A Structure-based Approach to combat Zoonotic Poxviruses

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

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Poxviruses are large cytosolic DNA viruses with a propensity to cause zoonoses. They are present in animal reservoirs and responsible for a large spectrum of disorders, including human smallpox. Although only few causative treatment options are available, vaccination with the non-pathogenic vaccinia virus enabled the eradication of the smallpox-causing variola virus, responsible for an estimated 300 million death toll in the 20th century. However, the herd immunity against poxviruses is dwindling in humans. Accordingly, a recent study ranks monkeypox virus among one of the most threatening viruses for its pandemic 'spillover' risk. The researchers outline a structure-based drug design strategy to combat the risk imposed by poxviral reservoirs. The team aims at targeting the unique poxviral transcription machinery, which relies exclusively on virus-encoded proteins. As a basis, the team recently reported the isolation and comprehensive structural investigation of this machinery in different phases of action. This now enables the identification and design of small molecules that interfere with poxviral gene expression and their subsequent conversion into specific antiviral drugs. Because the transcription machineries of Poxviridae and Asfarviridae are highly similar, this research is also likely to be of relevance for the economically highly threatening Asfarvirus-linked swine fever disease.

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