Researchers make breakthrough against poxviruses

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Smallpox has a nasty history throughout the world. Caused by poxviruses, smallpox is one of the few disease-causing agents against which the human body's immune system is ineffective in its defense.

A major breakthrough by Junpeng Deng, a structural biologist in the Division of Agricultural Sciences and Natural Resources (DASNR) at Oklahoma State University, and his first-year Ph.D. student, Brian Krumm, may be the first step towards a pharmaceutical medication for smallpox and the emerging human monkeypox.

The human immune system is rendered helpless against poxviruses partly because the viruses block a human immune molecule, interleukin-18 (IL-18), from sending out a signal to the immune system. The body acts as if everything is fine and the deadly disease takes over.

Deng and Krumm joined an ongoing project midway through 2007 and Krumm found what he was looking for in December 2008. They solved a three-dimensional crystal structure of a poxvirus protein in the act of disarming the IL-18.

"We capped a lot of others' research. This is additional information provided," said Krumm, who is credited as the major contributor to the research. "We also show many things through the structure that can't be revealed through traditional molecular biology and immunology."

The study is published in the Dec. 22 early online edition of the

Proceedings of the National Academy of Sciences of the United States of America.

"We know now how the proteins communicate with each other," Deng said. "In the future, we can design a drug to stop the poxvirus from blocking the IL-18 protein."

As there is currently no medication for poxvirus-caused diseases, this research could aid national and international security efforts against potential poxvirus use as bioterrorism.

Deng called the finding an example of "killing two birds with one stone."

"At this time we only have very limited medication to treat autoimmune diseases," he said.

For example, rheumatoid arthritis is one of the most prevalent autoimmune diseases in which IL-18 is too active, leading to the body attacking its own cells. Deng said seeing how IL-18 interacts with the poxviruses will help with the development of effective inhibitors against overreaction.

"There are still a lot of questions to be answered. This is just the beginning," Deng said. "This opened up a new area to explore: How we design medication for autoimmune diseases. We want to provide more and more structural insights."

Deng and Krumm will continue to do research in the lab created two years ago in November 2006, when Deng joined OSU with funding provided by a start-up fund from DASNR.

"Junpeng is a relatively new assistant professor at OSU and has already demonstrated some excellent work," said Gary Thompson, head of the

department of biochemistry and molecular biology. "I'm really impressed with not only Junpeng, but also the quality of work from his Ph.D. students."

Deng and Krumm did their research in the lab at OSU, but recognize the help they had from other researchers.

"Credit also goes to Yan Xiang and Xiangzhi Meng, our collaborators at the University of Texas Health Science Center at San Antonio," Deng said of the multi-institutional effort. "I believe our excellent collaboration will bring more success in the future."

Source: Oklahoma State University