Promising cancer treatment found by scraping the ocean floor

Researchers at Loma Linda University School of Medicine (LLUSM) and their commercial partner, Scion BioMedical, Inc., are developing a potentially powerful new resource in the battle against bladder cancer from an extract of crab, lobster and shrimp shells.

"Chitosan is amazing," says Wolff Kirsch, M.D., director of the Neurosurgery Center for Research, Training and Education at LLUSM. "It promotes hemostasis, or blood-clotting, potentially immunizes against superficial bladder cancer and fights inflammation."

Bladder cancer is deadly. Although the specific condition targeted in this study — a type of bladder cancer that does not spread into the muscles of the bladder wall — is not as dangerous as more advanced forms, there is strong demand for better treatments.

Kirsch says the idea of using chitosan ("kite-o-san") as a treatment for bladder cancer originated in pioneering research by David Zaharoff, Ph.D., and John W. Greiner, Ph.D., at the NCI. But he credits a conversation between Andrew Crofton, an LLUSM graduate student, and James L. Gulley, M.D., Ph.D., chief of the genitourinary malignancies branch at the NCI Center for Cancer Research, and a 1995 LLUSM graduate, with creating a potential solution to a problem that plagued those earlier studies.

During that discussion, Crofton told Gulley he and Kirsch have developed a procedure for purifying chitosan with nitrogen gas plasma to enable its use as an implantable blood-clotting agent in surgery.

Gulley became very interested. He said the NCI had tested the combination of chitosan and interleukin-12 (IL-12), an immune molecule, and found it to be highly effective against bladder cancer in mice. However, the tests had to be suspended because of the lack of sufficiently purified chitosan to safely implant in humans.

As they talked, Gulley and Crofton suddenly realized nitrogen gas plasma might be the solution.

Kirsch, who has been studying chitosan for more than 20 years, was delighted when Crofton said the NIH might be interested in funding research into his nitrogen gas plasma process.

Because chitosan is harvested from the sea, Kirsch says it contains very high level of endotoxins.

"We've developed a patented process for cleaning it up with nitrogen gas plasma," he reports. "LLUSM holds the patent on the process, and we partnered with the only company currently capable of producing biomedical-grade chitosan from crustaceans: Scion BioMedical, Inc."

Before chitosan can be tested on humans, however, pre-clinical studies must establish that the plasma-treated variety meets baseline values for cleanliness and safety without significant loss of functionality.

To accomplish this, Kirsch and Crofton submitted a Phase I SBIR grant application to NCI under the name of Scion BioMedical, Inc. The acronym, which stands for "small business innovative research," denotes grants from the U.S. government to enable small businesses to conduct research and develop projects with commercial potential. Based in Miami, Florida, Scion will produce the biomedical-grade chitosan in Washington State.

If the initial study is successful, purified chitosan will then be subjected to a far more extensive SBIR Phase II review to establish that it meets the "safety and efficacy" standards of the Food and Drug Administration (FDA). The Phase II study will also compare the performance and cost of the chitosan and IL-12 combination to similar products.

Kirsch conceived the idea for using nitrogen gas plasma to produce a grade of chitosan that meets FDA standards for internal use by humans.

On August 11, 2014, he and Crofton learned their application for an initial $225,000 SBIR Phase I study had been approved by the NCI. Under NIH guidelines, Kirsch will serve as principal investigator with Crofton and Sam Hudson, Ph.D., from North Carolina State University, as co-investigators. The trio will conduct the research at LLUSM as Scion employees, and Scion will administer the research funds.

According to Louis R. Rose, president & CEO of Scion, his company will supply the chitosan that will be "depyrogenated" at LLUSM. The word denotes the process of inactivating toxins that produce fever and inflammation.

"Scion BioMedical Corp. is a U.S.-based biomedical technology company that develops medical solutions for hemostasis, wound management, infection control, antimicrobial barrier protection, and drug delivery systems," Rose explains. "We are pleased and proud to partner together with the illustrious research team headed by Dr. Wolff Kirsch of Loma Linda University and Dr. Sam Hudson of North Carolina State University. Together we hope to discover immunotherapies that can change the face of medicine and improve the lives of patients. This is our mission and our collective goal."

At 83 years of age, Kirsch is excited that a humane new procedure will allow him to study chitosan without putting laboratory animals at risk.

"In the past, the only method for testing chitosan for endotoxins was to inject it into rabbits and see if they exhibited a fever," he reports. "Now there are more sophisticated tests available involving horseshoe crabs. Horseshoe crab blood cells look like amoebas. In the presence of pyrogens, they coagulate."

He is also proud of two of his students.

"Andrew Crofton is one of the most talented graduate students I've ever worked with," Kirsch explains, noting that Crofton recently made chitosan the subject of his doctoral dissertation.

"I was on the dissertation committee when Gulley defended his research on an amino acid I discovered several years earlier," Kirsch continues. "I knew he was destined for a very bright future, and he has achieved it. He was decorated by President Barack Obama in 2011 with the Presidential Early Career Award for Scientists and Engineers."

Crofton hopes the project will save lives.

"We believe nitrogen plasma will enable us to decontaminate chitosan without degrading it, and thus preserve its functionality," he notes. "Achieving this objective would be a tremendous advance since chitosan has a long list of extraordinarily useful biomedical properties."

Kirsch takes a similar big-picture view.

"Chitosan," he concludes, "has potential to make real strides against bladder cancer. And that's a pretty big deal!"

Louis R. Rose

Wolff Kirsch, M.D. with Andrew Crofton and Nicholas Sanchez, School of Medicine Graduate Students