Chemist working to help healing process

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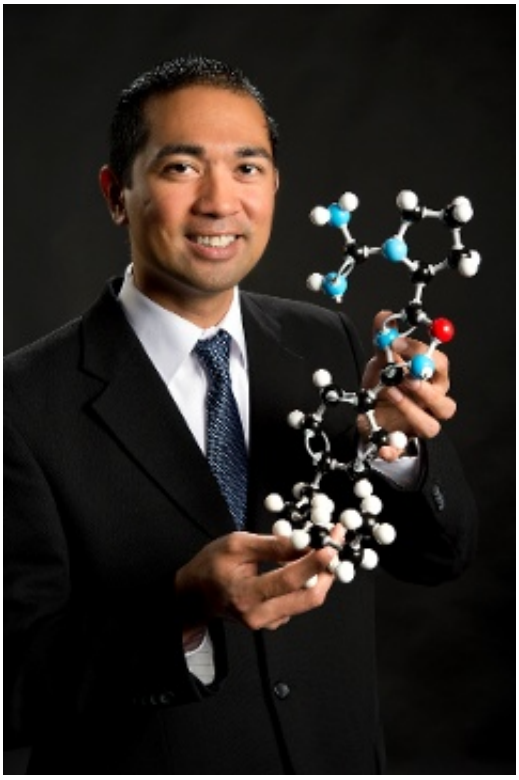

Webster Santos

The human body in all its complexity, sometimes is a little overzealous in making repairs. These repairs can, in some instances, lead to more problems.

For organic chemist Webster Santos, associate professor of chemistry, helping the body turn off its healing mechanisms in time to prevent fibrosis is a goal with an end in sight.

Building organic molecules in his lab, Santos, a native of Pampanga, Philippines, had been working on a compound he thought would be used to treat cancer.

"We've been working on this compound since around 2009," he said, "and it basically boils down to the fact we found a structure that we modified for a target enzyme and we're continuing to work on it with the eye toward it becoming a drug to fight fibrosis."

When the body is damaged, cells work to repair the tissue. However, when they're done, they don't always stop, creating more layers on the healed tissue that are fibrous in nature, and stiffer than the original tissue. This fibrosis can often cause complications. In fact, 45 percent of deaths in America each year have some sort of fibrotic component and more than 10 percent of Americans will suffer some sort of kidney fibrosis. Santos said this costs more than $35 billion each year.

"There isn't a single drug that treats fibrosis pathology – we hope to be the first," he said.

To help the team on their way, the National Institute of Health in September awarded Santos and his partner, Kevin Lynch, professor and vice chair of pharmacology at the University of Virginia, a $1.15 million three-year grant. Together with several other backers, Santos and Lynch founded Sphynkx Therapeutics in 2010 and licensed the patent rights from Virginia Tech Intellectual Properties and UVA Licensing & Ventures group.

"This started because Kevin, whom I've known for some time, called and said he needed an inhibitor for an enzyme he was working with," Santos explained. "I would make one and send it to him, and he'd tell me it didn't work, so I'd do it again. He'd tell me where it did work, and I'd modify it again. That went on for quite a while, but we knew we were

getting closer as he kept finding more activity with the compound. Initially we thought it was going to be an anti-cancer drug, but it turned out it worked pretty well for fibrosis."

The compound Santos works on deals with Sphingosine kinases, a protein that makes a ubiquitous signaling molecule in the blood of everyone that tells cells to grow, and multiply, and divide. In their original work, Santos thought the inhibitor he was helping create would tell the molecule to have the opposite effect – to essentially stop making more cells and die.

"We originally thought having the compound tell the cell to die would be good for cancer," Santos said. "But after testing we found it didn't work the way we had hoped, but an expert at the University of Virginia in the renal area had a knock-out of the enzyme and he had shown that the compound was protective toward kidney fibrosis. So we gave him our compound to test and it mimicked the knock-out model and showed it could work toward that end."

"What's involved is a lot of cell signaling," Santos explained. "The molecule signals the molecules that bind to the cell's surface receptors and it has a lot of impact telling cells when to stop and when to grow; when to repair, and when to stop repairing; and telling cells when to change from one type of cell to another type. The enzyme we're working on is involved in all of this."

Building the compound takes weeks to create as the chemists try to get the correct bonds to form. A task made more difficult with natural products.

"It's like building anything else," Santos said. "Building a bicycle is relatively easy whereas building a high performance sports car or a space shuttle is not. They both have a group of pieces that need to go together,

but one is far more complex with more connections that have to be made at a higher tolerance."

While the ultimate goal for Santos and his team is to create a viable drug, the end is still some distance off, but he feels it's within reach.

"We hope to have an investigational new drug in the next two to three years and then it will start the Food and Drug Administration clinical trials, but we're quite far down the road. We need to do a good deal more work before we get to the stage of having an orally administered drug – but we're getting there."

Santos received his bachelors and doctoral degrees from the University of Virginia in 1997 and 2002 respectively and he conducted his post-doctoral work at Harvard University before coming to Virginia Tech in 2006.

Provided by Virginia Tech