

Scientists learn how poxviruses defeat the body's host defense

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Smallpox virus magnified approximately 370,000 times. Smallpox, which killed millions of humans through the ages, ranks among the world's most feared bioterrorism agents. In a new report, virologists from the School of Medicine at the University of Texas Health Science Center at San Antonio and collaborators at Oklahoma State University demonstrate how poxviruses such as smallpox defeat the body's host immune defenses. Credit: CDC / Dr. Fred Murphy; Sylvia Whitfield

Smallpox virus, which killed millions of humans through the ages, ranks among the world's most feared bioterrorism agents. Human monkeypox continues to occur sporadically in remote African villages.

In a new report, virologists from the School of Medicine at The University of Texas Health Science Center at San Antonio and their collaborators at Oklahoma State University demonstrate how poxviruses such as smallpox defeat the body's host immune defenses. The implications extend beyond <u>viral infections</u> to cancer therapy, said senior author Yan Xiang, Ph.D., associate professor in the Department of Microbiology and Immunology, UT Health Science Center.

Dr. Xiang and colleagues revealed how a molecule on the poxviruses defeats a host restriction factor called SAMD9 in humans and animals. In addition to protecting against viruses, SAMD9 suppresses tumors, and mutations in the human SAMD9 gene are responsible for a life-threatening cancer called normophosphatemic familiar tumoral calcinosis. SAMD9 is also implicated in myeloid leukemias and lung cancer.

"There is an 'arms race' occurring between pathogens (disease-causing agents) and their hosts," Dr. Xiang said. "To survive in their hosts, many pathogens utilize specific inhibitors of the host restriction factors. SAMD9 is an evolutionally conserved immune barrier, but it has been



successfully overcome by diverse poxviruses." First author of the study is Xiangzhi Meng, Ph.D., an assistant professor in microbiology and immunology at the Health Science Center.

The discovery was described in December in *Proceedings of the National Academy of Sciences*.

More information: X. Meng et al. Structural basis for antagonizing a host restriction factor by C7 family of poxvirus host-range proteins, *Proceedings of the National Academy of Sciences* (2015). DOI: 10.1073/pnas.1515354112

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