Undergraduate Research Symposium May 18, 2018 Mary Gates Hall

Online Proceedings

Poster Session 2

Balcony, Easel 118

1:00 PM to 2:30 PM

Uncovering the Molecular Mechanism of Influenza Virus Restriction by Mx Proteins

Rachel Eguia, Recent Graduate, Biochemistry, Biophysics, and Molecular Biology, University of Washington
UW Post-Baccalaureate Research Education Program
Mentor: Gabriele Varani, Chemistry

The innate immune system employs various tactics to protect our bodies against foreign pathogens. For example, during a viral infection, virus particles selfishly enter a host cell to propagate and make copies to infect neighboring cells. But during this infection, the host's innate immune system recognizes certain pathogen-associated molecular motifs which signals for the production of proteins, known as restriction factors. These restriction factors can then block the viral pathogen by inhibiting various steps in the viral life cycle. One class of restriction factors active against influenza virus, are Mx proteins. Previous research indicates that these proteins may exert their antiviral activity by inhibiting the processivity of the viral RNA-dependent RNA polymerase during transcription and synthesis of influenza viral RNA (vRNA). Based on these findings, we hypothesized that the production of longer vRNA segments will be blocked in the presence of Mx proteins, with minimal effect on the production of shorter vRNA segments. To test this hypothesis, I designed fluorescent reporter constructs that mimicked the sizes of both short and long influenza genome segments and measured the ratio of short to long vRNA segments in the presence or absence of Mx using flow cytometry. Preliminary results indicate that Mx localized to the cell nucleus restricts the production of long vRNA segments, supporting our hypothesis. In contrast, Mx that is cytoplasmically-localized does not seem to have any effect on the production of long vRNA segments. Overall, this research will elucidate the previously unknown mechanism of viral restriction by Mx proteins, while also giving us insights into mechanisms of pathogen recognition by the innate immune system.

Session 2R

Exploring Protein Function at Scales from Whole Tissues to Single Atoms

Session Moderator: Celeste Berg, Genome Sciences

JHN 111

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Selective Inhibition of PARP4

Ashley Person, Junior, Biochemistry, Biophysics, and Molecular Biology, Whitman College
Mentor: Mike Cohen

Poly-ADP-ribose polymerases (PARPs) are enzymes that catalyze the post-translational transfer of adenosine diphosphate (ADP) from NAD+ to target proteins. Of the 17 PARPs, some have been studied extensively and are known to have important cellular functions while little is currenty understood about others. A cellular imbalance of one of these PARP enzymes, PARP4, has been correlated with several disease states, including cancers, though its cellular roles are largely unknown. Inhibitors of PARP4 are useful as tools to investigate the enzyme's functions and evaluate the inhibitors' therapuetic potential. In this research, several compounds were tested as inhibitors of PARP4 using a PARP inhibition screening assay. Initial results identified a potent, somewhat selective compound, and revealed which parts of the compound were important for PARP4 inhibition. This was used to direct the synthesis and testing of potentially more selective inhibitors of PARP4. This presentation discusses the inhibition results and their significance towards learning more about PARP4 biology, which can help inform researchers of this enzyme's role in disease states and give insight into developing treatments for such diseases.