

A lifetime of research may be leading to a life-saving treatment for shock

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A 200-patient Phase 2 clinical pilot study will be initiated this month to test the efficacy and safety of a new use, and method of administering, an enzyme inhibitor for critically ill patients developed by University of California, San Diego Bioengineering Professor Geert Schmid-Schönbein. Conditions expected to qualify for the study include new-onset sepsis and septic shock, post-operative complications, and new-onset gastrointestinal bleeding.

This new use of a Food and Drug Administration-approved drug is based on decades of research by Schmid-Schönbein on the microvascular and cellular reactions that lead to multi-organ failure after a patient has gone into shock, which is the second-leading cause of in-hospital deaths in the United States.

Schmid-Schönbein and his colleagues at the UC San Diego Jacobs School of Engineering discovered that under conditions of shock, the epithelial cell barrier that lines the small intestine becomes permeable causing potent digestive enzymes to be carried into the bloodstream and lymphatic system where they digest and destroy healthy tissue, a process he named Autodigestion. The treatment involves blocking the enzymes with an enzyme inhibitor.

In 2005, the team's protocol was licensed to San Diego-startup Inflammagen Therapeutics under an agreement developed by UC San Diego's Technology Transfer Office. Inflammagen Therapeutics, a development-stage, critical care company, developed the Inflammagen

Shok-Pak, a drug/delivery platform that delivers the [enzyme inhibitor](#) through a nasogastric tube directly into the stomach and lumen of the intestine, preventing shock and multi-organ failure. Schmid-Schönbein serves as a scientific advisor to Inflammagen but is not an employee of the company. Instead, he has chosen to focus on continuing to conduct fundamental research on autodigestion at UC San Diego.

"We are testing for the first time whether it is possible to help severely ill patients by blocking autodigestion, a condition in which digestive enzymes not only break down food inside the intestine but also the intestine itself," Schmid-Schönbein said. "We have pre-clinical results that this treatment can save lives."

To date, Inflammagen Shok-Pak has been used successfully outside the United States as a rescue therapy in 15 patients, most of whom were diagnosed with life-threatening conditions. In addition, pre-clinical studies of the technology in two animal species have demonstrated significant increases in long-term survival.

"Currently, patients in shock who survive their initial insult don't necessarily survive long-term. In addition, morbidity is very high in those patients that do survive. Our animal studies suggest that the treatment could improve functional outcomes and reduce the time patients remain in intensive care, as well as increase long-term survival rates," said principal investigator Dr. Erik Kistler, who currently serves as an assistant clinical professor in the Department of Anesthesiology and Critical Care at the UC San Diego School of Medicine and the Veterans Administration Healthcare System, San Diego. "While ICU costs can approach one-third of the entire hospital costs, decreasing ICU time by even a small percentage a day will have significant financial savings for patients and payors as well as result in significantly improved patient wellness," said Kistler, who earned a doctorate (1998) and master's (1994) in bioengineering from the Jacobs School of Engineering

as a student of Schmid-Schönbein's.

The Phase 2 pilot is designed as a double-blind, standard-therapy controlled study of 200 critically ill ICU patients. The goal is to determine the safety and efficacy of the gastrointestinal administration of Inflammagen Shok-Pak in the reduction of morbidity, which is defined as the incidence of disease. The team wants to know whether the treatment will reduce the time patients spend in intensive care and the hospital, and improve long-term survival rates. To determine this, researchers will follow up with patients 28 days and six months after discharge. The Phase 2 [pilot study](#) will be conducted at the Intensive Care Unit (ICU) at the VA San Diego Healthcare System, with additional sites being added as appropriate.

John Rodenrys, CEO of Inflammagen Therapeutics, remarked, "Initiation of the Phase 2 pilot study is a key milestone in the development of Inflammagen Shok-Pak as a potential treatment for sepsis and septic shock, which may result in multi-organ failure, a highly-invasive condition for which there is currently no effective therapy option."

Hank Loy, president of Inflammagen Therapeutics, added, "We look forward to working with the investigative team at the VA San Diego Healthcare System and expect their experiences to demonstrate the benefits of Inflammagen Shok-Pak, which have been evident in the pre-clinical studies and ex-U.S. patient experiences."

Inflammagen Shok-Pak was developed based on Schmid-Schönbein's research at the UC San Diego Jacobs School of Engineering and was supported by the National Institutes of Health and the UC San Diego Jacobs School of Engineering's von Liebig Center for Entrepreneurism and Technology Advancement, which provides advisory services and seed funding to accelerate the commercialization of research at

universities throughout Southern California. It was during an informal meeting hosted by the von Liebig Center that Schmid-Schönbein met Rodenrys, then a senior managing director of Leading Ventures, a La Jolla venture capital firm that specializes in promising, early stage technologies. Leading Ventures is now Leading Biosciences.

Schmid-Schönbein was awarded the 2008 Landis Award for his discovery of autodigestion. His current work is focused on the trigger mechanisms that produce multiple organ injury mechanisms and inflammation, one of which is due to digestive enzymes via the autodigestion process. He directs the UC San Diego Microcirculation Laboratory where he and his team are studying other forms of autodigestion also in chronic hypertension, diabetes, obesity and other diseases.

"We are basic scientists, we are not clinicians," said Schmid-Schönbein. "But the question is how do you apply yourself? Part of my goal is to increase the number of engineers who are educated in what could become a separate branch of bioengineering, called 'disease analysis.' We use the tools of [bioengineering](#) analysis to make new contributions to the understanding of the origin of diseases important to society."

Provided by University of California - San Diego

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