Scientists discover how smallpox may derail human immune system

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University of Florida researchers have learned more about how smallpox conducts its deadly business — discoveries that may reveal as much about the human immune system as they do about one of the world's most feared pathogens.

In findings to be published this week in the online early edition of the Proceedings of the National Academy of Sciences, scientists describe how they looked at all of the proteins produced by the smallpox virus in concert with human proteins, and discovered one particular interaction that disables one of the body's first responders to injury — inflammation.

"This virus that has killed more humans than any other contains secrets about how the human immune system works," said Grant McFadden, Ph.D., a professor of molecular genetics and microbiology at the College of Medicine and a member of the UF Genetics Institute. "I'm always amazed at how sophisticated these pathogens are, and every time we look, they have something new to teach us about the human immune system."

With researchers from the University of Alberta, the Centers for Disease Control and Prevention and a private company called Myriad Genetics, UF researchers for the first time systematically screened the smallpox proteome — the entire complement of new proteins produced by the virus — during interactions with proteins from human DNA.

These protein-on-protein interactions resulted in a particularly devastating pairing between a viral protein called G1R and a human protein called human nuclear factor kappa-B1, which is believed to play a role in the growth and survival of both healthy cells and cancer cells by activating genes involved in immune responses and inflammation.

"One of the strategies of the virus is to inhibit inflammation pathways, and this interaction is an inhibitor of human inflammation such that we have never seen before," McFadden said. "This helps explain some of the mechanisms that contribute to smallpox pathogenesis. But another side of this is that inflammation can sometimes be harmful or deadly to people, and we may learn a way to inhibit more dangerous inflammation from this virus."

Smallpox is blamed for an estimated 300 million deaths in the 20th century alone, and outbreaks have occurred almost continuously for thousands of years. The disease was eradicated by a worldwide vaccination campaign, and the last case of smallpox in the United States was in 1949, according to the CDC. The last naturally occurring case in the world was in Somalia in 1977.

With the exception of stores of the virus held in high-containment facilities in the United States and Russia, smallpox no longer exists on the planet. Since it was no longer necessary for prevention, and because the vaccines themselves were risky, routine vaccination against smallpox was stopped. However, public health concerns regarding the possible re-emergence of the virus through bioterrorism have led to renewed interest in the development of treatments for the disease and safer vaccines.

Source: University of Florida (news : web)