

Human intestinal diamine oxidase (DAO) activity in Crohn's disease: a new marker for disease assessment?

Oral p38 mitogen-activated protein kinase inhibition with BIRB 796 for active Crohn's disease: a randomized, double-blind, placebo-controlled trial.

A meta-analysis of the placebo rates of remission and response in clinical trials of active Crohn's disease.

CLUSTER 52 (124-116)

(53 Records)

*Clinical therapy and treatment for neurodegenerative and autoimmune diseases, with emphasis on stem cell transplantation, especially for treating MS

Cluster Syntax Features

Descriptive Terms

patient 31.5%, therapi 2.1%, transplant 1.9%, treatment 1.6%, relaps 1.5%, pregnanc 1.3%, dose 1.0%, treat 1.0%, clinic 0.8%, physician 0.7%, adr 0.7%, crh 0.7%, patients.treated 0.7%, ribavirin 0.7%, complic 0.7%, peg 0.7%, disabl 0.7%, symptom 0.6%, epsilon4 0.5%, medic 0.5%, advers 0.5%, progress 0.5%, diseas 0.5%, liver 0.5%, rate 0.5%

Discriminating Terms

patient 17.0%, cell 1.6%, relaps 1.0%, transplant 1.0%, protein 1.0%, therapi 1.0%, pregnanc 0.9%, gene 0.8%, receptor 0.7%, activ 0.7%, tnf 0.7%, express 0.6%, genom 0.6%, genet 0.5%, adr 0.5%, crh 0.5%, ribavirin 0.5%, neuron 0.5%, induc 0.5%, peg 0.5%, signal 0.5%, physician 0.5%, patients.treated 0.5%, human 0.5%, kinas 0.5%

Single Word Terms

patient 52, diseas 28, treatment 25, clinic 25, therapi 19, treat 19, dose 17, rate 15, activ 15, drug 15, on 14, therapeut 13, new 13, respons 12, control 12, data 11, two 11, phase 11, safeti 11, medic 11, toxic 10, complic 10, three 10, progress 10, relaps 10

Double Word Terms

patients.treated 11, multiple.sclerosis 7, treatment.patients 6, patients.chronic 6, relapsing.remitting 5, secondary.progressive 5, confidence.interval 5, hematopoietic.stem 4, cell.transplantation 4, patients.patients 4, treated.patients 4, patients.progressive 4, stem.cells 4, health.care 4, stem.cell 4, odds.ratio 3, liver.transplantation 3, clinical.features 3, one.patient 3, depressed.patients 3, phase.clinical 3, monoclonal.antibody 3, therapeutic.patients 3, eight.patients 3, therapeutic.agents 3

Triple Word Terms

stem.cell.transplantation 4, expanded.disability.status 3, patients.crohn.disease 3, disability.status.scale 3, hematopoietic.stem.cell 3, magnetic.resonance.imaging 3, patients.ulcerative.colitis 3, relapsing.remitting.multiple 2, apoe.epsilon4.allele 2,

status.scale.edss 2, carmustine.etoposide.cytosine 2, cytosine.arabinoside.melphalan 2, etoposide.cytosine.arabinoside 2, stem.cells.mobilized 2, clinicaltrials.gov.number 2, patients.major.depressive 2, transplantation.hsct.treatment 2, stem.cells.transplantation 2, selective.serotonin.reuptake 2, inflammatory.bowel.disease 2, treated.wilson.disease 2, proton.pump.inhibitors 2, ribavirin.patients.hcv 2, patients.hcv.genotype 2, patients.chronic.hepatitis 2

Medical therapy for ulcerative colitis.

A phase I clinical trial of the treatment of Crohn's fistula by adipose mesenchymal stem cell transplantation.

Hematopoietic stem cell transplantation for multiple sclerosis. A retrospective multicenter study.

The window of therapeutic opportunity in multiple sclerosis: evidence from monoclonal antibody therapy.

N-acetyltransferase 2 slow acetylator genotype associated with adverse effects of sulphasalazine in the treatment of inflammatory bowel disease.

Alemtuzumab vs. Interferon beta-1a in early multiple sclerosis.

Hematopoietic stem cell transplantation for multiple sclerosis.

Gastrointestinal damage associated with the use of nonsteroidal antiinflammatory drugs.

Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS).

Treating gastro-oesophageal reflux disease during pregnancy and lactation: what are the safest therapy options?

Autologous stem cell transplantation for progressive multiple sclerosis: update of the European Group for Blood and Marrow Transplantation autoimmune diseases working party database.

CARD15/NOD2 mutational analysis and genotype-phenotype correlation in 612 patients with inflammatory bowel disease.

Autologous hematopoietic stem cell transplantation suppresses Gd-enhanced MRI activity in MS.

N-acetyltransferase 1 and 2 genotypes do not predict response or toxicity to treatment with mesalamine and sulfasalazine in patients with ulcerative colitis.

CLUSTER 21 (124-116)

(31 Records)

*Diagnosis, rating, treatment, and epidemiology of depressive disorders, and their relation to other illnesses

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Cluster Syntax Features

Descriptive Terms

depress 16.9%, care 10.4%, medic 5.8%, disord 4.6%, anxieti 3.5%, health 3.0%, mental 1.9%, diagnos 1.6%, comorbid 1.5%, health.care 1.2%, lifetim 1.1%, primary.care 1.1%, unconvent 1.1%, hospit 1.0%, scale 0.9%, ill 0.9%, psychometr 0.9%, major.depression 0.7%, survei 0.6%, primari 0.6%, dsm 0.6%, behavior 0.6%, instrument 0.5%, stress 0.5%, prime 0.5%

Discriminating Terms

depress 9.9%, care 6.2%, medic 3.1%, anxieti 2.1%, cell 1.8%, disord 1.7%, health 1.3%, mental 1.1%, gene 1.0%, protein 1.0%, diagnos 1.0%, comorbid 0.9%, activ 0.8%, receptor 0.8%, primary.care 0.7%, health.care 0.7%, lifetim 0.7%, unconvent 0.7%, tnf 0.6%, diseas 0.6%, express 0.6%, hospit 0.5%, psychometr 0.5%, ill 0.5%, genom 0.5%

Single Word Terms

depress 16, health 16, disord 13, care 13, clinic 13, medic 12, anxieti 10, popul 10, data 10, survei 9, treatment 9, scale 9, rate 9, mental 8, diagnost 8, primari 8, set 8, interview 8, gener 8, patient 8, major 8, state 8, ag 8, diseas 8, on 7

Double Word Terms

health.care 8, mental.health 5, primary.care 5, major.depression 4, main.measures 4, anxiety.depression 4, depression.anxiety 4, mental.disorders 4, composite.diagnostic 3, anxiety.disorders 3, care.patients 3, diagnostic.interview 3, criterion.standard 3, comorbidity.survey 3, care.physicians 3, adult.patients 3, medical.surgical 3, care.treatment 3, data.collected 3, rating.scale 3, health.survey 3, disorder.kappa 2, diagnoses.mental 2, treatment.referral 2, kappa.accuracy 2

Triple Word Terms

composite.diagnostic.interview 3, primary.care.physicians 3, health.care.treatment 3, site.avoid.sampling 2, mental.disorders.primary 2, avoid.sampling.bias 2, bias.primary.care 2, face.household.survey 2, primary.care.mental 2, independent.mental.health 2,

diagnostic.statistical.manual 2, primary.health.care 2, household.survey.conducted 2, hospital.anxiety.depression 2, statistical.manual.mental 2, anxiety.depression.scale 2, manual.mental.disorders 2, face.face.household 2, comorbidity.survey.replication 2, version.composite.diagnostic 2, disorders.comorbidity.survey 2, care.treatment.referral 2, health.care.patients 2, diagnoses.independent.mental 2, sampling.bias.primary 2

Depressive disorders and immunity: 20 years of progress and discovery.

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data.

Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey.

The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R).

Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication.

Hospital Anxiety and Depression Scale (HAD): some psychometric data for a Swedish sample.

Case-finding instruments for depression in primary care settings.

Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study.

Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire.

Association within a family of a balanced autosomal translocation with major mental illness.

Functional status in coronary artery disease: a one-year prospective study of the role of anxiety and depression.

The hospital anxiety and depression scale.

A global measure of perceived stress.

A rating scale for depression.

Development of a rating scale for primary depressive illness.

Treatment of depression in primary care: where we are, where we can go.

CLUSTER 39 (124-116)

(45 Records)

*Items and rating scales in health and quality-of-life surveys/questionnaires

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Cluster Syntax Features

Descriptive Terms

item 13.8%, health 11.8%, scale 6.9%, measur 4.3%, instrument 3.3%, survei 2.9%, reliabl 2.6%, score 2.5%, questionnair 2.4%, health.status 1.5%, dimens 1.3%, rate 1.3%, statu 1.1%, complianc 0.9%, coeffici 0.8%, data 0.7%, patient 0.7%, time 0.7%, test 0.6%, discrimin 0.6%, correl 0.5%, sampl 0.5%, mail 0.5%, diari 0.5%, health.survey 0.4%

Discriminating Terms

item 8.6%, health 6.6%, scale 3.8%, instrument 2.0%, measur 2.0%, cell 1.8%, survei 1.6%, reliabl 1.5%, questionnair 1.4%, score 1.2%, gene 1.0%, protein 1.0%, health.status 0.9%, activ 0.9%, dimens 0.8%, receptor 0.8%, tnf 0.6%, genet 0.6%, express 0.6%, complianc 0.5%, statu 0.5%, coeffici 0.5%, genom 0.5%, kinas 0.5%, diseas 0.4%

Single Word Terms

health 30, measur 22, gener 20, data 20, scale 19, patient 18, rate 18, item 17, score 16, survei 14, test 14, instrument 14, diseas 13, respons 13, function 12, reliabl 12, clinic 12, popul 12, statu 12, questionnair 12, sampl 11, chronic 11, time 11, on 11, form 11

Double Word Terms

health.status 9, health.survey 9, response.rate 6, physical.functioning 5, data.collected 5, general.health 5, general.population 5, social.functioning 5, scales.reliability 4, short.form 4, rheumatoid.arthritis 3, confidence.intervals 3, form.health 3, item.scales 3, functioning.scale 3, missing.data 3, cronbach.alpha 3, internal.consistency 3, correlation.coefficients 3, visual.analogue 3, scale.scores 3, analogue.scale 3, bodily.pain 3, health.role 3, iqola.project 3

Triple Word Terms

visual.analogue.scale 3, form.health.survey 3, short.form.health 3, multi.item.scales 3, sickness.impact.profile 2, coop.poster.charts 2, health.life.instruments 2, operating.characteristic.roc 2, physical.functioning.bodily 2, functioning.bodily.pain 2, receiver.operating.characteristic 2, physical.mental.health 2, nottingham.health.profile 2, health.role.emotional 2, iqola.project.test 2, item.internal.consistency 2, life.iqola.project 2,

project.test.appropriateness 2, mos.item.short 2, physical.functioning.scale 2, test.retest.reliability 2, world.health.organization 2, general.health.perceptions 2, health.status.indicators 2, low.back.pain 2

Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations.

Clinical impact versus factor analysis for quality of life questionnaire construction.

Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States.

A sensitive and reliable locomotor rating scale for open field testing in rats.

Translation and performance of the Norwegian SF-36 Health Survey in patients with rheumatoid arthritis. I. Data quality, scaling assumptions, reliability, and construct validity.

Work losses related to inflammatory bowel disease in the United States: results from the National Health Interview Survey.

How should importance and severity ratings be combined for item reduction in the development of health status instruments?

Depression: influence on time estimation and time experiments.

The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs.

Comparisons of the costs and quality of norms for the SF-36 health survey collected by mail versus telephone interview: results from a national survey.

Individual-patient monitoring in clinical practice: are available health status surveys adequate?

Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation.

The Sickness Impact Profile: development and final revision of a health status measure.

Barriers to the use of health status measures in clinical investigation, patient care, and policy research.

Statistical methods for assessing agreement between two methods of clinical measurement.

Intraclass correlations: uses in assessing rater reliability.

Mode of questionnaire administration can have serious effects on data quality.

CLUSTER 37 (124-116)

(37 Records)

*Meta-analyses and reviews, especially controlled clinical trials

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Cluster Syntax Features

Descriptive Terms

trial 21.4%, meta 7.2%, topic 5.4%, journal 3.3%, clinic 2.8%, bia 2.7%, controlled.trials 2.0%, clinical.trials 1.9%, randomis 1.9%, medicin 1.5%, random 1.3%, acupunctur 0.9%, medic 0.8%, test 0.8%, outcom 0.8%, standard 0.8%, design 0.7%, terminolog 0.7%, report 0.7%, randomized.controlled.trials 0.7%, rct 0.7%, randomized.controlled 0.6%, statist 0.6%, intervent 0.6%, consort 0.5%

Discriminating Terms

trial 12.5%, meta 4.1%, topic 3.1%, journal 2.1%, cell 1.7%, bia 1.5%, controlled.trials 1.2%, randomis 1.1%, clinical.trials 1.0%, protein 1.0%, gene 1.0%, clinic 0.8%, activ 0.8%, receptor 0.8%, medicin 0.7%, random 0.6%, diseas 0.6%, tnf 0.6%, acupunctur 0.6%, express 0.5%, genet 0.5%, genom 0.5%, kinas 0.5%, human 0.4%, terminolog 0.4%

Single Word Terms

trial 25, clinic 21, control 13, random 13, design 12, meta 12, medicin 10, bia 10, standard 10, journal 10, data 10, search 9, gener 9, model 9, topic 9, medic 9, on 8, patient 8, multipl 8, number 8, measur 8, interpret 8, therapi 7, treatment 7, methodolog 7

Double Word Terms

controlled.trials 12, clinical.trials 11, randomized.controlled 7, medical.journals 5, reporting.trials 4, multiple.sclerosis 4, sample.size 4, trials.rcts 4, trials.journals 3, double.blind 3, trials.bias 3, randomised.controlled 3, regression.models 3, clinical.outcomes 3, data.sources 3, meta.analytic 3, trials.meta 3, randomised.clinical 3, complementary.medicine 3, trials.trials 3, randomized.trials 3, cross.validation 2, meta.regression 2, large.trials 2, diagnostic.test 2

Triple Word Terms

randomized.controlled.trials 6, randomised.clinical.trials 3, controlled.trials.rcts 3, randomised.controlled.trials 3, checklist.flow.diagram 2, general.medical.journals 2, clinical.trials.trials 2, bias.funnel.plots 2, complementary.medicine.cam 2, trials.double.blind 2, funnel.plots.meta 2, controlled.trials.meta 2, controlled.trials.topic 2,

reporting.randomized.controlled 2, controlled.clinical.trials 1, hydroxy.methylglutaryl.coenzyme 1, placebo.controlled.trials 1, odds.ratio.confidence 1, ratio.confidence.interval 1, statins.anti.inflammatory 1, randomized.clinical.trials 1, clinical.trials.rcts 1, rheumatoid.arthritis.clinical 1, arthritis.clinical.trials 1, patient.physician.global 1

Measuring inconsistency in meta-analyses.

Predictive ability of DNA microarrays for cancer outcomes and correlates: an empirical assessment.

Assessing the quality of reports of randomized clinical trials: is blinding necessary?

Interventions to enhance medication adherence in chronic medical conditions: a systematic review.

Quantitative synthesis in systematic reviews.

Before there were standards: the role of test animals in the production of empirical generality in physiology.

Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis.

Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses.

Characteristic and incidental (placebo) effects in complex interventions such as acupuncture.

Location bias in controlled clinical trials of complementary/alternative therapies.

Use of methodological standards in diagnostic test research. Getting better but still not good.

Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials.

Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy.

Improving the quality of reporting of randomized controlled trials. The CONSORT statement.

Lessons for clinical trials from natalizumab in multiple sclerosis.

Bias in analytic research.

CLUSTER 42

(40 Records)

*Drug development, interactions, adverse effects, testing, and evaluation

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Cluster Syntax Features

Descriptive Terms

drug 37.2%, pharmaceut 2.9%, pharmacogenet 2.5%, advers 1.9%, pharmacogenom 1.6%, proteom 1.4%, adverse.drug 1.2%, topic 1.1%, biomark 1.1%, clinic 1.0%, test 1.0%, pharmacokinet 0.9%, medicin 0.7%, drug.drug 0.6%, therapi 0.6%, variabl 0.5%, surveil 0.5%, mass.spectrometry 0.5%, spectrometri 0.5%, startl 0.4%, valid 0.4%, drug.response 0.4%, pipelin 0.4%, hiv 0.4%, drug.therapy 0.4%

Discriminating Terms

drug 21.3%, pharmaceut 1.9%, cell 1.9%, pharmacogenet 1.6%, advers 1.1%, pharmacogenom 1.1%, activ 1.0%, adverse.drug 0.8%, gene 0.8%, proteom 0.8%, biomark 0.7%, tnf 0.7%, receptor 0.6%, pharmacokinet 0.5%, express 0.5%, topic 0.5%, kinas 0.5%, neuron 0.5%, diseas 0.4%, signal 0.4%, drug.drug 0.4%, protein 0.4%, alpha 0.4%, autophagi 0.4%, function 0.4%

Single Word Terms

drug 34, clinic 17, diseas 13, therapi 11, genet 11, respons 10, protein 10, advers 10, data 10, therapeut 10, patient 10, potenti 9, test 9, pharmacogenet 8, human 8, factor 7, safeti 7, major 7, pharmacokinet 7, pharmaceut 7, variabl 7, on 7, new 7, complex 7, advanc 7

Double Word Terms

adverse.drug 8, drug.drug 5, drug.metabolizing 5, drug.administration 4, mass.spectrometry 4, metabolizing.enzymes 4, drug.safety 4, drug.response 4, drug.reactions 4, drug.therapy 4, pharmacokinetic.pharmacodynamic 3, polymorphisms.drug 3, clinical.trials 3, appreciation.role 2, individualised.pharmacotherapy 2, clinical.case 2, therapeutic.index 2, localisation.human 2, preclinical.clinical 2, growing.number 2, role.drug 2, tissues.vectorial 2, variability.variability 2, drug.treatment 2, number.preclinical 2

Triple Word Terms

drug.metabolizing.enzymes 4, adverse.drug.reactions 4, clinical.trials.topic 2, movement.therapeutic.index 2, localisation.human.tissues 2, appreciation.role.drug 2, drug.transporters.pharmacokinetic 2, transporters.pharmacokinetic.pharmacodynamic 2,

number.preclinical.clinical 2, variability.variability.polymorphisms 2, inheritance.drug.response 2, role.drug.transporters 2, trials.topic.drug 2, topic.drug.drug 2, polymorphisms.drug.metabolizing 2, human.tissues.vectorial 2, food.drug.administration 2, growing.number.preclinical 2, drug.reactions.adrs 1, new.chemical.entities 1, transgenic.mice.expressing 1, blood.brain.barrier 1, selective.serotonin.reuptake 1, 450.enzyme.system 1, cytochrome.450.enzyme 1

Proposal for a new tool to evaluate drug interaction cases.

Herb-drug interactions: a literature review.

Genetic polymorphisms of drug transporters: pharmacokinetic and pharmacodynamic consequences in pharmacotherapy.

Hypothesis: comparisons of inter- and intra-individual variations can substitute for twin studies in drug research.

Timing of new black box warnings and withdrawals for prescription medications.

Physically crosslinked alginate/N,O-carboxymethyl chitosan hydrogels with calcium for oral delivery of protein drugs.

Potential role of pharmacogenomics in reducing adverse drug reactions: a systematic review.

Measuring the value of pharmacogenomics.

Protein biomarker discovery and validation: the long and uncertain path to clinical utility.

Pharmacogenetics and drug development: the path to safer and more effective drugs.

Complex disease-associated pharmacogenetics: drug efficacy, drug safety, and confirmation of a pathogenetic hypothesis (Alzheimer's disease).

Pharmacogenetics/genomics and personalized medicine.

New colorimetric cytotoxicity assay for anticancer-drug screening.

The tail suspension test: a new method for screening antidepressants in mice.

The development of polypharmacy. A longitudinal study.

Pharmacogenetics and pharmacogenomics: development, science, and translation.

Molecular basis of ethnic differences in drug disposition and response.

[Imputation of the unexpected or toxic effects of drugs. Actualization of the method used in France]

CLUSTER 17 (125-121)

(80 Records)

*The role of pro-inflammatory cytokine tnf-alpha in promoting inflammation

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Cluster Syntax Features

Descriptive Terms

tnf.alpha 22.0%, alpha 21.0%, tnf 19.6%, cytokin 1.8%, lp 1.1%, alpha.tnf 0.8%, alpha.tnf.alpha 0.8%, beta 0.7%, inflammatori 0.7%, necrosi 0.7%, necrosis.factor 0.6%, factor.alpha.tnf 0.6%, factor.alpha 0.6%, necrosis.factor.alpha 0.6%, product 0.5%, activ 0.5%, tumor.necrosis 0.5%, monocyt 0.5%, tumor.necrosis.factor 0.5%, inhibit 0.4%, factor 0.4%, receptor 0.4%, releas 0.4%, tumor 0.4%, anti 0.4%

Discriminating Terms

tnf.alpha 16.4%, alpha 13.7%, tnf 11.3%, cell 1.0%, gene 1.0%, protein 0.7%, genet 0.7%, diseas 0.6%, alpha.tnf 0.6%, genom 0.6%, alpha.tnf.alpha 0.6%, patient 0.5%, autophagi 0.5%, cytokin 0.5%, factor.alpha.tnf 0.4%, risk 0.4%, snp 0.4%, factor.alpha 0.4%, necrosis.factor.alpha 0.4%, control 0.3%, sequenc 0.3%, lp 0.3%, function 0.3%, test 0.3%, cancer 0.3%

Single Word Terms

alpha 80, tnf 74, factor 60, necrosi 57, activ 54, cell 51, tumor 47, cytokin 45, inflammatori 43, induc 39, protein 38, role 37, human 35, express 35, inhibit 35, receptor 34, diseas 33, product 33, level 33, regul 29, mediat 29, respons 25, mechan 25, signal 24, treatment 23

Double Word Terms

tnf.alpha 74, necrosis.factor 56, tumor.necrosis 46, alpha.tnf 45, factor.alpha 43, factor.tnf 13, lipopolysaccharide.lps 12, tumour.necrosis 11, tnf.receptor 10, lps.induced 10, inflammatory.diseases 10, alpha.production 10, proinflammatory.cytokines 10, animal.models 9, inflammatory.cytokines 9, pro.inflammatory 9, alpha.induced 8, nuclear.factor 8, inflammatory.cytokine 8, cell.line 8, anti.tnf 8, alpha.release 8, alpha.1beta 7, dependent.manner 7, anti.inflammatory 7

Triple Word Terms

tumor.necrosis.factor 45, alpha.tnf.alpha 44, necrosis.factor.alpha 43, factor.alpha.tnf 40, necrosis.factor.tnf 13, tumour.necrosis.factor 11, factor.tnf.alpha 10, tnf.alpha.production 10, tnf.alpha.induced 8, tnf.alpha.release 8, anti.tnf.alpha 7, tnf.alpha.1beta 7, induction.tnf.alpha 6,

pro.inflammatory.cytokines 6, cytokines.tnf.alpha 6, 1beta.tnf.alpha 6, tnf.alpha.tnf 6, inhibition.tnf.alpha 5, tnf.alpha.mrna 5, tnf.alpha.receptors 5, release.tnf.alpha 5, expression.tnf.alpha 5, mitogen.activated.protein 5, central.nervous.system 5, tnf.alpha.interleukin 5

HMG-1 as a mediator of acute lung inflammation.

Glucocorticoids and tumor necrosis factor alpha cooperatively regulate toll-like receptor 2 gene expression.

Membrane tumor necrosis factor-alpha (TNF-alpha) expressed on HTLV-I-infected T cells mediates a costimulatory signal for B cell activation--characterization of membrane TNF-alpha.

The role of glial reaction and inflammation in Parkinson's disease.

Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance.

Tumor necrosis factor alpha: a key component of the obesity-diabetes link.

TNF alpha and the TNF receptor superfamily: structure-function relationship(s).

TNF- alpha inhibitors.

Tumor necrosis factor-alpha and FMLP receptors are functionally linked during FMLP-stimulated activation of adherent human neutrophils.

Identification of sphingomyelin turnover as an effector mechanism for the action of tumor necrosis factor alpha and gamma-interferon. Specific role in cell differentiation.

The influence of tetracyclines on T cell activation.

TNF-alpha upregulates adenosine 2b (A2b) receptor expression and signaling in intestinal epithelial cells: a basis for A2bR overexpression in colitis.

Tumor necrosis factor-alpha inhibits seizures in mice via p75 receptors.

p38 map kinase regulates TNF-alpha production in human astrocytes and microglia by multiple mechanisms.

An essential role for NF-kappaB in preventing TNF-alpha-induced cell death.

Anti-TNF-alpha therapies: the next generation.

Cytokines in inflammatory bowel disease.

TNF alpha--a pivotal role in rheumatoid arthritis?

CLUSTER 25 (125-121)

(67 Records)

*The role of tnf and its receptors in signal transduction and induction of nf-kappa B responses

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Cluster Syntax Features

Descriptive Terms

tnf 49.0%, tumor 2.4%, kappa 2.3%, necrosi 1.9%, necrosis.factor 1.8%, tumor.necrosis 1.7%, tumor.necrosis.factor 1.6%, receptor 1.2%, factor.tnf 1.1%, necrosis.factor.tnf 1.0%, cytokin 0.9%, factor 0.9%, signal 0.9%, mtnf 0.7%, etanercept 0.6%, arthriti 0.5%, alpha 0.5%, solubl 0.5%, endotoxin 0.5%, tnf.receptor 0.4%, infliximab 0.4%, rheumatoid 0.3%, induc 0.3%, cell 0.3%, activ 0.3%

Discriminating Terms

tnf 33.2%, gene 1.1%, kappa 1.1%, necrosis.factor 1.1%, tumor.necrosis 1.0%, necrosi 1.0%, cell 1.0%, tumor 1.0%, tumor.necrosis.factor 1.0%, factor.tnf 0.8%, necrosis.factor.tnf 0.8%, genet 0.7%, protein 0.7%, genom 0.6%, mtnf 0.5%, patient 0.5%, express 0.5%, autophagi 0.5%, diseas 0.5%, risk 0.5%, etanercept 0.4%, kinas 0.4%, snp 0.4%, drug 0.3%, stress 0.3%

Single Word Terms

tnf 58, factor 55, necrosi 51, tumor 49, cell 42, induc 34, activ 33, receptor 33, mediat 31, signal 26, protein 26, diseas 26, function 25, two 25, inflammatori 25, cytokin 25, alpha 25, respons 21, regul 20, mechan 20, immun 19, role 19, human 19, solubl 18, treatment 18

Double Word Terms

necrosis.factor 50, tumor.necrosis 45, factor.tnf 37, tnf.receptor 15, tnf.alpha 12, tnf.receptors 11, soluble.tnf 10, factor.alpha 9, rheumatoid.arthritis 9, anti.tnf 8, transmembrane.tnf 7, tnf.tnf 6, cell.death 6, tumour.necrosis 6, cell.surface 6, kappa.activation 6, immune.responses 5, tnf.induced 5, induced.apoptosis 5, tnf.family 5, wild.type 5, alpha.tnf 5, reverse.signaling 5, receptor.tnf 5, dependent.manner 4

Triple Word Terms

tumor.necrosis.factor 44, necrosis.factor.tnf 37, necrosis.factor.alpha 9, tumour.necrosis.factor 6, factor.alpha.tnf 4, cell.surface.receptors 4, factor.alpha.tnfalpha 3, tnf.family.members 3, two.tumor.necrosis 3, tnf.alpha.mtnf 3, signaling.transmembrane.tnf 3, nuclear.factor.kappa 3,

programmed.cell.death 3, receptors.tumor.necrosis 3, soluble.tnf.receptors 3, reverse.signaling.transmembrane 3, membrane.bound.tnf 2, mice.secreted.tnf 2, reactive.oxygen.species 2, tnf.ligand.members 2, central.nervous.system 2, tnf.deficient.mice 2, p55.tnf.receptor 2, necrosis.factor.receptors 2, factor.tnf.interleukin 2

Tumor necrosis factor identified in multiple sclerosis brain.

TRADD-TRAF2 and TRADD-FADD interactions define two distinct TNF receptor 1 signal transduction pathways.

Formation of ion-permeable channels by tumor necrosis factor-alpha.

Uncoupling the proinflammatory from the immunosuppressive properties of tumor necrosis factor (TNF) at the p55 TNF receptor level: implications for pathogenesis and therapy of autoimmune demyelination.

Failure to regulate TNF-induced NF-kappaB and cell death responses in A20-deficient mice.

Tumor necrosis factors alpha and beta protect neurons against amyloid beta-peptide toxicity: evidence for involvement of a kappa B-binding factor and attenuation of peroxide and Ca2+ accumulation.

Inhibition of human monocyte TNF production by adenosine receptor agonists.

Cloning and expression of cDNAs for two distinct murine tumor necrosis factor receptors demonstrate one receptor is species specific.

Production of tumor necrosis factor and other cytokines by astrocytes stimulated with lipopolysaccharide or a neurotropic virus.

Signal transduction by tumor necrosis factor and its relatives.

TNF receptor subtype signalling: differences and cellular consequences.

In vivo pattern of lipopolysaccharide and anti-CD3-induced NF-kappa B activation using a novel gene-targeted enhanced GFP reporter gene mouse.

Tumor necrosis factor (TNF)-mediated neuroprotection against glutamate-induced excitotoxicity is enhanced by N-methyl-D-aspartate receptor activation. Essential role of a TNF receptor 2-mediated phosphatidylinositol 3-kinase-dependent NF-kappa B pathway.

Increased tumor necrosis factor production by monocytes in alcoholic hepatitis.

Blocking soluble tumor necrosis factor signaling with dominant-negative tumor necrosis factor inhibitor attenuates loss of dopaminergic neurons in models of Parkinson's disease.

CLUSTER 8 (125-121)

(37 Records)

*Transcription factor nf-kappa B and its role in inflammatory and innate immune responses

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Cluster Syntax Features

Descriptive Terms

kappab 50.1%, ikk 2.4%, nuclear 1.9%, activ 1.7%, ikappab 1.5%, factor.kappab 1.4%, kappab.pathway 1.2%, factor 1.1%, nuclear.factor 0.9%, kappab.activation 0.9%, transcript 0.8%, nuclear.factor.kappab 0.7%, pathwai 0.7%, cyld 0.7%, transcription.factor 0.7%, kappab.kappab 0.6%, regul 0.6%, factor.kappab.kappab 0.6%, activation.kappab 0.5%, ikappabalpha 0.5%, phosphoryl 0.4%, signal 0.4%, kinas 0.4%, deubiquitin 0.4%, p65 0.4%

Discriminating Terms

kappab 33.0%, ikk 1.7%, cell 1.2%, ikappab 0.9%, factor.kappab 0.9%, kappab.pathway 0.8%, nuclear 0.8%, patient 0.7%, diseas 0.7%, receptor 0.6%, kappab.activation 0.6%, gene 0.6%, genet 0.6%, nuclear.factor 0.6%, protein 0.5%, nuclear.factor.kappab 0.5%, genom 0.4%, cyld 0.4%, autophagi 0.4%, kappab.kappab 0.4%, risk 0.4%, factor.kappab.kappab 0.4%, drug 0.4%, ikappabalpha 0.4%, activation.kappab 0.3%

Single Word Terms

kappab 37, activ 34, factor 34, regul 26, nuclear 24, transcript 23, cell 21, protein 18, induc 18, respons 18, signal 18, pathwai 17, function 17, gene 17, kinas 16, inhibit 15, express 15, mechan 14, mediat 14, subunit 12, ikk 12, role 12, human 12, ikappab 12, control 12

Double Word Terms

factor.kappab 22, nuclear.factor 20, kappab.activation 15, transcription.factor 14, kappab.kappab 12, activation.kappab 11, necrosis.factor 9, ikappab.kinase 9, transcription.factors 8, tumor.necrosis 7, kinase.ikk 7, gene.expression 6, kappab.activity 6, kappab.pathway 5, induced.kappab 5, kappab.nuclear 5, activation.transcription 5, kappab.signaling 5, factor.kappa 5, nuclear.translocation 4, kappab.human 4, kappa.kappab 4, inhibition.kappab 4, role.kappab 4, reporter.gene 4

Triple Word Terms

nuclear.factor.kappab 15, factor.kappab.kappab 12, ikappab.kinase.ikk 7,

transcription.factor.kappab 7, tumor.necrosis.factor 7, nuclear.factor.kappa 5, activation.transcription.factor 4, factor.kappa.kappab 4, activation.nuclear.factor 3, induced.kappab.activation 3, kinase.ikk.complex 3, necrosis.factor.alpha 3, transcription.factor.nuclear 3, factor.nuclear.factor 3, necrosis.factor.tnf 3, kappab.dependent.reporter 2, factor.tnf.induced 2, tnfr.factor.traf2 2, factor.receptor.tnfr 2, linked.polyubiquitin.chains 2, tnf.induced.kappab 2, beta.activation.kappab 2, nuclear.translocation.p65 2, ikappabalpha.nuclear.translocation 2, family.transcription.factors 2

Substituted trans-stilbenes, including analogues of the natural product resveratrol, inhibit the human tumor necrosis factor alpha-induced activation of transcription factor nuclear factor kappaB.

The p65 (RelA) subunit of NF-kappaB interacts with the histone deacetylase (HDAC) corepressors HDAC1 and HDAC2 to negatively regulate gene expression.

Autocrine tumor necrosis factor alpha links endoplasmic reticulum stress to the membrane death receptor pathway through IRE1alpha-mediated NF-kappaB activation and down-regulation of TRAF2 expression.

A nuclear export signal in the N-terminal regulatory domain of IkappaBalpha controls cytoplasmic localization of inactive NF-kappaB/IkappaBalpha complexes.

Modulatory properties of various natural chemopreventive agents on the activation of NF-kappaB signaling pathway.

Phosphorylation meets ubiquitination: the control of NF-[kappa]B activity.

NF-kappaB at the crossroads of life and death.

NF-kappaB in cancer: from innocent bystander to major culprit.

NF-kappaB: linking inflammation and immunity to cancer development and progression.

The tumour suppressor CYLD negatively regulates NF-kappaB signalling by deubiquitination.

A pervasive role of ubiquitin conjugation in activation and termination of IkappaB kinase pathways.

Nuclear factor-kappaB: its role in health and disease.

NF-kappaB regulation in the immune system.

Inhibition of NF-kappa B by S-nitrosylation.

Nuclear factor-kappaB contributes to infarction after permanent focal ischemia.

CLUSTER 55 (125-121)

(66 Records)

*The role of neurons, minocycline, nerve growth factor, and microglia in protection of the CNS against neuroinflammatory processes and eventual neurodegeneration

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Cluster Syntax Features

Descriptive Terms

neuron 17.4%, minocyclin 3.5%, ngf 2.8%, microglia 2.1%, mptp 2.1%, brain 1.7%, motor 1.7%, mice 1.3%, neuroprotect 1.3%, al 1.2%, bdnf 1.0%, induc 0.9%, glutam 0.9%, motor.neuron 0.8%, glial 0.7%, gdnf 0.7%, ischemia 0.7%, neurotrophin 0.7%, express 0.7%, pacap38 0.6%, ischem 0.6%, injuri 0.6%, neurotroph 0.6%, stroke 0.6%, astrocyt 0.5%

Discriminating Terms

neuron 10.7%, minocyclin 2.7%, ngf 2.4%, mptp 1.7%, microglia 1.3%, motor 1.2%, cell 0.9%, neuroprotect 0.9%, protein 0.9%, al 0.8%, bdnf 0.8%, tnf 0.8%, gene 0.7%, genom 0.6%, motor.neuron 0.6%, patient 0.6%, glutam 0.6%, pacap38 0.5%, gdnf 0.5%, kinas 0.5%, neurotrophin 0.5%, glial 0.5%, genet 0.5%, risk 0.5%, autophagi 0.5%

Single Word Terms

neuron 61, cell 42, activ 38, induc 37, diseas 33, brain 33, express 30, factor 28, model 24, treatment 22, mice 21, respons 20, receptor 20, protein 19, system 18, potenti 18, protect 18, death 17, rat 17, surviv 17, injuri 17, neuroprotect 17, therapeut 16, function 16, glial 16

Double Word Terms

nervous.system 11, parkinson.disease 10, neurotrophic.factor 10, nerve.growth 9, central.nervous 8, derived.neurotrophic 8, substantia.nigra 8, nitric.oxide 8, growth.factor 8, factor.ngf 7, wild.type 7, phenyl.tetrahydropyridine 7, dopaminergic.neurons 7, motor.neuron 7, methyl.phenyl 7, lateral.sclerosis 6, tetrahydropyridine.mptp 6, gene.expression 6, alzheimer.disease 6, spinal.cord 6, brain.tissue 6, brain.derived 6, cell.death 6, amyotrophic.lateral 6, oxide.synthase 6

Triple Word Terms

derived.neurotrophic.factor 8, nerve.growth.factor 8, growth.factor.ngf 7,

methyl.phenyl.tetrahydropyridine 7, central.nervous.system 7, nitric.oxide.synthase 6, amyotrophic.lateral.sclerosis 6, brain.derived.neurotrophic 6, phenyl.tetrahydropyridine.mptp 6, neurotrophic.factor.bdnf 5, lateral.sclerosis.als 5, middle.cerebral.artery 5, wild.type.mice 4, inducible.nitric.oxide 4, nigra.pars.compacta 4, substantia.nigra.pars 4, green.fluorescent.protein 4, parkinson.disease.neurodegenerative 3, disease.neurodegenerative.disorder 3, reactive.oxygen.species 3, cerebral.artery.occlusion 3, model.parkinson.disease 3, model.huntington.disease 3, mptp.induced.dopaminergic 3, fluorescent.protein.gfp 3

Interleukin-18 involvement in hypoxic-ischemic brain injury.

Glutamate regulation of GDNF gene expression in the striatum and primary striatal astrocytes.

Neuroinflammatory processes in Parkinson's disease.

BDNF-induced white matter neuroprotection and stage-dependent neuronal survival following a neonatal excitotoxic challenge.

CNTF and LIF act on neuronal cells via shared signaling pathways that involve the IL-6 signal transducing receptor component gp130.

Microglia: a sensor for pathological events in the CNS.

Minocycline slows disease progression in a mouse model of amyotrophic lateral sclerosis.

Activation of innate immunity in the CNS triggers neurodegeneration through a Toll-like receptor 4-dependent pathway.

Inducible nitric oxide synthase stimulates dopaminergic neurodegeneration in the MPTP model of Parkinson disease.

Nerve growth factor and basic fibroblast growth factor protect rat cerebellar granule cells in culture against ethanol-induced cell death.

Comparison of seizure phenotype and neurodegeneration induced by systemic kainic acid in inbred, outbred, and hybrid mouse strains.

Granulocyte-colony stimulating factor is neuroprotective in a model of Parkinson's disease.

Neurotrophins inhibit major histocompatibility class II inducibility of microglia: involvement of the p75 neurotrophin receptor.

Control of glial immune function by neurons.

Improving the transfection efficiency of post-mitotic neurons.

NF-kappa B: a crucial transcription factor for glial and neuronal cell function.

CLUSTER 36 (125-121)

(57 Records)

*Role of the enteric nervous system in controlling gastrointestinal system, and the role of myenteric neurons in gastrointestinal function and disease

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Cluster Syntax Features

Descriptive Terms

neuron 20.7%, enter 6.5%, myenter 6.1%, nervou 2.1%, nervous.system 1.9%, enteric.nervous 1.6%, gastrointestin 1.5%, innerv 1.5%, intestin 1.4%, enteric.nervous.system 1.4%, gut 1.4%, plexu 1.2%, system 1.1%, ag 1.1%, myenteric.plexus 1.0%, en 1.0%, myenteric.neurons 0.9%, nerv 0.9%, gdnf 0.8%, rat 0.8%, glia 0.8%, enteric.neurons 0.7%, stain 0.6%, ganglia 0.6%, colon 0.6%

Discriminating Terms

neuron 10.8%, enter 4.2%, myenter 4.2%, enteric.nervous 1.1%, innerv 1.0%, nervou 1.0%, enteric.nervous.system 0.9%, nervous.system 0.9%, cell 0.9%, gene 0.8%, gut 0.8%, gastrointestin 0.8%, plexu 0.8%, activ 0.7%, myenteric.plexus 0.7%, protein 0.7%, tnf 0.7%, diseas 0.7%, en 0.7%, myenteric.neurons 0.6%, intestin 0.6%, genet 0.6%, patient 0.6%, gdnf 0.5%, genom 0.5%

Single Word Terms

neuron 50, enter 34, cell 33, system 32, nervou 30, myenter 27, function 25, intestin 25, gut 21, gastrointestin 21, express 21, protein 20, nerv 20, rat 20, plexu 20, role 18, receptor 17, number 16, innerv 16, small 15, control 15, stain 15, factor 15, activ 14, colon 14

Double Word Terms

nervous.system 30, enteric.nervous 21, myenteric.plexus 18, enteric.neurons 14, myenteric.neurons 14, system.ens 11, gastrointestinal.tract 10, central.nervous 8, vasoactive.intestinal 7, small.intestine 7, glial.cells 6, nerve.fibers 6, neurotrophic.factor 6, protein.gene 5, cell.line 5, derived.neurotrophic 5, gene.product 5, small.large 5, neurons.myenteric 5, gastrointestinal.motility 5, cell.loss 5, gene.peptide 4, afferent.neurons 4, neurons.small 4, fischer.344 4

Triple Word Terms

enteric.nervous.system 21, nervous.system.ens 11, central.nervous.system 8,

derived.neurotrophic.factor 5, protein.gene.product 5, calcitonin.gene.peptide 4, glial.fibrillary.acidic 4, cell.line.derived 4, vasoactive.intestinal.polypeptide 4, glial.cell.line 4, line.derived.neurotrophic 4, primary.afferent.neurons 4, neurons.myenteric.plexus 4, fischer.344.rats 4, neurotrophic.factor.gdnf 3, myenteric.plexus.small 3, plexus.small.intestine 3, number.myenteric.neurons 3, nitric.oxide.synthase 3, dopamine.beta.hydroxylase 3, fibrillary.acidic.protein 3, intestinal.polypeptide.vip 3, vasoactive.intestinal.peptide 3, small.large.intestines 3, intestinal.peptide.vip 3

Gene targeting reveals a critical role for neurturin in the development and maintenance of enteric, sensory, and parasympathetic neurons.

The effects of age on the overall population and on sub-populations of myenteric neurons in the rat small intestine.

Enteric dopaminergic neurons: definition, developmental lineage, and effects of extrinsic denervation.

Physiological modulation of intestinal motility by enteric dopaminergic neurons and the D2 receptor: analysis of dopamine receptor expression, location, development, and function in wild-type and knock-out mice.

Choline acetyltransferase immunoreactivity of putative intrinsic primary afferent neurons in the rat ileum.

Distribution of adrenergic receptors in the enteric nervous system of the guinea pig, mouse, and rat.

Changes in chemical coding of myenteric neurones in ulcerative colitis.

As the gut ages: timetables for aging of innervation vary by organ in the Fischer 344 rat.

Aging of the myenteric plexus: neuronal loss is specific to cholinergic neurons.

Loss of glia and neurons in the myenteric plexus of the aged Fischer 344 rat.

Quantification of neurons in the myenteric plexus: an evaluation of putative pan-neuronal markers.

Alimentary tract innervation deficits and dysfunction in mice lacking GDNF family receptor alpha2.

Glial cells in the gut.

Ageing of the enteric nervous system.

CLUSTER 9 (125-121)

(29 Records)

* Peroxisome proliferator-activated receptors, especially PPAR-gamma, with emphasis on their role in the regulation of inflammation

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Cluster Syntax Features

Descriptive Terms

ppar 21.1%, ppargamma 11.9%, peroxisom 2.9%, ppar.gamma 2.8%, gamma 2.6%, macrophag 1.9%, peroxisome.proliferator 1.7%, proliferator.activated 1.6%, receptor 1.4%, peroxisome.proliferator.activated 1.4%, ppar.alpha 1.3%, kappab 1.2%, lxr 1.2%, prolifer 1.1%, ligand 1.0%, activ 0.9%, nuclear 0.9%, proliferator.activated.receptor 0.9%, activated.receptor 0.8%, pgj 0.8%, mppar 0.8%, agonist 0.8%, adipocyt 0.7%, lipid 0.7%, express 0.7%

Discriminating Terms

ppar 14.5%, ppargamma 8.2%, peroxisom 2.0%, ppar.gamma 1.9%, cell 1.2%, peroxisome.proliferator 1.1%, gamma 1.1%, proliferator.activated 1.1%, peroxisome.proliferator.activated 0.9%, ppar.alpha 0.9%, protein 0.8%, lxr 0.8%, diseas 0.8%, patient 0.8%, macrophag 0.6%, tnf 0.6%, proliferator.activated.receptor 0.6%, pgj 0.6%, mppar 0.6%, genet 0.6%, activated.receptor 0.5%, genom 0.5%, neuron 0.5%, adipocyt 0.5%, human 0.4%

Single Word Terms

receptor 27, activ 25, prolifer 22, peroxisom 22, express 21, factor 19, regul 19, respons 18, gene 18, nuclear 17, role 17, cell 16, gamma 16, ppar 16, inflammatori 16, transcript 16, inhibit 15, ligand 14, induc 14, bind 13, kappab 11, macrophag 11, inflamm 11, lipid 10, protein 10

Double Word Terms

proliferator.activated 22, peroxisome.proliferator 21, activated.receptor 17, receptor.gamma 12, gene.expression 9, nuclear.receptor 9, ppar.gamma 8, gamma.ppargamma 7, transcription.factors 7, gamma.ppar 6, dna.binding 6, activated.receptors 6, inflammatory.responses 6, nuclear.factor 6, receptor.superfamily 5, anti.inflammatory 5, transcription.factor 5, lipid.metabolism 5, receptors.ppars 5, gamma.agonists 4, deoxy.delta 4, inflammatory.gene 4, glucose.homeostasis 4, binding.activity 4, ligand.dependent 4

Triple Word Terms

peroxisome.proliferator.activated 21, proliferator.activated.receptor 17, activated.receptor.gamma 12, receptor.gamma.ppargamma 7, proliferator.activated.receptors 5, activated.receptors.ppars 5, gamma.ppar.gamma 4, dna.binding.activity 4, receptor.gamma.ppar 4, ppar.gamma.agonists 4, necrosis.factor.alpha 3, nuclear.receptor.superfamily 3, inducible.nitric.oxide 3, nitric.oxide.synthase 3, ppar.alpha.agonists 3, inflammatory.response.genes 3, inflammatory.gene.expression 3, deoxy.delta.prostaglandin 3, tumor.necrosis.factor 3, nuclear.factor.kappab 3, ppar.beta.delta 2, ppar.gamma.ppar 2, steroidal.anti.inflammatory 2, ppar.gamma.member 2, gamma.ppargamma.ligand 2

PPAR-gamma agonists inhibit production of monocyte inflammatory cytokines.

Reciprocal regulation of inflammation and lipid metabolism by liver X receptors.

Roles of PPARs in health and disease.

Involvement of IL-10 in peroxisome proliferator-activated receptor gamma-mediated anti-inflammatory response in asthma.

An overview on biological mechanisms of PPARs.

Peroxisome proliferator-activated receptors alpha and gamma are activated by indomethacin and other non-steroidal anti-inflammatory drugs.

A SUMOylation-dependent pathway mediates transrepression of inflammatory response genes by PPAR-gamma.

Sirt1 promotes fat mobilization in white adipocytes by repressing PPAR-gamma.

The peroxisome proliferator-activated receptor-gamma is a negative regulator of macrophage activation.

Expression of the peroxisome proliferator-activated receptor gamma (PPARgamma) in human atherosclerosis and regulation in macrophages by colony stimulating factors and oxidized low density lipoprotein.

mPPAR gamma 2: tissue-specific regulator of an adipocyte enhancer.

Peroxisome proliferator-activated receptor-alpha and retinoid X receptor agonists inhibit inflammatory responses of astrocytes.

The role of PPARs in inflammation and immunity.

Emerging roles of PPARs in inflammation and immunity.

Peroxisome proliferator-activated receptors in inflammation control.

CLUSTER 6 (125-121)

(26 Records)

* Cannabinoids and endocannabinoids, especially their effects on the immune and neural systems, and the role played by their receptors

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Cluster Syntax Features

Descriptive Terms

cannabinoid 32.1%, cannabinoid.receptor 4.6%, endocannabinoid 4.2%, receptor 4.0%, cb1 3.3%, faah 2.7%, anandamid 2.5%, cb2 2.3%, thc 1.2%, endogen 1.2%, memori 1.2%, agonist 1.0%, delta 0.9%, tetrahydrocannabinol 0.7%, marijuana 0.6%, delta.thc 0.6%, extinct 0.6%, cannabinoid.receptors 0.6%, acid 0.5%, 940 0.5%, cisaprid 0.5%, antagonist 0.4%, endogenous.cannabinoid 0.4%, resolut 0.4%, arachidonoylglycerol 0.4%

Discriminating Terms

cannabinoid 21.0%, cannabinoid.receptor 3.0%, endocannabinoid 2.7%, cb1 2.2%, faah 1.7%, anandamid 1.6%, cb2 1.5%, cell 1.3%, gene 0.9%, thc 0.8%, diseas 0.7%, protein 0.7%, tnf 0.6%, activ 0.6%, memori 0.6%, genet 0.6%, receptor 0.6%, patient 0.6%, endogen 0.5%, tetrahydrocannabinol 0.5%, delta 0.5%, genom 0.4%, kinas 0.4%, factor 0.4%, marijuana 0.4%

Single Word Terms

receptor 23, cannabinoid 19, acid 14, inhibit 13, activ 13, level 12, endogen 12, express 12, mediat 12, role 11, system 11, agonist 11, respons 10, cb1 10, antagonist 10, select 10, brain 10, function 9, endocannabinoid 9, cell 8, drug 8, tissu 8, cellular 8, action 8, central 8

Double Word Terms

cannabinoid.receptor 13, cannabinoid.receptors 8, endogenous.cannabinoid 7, mass.spectrometry 6, hydrolase.faah 5, fatty.acid 5, delta.tetrahydrocannabinol 5, central.nervous 5, nervous.system 5, acid.amide 5, endocannabinoid.levels 5, amide.hydrolase 5, messenger.rna 5, chromatography.mass 4, background.amp 4, amp.aims 4, antagonist.sr141716a 4, deficient.mice 4, cannabinoid.system 4, cell.lines 4, cb1.receptors 4, cannabinoid.cb1 4, levels.endocannabinoids 3, adenylate.cyclase 3, mrna.levels 3

Triple Word Terms

fatty.acid.amide 5, acid.amide.hydrolase 5, amide.hydrolase.faah 5, background.amp.aims 4, central.nervous.system 4, chromatography.mass.spectrometry 4, polymerase.chain.reaction 3,

reverse.transcription.polymerase 3, tetrahydrocannabinol.delta.thc 3, messenger.rna.mrna 3, delta.tetrahydrocannabinol.delta 3, transcription.polymerase.chain 3, endogenous.cannabinoid.system 3, liquid.chromatography.mass 3, gamma.aminobutyric.acid 3, faah.messenger.rna 2, binding.radiolabeled.cannabinoid 2, dose.dependent.manner 2, nervous.system.cns 2, cannabinoid.receptors.endogenous 2, inflammatory.bowel.diseases 2, endocannabinoids.anandamide.arachidonoylglycerol 2, cannabinoid.receptor.cb1 2, endocannabinoid.levels.isotope 2, hydrolase.faah.catalyzes 2

International Union of Pharmacology. XXVII. Classification of cannabinoid receptors.

An endogenous cannabinoid tone attenuates cholera toxin-induced fluid accumulation in mice.

Emerging role of cannabinoids in gastrointestinal and liver diseases: basic and clinical aspects.

Possible endocannabinoid control of colorectal cancer growth.

The endogenous cannabinoid system controls extinction of aversive memories.

Structure of a cannabinoid receptor and functional expression of the cloned cDNA.

Identification of an endogenous 2-monoglyceride, present in canine gut, that binds to cannabinoid receptors.

Molecular characterization of a peripheral receptor for cannabinoids.

Cannabinoids and the gastrointestinal tract.

Targeting endocannabinoid degradation protects against experimental colitis in mice: involvement of CB1 and CB2 receptors.

2-Arachidonoylglycerol: a possible endogenous cannabinoid receptor ligand in brain.

Cannabinoids inhibit N- and P/Q-type calcium channels in cultured rat hippocampal neurons.

Cannabinoids inhibit emesis through CB1 receptors in the brainstem of the ferret.

Identification and functional characterization of brainstem cannabinoid CB2 receptors.

Immunomodulation by cannabinoids is absent in mice deficient for the cannabinoid CB(2) receptor.

Fatty acid amide hydrolase controls mouse intestinal motility in vivo.

CLUSTER 59 (125-121)

(72 Records)

*Receptors, especially histamine, dopamine, and opoid, and their impact on immune and neural functions

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Cluster Syntax Features

Descriptive Terms

receptor 24.7%, histamin 9.0%, dopamin 3.3%, opioid 2.1%, bind 1.7%, ligand 1.4%, lymphocyt 1.0%, cell 0.9%, subtyp 0.8%, dopamine.receptor 0.8%, agonist 0.7%, cort 0.7%, express 0.6%, action 0.6%, antagonist 0.6%, brain 0.6%, rxr 0.5%, site 0.5%, prostanoid 0.4%, activ 0.4%, mast 0.4%, drug 0.4%, pharmacolog 0.4%, pge 0.4%, histamine.receptor 0.3%

Discriminating Terms

receptor 14.4%, histamin 7.3%, dopamin 2.6%, opioid 1.8%, diseas 0.9%, gene 0.9%, tnf 0.8%, patient 0.7%, ligand 0.7%, dopamine.receptor 0.7%, genet 0.7%, subtyp 0.6%, genom 0.6%, cort 0.6%, protein 0.6%, lymphocyt 0.5%, autophagi 0.5%, risk 0.5%, cell 0.5%, death 0.4%, bind 0.4%, rxr 0.4%, snp 0.4%, kinas 0.4%, prostanoid 0.4%

Single Word Terms

receptor 66, cell 40, activ 34, express 32, function 31, ligand 26, protein 26, bind 25, role 23, human 22, action 21, target 20, brain 20, system 19, induc 19, site 18, regul 18, mediat 18, respons 17, diseas 17, antagonist 17, acid 17, molecular 16, mechan 16, tissu 16

Double Word Terms

cell.surface 7, central.nervous 7, nervous.system 7, nuclear.receptors 6, protein.coupled 6, amino.acid 6, radioligand.binding 5, histamine.receptor 5, binding.sites 5, coupled.receptors 5, receptor.family 5, receptor.binding 5, receptor.subtypes 4, rheumatoid.arthritis 4, high.affinity 4, dopamine.receptor 4, agonists.antagonists 4, retinoid.receptor 4, receptor.subtype 4, binding.site 4, receptor.antagonist 4, peripheral.blood 4, cerebral.cortex 4, receptor.activation 4, receptor.antagonists 4

Triple Word Terms

central.nervous.system 7, protein.coupled.receptors 5, protein.coupled.receptor 3, gamma.aminobutyric.acid 3, peripheral.blood.lymphocytes 3, retinoid.receptor.rxr 3, beta1.integrin.mediated 2, vitamin.receptor.vdr 2, cells.myeloid.lineage 2, numbers.mast.cells 2,

human.peripheral.blood 2, expressed.sequence.tag 2, response.elements.target 2, elements.target.genes 2, binding.nuclear.receptors 2, dna.response.elements 2, soluble.beta.glucan 2, functions.adhesion.molecule 2, ep1.ep2.ep3 2, cyclase.activating.polypeptide 2, adenylate.cyclase.activating 2, ep2.ep3.ep4 2, activating.polypeptide.pacap 2, receptor.tyrosine.kinases 2, metabotropic.glutamate.receptors 2

Nicotinic acetylcholine receptors as drug targets.

Prostaglandin E2 regulates the nuclear receptor NR4A2 in colorectal cancer.

Histamine H4 receptor expression in human synovial cells obtained from patients suffering from rheumatoid arthritis.

Acute liver failure and hyperammonemia increase peripheral-type benzodiazepine receptor binding and pregnenolone synthesis in mouse brain.

The utilization of recombinant prostanoid receptors to determine the affinities and selectivities of prostaglandins and related analogs.

Ligand binding specificities of the eight types and subtypes of the mouse prostanoid receptors expressed in Chinese hamster ovary cells.

Retinoid X receptor interacts with nuclear receptors in retinoic acid, thyroid hormone and vitamin D3 signalling.

Molecular physiology of kainate receptors.

An estrogen receptor-beta agonist is active in models of inflammatory and chemical-induced pain.

Dopamine interacts directly with its D3 and D2 receptors on normal human T cells, and activates beta1 integrin function.

Cloning and functional expression of the human histamine H3 receptor.

Structural design and molecular evolution of a cytokine receptor superfamily.

Mu, delta, and kappa opioid receptor mRNA expression in the rat CNS: an in situ hybridization study.

Molecular analysis of nicotinic receptor expression in autism.

Dopamine receptor expression on human T- and B-lymphocytes, monocytes, neutrophils, eosinophils and NK cells: a flow cytometric study.

Tissue-specific mRNA expression profiles of human nuclear receptor subfamilies.

CLUSTER 7 (125-121)

(30 Records)

*Adenosine, especially adenosine receptors, and their role in regulation of the innate immune system and impact on the Central Nervous System

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Cluster Syntax Features

Descriptive Terms

adenosin 36.3%, receptor 11.8%, adenosine.receptor 4.6%, adenosine.receptors 1.7%, a2b 1.7%, agonist 1.6%, neca 1.5%, a2a 1.5%, purinerg 1.3%, antagonist 1.0%, p2x 0.7%, rat 0.6%, bind 0.5%, select 0.5%, subtyp 0.5%, atp 0.4%, purin 0.4%, adenosine.a2b 0.4%, radioligand 0.4%, cd73 0.3%, tissu 0.3%, a2a.adenosine 0.3%, pyrimidin 0.3%, receptor.adenosine 0.3%, inflammatori 0.3%

Discriminating Terms

adenosin 23.5%, receptor 4.0%, adenosine.receptor 3.0%, adenosine.receptors 1.1%, a2b 1.1%, neca 1.0%, a2a 1.0%, gene 1.0%, cell 0.9%, diseas 0.9%, purinerg 0.8%, patient 0.8%, agonist 0.8%, protein 0.7%, activ 0.7%, tnf 0.6%, genom 0.5%, antagonist 0.5%, p2x 0.4%, factor 0.4%, neuron 0.4%, kinas 0.4%, autophagi 0.4%, risk 0.4%, alpha 0.4%

Single Word Terms

adenosin 28, receptor 27, cell 21, activ 14, antagonist 13, agonist 12, select 12, respons 11, rat 11, express 11, protein 11, tissu 10, mediat 10, function 10, role 10, signal 10, a2a 9, subtyp 9, inhibit 9, bind 9, model 8, human 8, order 8, clone 8, ligand 8

Double Word Terms

adenosine.receptor 14, adenosine.receptors 13, selective.agonist 5, receptor.adenosine 5, adenosine.purinergic 4, coupled.receptors 4, adenosine.a2b 4, protein.coupled 4, high.affinity 4, a2a.adenosine 4, amino.acids 4, wild.type 4, polymerase.chain 3, receptor.cloned 3, adenosine.agonists 3, purinergic.receptors 3, immune.cells 3, selective.antagonists 3, selective.antagonist 3, receptor.activation 3, rat.brain 3, ovary.cells 3, chain.reaction 3, hamster.ovary 3, encodes.protein 3

Triple Word Terms

protein.coupled.receptors 4, chinese.hamster.ovary 3, wild.type.mice 3, hamster.ovary.cells 3, polymerase.chain.reaction 3, adenosine.receptor.agonist 3, central.nervous.system 3, radioligand.binding.adenosine 2, phenyl.propyladenosine.pia 2, ovary.cells.stably 2, coupled.adenylate.cyclase 2, adenosine.a2b.receptors 2, stimulated.camp.accumulation 2, binding.adenosine.receptor 2, receptor.deficient.mice 2, adenosine.purinergic.receptors 2, adenosine.receptor.subtype 2, adenosine.receptor.mrnas 2, amino.acid.sequence 2, brain.cdna.library 2, cdna.library.probe 2, rat.brain.cdna 2, cloned.rat.brain 2, site.directed.mutagenesis 2, a2a.adenosine.receptor 2

Grafts of adenosine-releasing cells suppress seizures in kindling epilepsy.

Cloned adenosine A3 receptors: pharmacological properties, species differences and receptor functions.

Adenosine A(2A) receptor activation promotes wound neovascularization by stimulating angiogenesis and vasculogenesis.

Medicinal chemistry of adenosine A3 receptor ligands.

Molecular physiology of P2X receptors.

Activation of A2A adenosine receptor attenuates intestinal inflammation in animal models of inflammatory bowel disease.

Role of G-protein-coupled adenosine receptors in downregulation of inflammation and protection from tissue damage.

Molecular cloning and expression of the cDNA for a novel A2-adenosine receptor subtype.

Molecular cloning and characterization of the human A3 adenosine receptor.

Signalling from adenosine receptors to mitogen-activated protein kinases.

Use of the A(2A) adenosine receptor as a physiological immunosuppressor and to engineer inflammation in vivo.

The A2b adenosine receptor mediates cAMP responses to adenosine receptor agonists in human intestinal epithelia.

The cytolytic P2Z receptor for extracellular ATP identified as a P2X receptor (P2X7).

A binding site model and structure-activity relationships for the rat A3 adenosine receptor.

Molecular cloning and characterization of an adenosine receptor: the A3 adenosine receptor.

Characterization of the A2 adenosine receptor labeled by [3H]NECA in rat striatal membranes.

CLUSTER 24 (125-121)

(32 Records)

*Role of matrix metalloproteinases in modulating inflammatory and immune responses, and the role of ghrelin in the gastric system and in the inhibition of cell death

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Cluster Syntax Features

Descriptive Terms

mmp 23.3%, ghrelin 15.6%, par 6.0%, matrix 2.7%, metalloproteinas 2.0%, ligand 1.3%, receptor 1.3%, rage 1.1%, gh 1.0%, tissu 0.9%, rat 0.9%, proteas 0.8%, gelatinas 0.8%, hormon 0.7%, mcp 0.7%, dkk 0.6%, sulfhydryl 0.6%, proteinas 0.6%, epitheli 0.5%, chemokin 0.5%, matrix.metalloproteinases 0.5%, inflamm 0.5%, neutrophil 0.5%, minocyclin 0.4%, cell 0.4%

Discriminating Terms

mmp 15.2%, ghrelin 10.5%, par 3.9%, matrix 1.6%, metalloproteinas 1.2%, gene 0.9%, diseas 0.8%, rage 0.8%, cell 0.7%, patient 0.7%, gh 0.7%, tnf 0.6%, protein 0.5%, gelatinas 0.5%, genet 0.5%, genom 0.5%, ligand 0.5%, mcp 0.4%, autophagi 0.4%, risk 0.4%, dkk 0.4%, proteas 0.4%, alpha 0.4%, kinas 0.4%, proteinas 0.4%

Single Word Terms

receptor 21, activ 18, tissu 18, cell 16, protein 15, role 13, metalloproteinas 12, express 12, function 12, extracellular 12, regul 12, matrix 12, stimul 11, inflamm 11, mmp 10, hormon 9, respons 9, signal 9, ligand 8, molecul 8, rat 8, mediat 8, growth 8, releas 8, peptid 8

Double Word Terms

matrix.metalloproteinase 8, matrix.metalloproteinases 6, extracellular.matrix 6, protein.coupled 5, growth.hormone 5, metalloproteinase.mmp 5, cell.migration 4, activated.receptors 4, receptors.pars 4, membrane.type 3, metalloproteinases.mmps 3, protein.mcp 3, adipose.tissue 3, growth.factor 3, play.role 3, ghrelin.stimulated 3, coupled.receptors 3, mmp.mmp 3, cell.line 3, cell.surface 3, tissue.destruction 3, release.growth 3, acylated.peptide 3, rat.ghrelin 3, rat.human 3

Triple Word Terms

matrix.metalloproteinase.mmp 5, activated.receptors.pars 4, release.growth.hormone 3, matrix.metalloproteinases.mmps 3, protein.coupled.receptors 3, growth.hormone.releasing 2, protein.coupled.receptor 2, undefined.physiological.functions 2, chemoattractant.protein.mcp 2,

glycation.end.products 2, growth.factor.vegf 2, member.immunoglobulin.superfamily 2, vascular.endothelial.growth 2, growth.hormone.pituitary 2, endothelial.growth.factor 2, metalloproteinase.mmp.activity 2, monocyte.chemoattractant.protein 2, proteinase.activated.receptors 2, high.affinity.binding 2, protease.activated.receptors 2, epithelial.cell.migration 2, extracellular.matrix.proteins 1, proliferator.activated.receptor 1, role.modulation.intestinal 1, membrane.type.matrix 1

Membrane-type 1 matrix metalloproteinase cleaves CD44 and promotes cell migration.

Ghrelin and des-acyl ghrelin inhibit cell death in cardiomyocytes and endothelial cells through ERK1/2 and PI 3-kinase/AKT.

The mitogenic and antiapoptotic actions of ghrelin in 3T3-L1 adipocytes.

Ghrelin is a growth-hormone-releasing acylated peptide from stomach.

Delayed minocycline inhibits ischemia-activated matrix metalloproteinases 2 and 9 after experimental stroke.

Ghrelin stimulates gastric acid secretion and motility in rats.

Matrix metalloproteinases: they're not just for matrix anymore!

Matrix metalloproteinase processing of monocyte chemoattractant proteins generates CC chemokine receptor antagonists with anti-inflammatory properties in vivo.

A role for ghrelin in the central regulation of feeding.

Matrix metalloproteinase-9 knockout confers resistance to corneal epithelial barrier disruption in experimental dry eye.

Matrix metalloproteinases process the laminin-5 gamma 2-chain and regulate epithelial cell migration.

The biology of the receptor for advanced glycation end products and its ligands.

Proteinase-activated receptors: transducers of proteinase-mediated signaling in inflammation and immune response.

How matrix metalloproteinases regulate cell behavior.

CLUSTER 35 (125-121)

(35 Records)

*The role of the cytokine osteopontin, the surface adhesion molecule CD44, and the membrane glycoprotein CD200 and its receptor CD200R in immune function (especially inflammation) mediation and regulation.

Cluster Syntax Features

Descriptive Terms

opn 38.0%, cd44 4.2%, cell 3.6%, cd200r 3.0%, osteopontin 2.8%, cd200 2.0%, mice 1.0%, osteoclast 0.8%, growth 0.7%, bone 0.7%, vegfr 0.6%, osteopontin.opn 0.6%, express 0.6%, igf 0.5%, procyanidin 0.4%, cytokin 0.4%, csf 0.4%, macrophag 0.4%, opn.mice 0.4%, regul 0.4%, blimp 0.4%, matrix 0.4%, ebv 0.3%, plasma 0.3%, respons 0.3%

Discriminating Terms

opn 27.7%, cd44 3.1%, cd200r 2.2%, osteopontin 2.0%, cd200 1.4%, diseas 0.8%, tnf 0.7%, protein 0.7%, genet 0.6%, patient 0.6%, osteoclast 0.6%, gene 0.5%, activ 0.5%, genom 0.5%, neuron 0.5%, kinas 0.5%, vegfr 0.4%, osteopontin.opn 0.4%, autophagi 0.4%, risk 0.4%, drug 0.4%, alpha 0.4%, igf 0.3%, death 0.3%, snp 0.3%

Single Word Terms

cell 34, express 20, receptor 19, activ 18, regul 18, mediat 17, respons 16, function 15, cytokin 14, induc 14, protein 14, osteopontin 13, tissu 12, factor 12, gene 12, differenti 11, role 11, opn 11, level 11, normal 10, growth 10, type 10, mice 10, signal 10, macrophag 9

Double Word Terms

osteopontin.opn 10, role.opn 5, growth.factor 5, cell.surface 5, growth.factors 5, embryonic.stem 4, cells.opn 4, stem.cells 4, cytokine.production 4, arginine.glycine 4, opn.secreted 4, epithelial.cells 4, cell.function 3, play.role 3, endothelial.cells 3, bone.marrow 3, wild.type 3, endothelial.cell 3, opn.cells 3, gene.expression 3, opn.cell 3, extracellular.matrix 3, control.opn 3, breast.cancer 3, myeloid.cell 3

Triple Word Terms

embryonic.stem.cells 4, osteopontin.opn.secreted 3, opn.cell.surface 2, bone.marrow.derived 2, opn.secreted.adhesive 2, cells.wild.type 2, growth.factor.rearrangement 2, autoimmune.encephalomyelitis.eae 2, wild.type.mice 2, interferon.gamma.opn 2,

recombination.embryonic.stem 2, experimental.autoimmune.encephalomyelitis 2, integrin.receptors.intracellular 2, arginine.glycine.aspartic 2, homologous.recombination.embryonic 2, extracellular.matrix.ecm 2, targeted.disruption.osteopontin 2, human.umbilical.vein 2, umbilical.vein.endothelial 2, growth.factors.cytokines 2, vein.endothelial.cells 2, cytokine.gene.expression 2, aspartic.acid.rgd 2, inhibited.cd200r.engagement 2, chronic.inflammatory.diseases 2

Roles of STAT3 in mediating the cell growth, differentiation and survival signals relayed through the IL-6 family of cytokine receptors.

Down-regulation of the macrophage lineage through interaction with OX2 (CD200).

Regulation of myeloid cell function through the CD200 receptor.

Soluble osteopontin inhibits apoptosis of adherent endothelial cells deprived of growth factors.

Altered wound healing in mice lacking a functional osteopontin gene (spp1).

CD44: structure, function, and association with the malignant process.

Reduced tolerance to acute renal ischemia in mice with a targeted disruption of the osteopontin gene.

Osteopontin: a key cytokine in cell-mediated and granulomatous inflammation.

Mice lacking osteopontin show normal development and bone structure but display altered osteoclast formation in vitro.

Osteopontin inhibits nitric oxide production and cytotoxicity by activated RAW264.7 macrophages.

Osteopontin: a multifunctional molecule regulating chronic inflammation and vascular disease.

T-bet-dependent expression of osteopontin contributes to T cell polarization.

Osteopontin.

Total absence of colony-stimulating factor 1 in the macrophage-deficient osteopetrotic (op/op) mouse.

Molecular mechanisms of CD200 inhibition of mast cell activation.

Intracellular osteopontin is an integral component of the CD44-ERM complex involved in cell migration.

CLUSTER 47 (125-121)

(71 Records)

*The opposing roles of different cytokines in regulating host immune response and especially inflammation, emphasing the interferons but mainly interferon-gamma

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Cluster Syntax Features

Descriptive Terms

ifn 12.0%, ifn.gamma 8.2%, gamma 7.6%, ino 7.0%, cytokin 4.6%, macrophag 3.5%, product 1.9%, mice 1.1%, cell 1.1%, monocyt 1.0%, stimul 0.8%, induc 0.8%, interferon 0.8%, inhibit 0.7%, inflammatori 0.7%, express 0.6%, lp 0.6%, interleukin 0.6%, tumor 0.6%, th1 0.6%, alpha 0.6%, mrna 0.5%, 1beta 0.5%, chemokin 0.5%, interferon.gamma 0.4%

Discriminating Terms

ifn 9.7%, ifn.gamma 6.7%, ino 5.4%, gamma 5.4%, cytokin 2.2%, macrophag 1.9%, gene 1.0%, patient 0.9%, protein 0.8%, genet 0.8%, diseas 0.7%, product 0.7%, genom 0.6%, receptor 0.5%, monocyt 0.5%, autophagi 0.5%, neuron 0.5%, interferon 0.5%, risk 0.5%, control 0.4%, kinas 0.4%, snp 0.4%, drug 0.4%, th1 0.4%, stress 0.4%

Single Word Terms

cell 56, cytokin 48, induc 43, gamma 42, product 42, activ 39, factor 38, ifn 38, inflammatori 37, express 35, inhibit 31, respons 31, stimul 30, human 28, macrophag 28, protein 28, interferon 27, role 27, alpha 26, regul 25, tumor 25, mediat 24, interleukin 24, level 24, necrosi 23

Double Word Terms

ifn.gamma 35, necrosis.factor 22, tumor.necrosis 20, nitric.oxide 20, interferon.gamma 19, oxide.synthase 15, factor.alpha 14, gamma.ifn 13, inducible.nitric 11, synthase.inos 11, tnf.alpha 10, anti.inflammatory 10, inflammatory.cytokines 8, cytokine.production 8, central.nervous 7, interferon.ifn 7, lipopolysaccharide.lps 7, gamma.production 7, proinflammatory.cytokines 7, nervous.system 7, immune.responses 6, growth.factor 6, deficient.mice 6, gene.expression 6, p40.subunit 5

Triple Word Terms

tumor.necrosis.factor 20, nitric.oxide.synthase 15, necrosis.factor.alpha 14, gamma.ifn.gamma 13, inducible.nitric.oxide 11, interferon.gamma.ifn 11, oxide.synthase.inos 10, ifn.gamma.production 7, central.nervous.system 7, interferon.ifn.gamma 5,

transforming.growth.factor 5, ifn.gamma.mediated 4, macrophage.cell.line 4, colony.stimulating.factor 4, macrophage.inflammatory.protein 4, ifn.gamma.induced 4, gamma.tumor.necrosis 4, growth.factor.beta 3, anti.ifn.gamma 3, ifn.gamma.inducible 3, inflammatory.protein.mip 3, wild.type.mice 3, multiple.sclerosis.anti 3, alpha.ifn.gamma 3, cytokines.tnf.alpha 3

Reciprocal expression of interferon gamma or interleukin 4 during the resolution or progression of murine leishmaniasis. Evidence for expansion of distinct helper T cell subsets.

Th1 CD4+ lymphocytes delete activated macrophages through the Fas/APO-1 antigen pathway.

Lactobacilli from human gastrointestinal mucosa are strong stimulators of IL-12 production.

Sequence-specific potent induction of IFN-alpha by short interfering RNA in plasmacytoid dendritic cells through TLR7.

Phosphatidylserine-dependent ingestion of apoptotic cells promotes TGF-beta1 secretion and the resolution of inflammation.

A pivotal involvement of IFN-gamma in the pathogenesis of acetaminophen-induced acute liver injury.

The IL-23/IL-17 axis in inflammation.

S-Nitrosoglutathione reduces inflammation and protects brain against focal cerebral ischemia in a rat model of experimental stroke.

Transient expression of IL-1beta induces acute lung injury and chronic repair leading to pulmonary fibrosis.

Regulation of macrophage chemokine expression by lipopolysaccharide in vitro and in vivo.

IL-23 drives a pathogenic T cell population that induces autoimmune inflammation.

The flavonoid baicalin exhibits anti-inflammatory activity by binding to chemokines.

Expression of type II nitric oxide synthase in primary human astrocytes and microglia: role of IL-1beta and IL-1 receptor antagonist.

Elevated serum levels of interferon-regulated chemokines are biomarkers for active human systemic lupus erythematosus.

Effects of IL-13 on phenotype, cytokine production, and cytotoxic function of human monocytes. Comparison with IL-4 and modulation by IFN-gamma or IL-10.

CLUSTER 30 (125-121)

(47 Records)

*The elicitation and orchestration of the host inflammatory response, emphasizing the elicitation by bacterial lipopolysaccharide and the role of toll-like receptors in activation of inflammatory responses through the assembly of receptor signaling complexes

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Cluster Syntax Features

Descriptive Terms

lp 20.5%, tlr 9.4%, tlr4 5.3%, microglia 3.0%, cd14 2.2%, receptor 1.8%, macrophag 1.5%, activ 1.4%, lipopolysaccharid 1.2%, vip 1.2%, signal 1.1%, toll 1.1%, jnk 0.9%, pacap 0.9%, induc 0.8%, mediat 0.8%, lps.induced 0.8%, myd88 0.7%, vip.pacap 0.7%, respons 0.7%, inflammatori 0.6%, chemokin 0.6%, bacteri 0.6%, tlr2 0.6%, immun 0.5%

Discriminating Terms

lp 14.6%, tlr 7.2%, tlr4 4.0%, microglia 1.8%, cd14 1.6%, cell 1.0%, diseas 0.9%, patient 0.9%, gene 0.8%, lipopolysaccharid 0.8%, vip 0.8%, genet 0.7%, toll 0.7%, genom 0.6%, pacap 0.6%, vip.pacap 0.5%, myd88 0.5%, lps.induced 0.5%, protein 0.5%, tnf 0.5%, macrophag 0.5%, autophagi 0.5%, risk 0.5%, tlr2 0.4%, data 0.4%

Single Word Terms

activ 37, receptor 36, mediat 34, cell 33, lp 30, induc 29, protein 28, respons 28, express 28, lipopolysaccharid 27, signal 25, factor 25, inflammatori 24, regul 22, macrophag 21, immun 21, product 21, role 20, toll 20, inhibit 19, human 18, tlr4 17, depend 16, mechan 16, tlr 16

Double Word Terms

lipopolysaccharide.lps 21, lps.induced 14, necrosis.factor 13, tumor.necrosis 13, toll.receptors 12, innate.immune 10, toll.receptor 9, receptors.tlrs 9, factor.alpha 9, immune.system 7, signal.transduction 7, inflammatory.response 6, cell.line 6, play.role 6, factor.kappab 6, gram.negative 6, inflammatory.responses 6, microglial.activation 6, anti.inflammatory 6, immune.response 6, nitric.oxide 5, transcription.factor 5, gene.expression 5, bacterial.lipopolysaccharide 5, intestinal.peptide 5

Triple Word Terms

tumor.necrosis.factor 13, necrosis.factor.alpha 9, toll.receptors.tlrs 9,

vasoactive.intestinal.peptide 5, lipopolysaccharide.lps.induced 5, intestinal.peptide.vip 5, bacterial.lipopolysaccharide.lps 5, innate.immune.system 5, nuclear.factor.kappab 5, macrophage.cell.line 4, peptide.vip.pituitary 4, pituitary.adenylate.cyclase 4, activating.polypeptide.pacap 4, vip.pituitary.adenylate 4, vip.pacap.inhibit 4, adenylate.cyclase.activating 4, cyclase.activating.polypeptide 4, inhibited.lps.induced 4, mediated.degeneration.dopaminergic 3, dose.dependent.manner 3, pathogen.molecular.patterns 3, inflammation.mediated.degeneration 3, activation.nuclear.factor 3, gram.negative.bacteria 3, innate.immune.responses 3

Lipopolysaccharide-mediated reactive oxygen species and signal transduction in the regulation of interleukin-1 gene expression.

Fas (CD95) induces macrophage proinflammatory chemokine production via a MyD88-dependent, caspase-independent pathway.

Role of Toll-like receptors in pathogen recognition.

TLR signaling.

LPS resistance in monocytic cells caused by reverse signaling through transmembrane TNF (mTNF) is mediated by the MAPK/ERK pathway.

Innate immunity and toll-like receptors: clinical implications of basic science research.

Toll-like receptor 4: the missing link of the cerebral innate immune response triggered by circulating gram-negative bacterial cell wall components.

Toll-like receptor 4 imparts ligand-specific recognition of bacterial lipopolysaccharide.

Negative regulation of toll-like receptor-mediated immune responses.

The vaccine adjuvant monophosphoryl lipid A as a TRIF-biased agonist of TLR4.

Human toll-like receptors mediate cellular activation by Mycobacterium tuberculosis.

Carbon monoxide differentially inhibits TLR signaling pathways by regulating ROS-induced trafficking of TLRs to lipid rafts.

Microglia initiate central nervous system innate and adaptive immune responses through multiple TLRs.

The family of five: TIR-domain-containing adaptors in Toll-like receptor signalling.

The repertoire for pattern recognition of pathogens by the innate immune system is defined by cooperation between toll-like receptors.

CLUSTER 61 (125-121)

(56 Records)

*Role of NO in the pathophysiology of stroke, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis, as well as reduce inflammation by inhibiting activation of nuclear factor-kappaB; role of nicotinic therapeutics to treat neurological diseases (Alzheimer's disease, Parkinson's disease, Tourette's syndrome), as well as therapy for ulcerative colitis

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Cluster Syntax Features

Descriptive Terms

nicotin 8.6%, behavior 4.6%, no 3.6%, relax 1.9%, rat 1.8%, mice 1.2%, anim 1.0%, metabol 1.0%, memori 0.9%, intestin 0.9%, brain 0.8%, ach 0.8%, learn 0.7%, respons 0.6%, model 0.6%, smoke 0.6%, level 0.6%, pain 0.6%, enzym 0.5%, arginin 0.5%, induc 0.5%, viscer 0.5%, chronic 0.5%, blood 0.5%, coliti 0.5%

Discriminating Terms

nicotin 6.5%, behavior 3.5%, no 2.8%, cell 1.6%, relax 1.6%, protein 1.1%, tnf 0.9%, patient 0.8%, rat 0.8%, ach 0.7%, genom 0.7%, memori 0.6%, kinas 0.6%, receptor 0.6%, genet 0.6%, learn 0.6%, alpha 0.5%, autophagi 0.5%, gene 0.5%, death 0.5%, activ 0.4%, viscer 0.4%, risk 0.4%, agrp 0.4%, snp 0.4%

Single Word Terms

induc 26, respons 25, activ 22, diseas 22, human 20, level 20, mediat 19, mechan 19, anim 19, function 18, express 17, model 17, system 16, rat 16, cell 16, brain 16, mice 15, behavior 15, regul 14, treatment 13, physiolog 13, gener 12, role 12, therapeut 12, reduc 12

Double Word Terms

nitric.oxide 10, gene.expression 6, ulcerative.colitis 6, nervous.system 5, blood.flow 5, inflammatory.bowel 4, bowel.disease 4, learning.memory 4, nitro.arginine 4, oxide.synthase 4, synthase.nos 4, animal.models 4, dose.dependent 3, endothelial.cells 3, gene.transcription 3, animal.model 3, central.nervous 3, inducible.nos 3, nos.isoforms 3, gastrointestinal.tract 3, hind.paw 3, nos.inos 3, physiological.behavioral 3, disease.ibd 3, behavioral.responses 3

Triple Word Terms

nitric.oxide.synthase 4, inflammatory.bowel.disease 4, inducible.nos.inos 3,

central.nervous.system 3, bowel.disease.ibd 3, cholinergic.nanc.neurotransmitter 2, oxide.synthase.nos 2, ulcerative.colitis.disease 2, inhibitor.nitro.arginine 2, colitis.disease.nonsmokers 2, rna.sirna.ventricular 2, somatic.gene.manipulation 2, wild.type.mice 2, sirna.ventricular.system 2, rna.interference.rnai 2, anti.inflammatory.anti 2, interfering.rna.sirna 2, adrenergic.non.cholinergic 2, non.adrenergic.non 2, arm.radial.maze 2, disease.ulcerative.colitis 2, non.cholinergic.nanc 2, short.interfering.rna 2, laser.capture.microdissection 1, gene.expression.profiles 1

Metabolism and disposition kinetics of nicotine.

Nitric oxide in inflammatory bowel disease: a universal messenger in an unsolved puzzle.

Hypothesis about mechanisms through which nicotine might exert its effect on the interdependence of inflammation and gut barrier function in ulcerative colitis.

7-Nitro indazole, an inhibitor of nitric oxide synthase, exhibits anti-nociceptive activity in the mouse without increasing blood pressure.

RJR-2403: a nicotinic agonist with CNS selectivity II. In vivo characterization.

Pharmacology of nicotine: addiction and therapeutics.

Murine taste-immune associative learning.

Inflammatory bowel disease and smoking: a review of epidemiology, pathophysiology, and therapeutic implications.

Non-adrenergic non-cholinergic relaxation mediated by nitric oxide in the canine ileocolonic junction.

Selective pharmacological inhibition of distinct nitric oxide synthase isoforms.

Targeting nitric oxide in the gastrointestinal tract.

Transport mechanisms of nicotine across the human intestinal epithelial cell line Caco-2.

The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine.

CLUSTER 48 (125-121)

(53 Records)

*Causes and treatments for inflammation

Cluster Syntax Features

Descriptive Terms

inflammatori 10.9%, anti.inflammatory 6.4%, cox 6.3%, inflamm 4.8%, nicotin 4.5%, anti 4.1%, cytokin 1.5%, vagu 1.5%, vagus.nerve 1.2%, glucocorticoid 1.1%, macrophag 1.0%, curcumin 1.0%, nerv 0.9%, acetylcholin 0.9%, inhibit 0.9%, kappa 0.6%, cyclooxygenas 0.6%, cholinerg 0.6%, interleukin 0.6%, diseas 0.5%, alpha7 0.5%, immun 0.5%, sepsi 0.5%, speci 0.4%, mechan 0.4%

Discriminating Terms

inflammatori 6.2%, cox 4.8%, anti.inflammatory 4.7%, nicotin 2.9%, inflamm 2.5%, anti 2.2%, cell 1.6%, vagu 1.2%, gene 1.1%, vagus.nerve 1.0%, protein 0.9%, patient 0.8%, curcumin 0.7%, glucocorticoid 0.7%, acetylcholin 0.6%, genom 0.6%, genet 0.6%, neuron 0.5%, nerv 0.5%, autophagi 0.5%, cyclooxygenas 0.4%, cholinerg 0.4%, alpha7 0.4%, risk 0.4%, function 0.4%

Single Word Terms

inflammatori 47, anti 35, inflamm 30, diseas 26, cytokin 25, inhibit 25, activ 24, mechan 24, induc 23, respons 20, receptor 20, cell 20, factor 18, mediat 18, immun 17, pathwai 16, system 16, human 15, stimul 14, drug 14, regul 14, interleukin 14, express 13, protein 12, releas 12

Double Word Terms

anti.inflammatory 33, necrosis.factor 11, inflammatory.pathway 9, vagus.nerve 8, nicotinic.acetylcholine 8, inflammatory.responses 8, pro.inflammatory 8, tumor.necrosis 8, acetylcholine.receptor 7, inflammatory.cytokines 7, inflammatory.disorders 5, immune.system 5, cytokine.release 5, tnf.alpha 5, immune.response 5, inflammatory.cytokine 5, alpha7.nicotinic 5, factor.alpha 5, nervous.system 5, inflammatory.drugs 5, inflammatory.bowel 5, cyclooxygenase.cox 5, inflammatory.response 5, inflammatory.activity 5, treatment.inflammatory 5

Triple Word Terms

anti.inflammatory.pathway 9, tumor.necrosis.factor 8, nicotinic.acetylcholine.receptor 7, anti.inflammatory.activity 5, necrosis.factor.alpha 5, anti.inflammatory.drugs 5,

alpha7.nicotinic.acetylcholine 5, inflammatory.bowel.disease 4, acetylcholine.receptor.alpha7nachr 4, pro.inflammatory.cytokines 4, cholinergic.anti.inflammatory 4, anti.inflammatory.agents 4, anti.inflammatory.mechanisms 4, inflammatory.pathway.alpha7 3, hypothalamic.pituitary.adrenal 3, inflammatory.drugs.nsaids 3, nonsteroidal.anti.inflammatory 3, tumour.necrosis.factor 3, selective.nicotinic.agonists 3, necrosis.factor.tnf 3, nicotinic.anti.inflammatory 3, stimulation.vagus.nerve 3, antioxidant.anti.inflammatory 3, immunosuppressive.anti.inflammatory 2, inflammatory.pathway.quot 2

Dampening inflammation.

Apoptosis and caspases regulate death and inflammation in sepsis.

Use of herbal preparations in the treatment of oxidant-mediated inflammatory disorders.

Inhibition of NF-kappa B by sodium salicylate and aspirin.

Anti-inflammatory activity of non-nucleoside adenosine deaminase inhibitor FR234938.

Selective expression of mitogen-inducible cyclooxygenase in macrophages stimulated with lipopolysaccharide.

Inflammation in atherosclerosis.

The anti-inflammatory activity of Scutellaria rivularis extracts and its active components, baicalin, baicalein and wogonin.

A cytokine-mediated link between innate immunity, inflammation, and cancer.

The cholinergic anti-inflammatory pathway.

The role of STATs in inflammation and inflammatory diseases.

NF-kappaB functions as a tumour promoter in inflammation-associated cancer.

Immunosuppressive and anti-inflammatory mechanisms of triptolide, the principal active diterpenoid from the Chinese medicinal herb Tripterygium wilfordii Hook. f.

The hygiene hypothesis and psychiatric disorders.

The role of galectins in the initiation, amplification and resolution of the inflammatory response.

Nicotine protects kidney from renal ischemia/reperfusion injury through the cholinergic anti-inflammatory pathway.

Curcumin: the Indian solid gold.

CLUSTER 57 (125-121)

(60 Records)

*Role of blood-brain barrier dysfunction in central nervous system disease

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Cluster Syntax Features

Descriptive Terms

brain 4.7%, bbb 4.6%, blood 3.6%, mdr1a 2.8%, system 2.6%, barrier 2.6%, nervou 2.3%, mpo 2.0%, blood.brain 1.9%, nervous.system 1.8%, cn 1.8%, brain.barrier 1.7%, blood.brain.barrier 1.5%, drug 1.4%, central.nervous 1.3%, central.nervous.system 1.3%, central 1.2%, neutrophil 1.0%, immun 1.0%, glycoprotein 1.0%, spinal 1.0%, agent 0.9%, cord 0.9%, spinal.cord 0.8%, mdr1a.mice 0.7%

Discriminating Terms

bbb 3.8%, mdr1a 2.3%, brain 2.1%, blood 2.1%, barrier 2.0%, mpo 1.6%, blood.brain 1.5%, brain.barrier 1.3%, nervou 1.3%, blood.brain.barrier 1.2%, cn 1.1%, gene 1.1%, cell 1.0%, nervous.system 1.0%, central.nervous 0.9%, central.nervous.system 0.8%, tnf 0.8%, receptor 0.7%, system 0.7%, spinal 0.6%, diseas 0.6%, genom 0.6%, genet 0.6%, cord 0.6%, glycoprotein 0.6%

Single Word Terms

system 35, brain 33, blood 27, cell 27, nervou 27, central 26, activ 25, function 25, barrier 22, role 21, protein 20, inflammatori 17, tissu 16, express 16, human 15, diseas 15, level 15, cn 15, organ 14, drug 14, new 14, inflamm 13, vivo 13, multipl 13, model 12

Double Word Terms

nervous.system 26, central.nervous 22, brain.barrier 19, blood.brain 19, system.cns 12, blood.vessels 9, endothelial.cells 9, multiple.sclerosis 9, barrier.bbb 8, spinal.cord 7, mdr1a.mice 5, emission.tomography 5, positron.emission 5, multidrug.resistance 4, mice.mdr1a 4, white.matter 4, tight.junctions 4, magnetic.resonance 4, play.role 4, autoimmune.encephalomyelitis 3, inflammatory.response 3, sclerosis.alzheimer 3, blood.borne 3, adhesion.molecules 3, experimental.autoimmune 3

Triple Word Terms

central.nervous.system 22, blood.brain.barrier 18, nervous.system.cns 12, brain.barrier.bbb 8, positron.emission.tomography 5, spinal.cord.injury 3, magnetic.resonance.imaging 3,

mdr1a.mice.mdr1a 3, emission.tomography.pet 3, experimental.autoimmune.encephalomyelitis 3, multiple.sclerosis.alzheimer 3, intestinal.peptide.vip 2, vasoactive.intestinal.peptide 2, macromolecular.contrast.agents 2, resonance.imaging.mri 2, cerebral.endothelial.cells 2, nervous.system.role 2, blood.tissue.barrier 2, chronic.relapsing.experimental 2, mouse.monoclonal.antibodies 2, capillary.blood.vessels 2, relapsing.experimental.autoimmune 2, barrier.endothelial.cells 2, tissue.barrier.sites 2, blood.brain.blood 2

Human TH17 lymphocytes promote blood-brain barrier disruption and central nervous system inflammation.

The blood-brain barrier: an overview: structure, regulation, and clinical implications.

Blood-brain barrier dysfunction in parkinsonian midbrain in vivo.

Blood-brain barrier transport of cytokines: a mechanism for neuropathology.

Blood-brain barrier abnormalities in longstanding multiple sclerosis lesions. An immunohistochemical study.

Polymorphonuclear leukocyte infiltration into cerebral focal ischemic tissue: myeloperoxidase activity assay and histologic verification.

Dopamine, a neurotransmitter, influences the immune system.

Close encounters of the monoamine kind: immune cells betray their nervous disposition.

Blood-brain barrier disruption in multiple sclerosis.

Conditional ablation of Stat3 or Socs3 discloses a dual role for reactive astrocytes after spinal cord injury.

Delivery of peptides and proteins through the blood-brain barrier.

How the blood talks to the brain parenchyma and the paraventricular nucleus of the hypothalamus during systemic inflammatory and infectious stimuli.

Radiolabeled compounds in diagnosis of infectious and inflammatory disease.

Disruption of the mouse mdr1a P-glycoprotein gene leads to a deficiency in the blood-brain barrier and to increased sensitivity to drugs.

Absence of the mdr1a P-Glycoprotein in mice affects tissue distribution and pharmacokinetics of dexamethasone, digoxin, and cyclosporin A.

P-glycoprotein in the blood-brain barrier of mice influences the brain penetration and pharmacological activity of many drugs.

CLUSTER 46 (125-121)

(48 Records)

*Immunity, autoimmunity, and the response of the immune system

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Cluster Syntax Features

Descriptive Terms

immun 22.7%, autoimmun 4.0%, immune.system 3.1%, respons 2.1%, host 2.1%, antigen 2.1%, system 1.8%, cell 1.7%, innat 1.4%, infect 1.2%, smoke 1.1%, cigarette.smoke 1.0%, inflammatori 1.0%, pathogen 0.9%, cigarett 0.9%, immune.responses 0.8%, chronic 0.8%, innate.immune 0.8%, toler 0.8%, microbi 0.8%, adapt 0.7%, immune.response 0.7%, nicotin 0.7%, receptor 0.6%, self 0.6%

Discriminating Terms

immun 14.9%, autoimmun 2.5%, immune.system 2.2%, host 1.3%, antigen 1.1%, gene 0.9%, protein 0.9%, innat 0.9%, cigarette.smoke 0.8%, tnf 0.8%, cigarett 0.7%, smoke 0.7%, patient 0.7%, genet 0.6%, immune.responses 0.6%, microbi 0.5%, neuron 0.5%, innate.immune 0.5%, pathogen 0.5%, autophagi 0.5%, toler 0.5%, genom 0.5%, kinas 0.5%, drug 0.4%, respons 0.4%

Single Word Terms

immun 44, cell 33, respons 31, system 27, activ 22, function 22, receptor 21, diseas 19, antigen 17, autoimmun 17, inflammatori 17, infect 17, chronic 15, regul 15, mediat 14, host 13, express 13, innat 13, mechan 12, anti 12, induc 11, inflamm 11, adapt 10, role 10, molecul 10

Double Word Terms

immune.system 20, innate.immune 12, immune.responses 11, immune.response 9, autoimmune.diseases 8, anti.inflammatory 7, immune.cells 7, dendritic.cells 6, regulatory.cells 5, adaptive.immune 4, toll.receptors 4, cigarette.smoke 4, bone.marrow 4, protein.tyrosine 3, inflammatory.response 3, antigen.cells 3, immune.function 3, type.diabetes 3, systemic.autoimmunity 3, nervous.system 3, costimulatory.molecules 3, innate.immunity 3, chronic.inflammatory 3, crohn.disease 3, homeostasis.immune 3

Triple Word Terms

innate.immune.system 7, potent.anti.inflammatory 3, adaptive.immune.system 3, homeostasis.immune.system 3, protein.tyrosine.kinase 2, hypothalamic.pituitary.adrenal 2, innate.immune.response 2, autoimmune.diseases.humans 2, pattern.recognition.receptors 2,

inflammatory.bowel.disease 2, cigarette.smoke.nicotine 2, maturation.dendritic.cells 2, expression.costimulatory.molecules 2, protective.immune.responses 2, control.immune.responses 2, pituitary.adrenal.axis 2, respiratory.tract.infection 2, cigarette.smoke.induced 2, dendritic.cells.mature 2, adaptive.immune.response 2, toll.receptors.tlrs 2, cells.mast.cells 2, mast.cells.granulocytes 2, cigarette.smoke.immune 2, activation.protein.tyrosine 1

Inflammation and metabolic disorders.

Molecular mechanisms of autoimmunity.

Effects of cigarette smoke on immune response: chronic exposure to cigarette smoke impairs antigen-mediated signaling in T cells and depletes IP3-sensitive Ca(2+) stores.

Chronic stress alters the immune response to influenza virus vaccine in older adults.

Failure to induce oral tolerance to a soluble protein in patients with inflammatory bowel disease.

Immune cell migration in inflammation: present and future therapeutic targets.

Evidence for an immune response in major depression: a review and hypothesis.

Cytokines for psychologists: implications of bidirectional immune-to-brain communication for understanding behavior, mood, and cognition.

Toll-like receptors and innate immunity.

Decoding the patterns of self and nonself by the innate immune system.

Recognition of microorganisms and activation of the immune response.

Regulatory T cells: friend or foe in immunity to infection?

Interleukin-10 and the interleukin-10 receptor.

How human neutrophils kill and degrade microbes: an integrated view.

See no evil, hear no evil, do no evil: the lessons of immune privilege.

Molecular imaging of lymphoid organs and immune activation by positron emission tomography with a new [(18)F]-labeled 2'-deoxycytidine analog.

Give us this day our daily germs.

Mechanisms of autoimmunity.

Effects of cigarette smoke on the immune system.

Immunomodulatory effects of cigarette smoke.

CLUSTER 44 (125-121)

(43 Records)

*Role of Copolymer 1 (a copolymer of amino acids) in the suppression of experimental autoimmune encephalitis (EAE), the animal model for multiple sclerosis, and the role of Th1 and Th2 cytokines in relation to autoimmunity and allergy.

Cluster Syntax Features

Descriptive Terms

cop 5.7%, eae 4.7%, antigen 4.5%, th1 4.0%, cell 3.9%, th2 3.6%, mhc 2.2%, cytokin 1.9%, sclerosi 1.7%, lesion 1.6%, multiple.sclerosis 1.5%, mice 1.3%, autoimmun 1.2%, multipl 1.0%, mhc.class 0.9%, mbp 0.9%, class 0.8%, cn 0.8%, th1.th2 0.8%, macrophag 0.7%, cd4 0.7%, helper 0.7%, immun 0.7%, copaxon 0.6%, respons 0.6%

Discriminating Terms

cop 4.6%, eae 3.6%, th1 3.0%, antigen 2.9%, th2 2.8%, mhc 1.4%, gene 1.1%, sclerosi 0.9%, multiple.sclerosis 0.9%, lesion 0.8%, genet 0.8%, tnf 0.7%, mbp 0.7%, protein 0.7%, mhc.class 0.7%, genom 0.6%, diseas 0.6%, neuron 0.6%, th1.th2 0.6%, helper 0.5%, copaxon 0.5%, activ 0.5%, autoimmun 0.5%, kinas 0.5%, autophagi 0.5%

Single Word Terms

cell 40, respons 25, cytokin 23, immun 21, diseas 20, multipl 20, sclerosi 20, induc 19, antigen 19, express 18, activ 17, protein 17, autoimmun 16, th2 15, mice 15, receptor 14, model 14, gamma 14, experiment 14, th1 14, product 13, encephalomyel 13, patient 12, helper 12, antibodi 12

Double Word Terms

multiple.sclerosis 19, experimental.autoimmune 12, autoimmune.encephalomyelitis 10, interferon.gamma 8, dendritic.cells 7, cd4.cells 7, myelin.basic 7, th1.th2 7, encephalomyelitis.eae 7, ifn.gamma 7, basic.protein 7, nervous.system 6, central.nervous 6, immune.response 6, glatiramer.acetate 6, copolymer.cop 6, anti.inflammatory 5, th2.cells 5, treated.mice 5, major.histocompatibility 5, protein.mbp 5, mhc.class 5, animal.model 5, suppressor.cells 4, system.cns 4

Triple Word Terms

experimental.autoimmune.encephalomyelitis 10, autoimmune.encephalomyelitis.eae 7, myelin.basic.protein 7, central.nervous.system 6, basic.protein.mbp 5, nervous.system.cns 4, major.histocompatibility.complex 4, transforming.growth.factor 4, expression.ifn.gamma 3, multiple.sclerosis.patients 3, th1.th2.cytokines 3, model.multiple.sclerosis 3, eae.animal.model 3, growth.factor.beta 3, copolymer.copolymer.cop 2, level.th2.cytokine 2, th2.cytokine.secretion 2, lymph.node.cells 2, ifn.gamma.production 2, acid.copolymer.copolymer 2, multiple.sclerosis.cop 2, helper.type.th1 2, amino.acid.copolymer 2, anti.inflammatory.cytokines 2, synthetic.amino.acid 2

Therapeutic efficacy of IL-17 neutralization in murine experimental autoimmune encephalomyelitis.

Cutting edge: generation of IL-18 receptor-deficient mice: evidence for IL-1 receptor-related protein as an essential IL-18 binding receptor.

Macrophage-derived IL-18-mediated intestinal inflammation in the murine model of Crohn's disease.

Copolymer 1 induces T cells of the T helper type 2 that crossreact with myelin basic protein and suppress experimental autoimmune encephalomyelitis.

Statins as a newly recognized type of immunomodulator.

In vivo mature immunological synapses forming SMACs mediate clearance of virally infected astrocytes from the brain.

Increased IL-23p19 expression in multiple sclerosis lesions and its induction in microglia.

Gene-microarray analysis of multiple sclerosis lesions yields new targets validated in autoimmune encephalomyelitis.

Epitope spreading initiates in the CNS in two mouse models of multiple sclerosis.

T helper type 1 lymphocytes drive inflammation in human atherosclerotic lesions.

The paradigm of Th1 and Th2 cytokines: its relevance to autoimmunity and allergy.

The expanding universe of T-cell subsets: Th1, Th2 and more.

Divergent pro- and antiinflammatory roles for IL-23 and IL-12 in joint autoimmune inflammation.

Multiple sclerosis: comparison of copolymer-1- reactive T cell lines from treated and untreated subjects reveals cytokine shift from T helper 1 to T helper 2 cells.

CLUSTER 1 (125-123)

(24 Records)

*The role of melatonin as a broad spectrum antioxidant, free radical scavenger, and anti-inflammatory agent.

Cluster Syntax Features

Descriptive Terms

melatonin 70.4%, radic 1.9%, antioxid 1.6%, scaveng 1.2%, pineal 0.9%, pineal.gland 0.6%, free.radical 0.5%, free 0.5%, glutathion 0.5%, gland 0.5%, melatonin.receptors 0.5%, peroxid 0.4%, action 0.4%, lipid.peroxidation 0.4%, oxid 0.4%, actions.melatonin 0.3%, indoleamin 0.3%, ccl4 0.3%, melatonin.receptor 0.3%, ino 0.2%, product 0.2%, lipid 0.2%, gsh 0.2%, radical.scavenging 0.2%, protect 0.2%

Discriminating Terms

melatonin 42.4%, cell 1.5%, gene 1.0%, protein 0.8%, diseas 0.7%, radic 0.7%, patient 0.6%, antioxid 0.6%, scaveng 0.6%, tnf 0.6%, genet 0.5%, pineal 0.5%, activ 0.5%, genom 0.4%, express 0.4%, kinas 0.4%, neuron 0.4%, pineal.gland 0.4%, factor 0.4%, alpha 0.3%, respons 0.3%, autophagi 0.3%, human 0.3%, risk 0.3%, receptor 0.3%

Single Word Terms

melatonin 24, oxid 16, reduc 14, radic 14, activ 13, scaveng 12, antioxid 12, induc 12, protect 12, action 11, free 11, product 10, level 10, cell 10, pineal 10, gener 9, concentr 9, vivo 9, treatment 9, damag 9, dose 8, enzym 8, vitro 8, condit 8, direct 8

Double Word Terms

free.radical 8, radical.scavenger 6, pineal.gland 6, vitro.vivo 6, oxidative.stress 6, actions.melatonin 6, free.radicals 5, radical.scavenging 5, nitric.oxide 5, oxidative.damage 4, melatonin.receptor 4, glutathione.gsh 4, lipid.peroxidation 4, melatonin.melatonin 3, malonaldehyde.hydroxyalkenals 3, vivo.melatonin 3, oxygen.nitrogen 3, hydroxyl.radical 3, action.melatonin 3, hormone.melatonin 3, melatonin.acetyl 3, melatonin.treatment 3, induced.oxidative 3, oxide.synthase 3, superoxide.dismutase 3

Triple Word Terms

free.radical.scavenger 5, free.radical.scavenging 4, nitric.oxide.synthase 3, induced.oxidative.damage 3, direct.free.radical 3, acetyl.formyl.methoxykynuramine 3,

generation.free.radicals 2, magnetic.resonance.nmr 2, concentration.malonaldehyde.hydroxyalkenals 2, nuclear.factor.kappa 2, vitro.vivo.melatonin 2, melatonin.potent.free 2, potent.free.radical 2, product.pineal.gland 2, melatonin.free.radical 2, nuclear.magnetic.resonance 2, formyl.methoxykynuramine.afmk 2, melatonin.anti.inflammatory 2, superoxide.dismutase.sod 2, oxide.synthase.inos 2, melatonin.acetyl.methoxytryptamine 2, reduced.glutathione.gsh 2, oxidative.stress.exposure 2, pineal.hormone.melatonin 2, reactive.oxygen.nitrogen 1

Anti-inflammatory effect of melatonin on A beta vaccination in mice.

Melatonin mitigates mitochondrial malfunction.

Anti-inflammatory actions of melatonin and its metabolites, N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK) and N1-acetyl-5-methoxykynuramine (AMK), in macrophages.

Potent protective effect of melatonin on in vivo paraquat-induced oxidative damage in rats.

Protective effect of melatonin in acetic acid induced colitis in rats.

Inhibition of cerebellar nitric oxide synthase and cyclic GMP production by melatonin via complex formation with calmodulin.

Melatonin reduces kainate-induced lipid peroxidation in homogenates of different brain regions.

Melatonin counteracts lipid peroxidation induced by carbon tetrachloride but does not restore glucose-6 phosphatase activity.

Biochemical reactivity of melatonin with reactive oxygen and nitrogen species: a review of the evidence.

Melatonin as an antioxidant: biochemical mechanisms and pathophysiological implications in humans.

Medical implications of melatonin: receptor-mediated and receptor-independent actions.

Interactions of melatonin and its metabolites with the ABTS cation radical: extension of the radical scavenger cascade and formation of a novel class of oxidation products, C2-substituted 3-indolinones.

Chemical and physical properties and potential mechanisms: melatonin as a broad spectrum antioxidant and free radical scavenger.

Melatonin as a naturally occurring co-substrate of quinone reductase-2, the putative MT3 melatonin membrane receptor: hypothesis and significance.

CLUSTER 29 (125-123)

(37 Records)

* Signalling pathways necessary for inducing key immune and inflammatory responses, emphasizing glycogen synthase kinase (gsk) and serine/threonine kinase Akt (protein kinase B-PKB), and the role of these kinases in phosphorylation of serine, threonine, and tyrosine residues in eukaryotic proteins

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Cluster Syntax Features

Descriptive Terms

akt 13.8%, kinas 13.0%, phosphoryl 3.6%, pkb 2.9%, gsk 2.0%, serin 1.8%, gsk3 1.6%, activ 1.6%, serine.threonine 1.6%, threonin 1.5%, protein 1.4%, signal 1.2%, kappa 1.2%, pten 1.1%, glycogen 1.1%, regul 1.0%, trx 0.9%, pathwai 0.7%, tor 0.6%, growth 0.6%, kinase.protein 0.6%, smad 0.6%, threonine.kinase 0.6%, serine.threonine.kinase 0.6%, kinase.akt 0.6%

Discriminating Terms

akt 9.9%, kinas 6.1%, pkb 2.1%, phosphoryl 1.7%, gsk 1.4%, gsk3 1.2%, serin 1.1%, serine.threonine 1.1%, threonin 1.0%, diseas 0.8%, patient 0.8%, pten 0.8%, glycogen 0.8%, cell 0.7%, trx 0.6%, genet 0.6%, receptor 0.5%, gene 0.5%, tnf 0.5%, genom 0.5%, tor 0.4%, kinase.protein 0.4%, autophagi 0.4%, threonine.kinase 0.4%, serine.threonine.kinase 0.4%

Single Word Terms

kinas 37, protein 29, activ 28, signal 25, cell 24, regul 23, phosphoryl 20, serin 20, threonin 18, role 15, pathwai 15, function 14, akt 14, factor 14, growth 13, target 13, inhibitor 12, transcript 11, express 11, depend 11, respons 11, glycogen 10, cellular 10, inhibit 10, synthas 10

Double Word Terms

serine.threonine 18, protein.kinase 14, threonine.kinase 10, synthase.kinase 10, glycogen.synthase 10, kinase.akt 9, kinase.protein 7, signaling.pathway 6, kinase.gsk 6, phosphatidylinositol.kinase 6, protein.serine 6, kinase.pkb 5, transcription.factors 5, threonine.kinases 5, phosphoinositide.kinase 4, akt.activity 4, tumor.suppressor 4, akt.protein 4, kinase.phosphorylation 4, kinase.activity 4, gene.expression 4, growth.factors 4, cell.proliferation 4, cell.survival 4, kappa.kinase 4

Triple Word Terms

glycogen.synthase.kinase 10, serine.threonine.kinase 10, protein.serine.threonine 6, synthase.kinase.gsk 6, serine.threonine.kinases 5, threonine.kinase.akt 5, protein.kinase.pkb 5, akt.protein.kinase 4, kinase.protein.serine 4, kappa.kinase.protein 4, pten.tumor.suppressor 3, target.rapamycin.tor 3, phosphoinositide.dependent.kinase 2, target.gene.activation 2, phosphatase.plays.role 2, family.transcription.factors 2, threonine.protein.kinase 2, pleckstrin.homology.domain 2, protein.kinase.glycogen 2, kinase.glycogen.synthase 2, kinase.protein.kinase 2, phosphorylation.beta.catenin 2, phosphorylation.glycogen.synthase 2, wnt.beta.catenin 2, growth.factors.cytokines 2

The Jak-STAT pathway.

Regulatory role of glycogen synthase kinase 3 for transcriptional activity of ADD1/SREBP1c.

From calcium to NF-kappa B signaling pathways in neurons.

Protein kinase CK2: structure, regulation and role in cellular decisions of life and death.

Control of beta-catenin phosphorylation/degradation by a dual-kinase mechanism.

Nuclear export of NF-ATc enhanced by glycogen synthase kinase-3.

AKT/PKB signaling: navigating downstream.

TGF-beta signaling by Smad proteins.

NF-kappaB activation by tumour necrosis factor requires the Akt serine-threonine kinase.

Phosphorylation and regulation of Akt/PKB by the rictor-mTOR complex.

PKB binding proteins. Getting in on the Akt.

Cdc42GAP regulates c-Jun N-terminal kinase (JNK)-mediated apoptosis and cell number during mammalian perinatal growth.

Recent advances in the protein kinase B signaling pathway.

TOR signaling in growth and metabolism.

Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor.

Shaping the nuclear action of NF-kappaB.

NF-kappaB in neuronal plasticity and neurodegenerative disorders.

The role of C/EBP isoforms in the control of inflammatory and native immunity functions.

The phosphoinositide 3-kinase pathway.

CLUSTER 40 (125-123)

(75 Records)

*The role of mitogen activated protein kinases in signal transduction and regulation pathways, and the use of MAPK inhibitors in reducing both the synthesis of pro-inflammatory cytokines and their signaling to reduce inflammation

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Cluster Syntax Features

Descriptive Terms

kinas 28.8%, mapk 4.3%, activ 2.8%, activated.protein 2.7%, protein.kinases 2.6%, signal 2.5%, mitogen 2.3%, mitogen.activated 2.2%, mitogen.activated.protein 2.2%, protein.kinase 2.2%, p38 2.2%, protein 1.9%, map 1.7%, map.kinase 1.5%, cascad 1.1%, erk 1.0%, pathwai 0.9%, activated.protein.kinase 0.8%, map.kinases 0.8%, inhibitor 0.7%, activated.protein.kinases 0.6%, mek 0.6%, phosphoryl 0.5%, regul 0.5%, raf 0.5%

Discriminating Terms

kinas 18.2%, mapk 3.0%, activated.protein 1.9%, protein.kinases 1.9%, mitogen.activated 1.6%, mitogen.activated.protein 1.6%, mitogen 1.6%, p38 1.4%, protein.kinase 1.4%, map.kinase 1.1%, cell 0.9%, patient 0.9%, diseas 0.9%, gene 0.9%, erk 0.7%, cascad 0.7%, tnf 0.7%, map 0.6%, activated.protein.kinase 0.6%, map.kinases 0.6%, signal 0.6%, genet 0.6%, genom 0.5%, autophagi 0.5%, human 0.4%

Single Word Terms

kinas 74, protein 72, activ 68, signal 53, mitogen 49, cell 42, regul 36, pathwai 36, inhibitor 31, factor 27, respons 26, mechan 24, inhibit 24, role 23, map 23, induc 22, bind 22, mediat 21, mapk 21, stress 20, p38 20, target 20, cascad 20, transduct 20, receptor 20

Double Word Terms

activated.protein 50, mitogen.activated 48, protein.kinase 43, protein.kinases 29, map.kinase 22, signal.transduction 17, kinase.mapk 13, kinase.kinase 12, extracellular.signal 12, signal.regulated 11, p38.mitogen 10, protein.map 10, kinase.inhibitors 9, signaling.pathways 9, map.kinases 9, kinase.erk 8, terminal.kinase 8, stress.activated 7, p38.map 7, regulated.kinase 7, transduction.pathways 6, binding.site 6, serine.threonine 6, kinase.jnk 6, kinase.activity 6

Triple Word Terms

mitogen.activated.protein 48, activated.protein.kinase 31, activated.protein.kinases 15,

protein.kinase.mapk 13, extracellular.signal.regulated 11, activated.protein.map 10, p38.mitogen.activated 10, p38.map.kinase 6, protein.kinases.mapks 6, signal.transduction.pathways 6, signal.regulated.kinase 6, protein.kinase.erk 5, protein.map.kinase 5, kinase.jnk.p38 5, terminal.kinase.jnk 5, protein.map.kinases 5, regulated.kinase.kinase 4, p38.map.kinases 4, tumor.necrosis.factor 4, map.kinase.signaling 4, signal.transduction.pathway 4, stress.activated.protein 4, signal.regulated.kinases 3, protein.kinase.inhibitors 3, regulated.kinases.erks 3

The protein kinase PKR is required for macrophage apoptosis after activation of Toll-like receptor 4.

Differential regulation of interleukin 1 receptor and Toll-like receptor signaling by MEKK3.

Intracellular signalling cascades regulating innate immune responses to Mycobacteria: branching out from Toll-like receptors.

Mitogen-activated protein kinase pathways mediated by ERK, JNK, and p38 protein kinases.

Redox regulation of cellular signalling.

MAPK signalling pathways as molecular targets for anti-inflammatory therapy--from molecular mechanisms to therapeutic benefits.

p38 MAP kinases: key signalling molecules as therapeutic targets for inflammatory diseases.

Distinct roles of the adaptor protein Shc and focal adhesion kinase in integrin signaling to ERK.

Mammalian mitogen-activated protein kinase signal transduction pathways activated by stress and inflammation.

Activation of the IkappaB alpha kinase complex by MEKK1, a kinase of the JNK pathway.

MEKK1 activates both IkappaB kinase alpha and IkappaB kinase beta.

A protein kinase involved in the regulation of inflammatory cytokine biosynthesis.

MAP kinase p38 inhibitors: clinical results and an intimate look at their interactions with p38alpha protein.

Signaling from G-protein-coupled receptors to mitogen-activated protein (MAP)-kinase cascades.

Raf-1 kinase inhibitor protein: structure, function, regulation of cell signaling, and pivotal role in apoptosis.

CLUSTER 22 (125-123)

(43 Records)

* The role of c-Jun amino-terminal kinases (JNKs) in JNK-mediated degenerative and inflammatory processes, and the balance between inhibiting JNKs to suppress pathological features while recognizing the JNKs are also essential regulators of physiological and pathological processes

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Cluster Syntax Features

Descriptive Terms

jnk 37.8%, phosphoryl 7.7%, kinas 4.1%, tau 1.9%, activ 1.9%, jnk1 1.7%, insulin 1.1%, stress 1.1%, p38 1.0%, termin 0.9%, sapk 0.7%, p38mapk 0.7%, signal 0.7%, ser 0.6%, pkr 0.5%, apoptosi 0.5%, induc 0.5%, kinase.jnk 0.4%, terminal.kinase 0.4%, jnk2 0.4%, neuron 0.4%, terminal.kinase.jnk 0.4%, cell 0.4%, motor 0.4%, bax 0.4%

Discriminating Terms

jnk 26.5%, phosphoryl 4.5%, tau 1.4%, jnk1 1.2%, kinas 1.1%, cell 0.8%, patient 0.8%, diseas 0.7%, gene 0.7%, insulin 0.6%, genet 0.6%, genom 0.5%, p38 0.5%, p38mapk 0.5%, tnf 0.5%, sapk 0.5%, receptor 0.5%, autophagi 0.4%, termin 0.4%, risk 0.4%, ser 0.4%, human 0.4%, system 0.3%, alpha 0.3%, pkr 0.3%

Single Word Terms

activ 38, kinas 37, cell 31, phosphoryl 28, jnk 28, protein 27, induc 23, signal 22, termin 22, express 21, respons 19, regul 19, function 17, gene 17, stress 17, role 17, mediat 16, inhibit 14, pathwai 14, transcript 13, mechan 13, bind 12, factor 12, p38 11, neuron 11

Double Word Terms

terminal.kinase 13, protein.kinase 12, kinase.jnk 12, activated.protein 9, mitogen.activated 7, terminal.kinases 7, kinases.jnks 7, signal.transduction 6, transcription.factor 6, amino.terminal 6, stress.activated 6, jnk.activation 5, kinase.activity 5, gene.expression 5, jnk.p38 4, alzheimer.disease 4, map.kinases 4, jnk.activated 4, insulin.resistance 4, cell.death 4, transgenic.mice 4, motor.neurons 4, p38.mitogen 3, transcriptional.activity 3, jnk.isoforms 3

Triple Word Terms

terminal.kinase.jnk 11, terminal.kinases.jnks 7, mitogen.activated.protein 7, activated.protein.kinase 7, amino.terminal.kinase 4, protein.kinase.p38mapk 3,

p38.mitogen.activated 3, signal.transduction.pathway 3, amyotrophic.lateral.sclerosis 3, lateral.sclerosis.als 3, extracellular.signal.regulated 2, induced.cell.death 2, kinase.mapk.cascades 2, sod1.mutant.mice 2, kinase.p38mapk.activated 2, motor.neurons.sod1 2, colocalized.phosphorylated.neurofilaments 2, signal.regulated.kinases 2, terminal.activation.domain 2, neurons.sod1.mutant 2, jnk1.jnk2.jnk3 2, member.map.kinase 2, nh2.terminal.kinase 2, brain.expression.activation 2, targeted.disruption.jnk 2

Identification of an oncoprotein- and UV-responsive protein kinase that binds and potentiates the c-Jun activation domain.

The c-Jun N-terminal kinases in cerebral microglia: immunological functions in the brain.

A central role for JNK in obesity and insulin resistance.

Signal transduction by the c-Jun N-terminal kinase (JNK)--from inflammation to development.

Phosphorylation of microtubule-associated protein tau on Ser 262 by an embryonic 100 kDa protein kinase.

JNK2 contains a specificity-determining region responsible for efficient c-Jun binding and phosphorylation.

From JNK to pay dirt: jun kinases, their biochemistry, physiology and clinical importance.

JNK phosphorylation of Bim-related members of the Bcl2 family induces Bax-dependent apoptosis.

Dissection of TNF receptor 1 effector functions: JNK activation is not linked to apoptosis while NF-kappaB activation prevents cell death.

Signaling from Rho to the actin cytoskeleton through protein kinases ROCK and LIM-kinase.

Targeting JNK for therapeutic benefit: from junk to gold?

JNK and p38 stresskinases--degenerative effectors of signal-transduction-cascades in the nervous system.

c-Jun, JNK/SAPK kinases and transcription factor NF-kappa B are selectively activated in astrocytes, but not motor neurons, in amyotrophic lateral sclerosis.

Activated p38MAPK is a novel component of the intracellular inclusions found in human amyotrophic lateral sclerosis and mutant SOD1 transgenic mice.

Possible involvement of phosphorylation of occludin in tight junction formation.

CLUSTER 0 (125-123)

(28 Records)

* Mesenchymal stem cells, especially their potential as cardiac therapeutics and immunomodulation agents.

Cluster Syntax Features

Descriptive Terms

msc 68.7%, mesenchym 2.2%, stem 1.8%, cell 1.3%, stem.cells 1.2%, marrow 1.1%, mesenchymal.stem 1.1%, cells.mscs 1.0%, mesenchymal.stem.cells 0.9%, differenti 0.7%, bone.marrow 0.6%, bone 0.6%, infarct 0.6%, stem.cells.mscs 0.6%, allogen 0.5%, transplant 0.4%, tissu 0.4%, cultur 0.3%, myocardi 0.3%, isol 0.2%, implant 0.2%, inject 0.2%, hla 0.2%, stromal 0.2%, lymphocyt 0.2%

Discriminating Terms

msc 41.3%, mesenchym 1.2%, gene 0.9%, protein 0.8%, diseas 0.7%, receptor 0.7%, patient 0.7%, stem 0.7%, activ 0.6%, cells.mscs 0.6%, mesenchymal.stem 0.6%, genet 0.5%, tnf 0.5%, stem.cells 0.5%, mesenchymal.stem.cells 0.5%, genom 0.4%, kinas 0.4%, marrow 0.4%, signal 0.4%, human 0.4%, neuron 0.3%, autophagi 0.3%, risk 0.3%, stem.cells.mscs 0.3%, allogen 0.3%

Single Word Terms

msc 28, cell 27, mesenchym 26, stem 25, marrow 20, bone 19, differenti 18, tissu 15, express 14, isol 13, cultur 11, induc 11, activ 10, growth 10, vivo 10, inject 10, inhibit 10, system 9, transplant 9, stromal 9, deriv 9, vitro 9, factor 9, diseas 9, expand 8

Double Word Terms

stem.cells 23, mesenchymal.stem 23, cells.mscs 22, bone.marrow 18, cells.msc 7, stromal.cells 7, growth.factor 5, mscs.isolated 5, stem.cell 5, ifn.gamma 5, msc.transplantation 4, myocardial.infarction 4, left.ventricular 4, labeled.mscs 4, marrow.derived 4, smooth.muscle 4, mscs.differentiate 4, marrow.stromal 4, marrow.aspirates 4, isolated.bone 3, cell.population 3, allogeneic.mscs 3, graft.host 3, host.disease 3, immune.system 3

Triple Word Terms

mesenchymal.stem.cells 22, stem.cells.mscs 19, marrow.stromal.cells 4, cells.bone.marrow 3, bone.marrow.aspirates 3, isolated.bone.marrow 3, mscs.isolated.bone 3, graft.host.disease 3,

mscs.bone.marrow 3, cells.mscs.inhibit 3, vascular.endothelial.growth 3, endothelial.growth.factor 3, stem.cells.msc 3, bone.marrow.derived 2, mesenchymal.stromal.cells 2, msc.treated.mice 2, stromal.cells.mscs 2, adult.stem.cells 2, migrated.forebrain.cerebellum 2, vitro.vivo.mscs 2, stem.cell.population 2, neural.cell.fates 2, autologous.allogeneic.mscs 2, msc.differentiate.multiple 2, major.histocompatibility.complex 2

Clarification of the nomenclature for MSC: The International Society for Cellular Therapy position statement.

Comparative analysis of mesenchymal stem cells from bone marrow, umbilical cord blood, or adipose tissue.

Marrow stromal cells migrate throughout forebrain and cerebellum, and they differentiate into astrocytes after injection into neonatal mouse brains.

Dynamic imaging of allogeneic mesenchymal stem cells trafficking to myocardial infarction.

Bone marrow mesenchymal stem cells inhibit the response of naive and memory antigen-specific T cells to their cognate peptide.

Role for interferon-gamma in the immunomodulatory activity of human bone marrow mesenchymal stem cells.

HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells.

Mesenchymal stem cells suppress lymphocyte proliferation in vitro and prolong skin graft survival in vivo.

Phenotypic and functional comparison of cultures of marrow-derived mesenchymal stem cells (MSCs) and stromal cells.

Mesenchymal stem cells reside in virtually all post-natal organs and tissues.

Transplantation of mesenchymal stem cells improves cardiac function in a rat model of dilated cardiomyopathy.

Mesenchymal stem cell engraftment in lung is enhanced in response to bleomycin exposure and ameliorates its fibrotic effects.

Mesenchymal stem cells and their potential as cardiac therapeutics.

Mobilization and homing of bone marrow stromal cells in myocardial infarction.

Mesenchymal stem cell implantation in a swine myocardial infarct model: engraftment and functional effects.

CLUSTER 43 (125-123)

(70 Records)

*Bone marrow-derived stem cells, especially for therapeutic purposes

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Cluster Syntax Features

Descriptive Terms

stem 13.6%, cell 9.1%, stem.cells 7.1%, marrow 6.2%, bone.marrow 3.7%, transplant 3.7%, bone 3.2%, differenti 2.6%, hematopoiet 2.2%, tissu 1.8%, adult 1.5%, stem.cell 1.4%, epc 1.3%, mesenchym 0.8%, progenitor 0.7%, deriv 0.7%, vector 0.6%, marrow.derived 0.5%, hematopoietic.stem 0.5%, lineag 0.5%, regener 0.5%, infarct 0.4%, myocardium 0.4%, stromal 0.4%, mesenchymal.stem 0.4%

Discriminating Terms

stem 9.2%, stem.cells 4.8%, marrow 4.0%, bone.marrow 2.4%, transplant 2.3%, bone 1.7%, cell 1.6%, hematopoiet 1.5%, differenti 1.1%, stem.cell 0.9%, epc 0.9%, activ 0.9%, protein 0.9%, diseas 0.7%, adult 0.7%, gene 0.7%, receptor 0.7%, tnf 0.7%, genom 0.5%, kinas 0.5%, mesenchym 0.5%, progenitor 0.5%, autophagi 0.4%, signal 0.4%, risk 0.4%

Single Word Terms

cell 69, stem 46, tissu 37, differenti 35, marrow 35, bone 33, transplant 32, express 31, adult 26, deriv 25, human 24, function 21, hematopoiet 20, mice 20, system 20, potenti 20, progenitor 18, popul 17, prolifer 17, therapi 17, diseas 17, protein 17, endotheli 16, activ 15, neuron 15

Double Word Terms

stem.cells 40, bone.marrow 32, stem.cell 22, marrow.derived 11, progenitor.cells 11, hematopoietic.stem 8, mesenchymal.stem 8, adult.bone 8, cell.lines 7, cell.types 7, peripheral.blood 7, donor.derived 7, marrow.cells 7, endothelial.cells 6, stromal.cells 6, derived.cells 5, cell.populations 5, hematopoietic.cells 5, human.bone 5, fluorescent.protein 5, cells.multiple 5, green.fluorescent 5, gene.therapy 5, endothelial.cell 5, immune.system 5

Triple Word Terms

bone.marrow.derived 8, mesenchymal.stem.cells 8, bone.marrow.cells 7, adult.bone.marrow 7, human.bone.marrow 5, hematopoietic.stem.cells 5, hematopoietic.stem.cell 5,

green.fluorescent.protein 5, marrow.derived.cells 5, stem.cell.population 4, endothelial.progenitor.cells 4, properties.stem.cells 3, progenitor.cells.epcs 3, stem.cell.transplantation 3, stem.cells.adult 3, transplanted.bone.marrow 3, stem.cells.isolated 3, central.nervous.system 3, neural.stem.cells 3, marrow.stem.cells 3, marrow.stromal.cells 3, self.renewal.differentiation 3, marrow.derived.mesenchymal 3, bone.marrow.stem 3, bone.marrow.transplantation 3

Plasticity of marrow-derived stem cells.

Bone marrow as a source of endothelial cells and NeuN-expressing cells After stroke.

In vivo derivation of glucose-competent pancreatic endocrine cells from bone marrow without evidence of cell fusion.

Regeneration of ischemic cardiac muscle and vascular endothelium by adult stem cells.

Pluripotency of mesenchymal stem cells derived from adult marrow.

Levels of p53 protein increase with maturation in human hematopoietic cells.

Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function.

A new human somatic stem cell from placental cord blood with intrinsic pluripotent differentiation potential.

Multi-organ, multi-lineage engraftment by a single bone marrow-derived stem cell.

Cell-intrinsic differences between stem cells from different regions of the peripheral nervous system regulate the generation of neural diversity.

Purified hematopoietic stem cells can differentiate into hepatocytes in vivo.

Treatment of severe acute graft-versus-host disease with third party haploidentical mesenchymal stem cells.

Multipotent stromal cells from human marrow home to and promote repair of pancreatic islets and renal glomeruli in diabetic NOD/scid mice.

Mesenchymal stem cells modified with Akt prevent remodeling and restore performance of infarcted hearts.

Transplanted bone marrow generates new neurons in human brains.

Dystrophin expression in the mdx mouse restored by stem cell transplantation.

CLUSTER 12 (125-123)

(42 Records)

*Caspases, especially their central role in apoptosis

Cluster Syntax Features

Descriptive Terms

caspas 49.8%, apoptosi 6.5%, death 1.5%, activ 1.3%, caspase.activation 1.2%, apoptot 1.0%, proteas 0.8%, mitochondri 0.7%, fmk 0.7%, cytochrom 0.7%, cell 0.7%, protein 0.6%, cell.death 0.6%, apoptosom 0.6%, apaf 0.6%, mitochondria 0.6%, pathwai 0.4%, procaspas 0.4%, cleav 0.4%, cleavag 0.4%, aif 0.4%, oligomer 0.4%, famili 0.4%, apic 0.3%, smac 0.3%

Discriminating Terms

caspas 33.2%, apoptosi 2.7%, gene 1.0%, patient 0.8%, caspase.activation 0.8%, tnf 0.6%, receptor 0.6%, diseas 0.6%, fmk 0.5%, genet 0.5%, cell 0.5%, genom 0.5%, kinas 0.4%, apoptosom 0.4%, alpha 0.4%, autophagi 0.4%, apaf 0.4%, cytochrom 0.4%, express 0.4%, proteas 0.4%, risk 0.4%, apoptot 0.3%, respons 0.3%, control 0.3%, human 0.3%

Single Word Terms

caspas 42, cell 35, apoptosi 34, activ 32, protein 28, death 22, induc 22, apoptot 19, proteas 18, famili 17, role 17, pathwai 17, signal 17, releas 14, inhibitor 14, regul 14, mediat 13, function 13, complex 13, mechan 13, inhibit 12, depend 12, two 12, plai 12, cytochrom 12

Double Word Terms

cell.death 15, caspase.activation 13, activation.caspase 8, apoptosis.caspase 8, caspase.caspase 6, proteases.caspases 6, induced.apoptosis 6, caspase.inhibitor 5, release.caspase 5, cytochrome.release 5, dna.fragmentation 5, cysteine.proteases 5, programmed.cell 5, endoplasmic.reticulum 5, caspase.independent 4, bcl.family 4, family.proteins 4, amino.acid 4, central.role 4, caspase.activity 4, caspase.activated 4, full.length 4, activation.caspases 4, play.role 4, death.receptor 4

Triple Word Terms

programmed.cell.death 5, apoptosis.programmed.cell 4, amino.acid.sequence 3, cysteine.proteases.caspases 3, induced.apoptosis.caspase 3, caspase.activation.cell 3, cytochrome.release.mitochondria 3, inhibitor.apoptosis.proteins 3, endoplasmic.reticulum.stress 3, apaf.cytochrome.complex 2, caspase.activation.caspase 2, molecular.sequence.data 2,

pathway.apoptosis.caspase 2, permeability.transition.pore 2, proteins.endoplasmic.reticulum 2, inhibition.caspase.activation 2, family.cysteine.proteases 2, cysteine.proteases.play 2, proteases.play.central 2, caspase.activation.binding 2, plays.central.role 2, caspase.independent.cell 2, pathogenesis.alzheimer.disease 2, caspases.amino.acid 2, acid.sequence.apoptosis 2

Multiple apoptotic caspase cascades are required in nonapoptotic roles for Drosophila spermatid individualization.

Cytochrome C-mediated apoptosis.

Active caspase-1 is a regulator of unconventional protein secretion.

The Jnk1 and Jnk2 protein kinases are required for regional specific apoptosis during early brain development.

Caspases 3 and 7: key mediators of mitochondrial events of apoptosis.

Caspases: pharmacological manipulation of cell death.

Cystamine inhibits caspase activity. Implications for the treatment of polyglutamine disorders.

DFF, a heterodimeric protein that functions downstream of caspase-3 to trigger DNA fragmentation during apoptosis.

The proteasome: a suitable antineoplastic target.

The serine protease Omi/HtrA2 regulates apoptosis by binding XIAP through a reaper-like motif.

Apoptosis in neurodegenerative disorders.

Induction of TNF receptor I-mediated apoptosis via two sequential signaling complexes.

The apoptosome activates caspase-9 by dimerization.

Interactions of fluorochrome-labeled caspase inhibitors with apoptotic cells: a caution in data interpretation.

Mitochondrial voltage-dependent anion channel is involved in dopamine-induced apoptosis.

Cyclin-dependent kinase inhibitors enhance the resolution of inflammation by promoting inflammatory cell apoptosis.

Pathways to caspase activation.

IAP family proteins--suppressors of apoptosis.

CLUSTER 13

(72 Records)

* Autophagy, its physiological and pathophysiological roles, and the role of Beclin, an essential mediator of autophagy

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Cluster Syntax Features

Descriptive Terms

autophagi 58.2%, beclin 3.2%, degrad 1.5%, cell 1.2%, autophag 1.1%, starvat 1.0%, death 0.8%, cell.death 0.8%, pathwai 0.7%, rapamycin 0.7%, protein 0.6%, lysosom 0.6%, nutrient 0.6%, mtor 0.5%, kinas 0.5%, aggreg 0.4%, cytoplasm 0.4%, organel 0.4%, autophagosom 0.4%, eukaryot 0.4%, cellular 0.3%, role 0.3%, induc 0.3%, role.autophagy 0.3%, surviv 0.3%

Discriminating Terms

autophagi 38.3%, beclin 2.1%, receptor 0.8%, patient 0.8%, gene 0.7%, tnf 0.7%, starvat 0.7%, activ 0.7%, autophag 0.6%, diseas 0.6%, degrad 0.6%, genom 0.5%, genet 0.5%, rapamycin 0.4%, express 0.4%, risk 0.4%, alpha 0.4%, inflammatori 0.4%, data 0.3%, human 0.3%, nutrient 0.3%, factor 0.3%, mtor 0.3%, snp 0.3%, sequenc 0.3%

Single Word Terms

autophagi 70, cell 59, protein 54, role 47, degrad 40, pathwai 37, induc 36, function 31, death 28, activ 27, autophag 27, lysosom 26, regul 26, mechan 26, cellular 23, gene 23, kinas 23, starvat 22, diseas 22, cytoplasm 22, inhibit 21, depend 19, compon 18, molecular 18, surviv 18

Double Word Terms

cell.death 25, role.autophagy 17, induced.autophagy 12, autophagy.induced 12, wild.type 9, programmed.cell 9, cells.autophagy 8, protein.kinase 8, inhibition.autophagy 8, target.rapamycin 7, autophagy.autophagy 7, eukaryotic.cells 7, huntington.disease 7, autophagy.induction 7, evolutionarily.conserved 7, cell.survival 7, death.autophagy 7, autophagy.cell 7, starvation.induced 7, autophagy.genes 7, induction.autophagy 7, protein.degradation 6, mammalian.target 6, kinase.activity 6, signaling.pathway 6

Triple Word Terms

programmed.cell.death 8, cell.death.autophagy 7, mammalian.target.rapamycin 6, form.programmed.cell 5, autophagic.cell.death 5, autophagy.cell.death 5, target.rapamycin.mtor 5, starvation.induced.autophagy 5, bulk.protein.degradation 4, mtor.inhibitor.rapamycin 4,

aggregate.prone.proteins 3, lived.proteins.cytoplasmic 3, cell.death.pathway 3, autophagy.induced.nutrient 3, ubiquitin.proteasome.system 3, degradation.lived.proteins 3, unfolded.protein.response 3, reactive.oxygen.species 3, terminal.kinase.jnk 3, cell.survival.cell 3, clearance.aggregate.prone 3, oxygen.species.ros 3, cell.death.cell 3, green.fluorescent.protein 3, induced.nutrient.starvation 3

Autophagy and human disease.

Increased susceptibility of cytoplasmic over nuclear polyglutamine aggregates to autophagic degradation.

Tor-mediated induction of autophagy via an Apg1 protein kinase complex.

Dual roles of autophagy in the survival of Caenorhabditis elegans during starvation.

Beclin-phosphatidylinositol 3-kinase complex functions at the trans-Golgi network.

Two distinct Vps34 phosphatidylinositol 3-kinase complexes function in autophagy and carboxypeptidase Y sorting in Saccharomyces cerevisiae.

Impairment of starvation-induced and constitutive autophagy in Atg7-deficient mice.

Loss of autophagy in the central nervous system causes neurodegeneration in mice.

Homeostatic levels of p62 control cytoplasmic inclusion body formation in autophagy-deficient mice.

The role of autophagy during the early neonatal starvation period.

Development by self-digestion: molecular mechanisms and biological functions of autophagy.

Eating oneself and uninvited guests: autophagy-related pathways in cellular defense.

Autophagy in cell death: an innocent convict?

Autophagy is induced in CD4+ T cells and important for the growth factor-withdrawal cell death.

Protection against fatal Sindbis virus encephalitis by beclin, a novel Bcl-2-interacting protein.

Induction of autophagy and inhibition of tumorigenesis by beclin 1.

Autophagy regulates programmed cell death during the plant innate immune response.

Growth factor regulation of autophagy and cell survival in the absence of apoptosis.

Autophagy in metazoans: cell survival in the land of plenty.

CLUSTER 53 (125-123)

(86 Records)

*Apoptosis-programmed cell death

Cluster Syntax Features

Descriptive Terms

death 14.7%, apoptosi 13.2%, cell.death 10.1%, cell 7.0%, apoptot 4.1%, bcl 3.7%, p53 1.1%, program 0.9%, fa 0.8%, programmed.cell 0.8%, bax 0.8%, induc 0.8%, programmed.cell.death 0.7%, mitochondri 0.7%, caspas 0.6%, flip 0.5%, pathwai 0.5%, activ 0.5%, mitochondria 0.5%, chop 0.4%, surviv 0.4%, protein 0.4%, cpp32 0.3%, mechan 0.3%, regul 0.3%

Discriminating Terms

death 9.6%, apoptosi 8.5%, cell.death 7.1%, apoptot 2.9%, bcl 2.7%, cell 1.0%, patient 1.0%, diseas 0.8%, receptor 0.8%, p53 0.8%, gene 0.7%, genom 0.6%, programmed.cell 0.6%, bax 0.6%, fa 0.6%, program 0.6%, programmed.cell.death 0.6%, risk 0.5%, kinas 0.5%, flip 0.4%, tnf 0.4%, genet 0.4%, alpha 0.4%, inflammatori 0.4%, snp 0.4%

Single Word Terms

cell 85, apoptosi 73, death 72, activ 48, apoptot 48, protein 45, induc 42, express 33, mechan 31, regul 30, pathwai 29, signal 27, role 27, inhibitor 26, gene 25, program 23, depend 23, level 22, mediat 22, human 21, inhibit 21, caspas 21, target 21, tissu 20, surviv 19

Double Word Terms

cell.death 62, programmed.cell 21, apoptotic.cell 14, induced.cell 11, apoptotic.cells 9, cell.survival 8, dna.fragmentation 8, cell.lines 8, death.apoptosis 7, bcl.bcl 7, induced.apoptosis 7, cell.line 7, reactive.oxygen 7, death.induced 6, necrosis.factor 6, pro.apoptotic 6, mediated.apoptosis 6, mitochondrial.membrane 6, cell.cycle 6, plays.role 6, cells.apoptosis 6, apoptotic.death 6, oxygen.species 6, caspase.activation 6, apoptosis.induced 5

Triple Word Terms

programmed.cell.death 20, apoptotic.cell.death 13, induced.cell.death 10, cell.death.apoptosis 6, reactive.oxygen.species 6, necrotic.cell.death 5, tumor.necrosis.factor 5, cell.death.pathway 4, cell.death.induced 4, autophagic.cell.death 4, small.interfering.rna 3, mitochondrial.permeability.transition 3, cell.survival.cell 3, relative.molecular.mass 3, cell.death.mechanism 3, cell.death.animal 3, type.cell.death 3, mediated.cell.death 3,

mitochondrial.transmembrane.potential 3, cell.death.molecular 3, apoptosis.programmed.cell 3, adp.ribose.polymerase 3, poly.adp.ribose 3, embryonic.fibroblasts.mefs 2, characteristic.morphological.biochemical 2

The biochemistry of apoptosis.

Death receptors: signaling and modulation.

Bcl-2 is an inner mitochondrial membrane protein that blocks programmed cell death.

The TNF receptor 1-associated protein TRADD signals cell death and NF-kappa B activation.

GRIM-19, a cell death regulatory protein, is essential for assembly and function of mitochondrial complex I.

Inhibition of death receptor signals by cellular FLIP.

Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics.

Annexin V for flow cytometric detection of phosphatidylserine expression on B cells undergoing apoptosis.

NO: an inhibitor of cell death.

Birth and death of bone cells: basic regulatory mechanisms and implications for the pathogenesis and treatment of osteoporosis.

Review of current evidence for apoptosis after spinal cord injury.

Mitochondrial permeability transition is a central coordinating event of apoptosis.

Apoptosis in development.

Mitochondria and apoptosis.

Identification and inhibition of the ICE/CED-3 protease necessary for mammalian apoptosis.

A rapid and simple method for measuring thymocyte apoptosis by propidium iodide staining and flow cytometry.

Apoptosis and necrosis: different execution of the same death.

Apoptosis in neural development and disease.

Analysis of cytosolic and lysosomal pH in apoptotic cells by flow cytometry.

ASK1 is essential for endoplasmic reticulum stress-induced neuronal cell death triggered by expanded polyglutamine repeats.

CLUSTER 28 (125-123)

(48 Records)

- Autophagosomes, a double-membrane vesicle which sequesters organelles and long-lived proteins and fuses with the lysosome to degrade the contents (autophagy), and LC3 (a microtuble-associated protein light chain and mammalian homolog of yeast Atg8), which has been used as a specific marker to monitor autophagy

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Cluster Syntax Features

Descriptive Terms

autophagosom 13.2%, lc3 9.6%, lysosom 8.8%, autophagi 6.0%, degrad 4.6%, autophag 2.4%, membran 2.1%, p62 1.8%, format 1.8%, protein 1.5%, macroautophagi 1.3%, aggreg 1.3%, vacuol 1.3%, ubiquitin 1.2%, conjug 1.1%, endosom 1.1%, autophagosome.formation 0.9%, organel 0.8%, apg5 0.8%, proteasom 0.7%, fusion 0.7%, yeast 0.5%, microtubul 0.5%, cytoplasm 0.5%, apg12 0.5%

Discriminating Terms

autophagosom 8.7%, lc3 6.5%, lysosom 5.5%, degrad 2.3%, autophagi 2.3%, autophag 1.4%, p62 1.2%, cell 1.0%, gene 0.9%, macroautophagi 0.8%, format 0.8%, vacuol 0.8%, receptor 0.7%, membran 0.7%, endosom 0.7%, aggreg 0.7%, patient 0.7%, tnf 0.7%, conjug 0.6%, autophagosome.formation 0.6%, genet 0.6%, activ 0.6%, diseas 0.6%, apg5 0.5%, genom 0.5%

Single Word Terms

protein 43, degrad 35, autophagi 32, cell 30, lysosom 29, membran 24, format 24, autophagosom 23, autophag 21, activ 20, pathwai 19, form 18, ubiquitin 17, system 17, vacuol 17, role 15, acid 15, lc3 15, inhibit 15, yeast 14, cytoplasm 14, two 14, complex 14, mediat 14, diseas 13

Double Word Terms

protein.degradation 10, autophagosome.formation 10, protein.aggregates 6, eukaryotic.cells 6, bulk.degradation 6, autophagic.vacuoles 6, cell.death 6, amino.acid 6, autophagic.degradation 5, cytoplasmic.components 5, conjugation.system 5, lysosome.vacuole 5, amino.acids 5, bulk.protein 4, autophagy.yeast 4, yeast.saccharomyces 4, chain.lc3 4, light.chain 4, saccharomyces.cerevisiae 4, essential.autophagy 4, neurodegenerative.diseases 4, endoplasmic.reticulum 4, wild.type 4, endosomes.lysosomes 3, lc3.lc3 3

Triple Word Terms

yeast.saccharomyces.cerevisiae 4, light.chain.lc3 4, bulk.protein.degradation 4, protein.light.chain 3, autophagy.bulk.degradation 3, fusion.autophagosomes.lysosomes 2, chronic.toxic.degenerative 2, protein.p62.sqstm1 2, bulk.degradation.proteins 2, polyubiquitinated.protein.aggregates 2, binding.protein.p62 2, endogenous.protein.degradation 2, protein.conjugation.system 2, microtubule.protein.light 2, essential.autophagy.yeast 2, ubiquitin.protein.conjugation 2, polyubiquitin.binding.protein 2, integral.membrane.proteins 2, toxic.degenerative.diseases 2, active.site.cysteine 2, pathway.eukaryotic.cells 2, system.essential.autophagy 2, protein.conjugating.enzyme 2, apg12p.apg5p.conjugate 2, bulk.degradation.cytoplasmic 2

LC3, a mammalian homologue of yeast Apg8p, is localized in autophagosome membranes after processing.

LC3, GABARAP and GATE16 localize to autophagosomal membrane depending on form-II formation.

Intracellular inclusions containing mutant alpha1-antitrypsin Z are propagated in the absence of autophagic activity.

Dissection of the autophagosome maturation process by a novel reporter protein, tandem fluorescent-tagged LC3.

Dynein-dependent Movement of Autophagosomes Mediates Efficient Encounters with Lysosomes.

Autophagy as a regulated pathway of cellular degradation.

Microtubules facilitate autophagosome formation and fusion of autophagosomes with endosomes.

The dynamics of autophagy visualized in live cells: from autophagosome formation to fusion with endo/lysosomes.

Lysosomes and autophagy in cell death control.

An insight into the mechanistic role of Beclin 1 and its inhibition by prosurvival Bcl-2 family proteins.

Formation of the approximately 350-kDa Apg12-Apg5.Apg16 multimeric complex, mediated by Apg16 oligomerization, is essential for autophagy in yeast.

LC3, an autophagosome marker, can be incorporated into protein aggregates independent of autophagy: caution in the interpretation of LC3 localization.

Mechanisms of chaperone-mediated autophagy.

CLUSTER 16 (125-123)

(50 Records)

* Regulatory T cells (especially CD4, CD25), which modulate the activity of self-reactive cells, and their role in autoimmune disease, and Foxp3, a key regulatory gene for the development of regulatory T cells.

Cluster Syntax Features

Descriptive Terms

cd4 10.4%, foxp3 9.4%, cd25 8.4%, cd4.cd25 5.7%, cell 4.7%, tgf 4.4%, regulatori 3.8%, regulatory.cells 3.7%, tgf.beta 3.5%, reg 3.5%, beta 2.4%, reg.cells 2.0%, mice 1.0%, treg 0.9%, cd25.cells 0.9%, cd4.cd25.cells 0.8%, suppress 0.8%, tcr 0.8%, self 0.7%, autoimmun 0.6%, antigen 0.5%, cd25.regulatory 0.5%, cd4.cd25.regulatory 0.5%, transforming.growth.factor 0.5%, transforming.growth 0.5%

Discriminating Terms

cd4 6.7%, foxp3 6.4%, cd25 5.7%, cd4.cd25 3.9%, tgf 2.8%, regulatory.cells 2.4%, reg 2.4%, tgf.beta 2.3%, regulatori 2.0%, reg.cells 1.4%, beta 0.8%, protein 0.7%, gene 0.7%, tnf 0.7%, cd25.cells 0.6%, treg 0.6%, cd4.cd25.cells 0.6%, diseas 0.5%, tcr 0.5%, receptor 0.5%, neuron 0.5%, genet 0.5%, genom 0.5%, kinas 0.5%, autophagi 0.4%

Single Word Terms

cell 44, activ 36, cd4 31, regulatori 31, express 30, function 29, mice 26, diseas 24, factor 24, induc 23, beta 23, cd25 23, autoimmun 21, immun 21, foxp3 20, suppress 20, tgf 19, regul 17, mediat 17, role 17, growth 17, respons 16, transform 16, peripher 16, protein 16

Double Word Terms

regulatory.cells 24, cd4.cd25 20, tgf.beta 18, transforming.growth 16, growth.factor 16, cd25.regulatory 13, cd25.cells 9, transcription.factor 8, factor.beta 8, cd4.cells 8, regulatory.cell 8, cell.activation 7, cells.foxp3 7, autoimmune.diseases 7, cells.regulatory 7, reg.cells 6, cd4.cd8 6, cell.function 6, factor.tgf 6, cells.suppress 6, cell.contact 5, self.tolerance 5, multiple.sclerosis 5, autoimmune.disease 5, factor.foxp3 5

Triple Word Terms

transforming.growth.factor 16, cd4.cd25.regulatory 13, cd25.regulatory.cells 11, cd4.cd25.cells 9, growth.factor.beta 8, growth.factor.tgf 6, cells.cd4.cd25 5, transcription.factor.foxp3 5, factor.tgf.beta 5, cells.tgf.beta 5, cells.regulatory.cells 4, cells.reg.cells 4, mice.cd4.cd25 4, cd4.regulatory.cells 4, beta.tgf.beta 4, factor.beta.tgf 4, regulatory.cell.function 3, cell.cell.contact 3, peripheral.cd4.cd25 3, tgf.beta.induced 3, suppressive.cd4.cd25 3, immunological.self.tolerance 3, human.cd4.cd25 3, cells.peripheral.blood 3, regulatory.cells.suppress 3

Glucocorticoids in T cell development and function*.

Induction of CD4+CD25+ regulatory T cells by copolymer-I through activation of transcription factor Foxp3.

Control of regulatory T cell development by the transcription factor Foxp3.

Defective regulatory and effector T cell functions in patients with FOXP3 mutations.

CD4+CD25high regulatory cells in human peripheral blood.

Human regulatory T cells and their role in autoimmune disease.

An essential role for Scurfin in CD4+CD25+ T regulatory cells.

TGF-beta increases retinal endothelial cell permeability by increasing MMP-9: possible role of glial cells in endothelial barrier function.

CD4(+)CD25(+) regulatory T cells can mediate suppressor function in the absence of transforming growth factor beta1 production and responsiveness.

Control of immune pathology by regulatory T cells.

Regulation of T cell development by the deubiquitinating enzyme CYLD.

FOXP3 and NFAT: partners in tolerance.

Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases.

Naturally arising Foxp3-expressing CD25+CD4+ regulatory T cells in immunological tolerance to self and non-self.

TGF-beta and IL-6 signals modulate chromatin binding and promoter occupancy by acetylated FOXP3.

CLUSTER 56 (125-123)

(79 Records)

*Oxidative stress and oxidative injury/damage

Cluster Syntax Features

Descriptive Terms

oxid 10.0%, stress 9.7%, antioxid 5.0%, ro 4.1%, oxidative.stress 3.6%, oxygen 3.6%, reactive.oxygen 2.2%, oxygen.species 2.0%, reactive.oxygen.species 2.0%, speci 2.0%, reactiv 2.0%, flavonoid 1.3%, glutathion 1.1%, damag 1.0%, nadph 1.0%, redox 0.8%, tea 0.7%, dna 0.7%, nadph.oxidase 0.6%, oxidas 0.6%, cell 0.6%, adapt 0.6%, protect 0.5%, kappab 0.5%, induc 0.5%

Discriminating Terms

oxid 6.3%, stress 6.0%, antioxid 3.7%, ro 3.2%, oxidative.stress 2.8%, oxygen 2.6%, reactive.oxygen 1.7%, reactive.oxygen.species 1.6%, oxygen.species 1.6%, speci 1.2%, reactiv 1.2%, flavonoid 1.0%, receptor 1.0%, gene 0.9%, tnf 0.8%, nadph 0.8%, cell 0.7%, genom 0.6%, glutathion 0.6%, genet 0.6%, patient 0.6%, tea 0.5%, protein 0.5%, redox 0.5%, diseas 0.5%

Single Word Terms

oxid 56, stress 49, oxygen 44, cell 42, activ 41, speci 40, reactiv 39, antioxid 36, diseas 34, induc 31, protein 29, role 26, mechan 25, cellular 25, gener 24, level 24, product 23, respons 23, human 22, enzym 22, function 22, ro 21, signal 21, protect 20, damag 20

Double Word Terms

reactive.oxygen 37, oxygen.species 36, oxidative.stress 36, species.ros 20, alzheimer.disease 9, cell.death 9, nadph.oxidase 8, lipid.peroxidation 8, play.role 7, antioxidant.enzymes 7, gene.expression 6, stress.induced 6, oxidative.damage 6, signal.transduction 6, stress.response 5, role.cellular 5, dna.damage 5, induced.apoptosis 5, superoxide.dismutase 5, nitric.oxide 5, parkinson.disease 5, ros.production 4, low.density 4, glutathione.gsh 4, free.radicals 4

Triple Word Terms

reactive.oxygen.species 36, oxygen.species.ros 20, low.density.lipoprotein 4, reduced.glutathione.gsh 3, production.reactive.oxygen 3, density.lipoprotein.ldl 3, ischemia.reperfusion.injury 3, intracellular.reactive.oxygen 3, nuclear.factor.kappab 3, biomarkers.oxidative.stress 3, toxic.reactive.oxygen 3, accumulation.reactive.oxygen 2,

dismutase.glutathione.peroxidase 2, glutathione.acetyl.cysteine 2, oxidative.stress.activates 2, glutathione.peroxidase.catalase 2, intracellular.antioxidant.enzymes 2, glutathione.transferase.gst 2, superoxide.dismutase.glutathione 2, cells.tumor.necrosis 2, induced.oxidative.stress 2, generation.reactive.oxygen 2, expression.oxidative.stress 2, oxidative.dna.damage 2, role.cellular.protection 2

Involvement of reactive oxygen species in Toll-like receptor 4-dependent activation of NF-kappa B.

Reactive oxygen species, cell signaling, and cell injury.

Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions.

NADPH oxidase.

Control of mitochondrial redox balance and cellular defense against oxidative damage by mitochondrial NADP+-dependent isocitrate dehydrogenase.

Biomarkers of oxidative stress study II: are oxidation products of lipids, proteins, and DNA markers of CCl4 poisoning?

Investigations of protective effects of the flavonoids quercetin and rutin on stress resistance in the model organism Caenorhabditis elegans.

Mitochondrial catalase and oxidative injury.

Oxidative stress and autophagy.

Two novel proteins activate superoxide generation by the NADPH oxidase NOX1.

Is NF-kappaB the sensor of oxidative stress?

Antioxidant enzymes and human diseases.

Effects of antioxidant enzymes in the molecular control of reactive oxygen species toxicology.

The NOX family of ROS-generating NADPH oxidases: physiology and pathophysiology.

The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer.

Reduction of diabetes-induced oxidative stress by phosphodiesterase inhibitors in rats.

Green tea polyphenols (flavan 3-ols) prevent oxidative modification of low density lipoproteins: an ex vivo study in humans.

Oxidative damage and Alzheimer's disease: are antioxidant therapies useful?

CLUSTER 49 (125-123)

(72 Records)

The role of oxides in tissue injury and disease, especially free radicals, nitric oxide, superoxides, and peroxides

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Cluster Syntax Features

Descriptive Terms

radic 12.3%, oxid 6.0%, superoxid 4.1%, peroxid 4.1%, lipid 3.9%, free 2.7%, peroxynitrit 2.1%, sod 1.6%, dismutas 1.4%, nitric 1.4%, nitric.oxide 1.4%, superoxide.dismutase 1.4%, hydrogen 1.3%, h2o2 1.3%, oxygen 1.3%, free.radicals 1.1%, free.radical 1.1%, hydrogen.peroxide 1.1%, catalas 1.0%, lipid.peroxidation 1.0%, mitochondri 0.9%, antioxid 0.8%, gsh 0.7%, metal 0.7%, copper 0.6%

Discriminating Terms

radic 8.6%, superoxid 2.8%, oxid 2.8%, peroxid 2.8%, lipid 2.2%, free 1.6%, peroxynitrit 1.5%, gene 1.1%, sod 1.1%, cell 1.0%, dismutas 1.0%, superoxide.dismutase 1.0%, hydrogen 0.9%, h2o2 0.9%, free.radicals 0.8%, receptor 0.8%, hydrogen.peroxide 0.8%, free.radical 0.7%, nitric.oxide 0.7%, nitric 0.7%, tnf 0.7%, patient 0.7%, catalas 0.7%, genet 0.7%, oxygen 0.6%

Single Word Terms

oxid 50, radic 41, superoxid 35, activ 34, cell 34, protein 29, free 28, peroxid 28, oxygen 27, lipid 25, mechan 24, induc 23, nitric 23, form 21, dismutas 21, gener 21, diseas 21, acid 20, stress 20, reactiv 20, role 20, product 20, hydrogen 19, mediat 19, tissu 19

Double Word Terms

nitric.oxide 23, superoxide.dismutase 21, free.radicals 18, free.radical 16, oxidative.stress 16, lipid.peroxidation 16, hydrogen.peroxide 16, dismutase.sod 10, reactive.oxygen 8, superoxide.anion 7, hydroxyl.radical 6, hydroxyl.radicals 6, glutathione.peroxidase 6, peroxide.h2o2 6, mitochondrial.respiratory 5, respiratory.chain 5, ischemia.reperfusion 5, xanthine.oxidase 5, oxygen.species 5, phosphate.dehydrogenase 5, glyceraldehyde.phosphate 5, tissue.injury 4, thiobarbituric.acid 4, derived.free 4, alzheimer.disease 4

Triple Word Terms

superoxide.dismutase.sod 10, hydrogen.peroxide.h2o2 6, mitochondrial.respiratory.chain 5, glyceraldehyde.phosphate.dehydrogenase 5, reactive.oxygen.species 5, nitric.oxide.synthase 4,

derived.free.radicals 4, role.oxidative.stress 4, free.radicals.play 3, free.radical.production 3, red.blood.cells 3, dismutase.sod.catalase 3, play.role.pathophysiology 3, hydrogen.ion.concentration 3, manganese.superoxide.dismutase 3, free.radical.generation 3, oxygen.free.radicals 3, membrane.sodium.channels 2, respiratory.distress.syndrome 2, oxidation.reduction.oxygen 2, pyrogallol.catalase.superoxide 2, cations.divalent.free 2, adp.ribose.synthetase 2, catalase.superoxide.dismutase 2, iron.oxygen.pyrogallol 2

Bcl-2 functions in an antioxidant pathway to prevent apoptosis.

Bright and dark sides of nitric oxide in ischemic brain injury.

Oxidative DNA damage induced by simultaneous generation of nitric oxide and superoxide.

Peroxynitrite-mediated tyrosine nitration catalyzed by superoxide dismutase.

Protein S-nitrosylation: a physiological signal for neuronal nitric oxide.

Oxidative stress and the pathogenesis of Parkinson's disease.

Interactions between superoxide and nitric oxide: implications in DNA damage and mutagenesis.

Free radicals as mediators of tissue injury and disease.

Myeloperoxidase: friend and foe.

Stimulation by nitroxides of catalase-like activity of hemeproteins. Kinetics and mechanism.

Role of nitric oxide in carcinogenesis and tumour progression.

Free radical tissue damage: protective role of antioxidant nutrients.

Role of superoxide dismutases in oxidative damage and neurodegenerative disorders.

Mitochondrial nitric oxide mediates decreased vulnerability of hippocampal neurons from immature animals to NMDA.

Oxygen-derived free radicals in postischemic tissue injury.

Apparent hydroxyl radical production by peroxynitrite: implications for endothelial injury from nitric oxide and superoxide.

Nitric oxide, superoxide, and peroxynitrite: the good, the bad, and ugly.

Biologically active metal-independent superoxide dismutase mimics.

Nitric oxide, cell bioenergetics and neurodegeneration.

CLUSTER 20 (125-123)

(40 Records)

*The role of the ubiquitin system in diverse cellular processes, especially the contribution of its dysfunction to neurodegenerative and immunological disorders.

Cluster Syntax Features

Descriptive Terms

ubiquitin 41.5%, proteasom 5.4%, protein 2.7%, catenin 2.4%, degrad 2.2%, beta.catenin 1.8%, conjug 1.2%, ligas 1.2%, ubiquityl 1.0%, substrat 0.9%, vcp 0.8%, cellular 0.8%, ubiquitin.chains 0.6%, regul 0.6%, cadherin 0.6%, beta 0.6%, ubiquitin.proteasome 0.4%, ubiquitin.protein 0.4%, domain 0.4%, polyubiquitin 0.4%, chain 0.4%, constel 0.4%, deubiquitin 0.3%, complex 0.3%, cyclin 0.3%

Discriminating Terms

ubiquitin 27.1%, proteasom 3.3%, catenin 1.6%, beta.catenin 1.2%, cell 0.9%, degrad 0.9%, gene 0.8%, ligas 0.8%, diseas 0.7%, ubiquityl 0.7%, conjug 0.7%, receptor 0.7%, patient 0.7%, tnf 0.6%, genet 0.6%, vcp 0.6%, activ 0.5%, neuron 0.5%, kinas 0.4%, ubiquitin.chains 0.4%, cadherin 0.4%, autophagi 0.4%, genom 0.4%, risk 0.4%, substrat 0.4%

Single Word Terms

protein 37, ubiquitin 33, regul 25, cell 24, degrad 21, proteasom 19, activ 18, mediat 16, function 16, control 15, pathwai 15, cellular 15, complex 15, target 14, substrat 13, type 12, role 12, signal 12, conjug 11, system 11, cycl 10, interact 10, chain 10, domain 10, promot 10

Double Word Terms

cell.cycle 9, ubiquitin.proteasome 8, cellular.proteins 6, ubiquitin.chains 6, ubiquitin.protein 6, beta.catenin 5, protein.degradation 5, cellular.cell 4, conjugation.ubiquitin 4, ubiquitin.proteins 4, transcription.factors 4, proteasome.system 4, cycle.progression 4, degradation.pathway 3, polyposis.coli 3, attachment.ubiquitin 3, proteins.degradation 3, proteins.ubiquitination 3, polyubiquitin.chain 3, adenomatous.polyposis 3, target.proteins 3, cell.cell 3, ubiquitin.ligase 3, 26s.proteasome 3, cysteine.proteases 3

Triple Word Terms

ubiquitin.proteasome.system 4, cell.cycle.progression 4, cellular.cell.cycle 3, adenomatous.polyposis.coli 3, innate.adaptive.immunity 2, ubiquitin.protein.conjugates 2,

polyubiquitin.chain.topology 2, k63.linked.ubiquitin 2, linked.ubiquitin.chains 2, domain.beta.catenin 2, formation.isopeptide.bond 2, lysosome.christian.duve 2, signal.transduction.protein 2, colon.cancer.cells 2, ubiquitin.protein.ligases 2, proteins.degradation.proteasome 2, proteasome.system.ups 2, malignancies.neurodegenerative.disorders 2, pathogenesis.diseases.malignancies 2, tumour.suppressor.gene 2, ubiquitin.proteasome.pathway 2, beta.catenin.degradation 2, polyposis.coli.apc 2, shed.light.structure 1, kda.cytoplasmic.protein 1

Protein regulation by monoubiquitin.

Weighing in on ubiquitin: the expanding role of mass-spectrometry-based proteomics.

Cortical stabilization of beta-catenin contributes to NHERF1/EBP50 tumor suppressor function.

Siah-1 mediates a novel beta-catenin degradation pathway linking p53 to the adenomatous polyposis coli protein.

Ubiquitin ligases and the immune response.

Proteasome-independent functions of ubiquitin in endocytosis and signaling.

Inducible nitric-oxide synthase is regulated by the proteasome degradation pathway.

A proteomics approach to understanding protein ubiquitination.

Mechanisms underlying ubiquitination.

Bacterial interference of ubiquitination and deubiquitination.

SseL, a Salmonella deubiquitinase required for macrophage killing and virulence.

IAPs, RINGs and ubiquitylation.

Themes and variations on ubiquitylation.

De-ubiquitination and ubiquitin ligase domains of A20 downregulate NF-kappaB signalling.

Ubiquitination and deubiquitination: targeting of proteins for degradation by the proteasome.

RNA interference of valosin-containing protein (VCP/p97) reveals multiple cellular roles linked to ubiquitin/proteasome-dependent proteolysis.

Ubiquitin-like proteins: new wines in new bottles.

RING finger proteins: mediators of ubiquitin ligase activity.

Ubiquitination on nonlysine residues by a viral E3 ubiquitin ligase.

CLUSTER 19 (125-123)

(38 Records)

*Unfolded protein response signaling pathway, including the role of molecular chaperones such as heat shock proteins in assisting the protein folding process in the endoplasmic reticulum, and the impact of unfolded or malfolded proteins on cell survival through stresses placed on the endoplasmic reticulum

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Cluster Syntax Features

Descriptive Terms

upr 16.4%, stress 6.3%, protein 4.1%, heat 3.5%, heat.shock 3.3%, unfold 2.6%, shock 2.5%, endoplasmic.reticulum 2.4%, endoplasm 2.4%, reticulum 2.4%, chaperon 2.2%, fold 1.6%, xbp 1.4%, ire1 1.3%, unfolded.protein 1.1%, atf6 1.1%, hypoxia 1.0%, response.upr 0.9%, unfolded.protein.response 0.9%, protein.response 0.9%, heat.shock.proteins 0.9%, shock.proteins 0.9%, protein.response.upr 0.8%, respons 0.7%, transcript 0.7%

Discriminating Terms

upr 11.6%, stress 2.7%, heat 2.2%, heat.shock 2.2%, unfold 1.8%, endoplasmic.reticulum 1.6%, endoplasm 1.6%, reticulum 1.5%, shock 1.5%, chaperon 1.4%, xbp 0.9%, ire1 0.9%, fold 0.8%, atf6 0.8%, receptor 0.8%, unfolded.protein 0.7%, patient 0.7%, tnf 0.7%, response.upr 0.7%, cell 0.6%, hypoxia 0.6%, unfolded.protein.response 0.6%, protein.response.upr 0.6%, heat.shock.proteins 0.6%, shock.proteins 0.6%

Single Word Terms

protein 36, cell 28, stress 28, endoplasm 25, reticulum 25, respons 24, activ 22, regul 21, factor 19, unfold 18, pathwai 17, transcript 17, function 16, fold 15, express 15, signal 15, gene 14, induc 14, upr 13, chaperon 13, cellular 12, mechan 12, role 11, shock 10, heat 10

Double Word Terms

endoplasmic.reticulum 25, unfolded.protein 15, protein.response 14, response.upr 13, heat.shock 10, transcription.factor 9, protein.folding 8, reticulum.stress 7, cell.death 6, molecular.chaperones 5, shock.proteins 5, upr.signaling 5, unfolded.proteins 5, signal.transduction 4, response.stress 4, shock.protein 4, transmembrane.protein 3, accumulation.unfolded 3, shock.response 3, genes.encoding 3, signaling.pathways 3, eukaryotic.cells 3, stress.induced 3, transcription.factors 3, transduction.pathways 3

Triple Word Terms

unfolded.protein.response 14, protein.response.upr 13, endoplasmic.reticulum.stress 7, heat.shock.proteins 5, heat.shock.protein 4, heat.shock.response 3, signal.transduction.pathways 3, response.upr.three 2, expression.heat.shock 2, accumulation.unfolded.proteins 2, cells.lethal.stress 2, cell.death.stress 2, transcription.genes.encoding 2, intracellular.signal.transduction 2, reticulum.stress.activates 2, apoptotic.cell.death 2, regulated.intramembrane.proteolysis 2, regulators.heat.shock 2, stress.endoplasmic.reticulum 2, inducible.factor.hif 2, hypoxia.inducible.factor 2, protein.disulfide.isomerase 2, translation.initiation.factor 2, unfolded.protein.signal 2, homologous.protein.chop 2

The role of molecular chaperones in protein folding.

Parkinsonian mimetics induce aspects of unfolded protein response in death of dopaminergic neurons.

The presence of malfolded proteins in the endoplasmic reticulum signals the induction of glucose-regulated proteins.

XBP-1 regulates a subset of endoplasmic reticulum resident chaperone genes in the unfolded protein response.

Proteasome inhibitors disrupt the unfolded protein response in myeloma cells.

The glucose-regulated proteins: stress induction and clinical applications.

IRE1 signaling affects cell fate during the unfolded protein response.

CHOP induces death by promoting protein synthesis and oxidation in the stressed endoplasmic reticulum.

Endoplasmic reticulum stress signaling in disease.

A transmembrane protein with a cdc2+/CDC28-related kinase activity is required for signaling from the ER to the nucleus.

The heat-shock response: regulation and function of heat-shock proteins and molecular chaperones.

Molecular chaperones and the stress of oncogenesis.

Roles of CHOP/GADD153 in endoplasmic reticulum stress.

Signal transduction from the endoplasmic reticulum to the cell nucleus.

Heat shock proteins as regulators of the immune response.

CLUSTER 62 (125-123)

(72 Records)

*Proteins, especially protein binding and its role in the activation of transcription factor NF-kappa B

Cluster Syntax Features

Descriptive Terms

protein 8.6%, bind 6.4%, kappa 4.1%, transcript 1.9%, subunit 1.9%, membran 1.6%, regul 1.3%, structur 1.2%, binding.proteins 1.2%, complex 1.2%, dna 1.2%, activ 1.2%, assembl 1.0%, interact 1.0%, peptid 0.9%, domain 0.9%, disc1 0.9%, cell 0.8%, gene 0.8%, mechan 0.7%, oncogen 0.7%, mmp 0.7%, dna.binding 0.7%, signal 0.7%, factor 0.7%

Discriminating Terms

bind 3.8%, protein 3.1%, kappa 2.8%, subunit 1.3%, patient 1.1%, binding.proteins 1.0%, tnf 0.9%, disc1 0.9%, assembl 0.7%, membran 0.7%, transcript 0.7%, diseas 0.7%, oncogen 0.6%, dna.binding 0.6%, cell 0.6%, autophagi 0.6%, neuron 0.5%, risk 0.5%, kinas 0.5%, membrane.proteins 0.5%, genom 0.5%, induc 0.5%, inflammatori 0.5%, p53 0.4%, snp 0.4%

Single Word Terms

protein 62, bind 41, activ 37, cell 37, gene 33, factor 31, regul 31, complex 27, transcript 27, mechan 27, function 25, signal 24, role 23, structur 23, interact 21, express 20, cellular 20, control 18, form 18, membran 17, system 17, diseas 17, depend 16, site 16, pathwai 16

Double Word Terms

transcription.factor 13, binding.proteins 10, gene.expression 10, transcription.factors 9, dna.binding 8, cell.cycle 6, expression.regulation 6, wild.type 5, proteins.transcription 5, plasma.membrane 5, signaling.pathways 5, cell.surface 5, tumor.suppressor 5, binding.sites 4, cell.growth 4, nervous.system 4, two.hybrid 4, binding.protein 4, yeast.two 4, binding.site 4, immune.system 4, molecular.mechanisms 3, binding.activity 3, transcriptional.activity 3, cell.types 3

Triple Word Terms

gene.expression.regulation 6, proteins.transcription.factors 4, yeast.two.hybrid 4, dna.binding.proteins 4, oncogene.proteins.fos 3, proto.oncogene.proteins 3, fos.proto.oncogene 3, proteins.fos.proto 3, genetics.gene.expression 2, camp.response.element 2,

element.binding.protein 2, human.disease.proteins 2, disrupted.schizophrenia.disc1 2, schizophrenia.disc1.gene 2, response.element.binding 2, transducer.activator.transcription 2, signal.transducer.activator 2, transcription.genes.encoding 2, tumor.suppressor.gene 2, activate.transcription.genes 2, cell.transformation.neoplastic 2, expression.regulation.genes 2, transformation.neoplastic.gene 2, activator.transcription.stat 2, nuclear.proteins.transcription 2

Function and activation of NF-kappa B in the immune system.

Macropinocytosis: searching for an endocytic identity and role in the uptake of cell penetrating peptides.

AP-1 function and regulation.

Regulated expression of the tyrosine hydroxylase gene by membrane depolarization. Identification of the responsive element and possible second messengers.

The NF-kappa B and I kappa B proteins: new discoveries and insights.

The large subunit of the mammalian mitochondrial ribosome. Analysis of the complement of ribosomal proteins present.

Predicting transmembrane protein topology with a hidden Markov model: application to complete genomes.

Protein phosphatase 2A: variety of forms and diversity of functions.

Regulation of the NF-kappa B/rel transcription factor and I kappa B inhibitor system.

Pharmacokinetic and pharmacodynamic considerations in the development of therapeutic proteins.

Calcineurin enhances MEF2 DNA binding activity in calcium-dependent survival of cerebellar granule neurons.

Binding interactions between peptides and proteins of the class II major histocompatibility complex.

Identification of 'tissue' transglutaminase binding proteins in neural cells committed to apoptosis.

Regulation of signaling protein function and trafficking by the hsp90/hsp70-based chaperone machinery.

The P-loop--a common motif in ATP- and GTP-binding proteins.

14-3-3 proteins associate with A20 in an isoform-specific manner and function both as chaperone and adapter molecules.

CLUSTER 63 (125-123)

(79 Records)

*The role of zinc in neurodegenerative diseases and as an antioxidant, and the role of amino acid as a zinc transporter

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Cluster Syntax Features

Descriptive Terms

zinc 5.0%, acid 3.6%, transport 3.3%, amino 2.5%, prx 2.0%, cy 1.9%, atpas 1.9%, protein 1.8%, drug 1.6%, assai 1.6%, amino.acid 1.4%, oxid 1.2%, peptid 1.2%, structur 1.0%, membran 1.0%, amyloid 0.8%, enzym 0.8%, nitrat 0.8%, bind 0.7%, potassium 0.7%, ion 0.7%, glycoprotein 0.7%, resist 0.7%, channel 0.6%, reaction 0.6%

Discriminating Terms

zinc 3.9%, transport 2.0%, prx 1.7%, acid 1.6%, cy 1.6%, atpas 1.6%, amino 1.4%, cell 1.2%, patient 0.9%, gene 0.9%, tnf 0.8%, amino.acid 0.8%, assai 0.8%, diseas 0.8%, receptor 0.7%, genet 0.7%, potassium 0.6%, genom 0.6%, nitrat 0.6%, amyloid 0.5%, autophagi 0.5%, ion 0.5%, peptid 0.5%, risk 0.5%, express 0.4%

Single Word Terms

protein 47, acid 40, activ 30, cell 28, mechan 26, amino 26, bind 24, oxid 23, site 20, role 19, two 19, system 18, membran 18, transport 18, tissu 17, on 17, structur 17, form 16, depend 15, enzym 15, function 15, high 14, sequenc 14, product 14, inhibit 14

Double Word Terms

amino.acid 19, amino.acids 7, nitric.oxide 6, acid.sequence 6, oxidative.stress 5, drug.resistance 5, catalytic.cycle 4, homology.amino 4, escherichia.coli 4, binding.sites 4, sequence.homology 4, multidrug.resistance 4, assay.sensitive 4, transport.system 4, alzheimer.disease 4, oxide.synthase 4, active.site 4, synthase.amino 3, indicators.reagents 3, arginine.nitric 3, acid.oxidoreductases 3, peroxiredoxin.prx 3, conductance.regulator 3, dodecyl.sulfate 3, binding.site 3

Triple Word Terms

amino.acid.sequence 6, nitric.oxide.synthase 4, sequence.homology.amino 4, amino.acid.oxidoreductases 3, synthase.amino.acid 3, arginine.nitric.oxide 3, oxide.synthase.amino 3, molecular.sequence.data 3, homology.amino.acid 3, sodium.dodecyl.sulfate 3, amino.acid.residues 3, amino.acids.amino 3,

antimicrobial.peptides.abundant 2, reagents.nitrates.nitrites 2, acid.transport.system 2, cystic.fibrosis.transmembrane 2, nitric.oxide.synthases 2, pterins.tetrahydropterin.dithiothreitol 2, hemoglobins.indicators.reagents 2, indicators.reagents.nitrates 2, high.molecular.weight 2, citrulline.nadp.arginine 2, amino.acid.transport 2, acid.oxidoreductases.chromatography 2, chromatography.ion.exchange 2

Is the multidrug transporter a flippase?

Control of zinc transfer between thionein, metallothionein, and zinc proteins.

Regulation of macrophage migration inhibitory factor and thiol-specific antioxidant protein PAG by direct interaction.

Zinc and disease of the brain.

Re-evaluation of amino acid PET studies: can the protein synthesis rates in brain and tumor tissues be measured in vivo?

Crystal structure of constitutive endothelial nitric oxide synthase: a paradigm for pterin function involving a novel metal center.

The antioxidant properties of zinc.

Absorption, transport, and hepatic metabolism of copper and zinc: special reference to metallothionein and ceruloplasmin.

Rapid induction of Alzheimer A beta amyloid formation by zinc.

Effects of amino acids on zinc transport in rat erythrocytes.

Cloning and characterization of a mammalian proton-coupled metal-ion transporter.

Investigation of the effect of metal ions on the reactivity of thiol groups in human 5-aminolaevulinate dehydratase.

CLUSTER 2 (125-123)

(17 Records)

*Role of prion protein (PrP) in neuronal dysfunction and progressive neurodegeneration due to protein misfolding, and the role of Poly(ADP-ribosyl)ation (PARylation) in inflammation, and neuronal function.

Cluster Syntax Features

Descriptive Terms

prp 10.5%, adp 10.5%, poly.adp 8.7%, parg 8.0%, poli 7.4%, adp.ribose 6.2%, ribos 5.9%, poly.adp.ribose 4.3%, hsp 1.4%, dna 1.3%, ation 1.3%, parp 1.3%, prp.res 1.2%, poly.adp.ribosyl 1.2%, ribosyl 1.2%, adp.ribosyl 1.2%, ribosyl.ation 1.1%, adp.ribosyl.ation 1.1%, re 1.0%, parg.110 0.6%, prion 0.6%, adp.ribose.polymerase 0.6%, ribose.polymerase 0.5%, nad 0.5%, 110 0.5%

Discriminating Terms

prp 6.1%, adp 6.0%, poly.adp 5.0%, parg 4.7%, poli 4.2%, adp.ribose 3.5%, ribos 3.4%, poly.adp.ribose 2.4%, cell 0.9%, gene 0.9%, hsp 0.8%, ation 0.8%, receptor 0.7%, prp.res 0.7%, diseas 0.7%, ribosyl 0.7%, poly.adp.ribosyl 0.7%, adp.ribosyl 0.7%, parp 0.7%, adp.ribosyl.ation 0.7%, ribosyl.ation 0.7%, patient 0.7%, tnf 0.6%, re 0.5%, activ 0.5%

Single Word Terms

protein 12, cell 11, polymeras 10, poli 10, damag 10, adp 10, activ 9, ribos 9, dna 8, cellular 8, role 7, function 7, parp 7, nuclear 6, death 6, parg 6, enzym 6, glycohydrolas 6, ribosyl 6, ation 6, prp 5, level 5, prion 5, form 5, deplet 5

Double Word Terms

poly.adp 10, adp.ribose 9, ribose.polymerase 8, dna.damage 7, ribosyl.ation 6, cell.death 6, adp.ribosyl 6, polymerase.parp 5, glycohydrolase.parg 5, ribose.glycohydrolase 5, prion.protein 4, spongiform.encephalopathies 3, role.poly 3, nuclear.proteins 3, dna.strand 3, enzyme.poly 3, heat.shock 3, activation.poly 3, protein.prp 3, transmissible.spongiform 3, nad.depletion 3, isoform.parg 2, parg.inhibitor 2, parg.inhibitors 2, modulation.poly 2

Triple Word Terms

poly.adp.ribose 9, adp.ribose.polymerase 8, adp.ribosyl.ation 6, poly.adp.ribosyl 6, adp.ribose.glycohydrolase 5, ribose.polymerase.parp 5, ribose.glycohydrolase.parg 4,

transmissible.spongiform.encephalopathies 3, enzyme.poly.adp 3, role.poly.adp 3, activation.poly.adp 3, dna.damage.activated 2, adp.ribose.polymers 2, parg.inhibitor.gallotannin 2, spongiform.encephalopathies.tses 2, protease.resistant.form 2, proteins.poly.adp 2, nuclear.proteins.poly 2, induced.cell.death 2, adp.ribose.units 2, prion.protein.prp 2, dna.strand.breaks 2, mice.wild.type 2, adp.ribose.par 2, parg.110.mice 2

Reversibility of scrapie inactivation is enhanced by copper.

Poly(ADP-ribose) in the cellular response to DNA damage.

Mice lacking the 110-kD isoform of poly(ADP-ribose) glycohydrolase are protected against renal ischemia/reperfusion injury.

Expression of hsp 27, hsp 60, hsc 70, and hsp 70 stress response genes in cultured human urothelial cells (UROtsa) exposed to lethal and sublethal concentrations of sodium arsenite.

Poly(ADP-ribosyl)ated chromatin domains: access granted.

Eight prion strains have PrP(Sc) molecules with different conformations.

Hyperbaric oxygen enhances the expression of prion protein and heat shock protein 70 in a mouse neuroblastoma cell line.

The most infectious prion protein particles.

Role of poly(ADP-ribose) synthetase in inflammation and ischaemia-reperfusion.

The poly(ADP-ribose) glycohydrolase inhibitor gallotannin blocks oxidative astrocyte death.

Poly(ADP-ribose) glycohydrolase mediates oxidative and excitotoxic neuronal death.

Physiology and pathophysiology of poly(ADP-ribosyl)ation.

A simple salting out procedure for extracting DNA from human nucleated cells.

Strain-dependent differences in beta-sheet conformations of abnormal prion protein.

Poly(ADP-ribose) accumulation and enhancement of postischemic brain damage in 110-kDa poly(ADP-ribose) glycohydrolase null mice.

Role of poly(ADP-ribose) glycohydrolase (PARG) in shock, ischemia and reperfusion.

CLUSTER 11 (125-123)

(23 Records)

*The role of infection in gastric diseases, especially helicobacter pylori

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Cluster Syntax Features

Descriptive Terms

pylori 16.3%, gastric 11.8%, infect 6.6%, metastas 4.9%, patient 3.3%, helicobact 3.0%, pylori.infection 2.5%, mesenter 2.5%, gastric.cancer 2.1%, helicobacter.pylori 1.7%, imag 1.2%, cancer 1.2%, calcif 1.0%, mass 1.0%, carcinoid 1.0%, mri 0.8%, gastriti 0.7%, node 0.7%, asd 0.6%, acid.secretion 0.5%, achalasia 0.5%, acid 0.5%, hiv 0.5%, signatur 0.4%, ulcer 0.4%

Discriminating Terms

pylori 10.2%, gastric 7.1%, metastas 3.0%, infect 3.0%, helicobact 1.8%, cell 1.6%, pylori.infection 1.6%, mesenter 1.5%, gastric.cancer 1.3%, helicobacter.pylori 1.0%, activ 0.9%, gene 0.9%, receptor 0.8%, protein 0.8%, calcif 0.6%, tnf 0.6%, carcinoid 0.6%, imag 0.5%, express 0.5%, genom 0.5%, mass 0.5%, kinas 0.5%, mri 0.4%, neuron 0.4%, genet 0.4%

Single Word Terms

patient 14, infect 13, diseas 11, pylori 9, factor 9, helicobact 9, cancer 8, two 7, gastric 7, pattern 6, clinic 6, on 6, ulcer 6, mass 6, risk 6, control 6, bacteri 5, primari 5, small 5, high 5, acid 5, metastas 5, mri 5, popul 5, detect 5

Double Word Terms

helicobacter.pylori 9, pylori.infection 8, gastric.cancer 4, carcinoid.tumors 4, resonance.imaging 4, imaging.mri 4, magnetic.resonance 4, risk.gastric 3, infection.gastric 3, bowel.wall 3, wall.thickening 3, metastases.patients 3, ulcer.disease 3, primary.tumor 3, small.bowel 3, lymph.node 3, patients.imaged 2, mesenteric.metastases 2, liver.metastases 2, odds.ratio 2, arterial.phase 2, nine.patients 2, age.matched 2, bacterial.agents 2, anti.bacterial 2

Triple Word Terms

helicobacter.pylori.infection 4, magnetic.resonance.imaging 4, resonance.imaging.mri 4, risk.gastric.cancer 3, bowel.wall.thickening 3, gastric.acid.secretion 2, soft.tissue.stranding 2, mesenteric.mass.radiating 2, worldwide.pylori.infection 2, infection.gastric.cancer 2, duodenal.ulcer.disease 2, anti.bacterial.agents 2, patients.nodal.metastases 2, surface.laser.desorption 1, ionization.mass.spectrometry 1, gene.expression.profile 1,

data.sources.four 1, kilogram.body.weight 1, humans.animal.models 1, four.electronic.databases 1, patients.men.women 1, men.women.age 1, gastro.oesophageal.reflux 1, bacterial.viral.infections 1, chronic.inflammation.carcinogenesis 1

MRI of carcinoid tumors: spectrum of appearances in the gastrointestinal tract and liver.

Cell wall-deficient (CWD) bacterial pathogens: could amylotrophic lateral sclerosis (ALS) be due to one?

Effect of diet and Helicobacter pylori infection to the risk of early gastric cancer.

Helicobacter pylori infection is a potential protective factor against conventional multiple sclerosis in the Japanese population.

Helicobacter pylori gastritis and gastric physiology.

Impaired gastric relaxation in patients with achalasia.

Evidence for Mycoplasma ssp., Chlamydia pneunomiae, and human herpes virus-6 coinfections in the blood of patients with autistic spectrum disorders.

Calcification and fibrosis in mesenteric carcinoid tumor: CT findings and pathologic correlation.

SENSE: sensitivity encoding for fast MRI.

Predicting progression to AIDS. An evaluation of two approaches.

Prevalence of Helicobacter pylori in patients with gastro-oesophageal reflux disease: systematic review.

Alterations in gastric acidity in patients infected with human immunodeficiency virus.

Midgut carcinoid tumors: CT findings and biochemical profiles.

Helicobacter pylori infection.

Clinical practice. Acute infectious diarrhea.

Carcinoid tumor of the small intestine: MDCT findings with pathologic correlation.

Helicobacter infection, chronic inflammation, and the development of malignancy.

Interleukin-1 polymorphisms associated with increased risk of gastric cancer.

Host-bacterial interactions in Helicobacter pylori infection.

CLUSTER 5 (125-123)

(22 Records)

*Childhood development disorders, especially autism

Cluster Syntax Features

Descriptive Terms

children 39.7%, autism 18.4%, autist 3.2%, children.autism 2.8%, disord 1.0%, disclosur 0.9%, development 0.8%, hai 0.7%, hay.fever 0.7%, concentr 0.6%, atop 0.6%, fever 0.5%, allerg 0.5%, interview 0.5%, diagnost 0.4%, abnorm 0.4%, nni 0.4%, autistic.children 0.4%, sibl 0.4%, level 0.4%, mother 0.4%, theori 0.4%, cotinin 0.3%, autistic.disorder 0.3%, sensitis 0.3%

Discriminating Terms

children 22.8%, autism 10.1%, autist 1.8%, children.autism 1.6%, cell 1.6%, gene 1.0%, protein 0.9%, activ 0.8%, receptor 0.7%, diseas 0.7%, patient 0.6%, tnf 0.6%, disclosur 0.5%, genet 0.5%, human 0.4%, genom 0.4%, neuron 0.4%, express 0.4%, hay.fever 0.4%, hai 0.4%, signal 0.4%, kinas 0.4%, induc 0.4%, respons 0.4%, development 0.3%

Single Word Terms

children 19, autism 13, disord 11, development 10, autist 9, on 9, factor 8, control 8, ag 8, two 7, abnorm 6, design 6, level 6, function 6, social 5, life 5, test 5, number 5, background 5, adult 5, brain 5, sampl 5, reduc 5, diseas 5, environment 5

Double Word Terms

children.autism 6, control.children 4, autistic.children 4, children.adults 4, allergic.diseases 3, children.children 3, immune.system 3, environmental.factors 3, pervasive.developmental 3, developmental.disorders 3, developmental.abnormalities 3, developmental.disorder 2, cerebral.cortex 2, social.developmental 2, liquid.chromatography 2, children.aged 2, children.developmental 2, young.children 2, play.children 2, autism.theories 2, confidence.interval 2, endothelial.cells 2, igm.autoantibodies 2, cross.sectional 2, landau.kleffner 2

Triple Word Terms

children.developmental.disorders 2, levels.children.autism 2, maturation.immune.system 2,

children.children.autism 2, social.developmental.abnormalities 2, landau.kleffner.syndrome 2, genetic.environmental.factors 2, autistic.spectrum.disorder 2, levels.elevated.children 2, autism.pervasive.developmental 2, young.children.autism 2, cerebral.white.matter 1, neurotrophic.factor.bdnf 1, dorsolateral.prefrontal.cortex 1, total.glutathione.concentrations 1, brain.derived.neurotrophic 1, glutathione.oxidized.glutathione 1, excretion.hydroxy.deoxyguanosine 1, urinary.excretion.hydroxy 1, pervasive.developmental.disorders 1, confidence.interval.risk 1, autism.spectrum.disorders 1, factors.oxidative.stress 1, interrater.test.retest 1, test.retest.reliability 1

Localization of white matter volume increase in autism and developmental language disorder.

Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism.

A clinicopathological study of autism.

Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders.

The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism.

Pilot study of a moderate dose multivitamin/mineral supplement for children with autistic spectrum disorder.

Increased excretion of a lipid peroxidation biomarker in autism.

Cohort study of sibling effect, infectious diseases, and risk of atopic dermatitis during first 18 months of life.

Porphyrinuria in childhood autistic disorder: implications for environmental toxicity.

The intestinal microflora in allergic Estonian and Swedish 2-year-old children.

Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey.

Cognitive underpinnings of pretend play in autism.

Mothers with HIV/AIDS and their children: disclosure and guardianship issues.

Passive smoking, salivary cotinine concentrations, and middle ear effusion in 7 year old children.

Family structure, neonatal infection, and hay fever in adolescence.

Visual function in patients undergoing long-term total parenteral nutrition.

CLUSTER 23 (125-123)

(28 Records)

*Iron regulation, and its relation to neural disorders, inflammation, and nitric-oxide mediated apoptosis; glutathione; nitric oxide and its relation to erdf

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Cluster Syntax Features

Descriptive Terms

iron 20.0%, glutathion 19.1%, particl 4.5%, edrf 3.0%, hepcidin 2.4%, heme 2.0%, reductas 2.0%, oxid 1.2%, disulfid 0.9%, glutathione.glutathione 0.9%, glutathione.disulfide 0.9%, imag 0.8%, shock 0.7%, thioredoxin 0.7%, iron.oxide 0.6%, glutathione.reductase 0.6%, simvastatin 0.5%, biolog 0.5%, biological.transport 0.5%, sam 0.5%, gsh 0.5%, erythrocyt 0.4%, cellular 0.4%, carbon 0.4%, peroxidas 0.4%

Discriminating Terms

iron 12.2%, glutathion 11.4%, particl 2.7%, edrf 1.9%, hepcidin 1.5%, heme 1.2%, reductas 1.2%, diseas 0.8%, cell 0.8%, receptor 0.8%, gene 0.8%, patient 0.7%, protein 0.7%, activ 0.6%, tnf 0.6%, glutathione.glutathione 0.6%, glutathione.disulfide 0.6%, disulfid 0.6%, genet 0.6%, express 0.5%, genom 0.5%, kinas 0.5%, thioredoxin 0.4%, iron.oxide 0.4%, human 0.4%

Single Word Terms

oxid 15, cell 14, iron 11, glutathion 10, regul 9, biolog 8, system 8, product 8, factor 8, induc 8, tissu 7, concentr 7, mechan 7, activ 7, major 7, cellular 7, protein 7, reductas 7, reaction 7, stress 6, function 6, two 6, liver 5, particl 5, mediat 5

Double Word Terms

glutathione.reductase 5, glutathione.disulfide 4, oxidative.stress 4, nitric.oxide 4, iron.oxide 3, derived.relaxing 3, iron.loading 3, glutathione.glutathione 3, major.cellular 3, signal.transduction 3, iron.content 3, cell.death 3, relaxing.factor 3, tomography.radiopharmaceuticals 2, imaging.fluorodeoxyglucose 2, hydroxymethylglutaryl.coa 2, induced.oxidative 2, redox.regulation 2, superoxide.dismutase 2, superparamagnetic.iron 2, role.iron 2, pigments.biliverdin 2, disulfide.glutathione 2, transmission.electron 2, glutathione.peroxidase 2

Triple Word Terms

derived.relaxing.factor 3, emission.tomography.radiopharmaceuticals 2, radionuclide.imaging.fluorodeoxyglucose 2, hydroxymethylglutaryl.coa.reductase 2, imaging.fluorodeoxyglucose.f18 2, induced.oxidative.stress 2, iron.induced.oxidative 2, glutathione.glutathione.disulfide 2, response.iron.loading 2, transmission.electron.microscopy 2, iron.oxide.particles 2, disulfide.glutathione.glutathione 2, pigments.biliverdin.bilirubin 2, bile.pigments.biliverdin 2, mechanisms.signal.transduction 2, relaxing.factor.edrf 2, coa.reductase.inhibitors 2, endothelium.derived.relaxing 2, glutathione.disulfide.glutathione 2, positron.emission.tomography 2, superparamagnetic.iron.oxide 2, proliferation.apoptotic.cell 1, leads.lipid.peroxidation 1, oxidative.stress.oxidative 1, apoptotic.cell.death 1

Balancing acts: molecular control of mammalian iron metabolism.

Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide.

Cellular non-heme iron content is a determinant of nitric oxide-mediated apoptosis, necrosis, and caspase inhibition.

S-Adenosylmethionine.

The heme oxygenase system: a regulator of second messenger gases.

Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization.

A COLORIMETRIC MICRO-METHOD FOR THE DETERMINATION OF GLUTATHIONE.

Dextran and albumin derivatised iron oxide nanoparticles: influence on fibroblasts in vitro.

Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor.

Selenium: biochemical role as a component of glutathione peroxidase.

Heme oxygenase-1/carbon monoxide: from basic science to therapeutic applications.

Glutathione and its role in cellular functions.

An asymmetric solar wind termination shock.

Iron and neurodegenerative disorders.

Iron-induced carcinogenesis: the role of redox regulation.

Superparamagnetic iron oxide contrast agents: physicochemical characteristics and applications in MR imaging.

Determination of glutathione and glutathione disulfide in biological samples.

APPENDIX 2 – SAMPLE NEW CONCEPTS FROM SHARED REFERENCES WITH NO MATCHING PHRASES

List of Concepts

Anthocyanins (water-soluble vacuolar pigments that may appear red, purple, or blue according to pH. They belong to a parent class of molecules called flavonoids)

Wogonin; Scutellaria rivularis extracts (Wogonin, a major component isolated from the flavonoid-rich Scutellaria rivularis species)

Trichothecenes (a very large family of chemically related mycotoxins produced by various species of Fusarium, Myrothecium, Trichoderma, Trichothecium, Cephalosporium, Verticimonosporium, and Stachybotrys. Trichothecenes belong to sesquiterpene compounds)

Pyroptosis (Pyroptosis is a form of programmed cell death associated with antimicrobial responses during inflammation. In contrast to apoptosis, pyroptosis requires the function of caspase-1)

Adalimumab (a TNF inhibitor that binds to TNFα, preventing it from activating TNF receptors; however, because TNFα is part of the immune system that protects the body from infection, adalimumab can lead to fatal infections.)

Cooked foods

Flippases (enzymes located in the membrane responsible for aiding the movement of phospholipid molecules between the two leaflets that compose a cell's membrane (transverse diffusion)).

1. Anthocyanins

LINKAGE

The shared reference (Wang and Mazza, 2002) showed anthocyanins induced TNF-alpha production and modulated the immune response. The PD paper (Dreiseitel et al, 2009) showed anthocyanins inhibited monamine oxidases (whose elevated activity has been implicated in neurodegenerative diseases), and the CD paper (Osman et al, 2008) showed that anthocyanins (blueberries) reduced inflammation in colitis.

SHARED REFERENCE

TI Effects of anthocyanins and other phenolic compounds on the production of tumor necrosis factor alpha in LPS/IFN-gamma-activated RAW 264.7 macrophages.
AB Flavonoids have been reported to demonstrate their benefits in lowering oxidative stress and beneficial effects on cardiovascular and chronic inflammatory diseases. Common phenolic compounds, including phenolic acids, flavonols, isoflavones, and- anthocyanins, present in fruits, vegetables, and grains were investigated for their effects on the production of tumor necrosis factor alpha (TNF-alpha) in LPS/IFN-gamma-activated RAW 264.7 macrophages. Gallic acid and (+)-catechin showed small but significant effects, whereas chlorogenic acid had no effect on TNF-alpha production. The flavonol quercetin inhibited TNF-alpha production, but kaempferol and myricetin induced the secretion of TNF-alpha. The isoflavone genistein was an inhibitor of TNF-alpha, whereas daidzein induced TNF-alpha production. Glycosylation of genistein changed its inhibitory effects to TNF-alpha induction, and glycosylation of daidzein had no effect on its activity. Anthocyanidins/anthocyanins and anthocyanin-rich extracts induced TNF-alpha production and acted as modulators of the immune response in activated macrophages. This is the first study to report the effects of anthocyanins and berry extracts on TNF-alpha production.
CR WANG J, 2002, J AGR FOOD CHEM, V50, P4183

PARKINSON'S CITING PAPER

Dreiseitel, A
Korte, G
Schreier, P
Oehme, A
Locher, S
Domani, M
Hajak, G
Sand, PG
TI Berry anthocyanins and their aglycons inhibit monoamine oxidases A and B
SO PHARMACOLOGICAL RESEARCH
AB Monoamine oxidases (MAO) are mitochondrial enzymes that catalyze the oxidation of monoamines in multiple tissues, including the brain. Elevated MAO activity has long been implicated in the

etiology of depression, anxiety, and neurodegenerative disease, fuelling the search for inhibitors in the prevention and treatment of these disorders. We hypothesized that emerging neuroprotective effects of anthocyanins from berry fruits may be explained by an affinity of these polyphenols for MAO isoforms A or B. Using a luminometric MAO assay, 25 anthocyanidins, anthocyanidin-3-glycosides, anthocyanidin-3,5-diglucosides, proanthocyanidins, and phenolic metabolites were examined. For MAO A and B, IC50 values in the low micromolar range were reached by anthocyanidins and anthocyanidin-3-glycosides. as opposed to values in the low millimolar range for phenolic acids. Kinetic analyses, performed with cyanidin and cyanidin-3-glucoside, indicated a competitive interaction of cyanidin with MAO A plus a mixed competitive and non-competitive mode of interaction of cyanidin with MAO B and of cyanidin-3-glucoside with both enzyme isoforms. Thus anthocyanins and their aglycons achieve MAO inhibition in vitro that is compatible with central nervous functionalities. For extrapolation of the present findings to in vivo effects, future studies will need to address in more detail the bioavailability of these dietary constituents.

CROHN'S CITING PAPER

AU Osman, N
Adawi, D
Ahrne, S
Jeppsson, B
Molin, G
TI Probiotics and blueberry attenuate the severity of dextran sulfate sodium (DSS)-induced colitis
SO DIGESTIVE DISEASES AND SCIENCES
AB We studied the anti-inflammatory properties of probiotic strains and blueberry in a colitis model. The disease activity index (DAI) was significantly lower on days 9 and 10 in all groups compared to the colitis control. Myeloperoxidase (MPO) and bacterial translocation to the liver and to the mesenteric lymph nodes (MLN) decreased significantly in all groups compared to colitis control. Cecal Enterobacteriaceae count decreased significantly in blueberry with and without probiotics compared to the other groups. Lactobacillus plantarum reisolated from the cecal content in the presence of blueberry, contrary to Lactobacillus fermentum. Colonic MDA decreased significantly in all groups, except the L. fermentum group, compared to the colitis control. The cecal concentration of acetic, propionic, and butyricbutyric acid was significantly higher in the L. plantarum group, while the L. fermentum group yielded the highest concentration of lactic acid compared with all other groups. Lactobacillus plantarum DSM 15313, Lactobacillus fermentum 35D, and blueberry alone and in combination improve the DAI, reduce bacterial translocation, and reduce inflammation.

2. Wogonin, baicalin, baicalein; Scutellaria rivularis extracts

LINKAGE

The shared reference (Lin and Shieh, 1996) described the anti-inflammatory activity of Scutellaria rivularis extracts. The PD paper (Cheng et al, 2008) described the neuroprotective effect of baicalein, and surmised its cause as increasing the levels of DA and 5-HT in the striatum, increasing the counts of dopaminergic neurons, inhibiting oxidative stress and the astroglia response. The CD paper (Latella et al, 2008) showed antifibrotic Scutellaria extracts are effective in preventing colonic fibrosis in TNBS-induced colitis, with the antifibrotic mechanism of action mediated by the inhibition of TGF-beta 1/Smad3 pathway.

SHARED REFERENCE

TI The anti-inflammatory activity of Scutellaria rivularis extracts and its active components, baicalin, baicalein and wogonin.
AB Five extracts (n-hexane, chloroform, ethyl acetate, n-butanol and water) of Scutellaria rivularis Benth. were evaluated for their anti-inflammatory activity against carrageenan-induced paw edema in rats and compared with indomethacin. The result indicated that chloroform extract proved to be the most effective in all of the extracts. Consequently, three major components (baicalin, baicalein and wogonin) of the chloroform extract were further tested for their anti-inflammatory activity using the same model. It was found that baicalin exhibits the greatest inhibition activity against carrageenan-induced rat paw edema.
CR LIN CC, 1996, AM J CHINESE MED, V24, P31

PARKINSON'S CITING PAPER

AU Cheng, YX
He, GR
Mu, X
Zhang, TT
Li, XX
Hu, JJ
Xu, B
Du, GH
TI Neuroprotective effect of baicalein against MPTP neurotoxicity: Behavioral, biochemical and immunohistochemical profile
SO NEUROSCIENCE LETTERS
AB 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) causes the damage of dopaminergic neurons as seen in Parkinson's disease (PD). Oxidative stress has been implicated in the pathogenesis of PD. Baicalein, isolated from the traditional Chinese herbal medicine Huangqin (Scutellaria baicalensis Georgi) has been, shown to have antioxidant effects. Here we investigated the effect of baicalein on MPTP-induced neurotoxicity in mice. Pretreatment with baicalein for a week was followed by challenge with MPTP for 4 consecutive days; the subsequent behavioral, biochemical and immunohistochemical manifestations in mice were determined and compared to those in

untreated mice and mice challenged only with MPTP. The present study showed that baicalein could improve the abnormal behavior in MPTP-treated mice. The protective effect may be caused by increasing the levels of DA and 5-HT in the striatum, increasing the counts of dopaminergic neurons, inhibiting oxidative stress and the astroglia response. These results suggest that baicalein possesses potent neuroprotective activity and may be a potential anti-Parkinson's disease drug that is worthy of further study.

CROHN'S CITING PAPER

AU Latella, G
Sferra, R
Vetuschi, A
Zanninelli, G
D'Angelo, A
Catitti, V
Caprilli, R
Gaudio, E
TI Prevention of colonic fibrosis by Boswellia and Scutellaria extracts in rats with colitis induced by 2,4,5-trinitrobenzene sulphonic acid
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION
AB Background Currently, no effective preventive measures or medical therapies are available for intestinal fibrosis and, thus, surgery remains the only available strategy in the management of fibrostenotic enteropathies, especially Crohn's disease. The aim of this study was to evaluate the efficacy of a combined therapy of anti-inflammatory Boswellia and antifibrotic Scutellaria extracts on the development of colonic fibrosis in rats. Materials and methods Chronic colonic inflammation-associated fibrosis was induced in rats by intracolonic administration of 2,4,5-trinitrobenzene sulphonic acid (TNBS). Sixty-four healthy male Sprague-Dawley rats were assigned to five groups: 8 controls, 14 TNBS, 14 TNBS orally treated with Boswellia extracts (50 mg kg(-1) day(-1)), 14 TNBS orally treated with Scutellaria extracts (150 mg kg(-1) day(-1)), and 14 TNBS orally treated with both Boswellia (50 mg kg(-1) day(-1)) and Scutellaria extracts (150 mg kg(-1) day(-1)). The colon was removed after 21 days of treatment and assessed by macroscopic, histological, morphometric and immunohistochemical analyses. For immunohistochemical analysis, alpha-smooth muscle actin (alpha-SMA), collagen types I-III, connective tissue growth factor (CTGF), transforming growth factor-beta1 (TGF-beta 1), Smad3, Smad7 and CD3 antibodies were used. Results Combined oral administration of Boswellia and Scutellaria significantly improved the course and macroscopic findings of TNBS-induced chronic colitis assessed by disease activity index, colon weight, length, adhesions, strictures, dilatation, thickness, oedema, ulcerations and extension of damage. The histological severity of the colonic fibrosis was also notably improved by the treatment and associated with a significant reduction in the colonic expression of alpha-SMA, collagen I-III, CTGF, TGF-beta 1, Smad3, and Smad7. Conclusions These data demonstrate that the prophylactic administration of anti-inflammatory Boswellia and antifibrotic Scutellaria extracts is

effective in preventing colonic fibrosis in TNBS-induced colitis. Their antifibrotic mechanism of action seems to be mediated by the inhibition of TGF-beta 1/Smad3 pathway.

3. Trichothecenes

LINKAGE

The shared reference (Pestka et al, 2004) states that trichothecenes are mycotoxins that can be immunostimulatory or immunosuppressive depending on dose, exposure frequency and timing of functional immune assay, and can induce MAPK-activation. The PD paper (Islam et al, 2008) shows that Satratoxin G (a macrocyclic trichothecene mycotoxin) induced apoptosis (in PC-12 neuronal cells) mediated by RNA-activated protein kinase. The CD papers (Maresca et al, 2008; Pinton et al, 2009) showed that the pro-inflammatory activity of enteropathogenic mycotoxins on human intestinal epithelial cells is mediated by both direct and indirect effects.

SHARED REFERENCE

TI Cellular and molecular mechanisms for immune modulation by deoxynivalenol and other trichothecenes: unraveling a paradox.
AB Macrophages, T cells, and B cells of the immune system are central targets of deoxynivalenol (DON) and other trichothecenes-mycotoxins that can be immunostimulatory or immunosuppressive depending on dose, exposure frequency and timing of functional immune assay. Notably, low dose trichothecene exposure transcriptionally and post-transcriptionally upregulates expression of cytokines, chemokines and inflammatory genes with concurrent immune stimulation, whereas high dose exposure promotes leukocyte apoptosis with concomitant immune suppression. DON and other trichothecenes, via a mechanism known as the ribotoxic stress response, bind to ribosomes and rapidly activate mitogen-activated protein kinases (MAPKs). The latter are important transducers of downstream signaling events related to immune response and apoptosis. Using cloned macrophages, our laboratory has identified two critical upstream transducers of DON-induced MAPK activation. One transducer is double-stranded RNA-(dsRNA)-activated protein kinase (PKR), a widely-expressed serine/theonine protein kinase that can be activated by dsRNA, interferon, and other agents. The second transducer is hematopoetic cell kinase (Hck), a non-receptor associated Src family kinase. Inhibitors and gene silencing studies have revealed that Hck and PKR play roles in DON induced gene expression and apoptosis. Future studies should focus on the molecular linkages between these kinases and trichothecene toxicity.
CR PESTKA JJ, 2004, TOXICOL LETT, V153, P61

PARKINSON'S CITING PAPER

AU Islam, Z
Hegg, CC
Bae, HK
Pestka, JJ
TI Satratoxin G-induced apoptosis in PC-12 neuronal cells is mediated by PKR and caspase independent
SO TOXICOLOGICAL SCIENCES

AB Satratoxin G (SG) is a macrocyclic trichothecene mycotoxin produced by Stachybotrys chartarum, a mold suggested to play an etiologic role in damp building-related illnesses. Acute intranasal exposure of mice to SG specifically induces apoptosis in olfactory sensory neurons of the nose. The PC-12 rat pheochromocytoma cell model was used to elucidate potential mechanisms of SG-induced neuronal cell death. Agarose gel electrophoresis revealed that exposure to SG at 10 ng/ml or higher for 48-h induced DNA fragmentation characteristic of apoptosis in PC-12 cells. SG-induced apoptosis was confirmed by microscopic morphology, hypodiploid fluorescence and annexin V-fluorescein isothiocyanate (FITC) uptake. Messenger RNA expression of the proapoptotic genes p53, double-stranded RNA-activated protein kinase (PKR), BAX, and caspase-activated DNAse was significantly elevated from 6 to 48 h after SG treatment. SG also induced apoptosis and proapoptotic gene expression in neural growth factor-differentiated PC-12 cells. Although SG-induced caspase-3 activation, caspase inhibition did not impair apoptosis. Moreover, SG induced nuclear translocation of apoptosis-inducing factor (AIF), a known contributor to caspase-independent neuronal cell death. SG-induced apoptosis was not affected by inhibitors of oxidative stress or mitogen-activated protein kinases but was suppressed by the PKR inhibitor C16 and by PKR siRNA transfection. PKR inhibition also blocked SG-induced apoptotic gene expression and AIF translocation but not caspase-3 activation. Taken together, SG-induced apoptosis in PC-12 neuronal cells is mediated by PKR via a caspase-independent pathway possibly involving AIF translocation.

CROHN'S CITING PAPER

Maresca, M
Yahi, N
Younes-Sakr, L
Boyron, M
Caporiccio, B
Fantini, J
TI Both direct and indirect effects account for the pro-inflammatory activity of enteropathogenic mycotoxins on the human intestinal epithelium: Stimulation of interleukin-8 secretion, potentiation of interleukin-1 beta effect and increase in the transepithelial passage of commensal bacteria
SO TOXICOLOGY AND APPLIED PHARMACOLOGY
AB Mycotoxins are fungal secondary metabolites responsible of food-mediated intoxication in animals and humans. Deoxynivalenol, ochratoxin A and patulin are the best known enteropathogenic mycotoxins able to alter intestinal functions resulting in malnutrition, diarrhea, vomiting and intestinal inflammation in vivo. Although their effects on intestinal barrier and transport activities have been extensively characterized, the mechanisms responsible for their pro-inflammatory effect are still poorly understood. Here we investigated if mycotoxin-induced intestinal inflammation results from a direct and/or indirect pro-inflammatory activity of these mycotoxins on human intestinal epithelial cells, using differentiated Caco-2 cells as model and interleukin 8 (IL-8)

as an indicator of intestinal inflammation. Deoxynivalenol was the only mycotoxin able to directly increase IL-8 secretion (10- to 15-fold increase). We also investigated if these mycotoxins could indirectly stimulate IL-8 secretion through: (i) a modulation of the action of pro-inflammatory molecules such as. the interleukin-1beta (IL-1 beta), and/or (ii) an increase in the transepithelial passage of non-invasive commensal Escherichia coli. We found that deoxynivalenol, ochratoxin A and patulin all potentiated the effect of IL-1 beta on IL-8 secretion (ranging from 35% to 138% increase) and increased the transepithelial passage of commensal bacteria (ranging from 12- to 1544-fold increase). In addition to potentially exacerbate established intestinal inflammation, these mycotoxins may thus participate in the induction of sepsis and intestinal inflammation in vivo. Taken together, our results suggest that the pro-inflammatory activity of enteropathogenic mycotoxins is mediated by both direct and indirect effects.

AU Pinton, P
Nougayrede, JP
Del Rio, JC
Moreno, C
Marin, DE
Ferrier, L
Bracarense, AP
Kolf-Clauw, M
Oswald, IP
TI The food contaminant deoxynivalenol, decreases intestinal barrier permeability and reduces claudin expression
SO TOXICOLOGY AND APPLIED PHARMACOLOGY
AB The gastrointestinal tract represents the first barrier against food contaminants as well as the first target for these toxicants. Deoxynivalenol (DON) is a mycotoxin that commonly contaminates cereals and causes various toxicological effects. Through consumption of contaminated cereals and cereal products, human and pigs are exposed to this mycotoxin. Using in vitro, ex vivo and in vivo approaches, we investigated the effects of DON on the intestinal epithelium. We demonstrated that, in intestinal epithelial cell lines from porcine (IPEC-1) or human (Caco-2) origin, DON decreases trans-epithelial electrical resistance (TEER) and increases in a time and dose-dependent manner the paracellular permeability to 4 kDa dextran and to pathogenic Escherichia coli across intestinal cell monolayers. In pig explants treated with DON, we also observed an increased permeability of intestinal tissue. These alterations of barrier function were associated with a specific reduction in the expression of claudins, which was also seen in vivo in the jejunum of piglets exposed to DON-contaminated feed. In conclusion, DON alters claudin expression and decreases the barrier function of the intestinal epithelium. Considering that high levels of DON may be present in food or feed, consumption of DON-contaminated food/feed may induce intestinal damage and has consequences for human and animal health.

4. Diversity of cell death processes, including pyroptosis (Pyroptosis is a form of programmed cell death associated with antimicrobial responses during inflammation. In contrast to apoptosis, pyroptosis requires the function of caspase-1)

LINKAGE

The shared reference (Fink and Cookson, 2005) describes the different types of cell death and the different mechanisms involved. The Parkinson's citing paper (Paris et al, 2009) showed that the copper-dopamine complex induces mitochondrial autophagy preceding caspase-independent (non-pyroptosis) apoptotic cell death. The Crohn's citing paper (Franchi et al, 2009) describes inflammasomes in caspase-1 activation (a pre-condition for pyroptosis) and subsequent release of proinflammatory cytokines such as interleukin-1 beta. The common theme is mechanisms other than pure necrosis or apoptosis cell death, and their subsequent role in neurodegenerative and inflammatory diseases.

SHARED REFERENCE

TI Apoptosis, pyroptosis, and necrosis: mechanistic description of dead and dying eukaryotic cells.
AB A wide variety of pathogenic microorganisms have been demonstrated to cause eukaryotic cell death, either as a consequence of infecting host cells or by producing toxic products. Pathogen-induced host cell death has been characterized as apoptosis in many of these systems. It is increasingly being recognized that cell death with some of the features of apoptosis may result from a variety of molecular pathways and that experimental techniques used to identify cell death often do not distinguish among these mechanisms. We propose that a clear understanding of the diversity of processes mediating cell death has been obscured by the simplicity of the nomenclature system commonly employed to describe eukaryotic cell death. This review presents a perspective on eukaryotic cell death and discusses experimental techniques used to study these processes.
CR FINK SL, 2005, INFECT IMMUN, V73, P1907

PARKINSON'S CITING PAPER

AU Paris, I
Perez-Pastene, C
Couve, E
Caviedes, P
LeDoux, S
Segura-Aguilar, J
TI Copper center dot Dopamine Complex Induces Mitochondrial Autophagy Preceding Caspase-independent Apoptotic Cell Death
SO JOURNAL OF BIOLOGICAL CHEMISTRY
AB Parkinsonism is one of the major neurological symptoms in Wilson disease, and young workers who worked in the copper smelting industry also developed Parkinsonism. We have reported the specific neurotoxic action of copper center dot dopamine complex in neurons

with dopamine uptake. Copper center dot dopamine complex (100 mu M) induces cell death in RCSN-3 cells by disrupting the cellular redox state, as demonstrated by a 1.9-fold increase in oxidized glutathione levels and a 56% cell death inhibition in the presence of 500 mu M ascorbic acid; disruption of mitochondrial membrane potential with a spherical shape and well preserved morphology determined by transmission electron microscopy; inhibition (72%, $p < 0.001$) of phosphatidylserine externalization with 5 mu M cyclosporine A; lack of caspase-3 activation; formation of autophagic vacuoles containing mitochondria after 2 h; transfection of cells with green fluorescent protein-light chain 3 plasmid showing that 68% of cells presented autophagosome vacuoles; colocalization of positive staining for green fluorescent protein-light chain 3 and Rhod-2AM, a selective indicator of mitochondrial calcium; and DNA laddering after 12-h incubation. These results suggest that the copper center dot dopamine complex induces mitochondrial autophagy followed by caspase-3-independent apoptotic cell death. However, a different cell death mechanism was observed when 100 mu M copper center dot dopamine complex was incubated in the presence of 100 mu M dicoumarol, an inhibitor of NAD(P) H quinone: oxidoreductase (EC 1.6.99.2, also known as DT-diaphorase and NQ01), because a more extensive and rapid cell death was observed. In addition, cyclosporine A had no effect on phosphatidylserine externalization, significant portions of compact chromatin were observed within a vacuolated nuclear membrane, DNA laddering was less pronounced, the mitochondria morphology was more affected, and the number of cells with autophagic vacuoles was a near 4-fold less.
[Cu-DA complex-induced mitochondrial autophagy is an early event of cell death that occurs after 2 h of exposure, followed by a caspase 3-independent apoptotic cell death characterized by late oligonucleosomal DNA fragmentation at 12 h.]

CROHN'S CITING PAPER

AU Franchi, L
 Wamer, N
 Viani, K
 Nunez, G
TI Function of Nod-like receptors in microbial recognition and host defense
SO IMMUNOLOGICAL REVIEWS
AB Nucleotide oligomerization domain (NOD)-like receptors (NLRs) are a specialized group of intracellular proteins that play a critical role in the regulation of the host innate immune response. NLRs act as scaffolding proteins that assemble signaling platforms that trigger nuclear factor-kappa B and mitogen-activated protein kinase signaling pathways and control the activation of inflammatory caspases. Importantly, mutations in several members of the NLR family have been linked to a variety of inflammatory diseases consistent with these molecules playing an important role in host-pathogen interactions and the inflammatory response. In this review, we focus on the role of Nod1 and Nod2 in host defense and in particular discuss recent finding regarding the role of Nlrc4,

Nlpr1, and Nlrp3 inflammasomes in caspase-1 activation and subsequent release of proinflammatory cytokines such as interleukin-1 beta.

5. Adalimumab

LINKAGE

The shared reference (Scheinfeld, 2004) focuses on side effects from tnf-alpha blockers, including Adalimumab. The Parkinson's citing paper (McCoy et al, 2008) showed that inhibition of tnf through nigral infusion of dominant-negative (DN-TNF) protein attenuates dopaminergic neuron loss and behavioral deficits resulting from striatal dopamine depletion. The Crohn's citing paper(s) (Jacobi et al, 2006; Biancone et al, 2007) describe the use of tnf-alpha blockers for 1) treating inflammatory skin disorders, including undesirable side effects, and 2) treating inflammatory bowel disorders despite potential side-effects of increased cancer risk.

SHARED REFERENCE

TI A comprehensive review and evaluation of the side effects of the tumor necrosis factor alpha blockers etanercept, infliximab and adalimumab.
AB For more than 5 years, infliximab and etanercept have been utilized to treat rheumatoid arthritis and Crohn's disease. There is therefore much post-approval data on their side effects. A variety of Medline searches were done at the beginning of June 2004 using the terms 'etanercept', 'infliximab' and 'adalimumab' and the words 'lymphoma', 'infection', 'congestive heart failure', 'demyelinating disease', 'lupus', 'antibodies', 'injection site reaction', 'systemic', 'side effects' and 'skin'. Approximately 150 articles were so identified. In addition, FDA and manufacturers' data obtained by internet searches using Google were reviewed. The important side effects that have been most extensively related to TNFalpha blockers include: lymphoma, infections, congestive heart failure, demyelinating disease, a lupus-like syndrome, induction of auto-antibodies, injection site reactions, and systemic side effects. The risk of these side effects is very low. Nevertheless, it is important for clinicians to be aware of these side effects when prescribing therapy.
CR SCHEINFELD N, 2004, J DERMATOL TREAT, V15, P280

PARKINSON'S CITING PAPER

AU McCoy, MK
Ruhn, KA
Martinez, TN
McAlpine, FE
Blesch, A
Tansey, MG
TI Intranigral lentiviral delivery of dominant-negative TNF attenuates neurodegeneration and behavioral deficits in hemiparkinsonian rats
SO MOLECULAR THERAPY
AB Neuroinflammatory processes have been implicated in the progressive loss of ventral midbrain dopaminergic (DA) neurons that give rise to Parkinson's disease (PD), a late-onset movement

disorder that affects 2% of the population over the age of 70 years. We have shown earlier, in two rat models of PD, that inhibition of the proinflammatory cytokine tumor necrosis factor (TNF) through nigral infusion of dominant-negative (DN-TNF) protein (XENP345) attenuates DA neuron loss. The objectives of this study were to develop a constitutive lentiviral vector encoding dominate-negative TNF, and to determine whether a gene therapy approach to deliver DN-TNF directly into the rodent substantia nigra could prevent or attenuate neurotoxin-induced DA neuron loss and associated behavioral deficits. Here we demonstrate that a single injection of lentivirus-expressing DN-TNF into rat substantia nigra, administered concomitant with a striatal 6-hydroxydopamine lesion, results in sufficiently high expression of inhibitor in vivo to attenuate both DA neuron loss and behavioral deficits resulting from striatal dopamine depletion. Our findings demonstrate the feasibility and efficacy of dominant-negative TNF gene transfer as a novel neuroprotective strategy to prevent or delay nigrostriatal pathway degeneration. This strategy holds the potential for therapeutic application in the treatment of PD.

CROHN'S CITING PAPER

AU Jacobi, A
 Mahler, V
 Schuler, G
 Hertl, M
TI Treatment of inflammatory dermatoses by tumour necrosis factor antagonists
SO JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY
AB Background The treatment of inflammatory skin diseases is at present often empirical as causal therapeutic approaches, based on an incomplete knowledge of the immune pathogenesis, are mostly unavailable. The currently applied treatments can in fact lead to remission of the disease; however, under certain circumstances undesirable side-effects must be expected. On the basis of experience gained in cytokine modulation therapy of chronic inflammatory diseases such as rheumatoid arthritis and psoriasis, the application of TNF-alpha inhibitors represents a novel, more specific, and effective therapeutic option for distinct chronic inflammatory diseases. Patients and methods The current status of the therapeutic effect of TNF-alpha blockers is discussed based on our own observations and a review of the current literature. Also discussed are potential undesirable side-effects and possible contraindications of this therapy. Results and conclusions Based on recent findings, the use of TNF-alpha blockers seems to be promising in the treatment of therapy-resistant inflammatory dermatoses. At present, guidelines for indications and contraindications of anti-TNF-alpha treatment of inflammatory skin disorders are rare. Such guidelines are necessary to improve the efficacy of anticytokine treatment and the reduction of side-effects.

AU Biancone, L

Calabrese, E
Petruzziello, C
Pallone, F
TI Treatment with biologic therapies and the risk of cancer in patients with IBD
SO NATURE CLINICAL PRACTICE GASTROENTEROLOGY & HEPATOLOGY
AB The proven involvement of cytokines in the pathophysiology of IBD has led to the development of powerful, selective, anticytokine drugs - so-called biologics - as a therapy for IBD. Although the efficacy of infliximab, a chimeric monoclonal IgG(1) antibody directed against tumor necrosis factor, is proven and the use of biologic agents is growing worldwide, there is concern about their long-term safety, which includes the risk of developing cancer. An increased risk of malignancies, particularly lymphoma, has been reported in some studies of infliximab-treated patients with IBD; however, the increased risk could be caused by the underlying chronic disease, severity of the disease, concomitant medications (e.g. conventional immunomodulators), infliximab itself, or all of these variables. At present, the data do not provide clear evidence for a causal association between infliximab and the increased cancer risk. In appropriately selected patients with severe, refractory Crohn's disease, the benefits of biologic therapy seem to outweigh the cancer risk. Multicenter, case - control studies in large populations, with a long-term follow-up are needed to define the outcome of patients with IBD treated with biologic therapies.

6. Cooked foods

LINKAGE

The shared reference (Layton et al, 1995) describes the cancer risk of heterocyclic amines (pyrolysis products formed during the cooking of meats/fish). The Parkinson's citing paper (Louis et al, 2008) showed that elevated blood concentrations of the co-mutagenic beta-carboline harmane, also found in cooked meats, are associated with elevated levels of essential tremor. The Crohn's citing paper (Forte et al, 2008) describes the increased risk of colorectal cancer associated with consumption of meat, and suggests that mutagenic compounds such as heterocyclic amines could be a possible causative factor.

SHARED REFERENCE

TI Cancer risk of heterocyclic amines in cooked foods: an analysis and implications for research.
AB Heterocyclic amines (HAs) are formed as pyrolysis products during the cooking of meats/fish. These substances are potent mutagens in the Ames/Salmonella assay and are also carcinogens in laboratory animals. In order to assess the magnitude of the cancer risk posed by their presence in the US diet, we estimated the average intakes of HAs, based on analyses of the concentrations of HAs in cooked foods and data from a dietary survey of the US population and quantified the cancer potencies of the individual compounds using dose-response data from animal bioassays. Measured concentrations of HAs in cooked foods were taken from a major review of the open literature. Only those concentrations that were associated with normal cooking conditions were chosen for use in estimating dietary intakes. The average consumption of HA-bearing foods was determined by analyzing statistically the intakes of 3563 individuals who provided 3 day dietary records in a USDA sponsored random survey of the US population during 1989. Dietary intakes of the five principal HAs in descending order were 2-amino-1-methyl-6-phenylimidazo [4,5-b]pyridine (PhIP) > 2-amino-9H-pyrido[2,3-b]indole (A alpha C) > 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx) > 2-amino-3,4,8-trimethylimidazo[4,5-f]quinoxaline (DiMeIQx) > 2-amino-3-methylimidazo[4,5-f]quinoline (IQ). The carcinogenic potencies, in contrast, were almost the reverse order: IQ > DiMeIQx > MeIQx > PhIP > A alpha C. An upper-bound estimate of the incremental cancer risk is 1.1 x 10(-4), using cancer potencies based on a body surface area basis. Nearly half (46%) of the incremental risk was due to ingestion of PhIP. Consumption of meat and fish products contributed the most (approximately 80%) to total risk.
CR LAYTON DW, 1995, CARCINOGENESIS, V16, P39

PARKINSON'S CITING PAPER

AU Louis, ED
Jiang, W
Pellegrino, KM
Rios, E

Factor-Litvak, P
Henchcliffe, C
Zheng, W
TI Elevated blood harmane (1-methyl-9H-pyrido[3,4-b]indole) concentrations in essential tremor
SO NEUROTOXICOLOGY
AB Essential tremor (ET) is a widespread late-life neurological disease. Genetic and environmental factors likely play an etiological role. Harmane (1-methyl-9H-pyrido[3,4-b]indole) is a potent tremor-producing neurotoxin. In 2002, we demonstrated elevated blood harmane concentrations in an initial sample of 100 ET cases compared to 100 controls. Between 2002 and 2007, we assembled a new and larger sample of ET cases and controls. We now attempt to replicate our previous findings. Cases and controls were frequency-matched on age, gender, and race. Blood harmane concentrations were quantified by high-performance liquid chromatography. Subjects comprised 150 ET cases and 135 controls (mean age 65.3 +/- 15.5 vs. 65.5 +/- 14.2 years, p = 0.94). Mean log blood harmane concentration was similar to 50% higher in cases than controls (0.50 +/- 0.54 g(-10)/ml vs. 0.35 +/- 0.62 g(-10)/ml, p = 0.038). In a logistic regression analysis, log blood harmane concentration was associated with ET (ORadjusted 1.56, 95% CI 1.01-2.42, p = 0.04), and odds of ET was 1.90 (95% CI 1.07-3.39, p = 0.029) in the highest versus lowest log blood harmane tertile. Log blood harmane was highest in ET cases with familial ET (0.53 +/- 0.57 g(-10)/ml), intermediate in cases with sporadic ET (0.43 +/- 0.45 g(-10)/ml) and lowest in controls (0.35 +/- 0.62 g(-10)/ml) (test for trend, p = 0.026). Blood harmane appears to be elevated in ET. The higher concentrations in familial ET suggests that the mechanism may involve genetic factors

CROHN'S CITING PAPER

TI Dietary chemoprevention of colorectal cancer
SO ANNALI ITALIANI DI CHIRURGIA
AB AIMS AND BACKGROUND: Colorectal cancer is the second cause of morbidity and death in Italy. Genetic and environmental factors, i.e. inappropriate nutrition, are strongly involved in the aetiology of colon cancer. In the present review the authors analyze the possible mechanisms by which certain nutritive factors may interfere with the complex process of carcinogenesis. METHODS: The authors identify studies by a literature search of Medline from January 1, 1970, through December 31, 2006 RESULTS: The mechanism of every protective compound is detailed, in particular the impact of antioxidant vitamins and minerals on tumor development. At present, the data suggest that vegetables are associated with lower risk and that their fibre content alone does not account for this association. Further, meat consumption is associated with an increased risk but this, too, is not explained solely by its fat content. Several microconstituents of the diet may be associated with reduced risk, including folate, methionine, calcium and vitamin D. Short chain fatty acids also contribute to colonic health. Nevertheless agricultural products contain several dangerous pesticides. Mutagenic compounds, particularly heterocyclic amines,

produced when protein is cooked, plausibly explain the meat association. CONCLUSIONS: Healthy nutrition is a necessary hut not sufficient condition for colon cancer prevention: accepted the feasibility of an accurate control on every patient’s diet, frequently the difficulty encountered in nutritional chemoprevention is to establish individual metabolic profiles.

7. Flippases (enzymes located in the membrane responsible for aiding the movement of phospholipid molecules between the two leaflets that compose a cell's membrane (transverse diffusion)).

LINKAGE

The shared reference (Higgins and Gottesman, 1992) addresses the transport of drugs out of cells. The Parkinson's citing paper (Pahnke et al, 2009) proposes that the activation of the excretion function of the blood-brain barrier might help to achieve better results in trials targeting the dissolution of cerebral amyloid-beta aggregates in Alzheimer's Disease. The Crohn's citing paper (Annese et al, 2006) examines two SNP polymorphisms of the MDR1 gene (whose product the P-glycoprotein (P-gp) functions as a transmembrane efflux pump thus influencing disposition and response of many drugs, some of whom (i.e. glucocorticoids) are central to IBD therapy. In addition P-gp is highly expressed in many epithelial surfaces, including the gastrointestinal tract (G-I) with a putative role in decreasing the absorption of endogenous or exogenous toxins, and perhaps host-bacteria interaction), and shows that a significant association between one allele and geneotype has been found with ulcerative colitis, whereas none could be found with CD.

SHARED REFERENCE

TI Is the multidrug transporter a flippase?
AB The phenomenon of multidrug resistance is correlated with the presence of a membrane protein, P-glycoprotein, which pumps a wide variety of drugs out of cells thus reducing their toxicity. However, the mechanism of this pumping action remains unclear. In this article, we suggest that several properties of the multidrug transporter may be explained if it acts as a 'flippase' to transport drugs from the inner leaflet of the lipid bilayer to the outer or to the external medium.
CR HIGGINS CF, 1992, TRENDS BIOCHEM SCI, V17, P18

PARKINSON'S CITING PAPER

PT J
AU Pahnke, J
Walker, LC
Scheffler, K
Krohn, M
TI Alzheimer's disease and blood-brain barrier function-Why have anti-beta-amyloid therapies failed to prevent dementia progression?
SO NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS
AB Proteopathies of the brain are defined by abnormal, disease-inducing protein deposition that leads to functional abrogation and death of neurons. Immunization trials targeting the removal of amyloid-beta plaques in Alzheimer's disease have so far failed to stop the progression of dementia, despite autopsy findings of

reduced plaque load. Here, we summarize current knowledge of the relationship between AD pathology and blood-brain barrier function, and propose that the activation of the excretion function of the blood-brain barrier might help to achieve better results in trials targeting the dissolution of cerebral amyloid-beta aggregates. We further discuss a possible role of oligomers in limiting the efficacy of immunotherapy

CROHN'S CITING PAPER

PT J
AU Annese, V
Valvano, MR
Palmieri, O
Latiano, A
Bossa, F
Andriulli, A
TI Multidrug resistance 1 gene in inflammatory bowel disease: A meta-analysis
SO WORLD JOURNAL OF GASTROENTEROLOGY
AB The MDR1 gene is an attractive candidate gene for the pathogenesis of inflammatory bowel disease (IBD) and perhaps response to therapy, with evidences at both functional and genetic levels. Its product, the P-glycoprotein (P-gp) functions as a transmembrane efflux pump thus influencing disposition and response of many drugs, some of whom (i.e. glucocorticoids) central to IBD therapy. In addition P-gp is highly expressed in many epithelial surfaces, included gastrointestinal tract (G-I) with a putative role in decreasing the absorption of endogenous or exogenous toxins, and perhaps host-bacteria interaction. Many genetic variations of MDR1 gene has been described and in some instances evidences for different P-gp expression as well drugs metabolism have been provided. However data are often conflicting due to genetic heterogeneity and different methodologies employed. Perhaps the greatest piece of evidence of the physiological importance of P-gp in the G-I tract has come from the description of the mdr1 knock-out mice model, which develops a spontaneous colitis in a specific pathogen-free environment. Studies investigating MDR1 gene polymorphism and predisposition to IBD have also shown conflicting results, owing to the known difficulties in complex diseases, especially when the supposed genetic contribution is weak. In this study we have undertaken a meta-analysis of the available findings obtained with two SNPs polymorphism (C3435T and G2677T/A) in IBD;a significant association of 3435T allele and 3435TT genotype has been found with UC (OR = 1.17, P = 0.003 and OR = 1.36, P =

0.017, respectively). In contrast no association with CD and the G2677T/A polymorphism could be demonstrated.