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Endonuclease substrate selectivity characterized with full - Length PA of influenza A virus polymerase

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The influenza A viral polymerase is a heterotrimer capable of both transcribing viral mRNAs and replicating the viral genome. To initiate synthesis of viral mRNA the virus uses a process known as "cap snatching" wherein the viral polymerase binds a host pre-mRNA and cleaves a short primer with a 5' end cap structure. Essential to this process is the enzymatic activity contained within the PA subunit. The N-terminal domain of PA has been demonstrated to have endonuclease activity in vitro and crystal structures of the PA N-terminal domain reveal a distinct active site. Here we sought to understand the biochemical nature of the PA endonuclease activity using, for the first time, the full-length PA protein. This full-length protein is active against both RNA and DNA in a cap-independent manner and can use several different divalent cations as cofactors. Different metal cofactors induce secondary structure changes, which correlate with cleavage patterns. Our in vitro assay was also able to demonstrate the minimal substrate size and sequence selectivity of the PA protein. Finally, we confirmed the observed endonuclease activity of the full length PA with a FRET based endonuclease assay, which is well suited for screening of novel anti-influenza agents.

Biography

Erin Noble completed her B.S. degree in Microbiology and Immunology in 2007 from the University of Rochester. She is in the process of completing her PhD research in the lab of Dr. Baek Kim at the University of Rochester. Her research focuses on understanding the biochemical nature of the influenza A virus polymerase complex and developing assays to characterize viral biochemical processes.

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