Cryo-Electron Microscopy Investigations of Seneca Valley Virus

Bostina, M.[1], Jayawardena, N.[1], Easingwood, R.[1], Strauss, M.[2], Wolf, M.[3] and Burga, L.[1]

[1] University of Otago, New Zealand, [2] Harvard Medical School, United States, [3] Okinawa Institute for Science and Technology, Japan

Seneca Valley Virus (SVV) is a newly emerged picornavirus with potent antitumour activity and is being explored for use as a therapeutic agent in the treatment of small cell lung cancers and paediatric solid tumors with neuroendocrine features.
Recently, we identified the anthrax toxin receptor 1 (ANTXR1) as the high-affinity receptor for SVV in cancer cells (1). This presents a unique example of a shared receptor between a mammalian virus and a bacterial toxin. From a therapeutical perspective, ANTXR1 constitutes a highly specific biomarker for the identification of potential patients for SVV virotherapy. ANTXR1 has been found to be overexpressed in 60% of human cancers and less-expressed in normal tissues. This finding opens the possibility of developing SVV as targeted therapy against a wider range of cancers. In addition, numerous reports show SVV to be an important emerging livestock pathogen for which a vaccine could be necessary.

We used cryo-electron microscopy in combination with other techniques to investigate the structural differences between the SVV procapsid and the native virion. We solved the procapsid structure at 5.9 Å and that of the full virion at 3.8 Å (2). We also solved the structure of the ANTXR1 decorated capsid at a resolution of 3.8 Å.

The exterior of SVV full capsid and procapsid appeared identical. Most of the differences occurred on the inside of the capsid, where the N-terminal end of VP1 is disordered in the procapsid, but becomes ordered in the full virion, in contact with the viral RNA. Unlike the majority of picornaviruses, most copies of VP0 were cleaved in both the procapsid and the full capsid of SVV. Variations in pH affected the stability of both the procapsid and the full virion. In addition, our receptor-capsid structure revealed the that ANTXR1 makes extensive contact with VP2 protein. The structure of the capsid solved at 3.1 Å, indicated subtle changes for all the capsid proteins.

Our results are revealing properties of the SVV procapsid, some of them novel to the picornavirus family. These results will aid to engineer a modified version of the procapsid to be used for targeted in vivo delivery in cancer therapy or to make a stable vaccine against SVV, which could be of great interest to the agricultural industry.

References
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