'RapidVax®' – A Novel Cellular Vaccine Platform To Target Rapidly Emerging Biological Threats

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The current COVID-19 pandemic underscored societal risks and vulnerabilities to battle biological threats, whether by an intentional attack, an accidental release, or naturally occurring drift in an infectious disease pathogen. The current pandemic highlights the need for a proven, safe, core vaccine strategy that can be engineered and modified in real-time to address emerging biological threats and ensure continual efficacy. Neutralizing the threat of biological weapons has been elusive due to the number of potential agents and the timeline required to develop a viable vaccine. **The cellular vaccine platform RapidVax® is in development** to leverage the immune-activating properties of heat shock protein gp96, a danger signal associated protein, as well as the T cell co-stimulatory properties of OX40L. Gp96 normally chaperones activation peptides to antigen presenting cells under times of cellular stress. These non-self peptide-gp96 complexes then stimulate antigen cross-presentation leading to a broad array of adaptive immune responses to confer **cellular and humoral immunity** against a wide range of antigens. OX40L co-stimulation of T cells has been demonstrated to promote the extension and expansion of T cell memory as well as the development of T follicular helper cells. The RapidVax platform is designed to rapidly address various disease settings by using a **stable cell-based platform amenable to stockpiling for rapid "plug and play" custom programming and "fill-finish"** against numerous pathogens. This capability has the potential to **dramatically shorten timelines to develop and test novel vaccines against emerging infectious agents.** Initial trials demonstrate a positive risk: benefit ratio after treating subjects with a gp96 based vaccine in non-small cell lung cancer - showing a favorable safety profile in over 250 cancer patients treated to date.[1,2] Furthermore, gp96/OX40L based cellular vaccines demonstrate prophylactic protection in mice and primate models against a range of infectious threat agents, including malaria, HIV/SIV, Zika and SARS-CoV-2 virus.[3-7] **RapidVax is a gp96/OX40L based allogeneic, off-the-shelf, cellular therapy platform** designed to utilize the toll-like receptor 2/4 stimulating adjuvant gp96 to chaperone engineered pathogen proteins directly to antigen presenting cells to facilitate their activation and antigen-specific stimulation of immune cells to produce pathogen targeting antibody and cytotoxic T-cell responses. Vaccines can be generated for any virus, bacteria, or parasite-specific threat by transfecting the stockpiled cell line with any pathogen-specific plasmid. Notably, this approach is complementary with the use of artificial intelligence and biosurveillance to predict emerging threats and antigenic targets. The **RapidVax platform is being designed to enable an accelerated response to a range of infectious agents by providing a flexible "plug and play" vaccine platform** which may be rapidly customized, manufactured, and deployed while stimulating long-lasting cellular and humoral immunity. This approach has the potential to provide long-term biodefense capability to protect U.S. forces and civilians in the event of future biological threats.

CORE VACCINE TECHNOLOGY

RapidVax is Built on 20 Years of Research Using gp96 as a Potent Antigen-Delivery & Adjuvant Platform

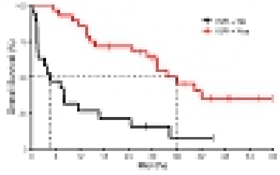
- Incorporating gp96 and a potent T cell memory co-stimulatory molecule, OX40L, RapidVax is designed to generate both cell-mediated and humoral immunity
- RapidVax cells are lethally irradiated rendering them replication incompetent with cells acting as a "mini-drug pump" to deliver immunogens directly to the body

CORE VACCINE SUPPORTING CLINICAL DATA

gp96 Clinical Proof-of-Concept:

HS110-102: Phase 1b/2 trial using gp96 cell-based vaccine with nivolumab to treat NSCLC

	HS-110 + Nivolumab				Nivolumab
	All	ISR	PD-L1		
OS (mos)	[illegible]	[illegible]	[illegible]	OS (mos)	[illegible]



- HS-110 is an allogeneic cell-based therapy designed to secrete multiple cancer testis antigens chaperoned by heat shock protein gp96
- The table represents the mOS in Checkpoint Inhibitor (CPI) naïve NSCLC patients treated with HS-110 and the PD-1 inhibitor nivolumab, exhibit favorable median overall survival compared to a historical control population treated with nivolumab alone
- Improved OS observed in a subsets of patients with injection site reaction (ISR) compared to subjects without an ISR

INTRODUCING RAPIDVAX "PLUG-AND-PLAY" VACCINE PLATFORM

Designed to Enable Manufacturing and Stockpiling of Unprogrammed gp96-based Vaccine

- RapidVax offers a fast, potent, highly differentiated platform to respond to known and unknown biological threats
- Rapid "plug and play" of relevant antigens upon the emergence of novel biological threats

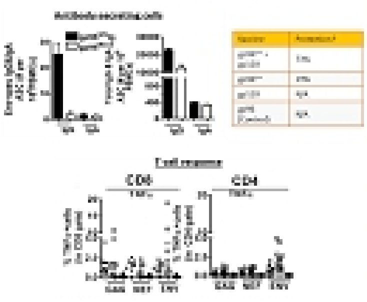
Cellular vaccine focused on generating long-lasting T-cell mediated immunity

RapidVax is Amenable to Stockpiling to Rapidly Respond to Any Biological Threat

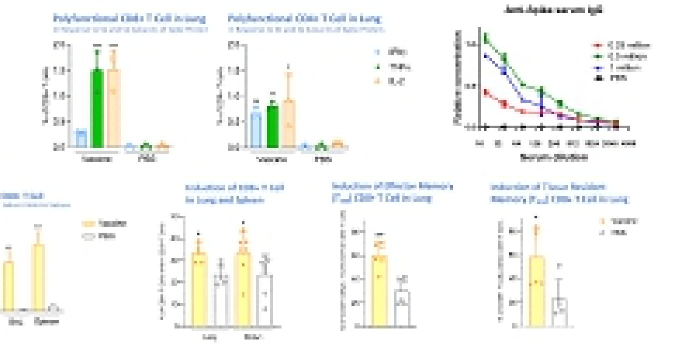
- Incorporates core gp96 vaccine technology and delivers potent costimulatory molecule, OX40L, in concert with specific cloned antigens
- This approach has the potential to accelerate the development and manufacturing of custom, adaptable vaccines

RAPIDVAX PROTOYPE VACCINES

HIV/SIV Prototype



COVID-19/SARS-CoV-2 Prototype



Demonstrated Efficacy in HIV/SIV Primate Model of Disease

- Protection against simian immunodeficiency virus (SIV) in NHPs
- Induction of humoral and cellular immunity
- Induction of Env-specific CD8+ T cells in mice
- Elevation of malaria-specific CD8+ T cells in mice

Building SARS-CoV-2 RapidVax Prototype

- Vaccine build starts with transfecting a cell line with plasmids expressing gp96-Ig, OX40L-Ig and Spike protein
- Expression kinetics of gp96, OX40L and Spike protein are measured in vitro, and cell dose is normalized to expressed components
- Stability of expression and proliferation capacity are measured

Immunogenicity of SARS-CoV-2 RapidVax Prototype

- Polyclonal immune response induced by RapidVax prototype expands CD8+ and CD4+ T cells expressing anti-viral cytokines, IFNγ, TNFα, IL-2
- Response to Spike protein subunits, S1 and S2, observed in the lung, bronchial alveolar fluid (BAL) and peripherally in the spleen
- Humoral immune response observed by induced anti-Spike IgG in the serum of mice; evidence of follicular helper T cell also observed

T cell Memory Induced by RapidVax Prototype

- T cell Memory observed post RapidVax prototype challenge
- Stimulation of effector, central and tissue resident memory T cells in the lung and spleen of immunized mice
- Induction of T cells against human immunodominant epitopes in HLA-A2 transgenic mice in the lung, BAL and spleen

Blackhawk Bio is a subsidiary of Heat Biologics

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"RapidVax®" – a Novel Cellular Countermeasure Platform Against Rapidly Emerging Biological Threats
For inquiries or questions please send a request to: info@blackhawk.bio