



Virulence Factor Ontology for Biosecurity

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MSR

Problem

- **Virulence factors are what make people, animals, and plants sick**

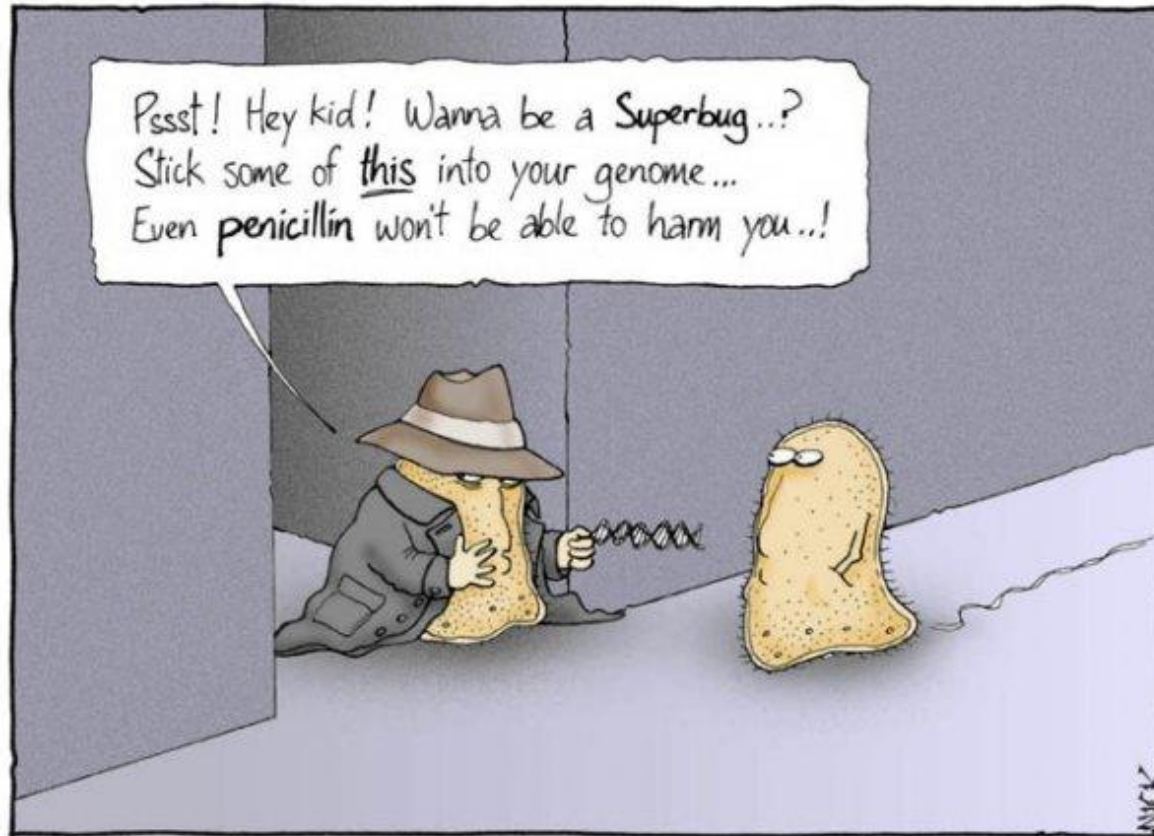
- **Pathogens use one or more of them**
 - There are many virulence factors
 - The virulence factor name may not tell you what it does

- **Mechanisms used may be shared by many pathogens**

- **The same kind of virulence factor may have a DIFFERENT name in a DIFFERENT closely related pathogen**

Background

The Antibiotic Resistance



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Objective

- **Create the ontologies/semantics for a catalog of known virulence factors and organisms**
 - **Goal: create an ontology that cuts across organisms and fields**
- **Populate by mapping existing sequence data**
 - **Using several existing virulence sequence databases and annotation efforts**
- **Potential uses**
 - **Detection of pathogens/virulence factors in environmental (metagenomic) samples**
 - **Development/discovery of drugs against pathogens**

Activities

- **Draft an ontology/semantics**
 - Working with various groups who have the starting ontologies, end-users, and generators of the primary data

- **Expand use cases**
 - Continue finding more use cases to help shape the ontology

Highlight

BVF (Gemina)

TVFac (LANL)

- ☐ Bacterial Virulence Factors
 - ☐ Adherence and Colonization Factors
 - ☐ Capsules and Surface Components
 - ☐ **Drug and Multidrug Resistance Factors**
 - ☐ Invasins
 - ☐ Pathogenesis Assistance Factors
 - ☐ Siderophores
 - ☐ **Toxins**
 - Adenylate Cyclase Toxin
 - Cord Factors
 - Cytotoxins
 - Diphtheria Toxin
 - Endotoxins
 - Enterotoxins
 - Exfoliatins
 - Exotoxins
 - Tetanus Toxin
 - ☐ Virulence Factors Encoded in Plasmids

- ☐ Toxin and virulence factors
 - ☐ Adhesins
 - ☐ Anti-immune responses
 - ☐ **Antibiotic Resistance**
 - ☐ **Endotoxins**
 - Endotoxin biosynthesis
 - Exotoxin activity
 - A-B toxins
 - ADP-ribosylating toxins
 - Enterotoxins
 - Heat-stable toxins
 - Insecticidal
 - Membrane-damaging toxins
 - Neurotoxins
 - Proteolytic toxins
 - RTX toxins
 - Superantigens
 - ☐ Intracellular survival
 - ☐ Invasins
 - ☐ Iron Acquisition
 - ☐ Phage-related
 - ☐ Regulation
 - ☐ Transport and secretion systems

Classes not captured in other ontologies

- Drug Resistance**
 - Antibiotics
 - Antivirals
- Toxins**

Mappings to existing ontologies

Gene Ontology/PAMGO
PATO, Sequence Ontology
Taxon IDs, ChemBI, MESH

Can we identify and annotate all known cholera toxins from databases and scientific literature with existing and possible ontology terms?

Demonstration

Vibrio Cholerae Toxins

■ Examples of toxins

- Cholera toxin subunit A (ctxA) →
- Accessory cholera enterotoxin (ace)
- Hemolysin (hlyA)
- Hemagglutinin protease (hap) →

Signal pathway activating toxin
cAMP signaling activating toxin

Pore-forming toxin

■ Examples of non-toxins with toxin in their names that are virulence factors

- Cholera toxin subunit B (ctxB)—delivery for ctxA
- Toxin coregulated pilin (tcpA)—adhesion
- Cholera toxin-positive regulatory protein (toxR)—transcription regulator
- Antitoxin-encoding gene (higA)—protection to ctxA

Impacts

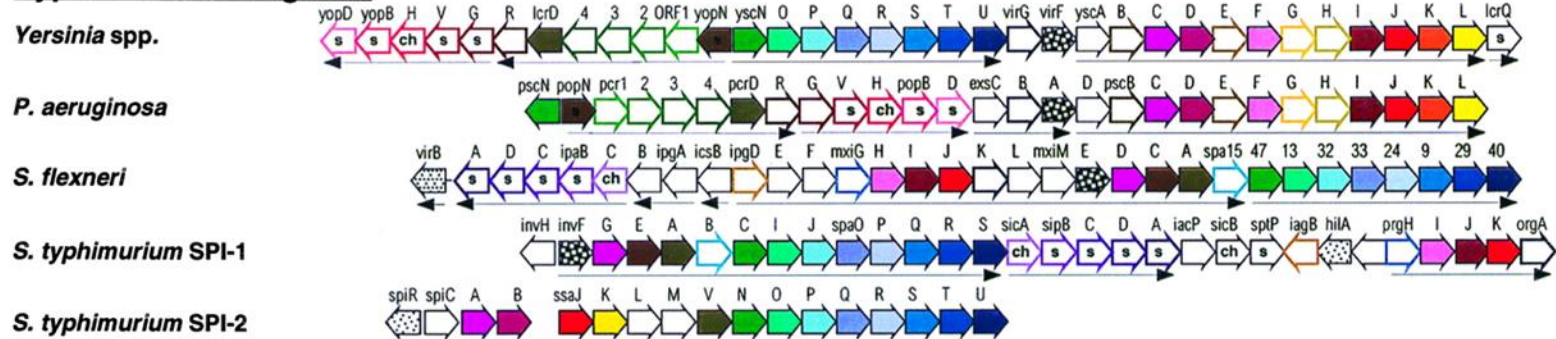
- **Development of an ontology will provide a unique resource for our sponsors**

- **An ontology will help capture knowledge about pathogens in an organized way**
 - It will make current resources (e.g., MVirDB) much more usable

- **We are bridging a variety of communities in generating the ontology**
 - E.g., DHS for signatures and NIAID for pathogen sequencing and annotation

Future Plans

Type III secretion genes



- **Expand list of organisms and virulence factors to annotate**
 - Capture information about pathogenicity islands (e.g., type III secretion genes)
- **Expand use cases to help drive the terms collected**
- **Draft Minimum Information about a Pathogen (MIP) and its genes**