

Human Monoclonal Antibodies Against H5N1 and Other Biothreats

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MSR in collaboration with MUSC



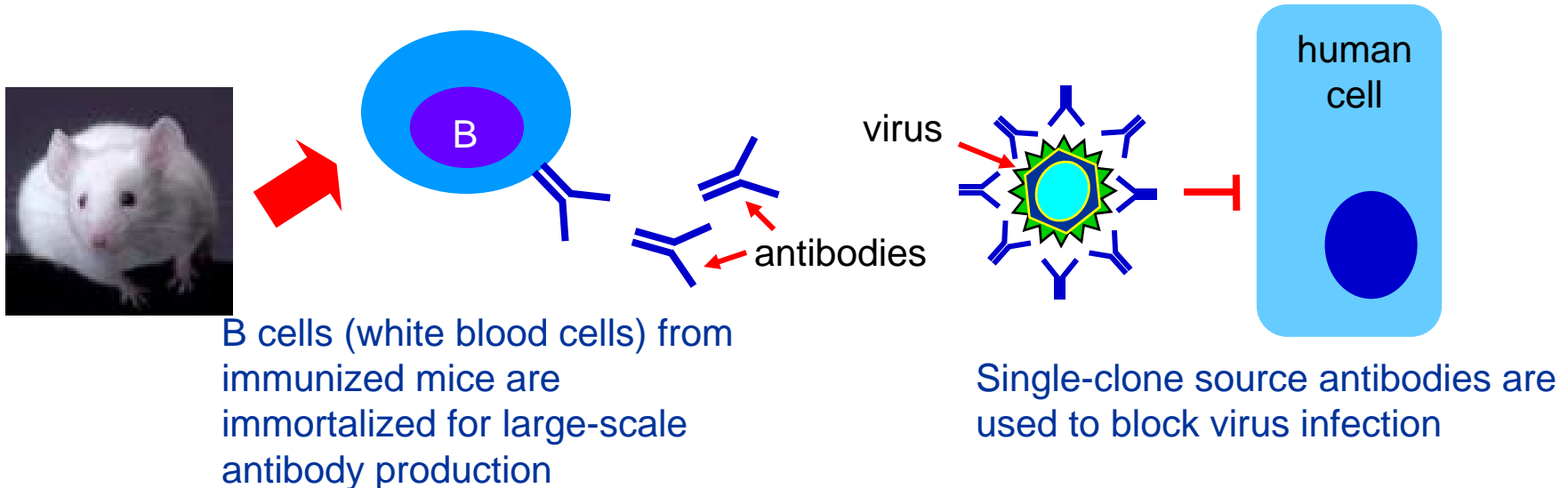
Problem



- **Can “naive” B cells of human origin be manipulated to produce antibodies able to bind to targets of concern?**
 - Many microbes and toxins remain a threat (BW or natural)
 - Vaccinations have covered only a small fraction of the spectrum
 - Antibody therapy is a promising alternative

Background

- Vaccination, drug, and antibody therapies are the best available interventions against infectious diseases and toxin exposure
- Where no vaccine or drugs are available, antibody therapy is a real option
- Antibody therapies continue to rely on animal or “humanized” sources



Objective



- **A new method for production of human monoclonal antibodies will be optimized for treatment of infectious diseases**
- **The resulting antibodies will be tested for therapeutic blocking of avian influenza viruses**
- **Use in detection and diagnosis will be tested**
- **The “contact point” between target viral proteins and antibodies will be mapped**

Activities

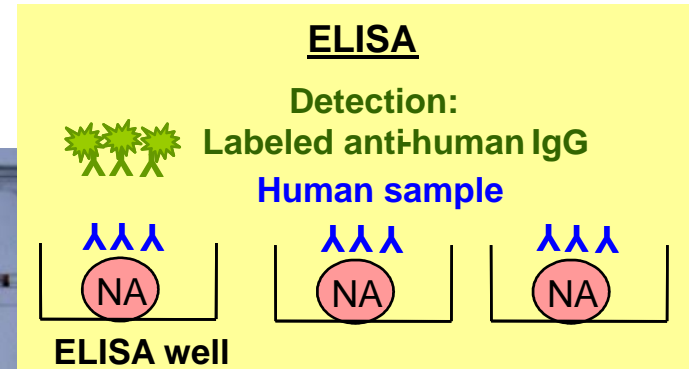
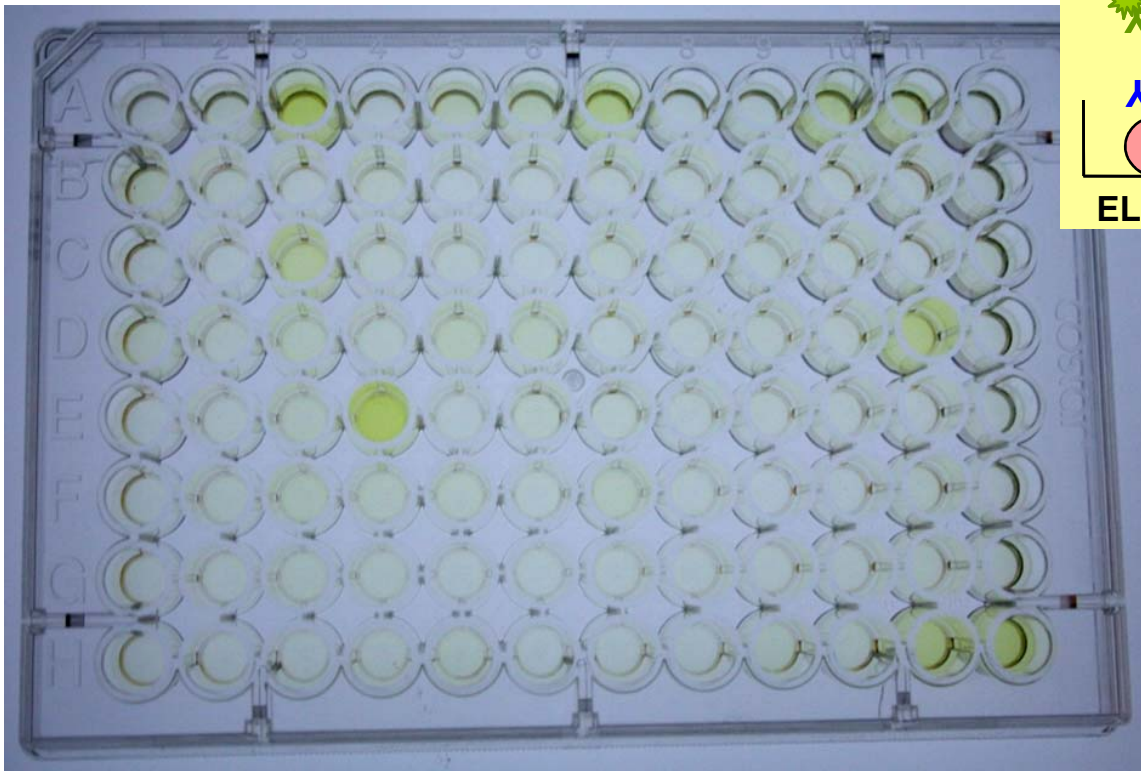


- **Human B cells are isolated from tonsils obtained after tonsillectomy**
- **B cells are manipulated to generate IgG antibody producing clones with indefinite lifespan**
- **The generated antibodies are tested for binding to target proteins on H5N1 avian influenza**
- **Mapping technologies will define antibody target contact points, identifying antibodies useful for detection, diagnostics, and therapeutics**

Highlight

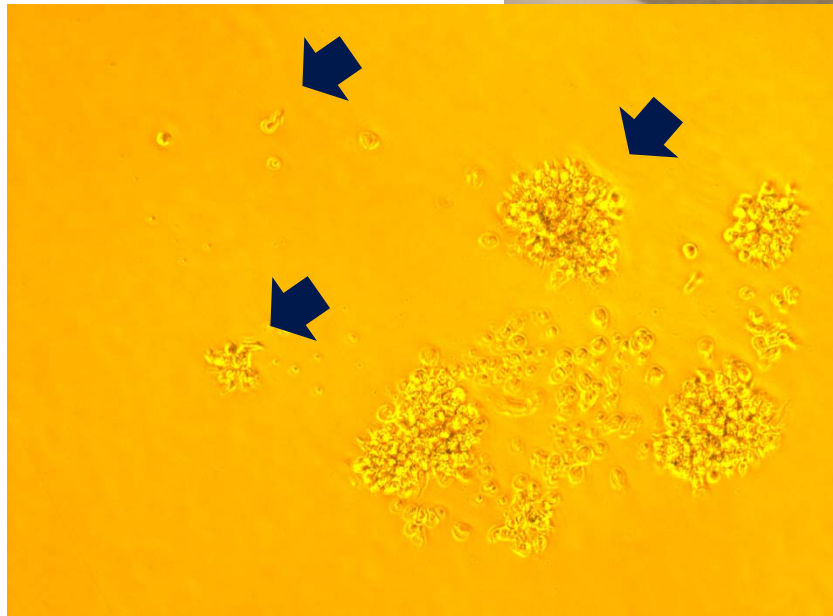
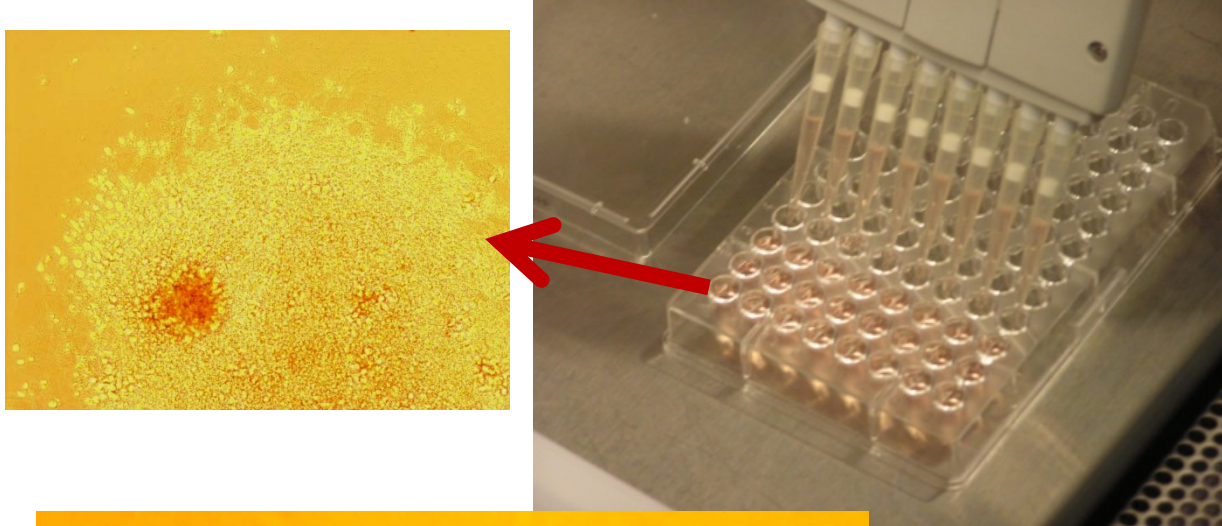
Generating NA Antibodies – MITRE Biolab

ELISA test results



Demonstration

Generating Antibodies – MITRE Biolab



Stack of 10 plates



Test by ELISA



B cell Subcloning



Four Rounds



Clonal B cell

Single B cell clones example

Impacts



- **Immortalized B cell clones will produce large-scale quantities of monoclonal antibodies**
- **H5N1 virus monoclonal antibodies are selected and purified for use as therapy against avian flu**
- **The antibodies will also be applied as diagnostic/detection reagents**
- **Program success will increase options to stop the threat of emerging influenza viruses**

Future Plans



- **Test neutralization of a highly pathogenic H5N1 strain**
- **Assess universal neutralization of influenza viruses**
- **Identify antibodies against other emerging biothreats**
- **Promote use towards National Security Stockpiling**