Defense Health Agency
MEDICAL TECHNOLOGY TRANSFER

The Defense Health Agency is a joint, integrated Combat Support Agency that enables the Army, Navy, and Air Force medical services to provide a medically ready force in both peacetime and wartime.

Targeting
- Crimean-Congo Hemorrhagic Fever
- Smallpox/Monkeypox
- Hantavirus
- COVID
- RNA Viruses
- Inflammatory Diseases
- Chronic Pain
- Cancer
- Non-Alcoholic Steatohepatitis (NASH)

Global Health Initiatives

9 Federally Funded Innovations to Improve Public Health Readiness

DHA Research and Development is seeking to license the following technologies.

1. **Partially humanized mouse monoclonal antibody that is protective in mouse models against Crimean-Congo hemorrhagic fever (CCHFV).**

Currently, Inventors demonstrated protection when the antibody is added before, and up to three days after exposure. To our knowledge, this is the first time any anti-CCHFV has worked as a true therapeutic. We plan to fully humanize this antibody and add modifications to extend the half-life. We will confirm the protective efficacy of the engineered antibody and then conduct IND-enabling safety studies followed by a Phase 1 clinical trial. Developed by: RIID. Tech ID 18-21.

2. **Novel DNA vaccine for Crimean-Congo hemorrhagic fever (CCHF) based on a clinically relevant CCHFV strain (Afg09-2990) isolated from a fatal case of a U.S. Army soldier.**

This DNA vaccine expresses the codon optimized full-length M-segment of the Afg09-2900 isolate from a single DNA plasmid in inventors' plasmid backbone which is approved for human use, pWRG7077. This vaccine was highly immunogenic and completely protective against Afg09-2990 challenge in mice. It also generated immune responses to regions of the M-segment that are known to correlate with protective immunity. Since this vaccine is a single DNA plasmid, we expect that it will be readily scalable from a manufacturing perspective. Developed by: RIID. Tech ID: 20-18.

3. **Self-neutralizing poxvirus vaccine platform.**

Uses recombinant, replication-competent vaccinia virus. ACAM2000 is problematic because of its ability to replicate in human tissue, however it has a robust immune response. The vector will encode a monoclonal that specifically neutralizes the vector itself to reduce the extent of infection and viral shedding. Could be used: (1) as a smallpox/monkeypox (orthopox) vaccine, (2)to deliver the monoclonal as a post-exposure therapeutic, or (3) as a vector to deliver a gene of interest. Developed by: RIID. Tech ID 20-04.

4. **COVID19 Surveillance Using NGS.**

Some highlights are:
a. Able to detect 46,000 samples on NextSeq2K, predicted capacity of 100,000
b. Works with nasal/oral swabs or saliva
c. 23,000 validated probes for COVID E and 23,000 for COVID S
d. Results are concordant with rapid & PCR in known positives from operational samples to a CDC EUA PCR Ct 32
e. Results are far superior to those obtained in-house with RT Lamp and Swabseq.
f. Cost can be as low as $3 to $5 per sample
Developed by: RIID. Tech ID 21-02.

Contact: Edward Diehl 301-619-2817 edward.e.diehl.civ@health.mil Web: *technologytransfer.health.mil*
DHA Research and Development, Office of Medical Technology Transfer, Fort Detrick MD 21702

5. Prolyl hydroxylase domain inhibitor (PHDi) that improves survivability and outcomes of trauma and hemorrhagic shock.

These are methods for treating erythropoietin-associated conditions by increasing endogenous erythropoietin in vitro and in vivo. Developed by: RIID. Tech ID: 22-04.

6. Base-modified ribonucleosides as prodrugs against RNA viral infections.

Since the specific modification of pyrimidine nucleobase in 2'-deoxyribonucleosides has resulted in the development of novel anti-cancer and anti-DNA-viral prodrugs, then the similarly modified ribonucleosides should also be capable of serving as pro-drugs against RNA viruses, such as alphavirus (VEEV, EEEV, and WEEV), Ebola, Marburg, Influenza, and COVID. The preliminary data have demonstrated that the specific substitution pattern of the modifying moiety attached to the nucleobase of the N-hydroxycytidine nucleoside leads to complete inhibition of the VEEV infection, while all other similarly modified derivatives without the specific substitution pattern in the modifying moiety have demonstrated rather negligible anti-viral activity. Developed by: RIID. Tech ID: 21-13.

7. Novel Clot Retraction Assay for Quality Monitoring of Platelet Products.

The invention includes the following: (1) a method for quantitative evaluation of clot retraction, (2) an algorithm to extract parameters from the time-series data, (3) a sample preparation method that can be used in austere conditions, and (4) a demonstration of fluorescent particles to measure clot retraction. Developed by: ISR. Tech ID: 22-084.

8. A3 Adenosine Receptor Positive Allosteric Modulators.

Selective A3AR agonists are sought as potential agents for treating inflammatory diseases, chronic pain, cancer and non-alcoholic steatohepatitis (NASH). In the past, the inventors modified 1H-Imidazo[4,5-c]quinolin-4-amine derivatives were reported as positive allosteric modulators (PAMs) of the A3AR. They have now invented new members of the same chemical class that contain sterically constrained, bridged modifications and cycloalkyl rings of various sizes, as well as modifications of the 4-arylamino group. They have added three-dimensionality to otherwise flat molecules, which helps distinguish their positive (desired) and negative (undesired) pharmacological effects on the action of A3AR agonists. Unlike agonists that have side effects, PAM action can be event- and site-specific because adenosine is endogenously elevated in response to localized distress signals within the body. They do not yet have in vivo results for these PAMs, because their activity is evident only in higher animals (primates, dogs, rabbits), but not rats and mice. Developed by: USUHS. Tech ID: 22-09.

9. Novel Hantavirus DNA vaccine .

Hantavax™ vaccine immunity appears to wane over time. Between 2005 and 2010, about 100,000 Korea Armed Forces personnel were vaccinated each year using Hantavax. Our vaccine elicits antibodies against the HTNV and PUUV hantaviruses, and may cross protect against Dobrava virus as well. The vaccine does not protect against other hantaviruses endemic to the US or South America (e.g. SNV, ANDV, etc). The pWRG/HTN-M(x) HTNV DNA vaccine and pWRG/PUU-M(s2) PUUV DNA vaccine were constructed using the base mammalian expression plasmid pWRG7077 expressing the HTNV M gene products G1 and G2, and the PUUV gene products G1 and G2, respectively. The final vaccine for Phase II clinical studies was manufactured by Althea Anjimoto (San Diego, CA). This vaccine has not been manufactured at scale higher than for Phase II clinical studies or proven to be able to be manufactured at high volume to date. Developed by: RIID - eight patents and applications.

Defense Health Agency
MEDICAL TECHNOLOGY TRANSFER

The Defense Health Agency is a joint, integrated Combat Support Agency that enables the Army, Navy, and Air Force medical services to provide a medically ready force in both peacetime and wartime.

Fentanyl Vaccine At-A-Glance

- **US Patent Application**
  17/792,378
- **Canadian Patent Application**
  3,167,191
- **Priority Date**
  13 JAN 2020
- **Title**
  Fentanyl Haptens for the Preparation of a Fentanyl Vaccine
- **Inventors**
  Torres, Oscar et al.
- **Laboratory**
  Walter Reed Army Institute of Research (WRAIR)
  Silver Spring, MD
- **Publications**
  Mol Pharm. 2020 Sep 8; 17(9): 3447–3460

Fentanyl Vaccine

Novel Vaccine that Blunts Fentanyl's Effects & Sequesters Fentanyl Analogs

DHA Research and Development, HJF, and NIAID seeks a partner interested in commercializing this technology.

The Market Need

Currently, there are no fentanyl vaccines approved by the U.S. The U.S. Drug Enforcement Agency has called fentanyl the "single deadliest drug threat our nation has ever encountered."

The fentanyl category of opioids accounted for 67,325 preventable deaths in 2021, representing a 26% increase over 2020[1]. People consume fentanyl both knowingly and unknowingly when it is mixed into or sold as other drugs, such as heroin, cocaine, or counterfeit pills. Forty two percent (42%) of counterfeit pills tested for fentanyl contained at least 2 mg of fentanyl, considered a potentially lethal dose[2]. Since fentanyl is between 50 to 100 times more potent than morphine, using a drug that has been contaminated with or replaced by fentanyl can greatly increase one's risk of overdose.

The current treatment for suspected opioid overdose is prompt administration of naloxone. However, due to the potency and pharmacodynamics of fentanyl, managing acute overdose with short-acting naloxone may not be effective. In addition, naloxone may not work when fentanyl is combined with non-opioid drugs such as xylazine. Prophylactic vaccination against fentanyl could be a cost-effective, long-lasting intervention to reduce the incidence or severity of fentanyl overdoses, potentially saving thousands of lives each year.

Technology

Researchers at the Walter Reed Army Institute of Research (WRAIR) working with the National Institute on Drug Abuse and the Henry Jackson Foundation have developed a vaccine formulation composed of a novel fentanyl haptens conjugated to tetanus toxoid and adjuvanted with liposomes containing monophosphoryl lipid A.

Contact: David Humphrey 301-619-6975 david.h.humphrey7.civ@health.mil Web: *technologytransfer.health.mil*
DHA Research and Development, Office of Medical Technology Transfer, Fort Detrick MD 21702

Defense Health Agency
MEDICAL TECHNOLOGY TRANSFER

(over)

Fentanyl Vaccine *(continued)*

Novel Vaccine that Blunts Fentanyl's Effects & Sequesters Fentanyl Analogs

Highlighted Benefits

The fentanyl haptens employed in the vaccine bind with high affinity to fentanyl and its analogs preventing the harmful effects of fentanyl in mouse studies. Haptens are used because opioids such as fentanyl are not immunogenic due to their small molecular size. Immunization with the hapten complex generates antibodies that can sequester fentanyl in the blood.

Impedes the ability of opioids to permeate the blood–brain barrier and prevents access to receptors in the brain. In animal studies, immunization with the fentanyl haptens produced antibodies with nanomolar infinities to fentanyl and its analogs such as cyclopropyl fentanyl, furanyl fentanyl, para-fluorofentanyl, and carfentanil, preventing fentanyl's harmful effects.

The antibodies do not have cross-reactivity with opioid abuse pharmacotherapies naltrexone, buprenorphine, and naloxone.

Applications

1. Counteract fentanyl misuse and accidental overdose
2. Medical countermeasure against fentanyl used as a chemical agent for incapacitation in military scenarios
3. Reduced risk for law enforcement, first responders, airport and customs personnel as well as their canine units technology has applicability in multiple market segments:

References

1. https://www.dea.gov/resources/facts-about-fentanyl
2. https://injuryfacts.nsc.org/home-and-community/safety-topics/drugoverdoses/data-details

Contact: David Humphrey 301-619-6975 david.h.humphrey7.civ@health.mil Web: *technologytransfer.health.mil*
DHA Research and Development, Office of Medical Technology Transfer, Fort Detrick MD 21702