Antibody therapies and universal vaccines for diseases of military importance

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VACCINE DEVELOPMENT

1. Phase-display antibody library (10^9 diversity)
2. Multiple rounds of phage library cross-panning against multiple pseudoviruses (linked to magnetic beads)
3. Reformating of broad-spectrum candidates to full-length human IgG antibodies
4. In vitro IgG neutralization assays against wide panel of viruses from family
5. In vivo protection assays in animal models (hamster/guinea pig)

Figure 3. Diagram of antibody discovery process using USAMRIID’s pseudovirion system and Centivax’s proprietary phage display antibody library platform.

UNIVERSAL INFLUENZA VACCINE

Figure 1. (Left) Centivax approach to universal influenza vaccine design. (Right) Results from ELISA binding assays from vaccinated animals against broad panel of influenza hemagglutinins.

Figure 2. Results from ferret study with heterologous virus challenge. Ferrets were protected from H1N1 and H3N2 “future” strains of influenza.

Figure 5. Crystal structures of D09 with 3FTXs reveal similarity in recognition between antibody and acetylcholine receptor (nAChR).

Figure 6. In-vivo protection by D09 with live challenge by recombinant α-neurotoxin and whole venom.

Figure 4. Balb/c mice (6-8 weeks old) were injected with 5x10^8 total CFU of S. aureus (JE2::lux) and received a single injection of PBS (vehicle control), Centi-ATOX-α2-β12, SEB-2081-β12, or combination (600 ug/mouse). Mantel-Cox survival curve analysis was performed (p=0.0001) for the duration of the sepsis study. Mice were monitored frequently and visually evaluated using the murine sepsis scoring system. Credit: NMRC Combat Wound Infections Division, WRAIR, Silver Springs, MD.

TREATING INFECTION, PREVENTING SEPSIS

Centivax’s strategy for treating bacterial wound infections is to target conserved epitopes on secreted toxins using a cocktail of monoclonal antibodies, depicted here. By neutralizing pathogenic toxins, our therapy will allow field-treated patients to survive until more advanced medical facilities are available.

MANUFACTURING ADVANTAGES

- Annual rush to GMP manufacture, approve, and sell a new vaccine
- Vaccine always mismatch to circulating strains (30-60% efficacy)
- Manufacturing delays are catastrophic financially
- Market is fractured between Northern/Southern hemisphere vaccines

- Same Centivax vaccine manufactured for decades without redesign
- Centivax vaccine works on all strains (80-90% efficacy)
- Centivax vaccine manufactured all year round & stockpiled
- Single Centivax vaccine for both hemispheres

Figure 7. Annual influenza vaccine US Supply Timeline

Figure 8. Centivax influenza vaccine Global Supply Timeline

ANTIBODY DISCOVERY PLATFORM

- Target
- Indication
- Tech
- Clones
- Tests
- Panel
- Market
- Partners

Figure 3. Diagram of antibody discovery process using USAMRIID’s pseudovirion system and Centivax’s proprietary phage display antibody library platform.

UNIVERSAL ANTIVENOM FOR SNAKEBITE

Figure 9. Crystal structures of C09 with 3FTX reveal similarity in recognition between antibody and acetylcholine receptor (nAChR).

Figure 10. In-vivo protection by C09 with live challenge by recombinant α-neurotoxin and whole venom.