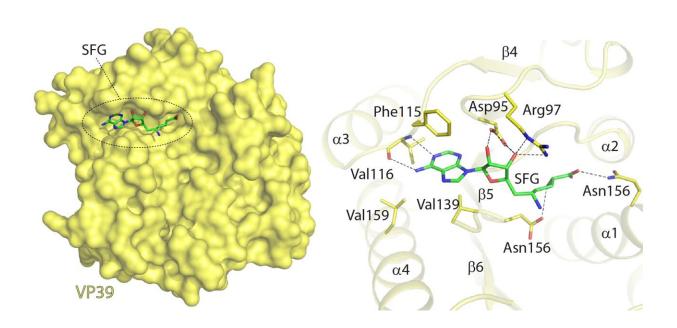


Researchers decipher the structure of protein methyltransferase from the mpox virus

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Sinefungin and SAH recognition by the monkeypox virus VP39 methyltransferase. Credit: Jan Silhan et al

Scientists from the Institute of Organic Chemistry and Biochemistry in Prague have deciphered the structure of the protein methyltransferase from the monkeypox virus. It is with the help of this protein that the virus escapes human immunity and causes the monkeypox disease. Based on this discovery, they have prepared substances that can block the function of methyltransferase.



The results of this research may constitute the first step towards creating a completely new group of antivirals. This applies not only to monkeypox, but also to diseases caused by other viruses, including COVID-19 induced by the SARS-CoV-2 coronavirus.

An article on the results of the work of the scientific groups led by Dr. Evžen Bouřa and Dr. Radim Nencka has now been published in *Nature Communications*. Both teams have for many years been studying viruses that cause serious diseases. In the past, they focused on the Zika virus from the flavivirus group or the SARS-CoV-2 virus from the coronavirus group.

Like other viruses, the monkeypox virus multiplies in a host cell. For it to defend itself against external attack, it needs to recognize which RNA molecules are its own and which are not. "Native RNA molecules carry a special marker called a cap for easier recognition. An unmarked molecule triggers an innate antiviral immunity response in infected cells. Therefore, viruses try to deceive the <u>human body</u> and, for example, the monkeypox virus confuses it by also adding a cap to its RNA," explains Evžen Bouřa.

The symptoms of monkeypox resemble those of smallpox, a disease that has already been eradicated. Until recently, the virus causing it was found only in Central and Western Africa. Its natural reservoirs reside in rodents and primates. In humans it can cause a disease with an estimated mortality rate of 3% to 6%. While this is less than in the case of smallpox, it is much higher than, for example, with COVID-19.

Recently, the <u>monkeypox virus</u> has spread worldwide, so it is no wonder that not only experts, but also the <u>general population</u> and public authorities are nervously watching the threat of another global viral pandemic. "Our colleagues perfectly combine <u>structural biology</u> and cutting-edge medicinal chemistry. Thanks to that, we are closer to



discovering new antivirals," says Prof. Jan Konvalinka, the director of IOCB Prague.

More information: Jan Silhan et al, Discovery and structural characterization of monkeypox virus methyltransferase VP39 inhibitors reveal similarities to SARS-CoV-2 nsp14 methyltransferase, *Nature Communications* (2023). DOI: 10.1038/s41467-023-38019-1

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