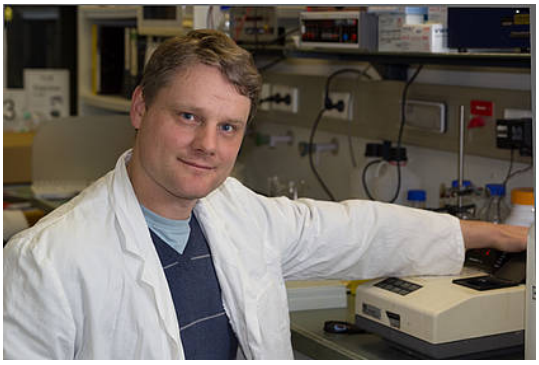
NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

SEMINAR

Tues, 8 Oct 2019 | 10 am | DBS Conference Room 1

Hosted by A/P Christoph Winkler



Atomic Structures of Vaccinia DNA-Dependent RNA Polymerase Complexes: The Mechanism of Poxvirus Transcription

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Poxviruses possess a complex DNA genome that is expressed and replicated exclusively in the cytoplasm of infected cells. Gene expression of this virus class has been studied mostly in *Vaccinia* virus (VV), which serves as a smallpox vaccine and is a promising tool in viral anti-cancer therapies. However, structural insight into the transcription machinery of VV has been lacking so far. Here we describe the biochemical and structural characterization of purified, catalytically active viral DNA-dependent RNA polymerase (vRNAP) enzyme complexes.

The vRNAP core enzyme resembles RNA polymerase II, but at the same time displays many virus-specific features, including transcription factor Rap94, whose five distinct domains intertwine with the core vRNAP assembly.

The complete vRNAP additionally contains the early transcription factor VETF, the mRNA processing and termination factors VTF/CE and NPH-I and the viral core protein E11. Strikingly, this compact, 0.85 MDa complex also comprises a host $tRNA^{Gln}$ as an integral component. The unit is capable of carrying out the entire early transcription process, including promotor recognition, initiation, elongation, mRNA capping and termination. The structure shows that Rap94 provides TFIIB-like functionality, that the vRNAP subunit Rpo30 resembles the Pol II elongation factor TFIIS, and that NPH-I resembles chromatin remodelers.

Structures of a co-transcriptional capping complex and of an elongation complex further reveal how nascent RNA is channeled from the vRNAP active site through the exit tunnel to the capping enzyme. This process is accompanied by large-scale rearrangements of accessory factors in the viral transcription machinery.

Our study allows unprecedented insight into the architecture of a viral multi-component transcription apparatus and reveals the principle mechanisms underlying the regulation, synthesis and co-transcriptional modification of poxvirus RNA.