JSTO in the News

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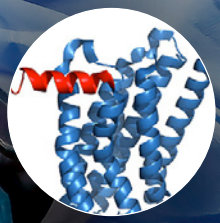

Natural Proteins.
Artificial Intelligence.

Strong Suit

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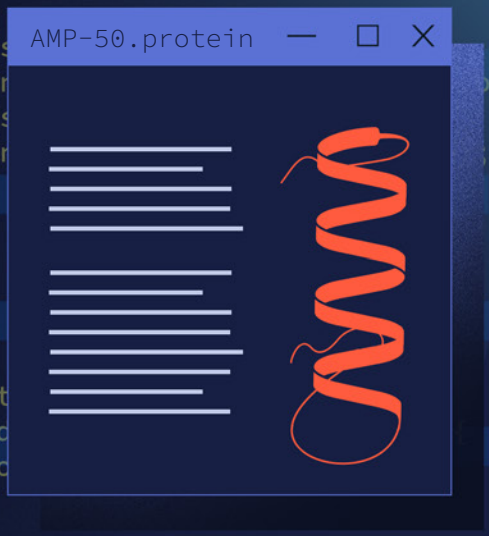
Front cover: A research assistant with the Naval Medical Research Center (NMRC) counts methicillin-resistant Staphylococcus aureus bacteria in the Combat Wounds Infections Division laboratory. Part of NMRC's Operationally Relevant Infections Department, the Combat Wound Infections Division develops and evaluates new treatments for combat injury related skin and soft tissue infections associated with multidrug-resistant organisms. (U.S. Navy photo by Michael Wilson)

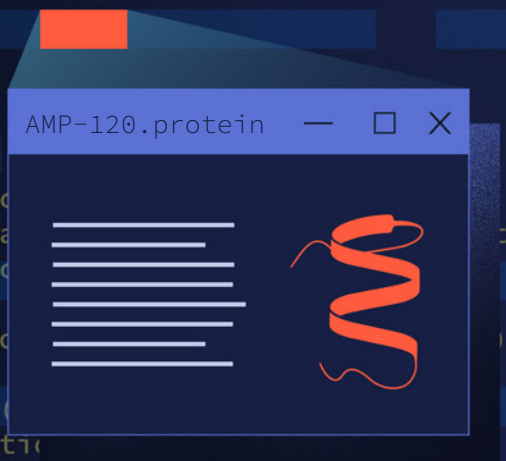
Inside cover: Oxygen tanks stand by for use by Marines during exercise Toxic Bayou at Kadena Air Base, Okinawa, Japan. The Marines conducted exercise Toxic Bayou to refine their skills in Countering Weapons of Mass Destruction operations across unique and challenging environments. (U.S. Marine Corps photo by Lance Cpl. Weston Brown)

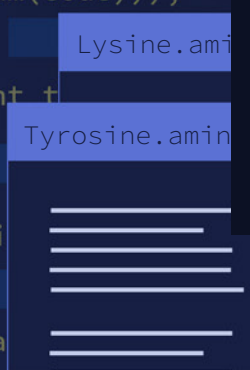
Back cover: A medic from the Massachusetts National Guard monitors a simulated patient as members of the unit prepare multiple soldiers for transport during a Tactical Combat Casualty Care training event at Camp Edwards, Mashpee, Mass. (U.S. National Guard photo by Capt. John Quinn)

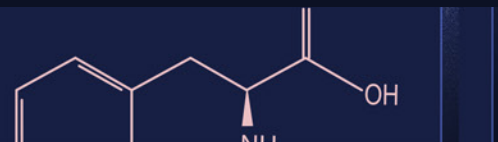
Natural Proteins. Artificial Intelligence.

Analysis of the human proteome may lead to potential antimicrobial treatments.





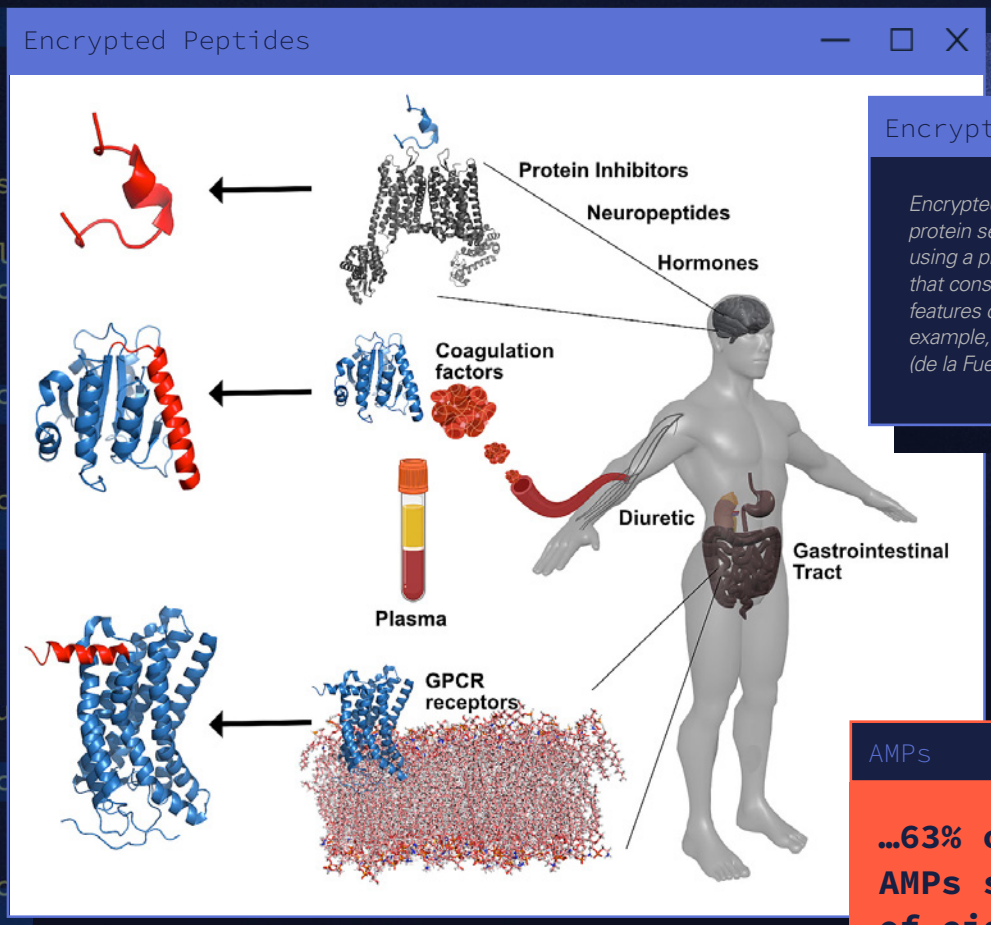




Antibiotic-resistant diseases are some of the most significant public health issues today. An artificial intelligence (AI) and machine-learning (ML) tool recently developed at the University of Pennsylvania (UPenn) searches for antibiotics that lie hidden within proteins naturally produced by the human body. These small protein antibiotics called antimicrobial peptides (AMPs) could be the key to developing new drugs that are effective against the increase in antibiotic resistance that threatens the health and readiness of the Joint Force.

Antibiotic resistance results from genetic or environmental adaptations that trigger new or preexisting defense mechanisms in bacteria, allowing them to evade the toxic effects of an antibiotic, persist, and cause disease. Decades of poor antibiotic stewardship and misuse sped up this naturally occurring phenomenon that caused the rise in antibiotic-resistant bacteria. Drug-resistant genes are more prevalent worldwide, which increases the opportunity for bacteria to acquire antibiotic resistance traits faster than ever.

Developing new antibiotics capable of eliminating drug-resistant bacteria is critical to our survival. The existing antibiotic drug development pipeline is expensive, lacks sufficient profit incentives necessary for motivating investments by the pharmaceutical industry, and is time-consuming. Drug development often takes over a decade before receiving Food and Drug Administration approval.



Encrypted Peptides

Encrypted peptides were identified within protein sequences from the human proteome using a physicochemical-guided scoring function that considered the main physicochemical features of antimicrobial peptides (AMPs), for example, length, charge, and hydrophobicity. (de la Fuente Lab/UPenn image)

AMPs

…63% of the synthesized AMPs suppressed growth of eight bacterial strains on the World Health Organization's watch list.

The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program invested in the UPenn research that led to the discovery of thousands of new human-derived AMPs hidden within sections of known proteins which can be used in new antibiotic development.

Scientists use AI/ML search tools to speed up the drug-discovery process by quickly mining through large amounts of data, which can expedite the development of new broad-spectrum therapeutics. Since there were no tools for rapid identification of human-derived antibiotics, the UPenn team created an ML tool that scanned the sequences of all human proteins, looking for AMPs. The resulting search led to identifying 2,603 new AMPs from which the team selected 55 candidate peptides that were synthesized, characterized, and validated in subsequent laboratory tests. A study of the biochemical characteristics of these 55 peptides demonstrated that they were different from all known AMPs to date and had biological functions unrelated to the immune system. They demonstrated significant clinical relevance as 63% of the synthesized AMPs suppressed growth of eight bacterial strains on the World Health Organization's watch list.

The UPenn report featured on the cover of the January 2022 issue of Nature Biomedical Engineering demonstrated their ground-breaking approach that uses an AI/ML algorithm to search within the human proteome to discover unique antimicrobials. The article provides the researchers' ML code that can be used by other scientists to broaden the search for AMPs in other organisms to discover new naturally occurring AMPs for antibiotic development. This could help create a new panel of antibiotics that expands the available antimicrobial spectrum to aid DTRA JSTO's efforts in protecting the Joint Force from antibiotic-resistant infections. ●

Drug Development Process

Drug Development Process

1. Drug discovery
Identify molecules that effectively kill bacteria that are also nontoxic to humans.

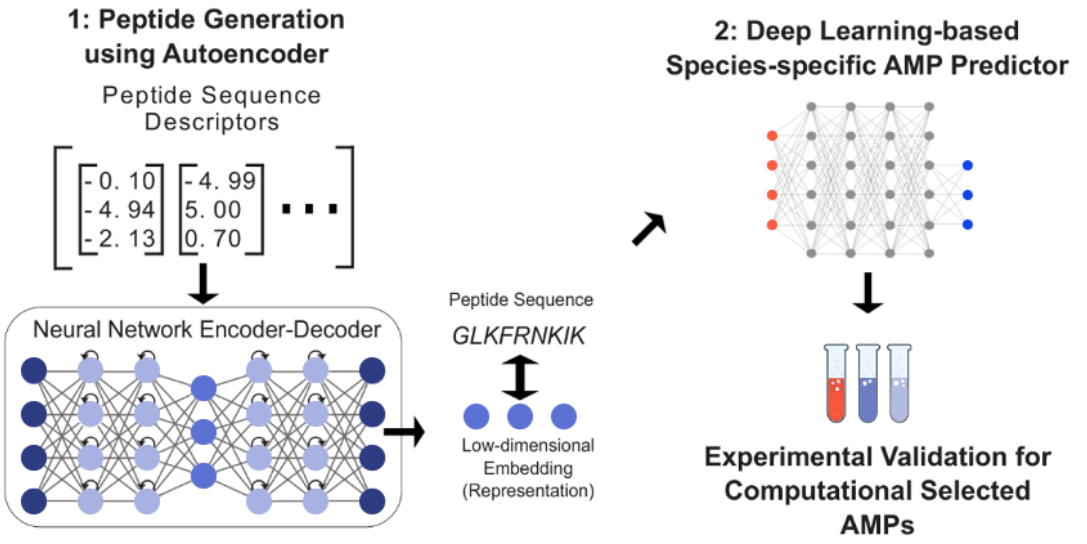
2. Preclinical research and development
Drug formulation and dosing optimization, cell culture and other studies to determine safety, toxicity, potency, effectiveness for treating disease, distribution throughout the body, metabolism, etc.

3. Clinical trials
Promising candidates are tested to see if they are safe and effective in people.

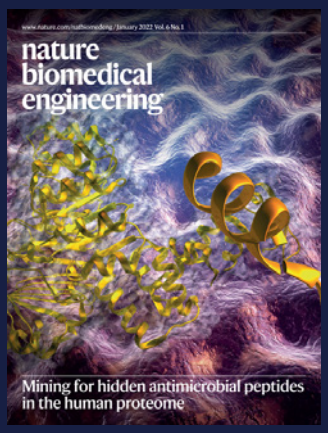
4. FDA approval
The FDA reviews regulatory documents that detail the manufacturing process and quality controls, pre-clinical and clinical trial data, and risk to benefit ratio.

5. Post-approval studies
Data collected from real world experience and additional clinical trials are periodically evaluated to assure continued safety and efficacy. Pharmaceutical companies often pursue new patient populations or disease indications for their drug.

Deep Learning



Learn More



Mining for hidden antimicrobial peptides in the human proteome

nature biomedical engineering,
January 2022, Vol 6, No 1

Click here to learn more

Deep Learning

A deep learning-based framework based on (1) peptide representation learning and novel peptide generation, and (2) AMP prediction and selection. (de la Fuente Lab/UPenn image)

STRONG SUIT

Advancements in tactical hazard protection are helping specialists stay on mission longer.

A new system of technologies for chemical and biological (CB) integrated protective gear that increases the time CB incident specialists can spend on mission also decreases the physical burden of the current Level A ensemble while still providing a high level of protection. The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program teamed with researchers at the U.S. Army Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC) and Soldier Center (DEVCOM SC), and industry partners to develop advanced suit, cooling, and respirator technologies for the protective gear that compose the Tactical All Hazards Ensemble (TacHazE).

TacHazE consists of a close-fitting, lightweight, and drapable protective garment; a powered cooling garment; and a full-spectrum respiratory protection system, which is a combination rebreather and Powered Air-Purifying Respirator (PAPR).

The third generation TacHazE suit, excluding the rebreather (top). TacHazE powered cooling garment worn under the TacHazE suit (bottom left and right). (Top: DEVCOM Soldier Center photo. Bottom left and right: Oceanit photos)

CB incident specialists may spend several hours at a time over many days or even weeks in the heavy, cumbersome Level A protective gear consisting of an impermeable suit and a self-contained breathing apparatus that limits user mobility and provides no moisture vapor transfer, which makes it hot. The users also wear oxygen bottles that typically last just one hour.

TacHazE combines new garment materials and respiratory technologies with a personal cooling system. When users face a large amount of toxic chemicals and deadly bacteria and viruses, this new ensemble would improve their mobility, suit temperature, and time on mission over the Level A ensemble.

TacHazE consists of a close-fitting, lightweight, and drapable protective garment; a powered cooling garment; and a full-spectrum respiratory protection system, which is a combination rebreather and Powered Air-Purifying Respirator (PAPR). Although the TacHazE garment fits tighter than the Level A suit, its fabric makes it easier to move in.

The TacHazE respiratory protection system is designed to extend mission time up to 4 hours in rebreather mode using a configuration with a weight comparable to a 60-minute air bottle. The system can also switch to a PAPR that allows the user to approach the mission site while breathing filtered external air for up to 8 hours. The TacHazE cooling garment keeps users comfortable while they work in the protective suits and reduces the physical burden associated with high levels of protection. The system comprises a cooling vest and miniature refrigeration unit that is powered by standard military rechargeable batteries.

In a recent showcase event at the Aberdeen Proving Ground in Edgewood, Md., a demonstration team of engineers from DEVCOM CBC, DEVCOM SC, and DTRA JSTO displayed the TacHazE system components, highlighted its operational improvements, and solicited user feedback from key personnel at the 20th Chemical, Biological, Radiological, Nuclear, and Explosives (CBRNE) Command

Maj. Gen. Antonio Munera, former commander of the 20th CBRNE Command, (right) examines the Tactical All Hazards Ensemble display (center on a manikin) at a technology showcase event hosted by DTRA JSTO at Aberdeen Proving Ground in Edgewood, Md. (U.S. Army photo by Marshall R. Mason)

and the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense. This user feedback will help improve the TacHazE to both ease the burden of effective incident responders' protective gear and increase the time they can work to counter CB threats. This achievement is yet another example of DTRA JSTO's proven history of successfully providing the Joint Force with critical capabilities. ●

JSTO in the News

For more information about improved cooling systems for protective garments, see **Keeping Your Cool** in *JSTO In The News*, November 2019.

Click here to learn more

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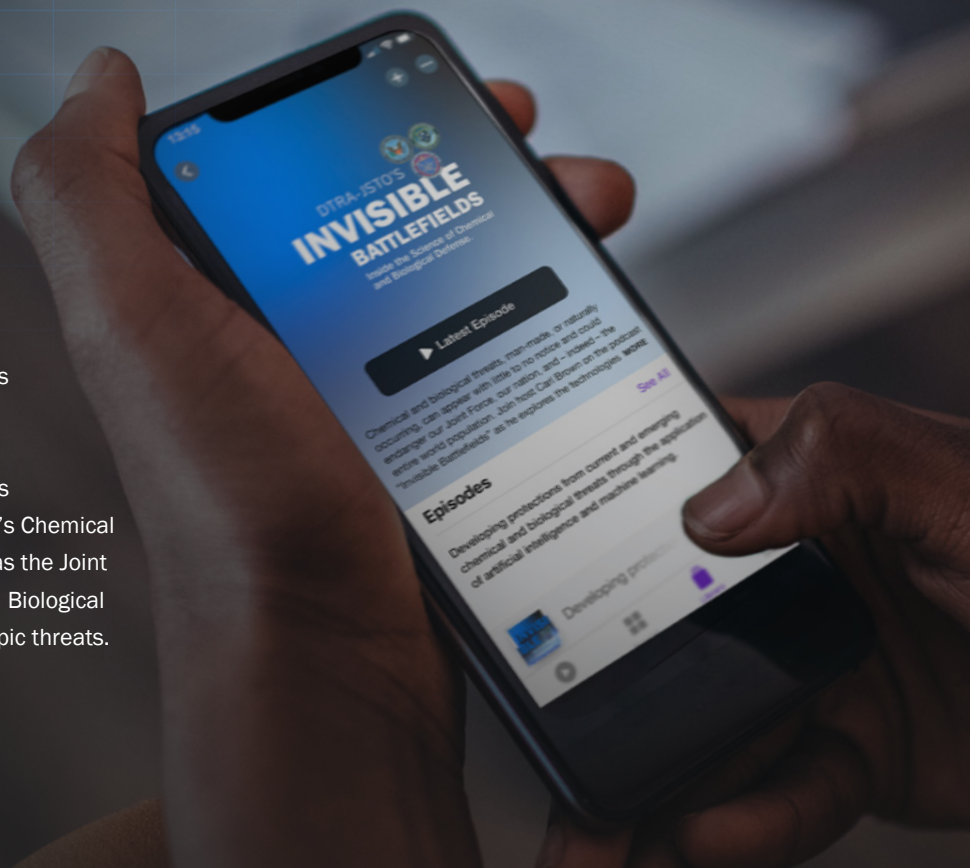
Invisible Battlefields: Inside the Science of Chemical and Biological Defense



Invisible Battlefields is a podcast meant to engage with the chemical and biological defense community and is another platform providing a voice highlighting the continuous collaborations that the DTRA JSTO program explores with industry partners, academia, and other government agencies concerning chemical and biological threats and protecting our Joint Force against them.

Join host Carl Brown as he explores the technologies developed by the Defense Threat Reduction Agency's Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office for the Chemical and Biological Defense Program to protect against these microscopic threats.

AVAILABLE NOW

EPISODE 01

Developing protections from current and emerging chemical and biological threats through the application of artificial intelligence and machine learning.

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Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department performing the role of Joint Science and Technology Office for the Chemical and Biological Defense Program. This publication highlights the department's advancements in protecting the Joint Force and citizens from chemical and biological threats through the innovative application of science and technology.

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