



# **Human Monoclonal Antibodies Against H5N1 Avian Influenza**

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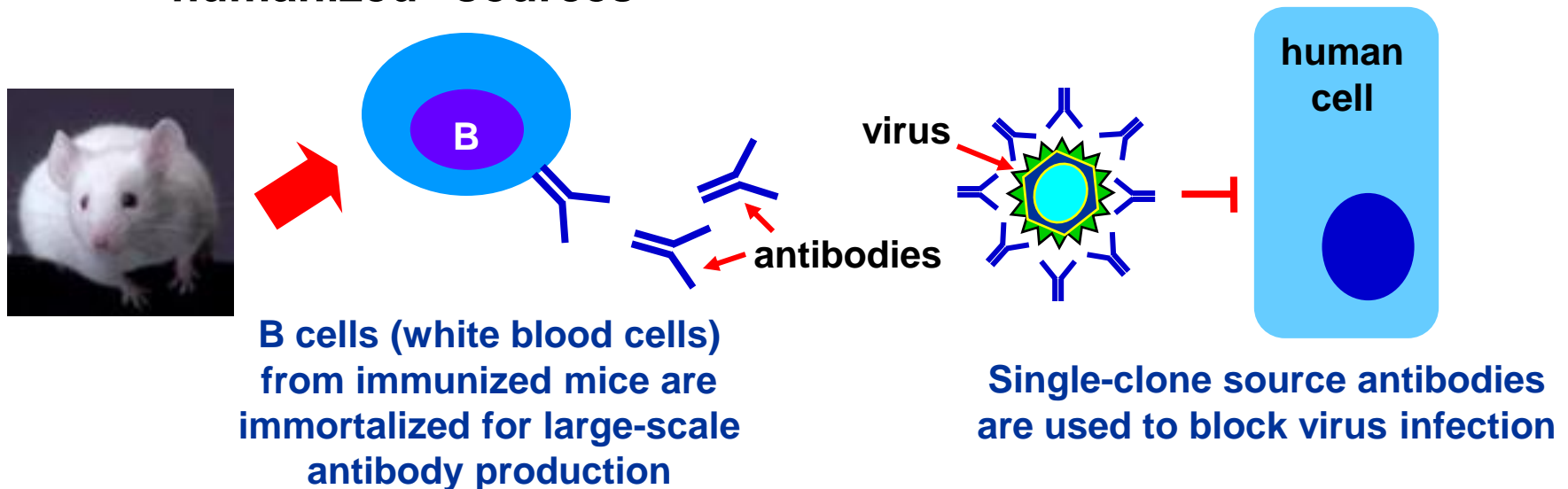
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# Problem

- **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 a detection assay also will be tested**
- **The “contact point” between target viral proteins and antibodies will be mapped**

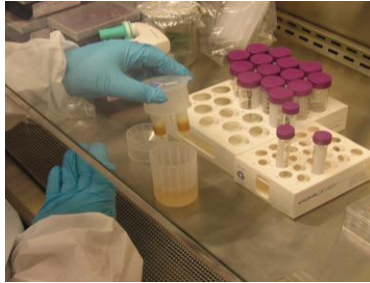
# Activities



- **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 diagnostics and therapeutics**

# Highlight

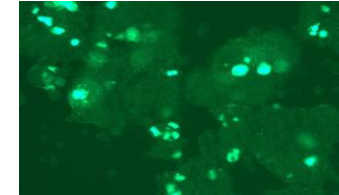
## 1. Efficient Immobilization of Human B cells



Epstein-Barr Virus concentration (EBV)

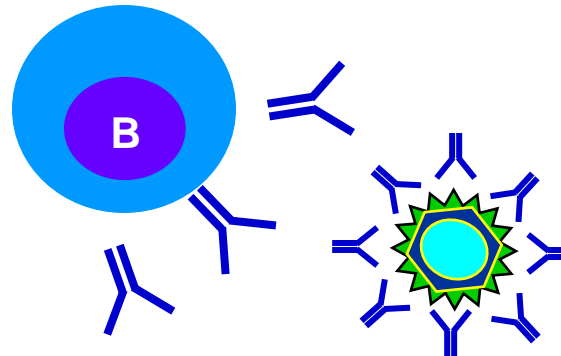
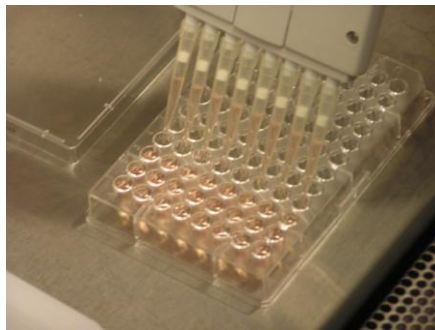


Tonsil extracted B cells are “spinfectd” with EBV

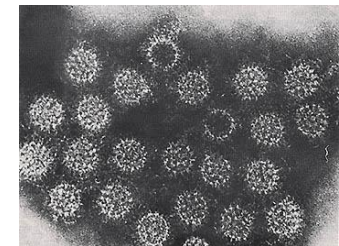


“Immortalized” B cells shown with fluorescent label

## 2. *In Vitro* Antibody Production



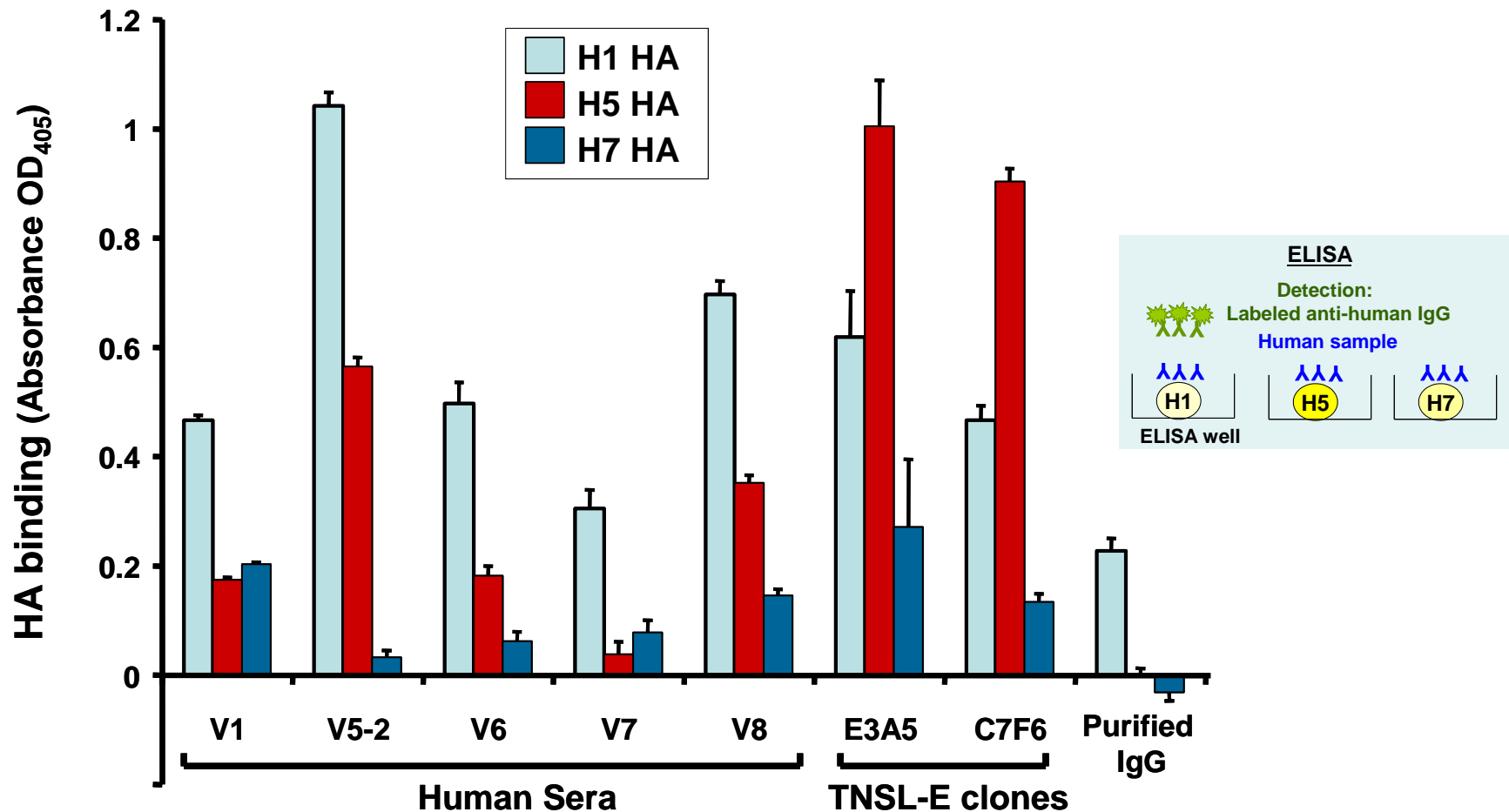
Antibody coated flu virus



Newly immortalized B cells are further treated to induce antibody secretion *in vitro*

B cells secreting antibodies against avian influenza H5N1 virus are isolated and expanded

# Demonstration



TNSL-E clones E3A5 and C7F6 secrete IgG that binds H5 HA with higher affinity than H1 or H7 HA, while human sera from healthy volunteers bind H1 HA with higher affinity. Sera from 5 healthy adult volunteers (diluted 1:1000), and supernatants from TNSL-E clones E3A5 and C7F6, were assayed for IgG binding to H1, H5 and H7 HA by ELISA. Mean absorbance  $\pm$  SD of samples and controls (n=3) are shown.

# 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 diagnostic/detection tools**
- **Program success will increase options to stop the threat of emerging influenza viruses**

# Future Plans

- **Assess universal neutralization of influenza viruses**
- **Identify antibodies against other emerging biothreats**
- **Plan stockpiles of therapies against BW agents (bacteria, viruses and toxins)**

