

EXPRESSING AND MULTIPLYING – viral gene expression

Abstract final identifier: P027

DEPHOSPHORYLATION OF RESPIRATORY SYNCYTIAL M2-1 PROTEIN BY THE CELLULAR PHOSPHATASE PP1 IS REQUIRED FOR ITS MRNA BINDING ABILITY

Jean-Francois Eleouet¹, Charles-Adrien Richard², Vincent Rincheval³, Christophe Cardone⁴, Camille Esneau¹, Sergei Nekhai⁵, Marie Galloux¹, Marie-Anne Rameix-Welti³, Christina Sizun⁴

¹Unite de Virologie et Immunologie Moleculaires, INRA Universite Paris-Saclay, ²Unite de Virologie et Immunologie Moleculaires, INRA, Jouy en Josas, ³UMR1173, INSERM-Universite de Versailles St Quentin, Montigny le retonneux, ⁴ICSN, CNRS-Universite Paris-Saclay, Gif-sur-Yvette, France, ⁵Center for Sickle Cell Disease, Howard University, Washington D.C., United States

Abstract: The M2-1 protein of respiratory syncytial virus (RSV) is essential for viral transcription. Previous reports suggested that dynamic regulation of M2-1 phosphorylation is critical for its function. M2-1 phosphorylation depends on the presence of the RSV phosphoprotein P, which is a multifunctional protein and the main cofactor of the large RNA polymerase L protein; formation of the P-M2-1 complex is required for viral transcription. However mechanisms involved in M2-1 phosphorylation and dephosphorylation *in vivo* have not been clarified. Using site-directed mutagenesis and NMR, we identified an RVxF-like motif located upstream of the M2-1 binding domain and involved in the capture of the host cell protein phosphatase-1 (PP1) by P and its recruitment to cytoplasmic inclusion bodies (IBs) where viral RNA synthesis occurs. We further show that the P-PP1 complex regulates M2-1 dephosphorylation and RSV transcription. In the absence of PP1 from inclusion bodies, M2-1 was excluded from IBs associated granules (IBAGs) formed by viral mRNA. These results suggest that M2-1 functions not only as a transcription antiterminator but plays also a critical role at late transcription steps.

Graphical Abstract:

