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

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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.

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Computational Structural Modeling of Evolutionary Conserved Region in Cyrano/OIP5-AS1

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lncRNAs play a wide range of cellular functions, and the roles they play in cell maintenance are of increasing importance. An unusually conserved lncRNA, OIP5-AS1 (known as Cyrano), plays a crucial role in stem cell differentiation and development. It has also been shown to interact with the miRNA miR-7 and the protein HuR. Although there is growing information about interactions of Cyrano, truly understanding this lncRNA's function is hindered by the lack of structural information. To gather information on the structure of the evolutionary conserved region of Cyrano, the secondary structure was elucidated using SHAPE and RNA prediction software. A 4-way junction was observed when assessing these data. The 2D predictions were used as constraints to generate 3D models of the 4-way junction. Overall, three separate prediction software generated topologically similar 3D models of Cyrano (RMSD range of 13.362 Å). These models produce a 4-way junction with 2 coaxial stacked helices (H1H2, H3H4). These modeled structures suggest a Family cH 4 way junction, where H1 and H3 interact forming an A-minor interaction between junction J(1,2) and Helix H3. This model is important as it aids in directing future experimental approaches for studying Cyrano, and also hint at a potentially important structural motif for Cyrano function.