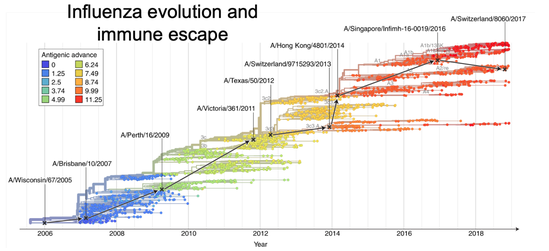
Antibody therapies and universal vaccines for diseases of military importance

Sangil Kim, Mark Bellin, Joel Christian Andrade, Sujeong Kim, Tim Friede, Sara Siebel Marr, J. David Gangemi, Nicholas L. Bayless, David Tsao, Sawsan Youssef, Jacob Glanville - **Centivax Inc., South San Francisco, CA**

VACCINE DEVELOPMENT



	TARGET	INDICATION	TECH	In vitro POC	In vivo POC	GMP	CLINICAL	MARKET SIZE	PARTNERS
MUTATING VIRUSES	Influenza	influenza	Broad-spectrum vaccine				2023	$6.2B*	GATES FOUNDATION
	HIV	HIV	Broad-spectrum vaccine				2024	>$5.0B	
	SARS-CoV-2	COVID-19	Broad-spectrum vaccine				2024	$13.6B	
MULTIDRUG RESISTANT PATHOGENS	MRSA	wound, pneumonia, bacteremia, sepsis	Broad-spectrum mAbs				2023	$3.9B	NMRC
	pseudomonas	wound, pneumonia, bacteremia, sepsis	Broad-spectrum mAbs				2023	$1.8B	NMRC
MUTATING CANCERS	ISTAR	cancer	Gene delivery				2024	>$60B**	
ANTIVIRAL	SARS-CoV-2	COVID-19, hospitalized (IV)	mAb				.***	$2B	NMRC, NIIMBL, CRL, MIDRP/USAMRIID
	SARS-CoV-2	COVID-19, outpatient injectable	mAb				.***	$2B	NMRC, NIIMBL, CRL, MIDRP/USAMRIID
AUTO-IMMUNITY	CXCR5	SLE, RA, MS, lymphomas, colorect.	mAb				2023	$24B	
	antivenom	universal anti-venom	Broad-spectrum mAbs				2023	$1.5B	NIH

UNIVERSAL INFLUENZA VACCINE

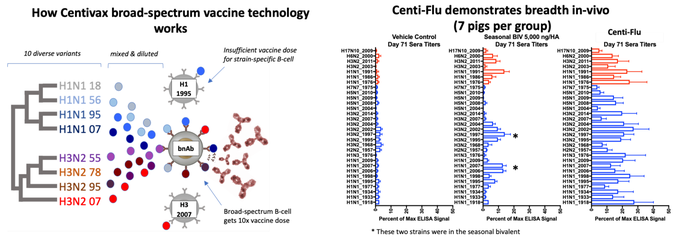


Figure 1. (Left) Centivax approach to universal influenza vaccine design. (Right) Results from ELISA binding assays from vaccinated animals against broad panel of influenza hemagglutinin.

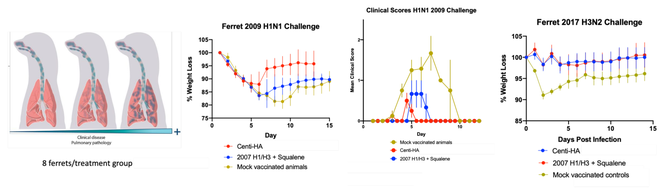
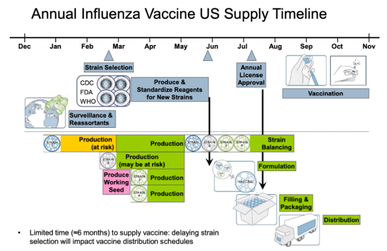
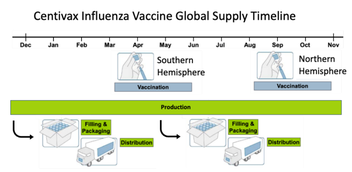


Figure 2. Results from ferret study with heterologous virus challenge. Ferrets were protected from H1N1 and H3N2 "future" strains of influenza.

MANUFACTURING ADVANTAGES



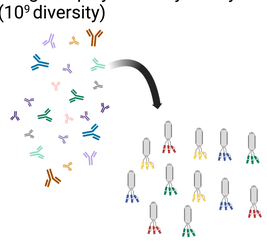


- Annual rush to GMP manufacture, approve, and sell a new vaccine
- Vaccine always mismatch to circulating strains (30-60% efficacy)
- Manufacturing delays are catastrophic financially
- Market is fractured between Northern/ Southern hemisphere vaccines

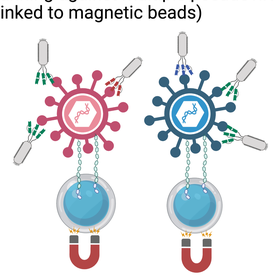
- Same Centivax vaccine manufactured for decades without redesign
- Centivax vaccine works on all strains (80-90% efficacy)
- Centivax vaccine manufactured all year round & stockpiled
- Single Centivax vaccine for both hemispheres

ANTIBODY DISCOVERY PLATFORM

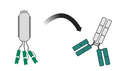
1. Phage-display antibody library (10^9 diversity)



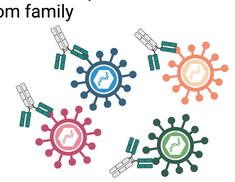
2. Multiple rounds of phage library cross-panning against multiple pseudoviruses (linked to magnetic beads)



3. Reformatting 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)

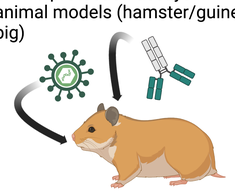
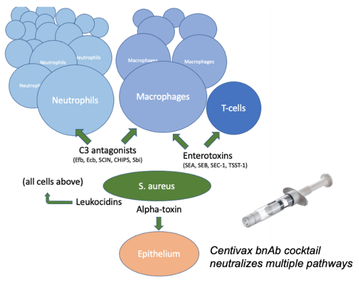


Figure 3. Diagram of antibody discovery process using USAMRIID's pseudovirion system and Centivax's prioprietary phage display antibody library platform.

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.

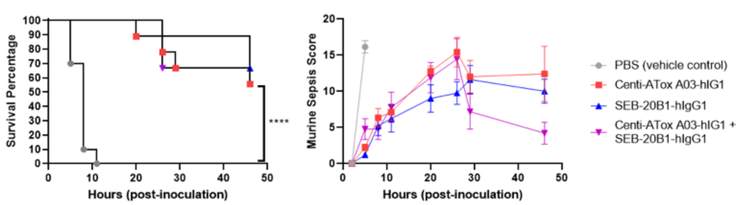
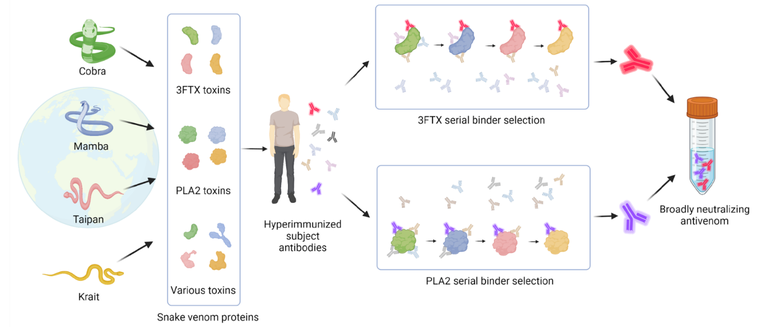


Figure 4. Balb/c mice (6-8 weeks old) were injected with 5x10^8 total CFU of *S. aureus* (*JE2::lux*) and received a single injection of PBS (vehicle control), Centi-ATOX-A03-hIG1, SEB-20B1-hIG1, or combination mAb (600 ug/mouse). Mantel-Cox survival curve analysis was performed (p****<0.0001) for the duration of the sepsis study. Mice were monitored frequently and visually evaluated using the murine sepsis scoring system[3]. Credit: NMRC Combat Wound Infections Division, WRAIR, Silver Springs, MD.

UNIVERSAL ANTIVENOM FOR SNAKEBITE



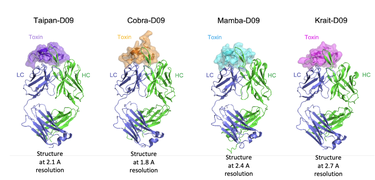


Figure 5. Crystal structures of D09 with 3FTXs reveal similarity in recognition between antibody and acetylcholine receptor (nAChR).

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