UC San Diego
UC San Diego News Center

October 21, 2020 | By Liezel Labios

Start-up Receives up to $15 M to Develop Nanoparticle Therapy for Sepsis Licensed from UC San Diego

San Diego-based Cellics Therapeutics, which was co-founded by UC San Diego nanoengineering Professor Liangfang Zhang, has received an award of up to $15M from Boston-based accelerator CARB-X to develop a macrophage cellular nanosponge—nanoparticles cloaked in the cell membranes of macrophages—designed to treat sepsis.

CARB-X, which stands for Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator, is a global non-profit partnership dedicated to supporting early development of antibacterial R&D to address the rising threat of drug-resistant bacteria.

In a paper published in *Proceedings of the National Academy of Sciences* in 2017, Zhang collaborated with the laboratory of Professor Victor Nizet at UC San Diego School of Medicine and Skaggs School of Pharmacy and Pharmaceutical Sciences to show that macrophage nanosponges can safely neutralize bacterial molecules that play a key role in sepsis, called endotoxins, as well as pro-inflammatory cytokines produced by the immune system. In this work, treatment with macrophage nanosponges protected mice from lethal sepsis caused by *E. coli* bacteria. The CARB-X award further validates the potential of macrophage cellular nanosponges to neutralize diverse inflammatory factors that play key biological roles in sepsis and other human diseases. As demonstrated in another recent study from the Zhang laboratory, this work could likewise position macrophage cellular nanosponges as a treatment for COVID-19 given its ability to neutralize SARS-CoV-2 and cytokine storm that the virus can cause.

The CARB-X funds will go to Cellics and the Nizet Laboratory to develop an appropriate animal model for bacterial sepsis to carefully assess the therapeutic potential of the nanosponges. Researchers will also identify the appropriate cell line to be used for manufacturing the nanosponges. The ultimate goal is to advance Cellics' manufacturing capabilities and scale up

production of the nanosponges. Cellics is currently on schedule to advance its lead product candidate, a red blood cell nanosponge for the treatment of MRSA pneumonia, to human clinical trials.

“Cellics is dedicated to the development of biomimetic nanomedicines to treat life threatening diseases. Our macrophage nanosponge technology leverages the natural receptors on human macrophage membranes to neutralize bacterial pore-forming toxins, endotoxins, and inflammatory cytokines that underlie sepsis,” said Dr. Steve Chen, president and chief medical officer, Cellics Therapeutics, Inc.

“Sepsis is a leading cause of death around the world that is made worse by the lack of effective preventatives and treatments for drug-resistant bacterial infections. Effective treatments are urgently needed,” said Erin Duffy, CARB-X R&D Chief. “CARB-X funds and supports early development of innovative antibiotics and other treatments that target the most dangerous drug-resistant bacteria. Cellics’ nanosponge product, if successful, could potentially transform the treatment of sepsis and save lives.”

Sepsis

Sepsis occurs when the body launches an uncontrolled immune response to an infection, triggering widespread inflammation that can lead to organ failure, septic shock and even death. The U.S. Centers for Disease Control and Prevention estimate that more than 1.5 million Americans get sepsis and about 250,000 die from this condition each year. A 2020 study in the leading medical journal *The Lancet* estimated that sepsis-related deaths represent 19.7% of all global deaths, exceeding cancer as a cause of human mortality.

Sepsis is usually treated with antibiotics. But while antibiotics can potentially eliminate sepsis-causing bacteria, they can’t keep inflammation in check.

Inflammation is triggered when macrophages recognize that the toxic endotoxins secreted by sepsis-causing bacteria are dangerous. In response, macrophages release proteins called pro-inflammatory cytokines, which in turn activate additional macrophages and other immune cells to produce more cytokines, setting off a dangerous domino effect of inflammation throughout the body.

Most recently, cytokine storm has emerged as a major issue in COVID-19, leading to organ injury and failure, and ultimately, if left unchecked, to death.

There is no currently approved treatment for sepsis. “To effectively manage sepsis, you need to manage this cytokine storm,” said Zhang.

Nanosponges stop the cascade that leads to sepsis by trapping endotoxins and pro-inflammatory cytokines onto their macrophage cell membranes, thus neutralizing them. The injected nanosponges vastly outnumber the organism’s own macrophages, ensuring that sepsis and a cytokine storm can be avoided. Also, since the nanosponges are covered in actual macrophage cell membranes, they can pass as the body’s own immune cells and circulate within the bloodstream without being evicted.

The nanosponge platform

Sepsis-fighting nanosponges are one example of the cell membrane cloaking technology pioneered by Zhang’s lab at UC San Diego. His group develops new nanomedicine therapies by disguising nanoparticles as the body’s own cells. Previous examples include red blood cell nanosponges to combat and prevent MRSA infections; nanoparticles cloaked in platelet cell membranes to repair wounded blood vessels; and cancer cell membrane cloaked nanoparticles to elicit multi-antigenic antitumor immunity for cancer immunotherapy.

In 2014, Zhang co-founded Cellics to further develop and commercialize this nanosponge technology. The company’s proprietary platform technology strips cell membranes of their intracellular contents and creates cellular nanosponges from these membranes to be leveraged as a therapeutic product. These nanosponges are designed to counteract diverse disease pathologies by acting as biomimetic decoys to sequester and neutralize biological molecules that would otherwise attack host cells.

Product development at Cellics currently emphasizes using nanosponges made of human red blood cell membranes and white blood cell membranes for the treatment of bacterial infections and inflammatory diseases. A similar working principle can be applied with membranes of other cell types, making cellular nanosponges suitable for large and diverse disease areas, including MRSA and COVID-19.

The mission of Cellics is to employ innovative biomimetic nanomedicines to address serious diseases with a high unmet medical need. The company’s initial primary focus at this time is on autoimmune and inflammatory diseases and difficult-to-treat infectious diseases. Cellics also aims to develop best-in-class vaccines for various diseases. The company is currently on schedule to advance its lead product candidate CTI-005 to human clinical trials for the treatment of MRSA pneumonia.

MEDIA CONTACT

Liezel Labios, 858-246-1124, llabios@ucsd.edu

UC San Diego's Studio Ten 300 offers radio and television connections for media interviews with our faculty, which can be coordinated via studio@ucsd.edu. To connect with a UC San Diego faculty expert on relevant issues and trending news stories, visit https://ucsdnews.ucsd.edu/media-resources/faculty-experts.