The Measles virus phosphoprotein - An intrinsically disordered chaperone that regulates nucleocapsid assembly

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Measles virus, a negative strand RNA virus, packages its genome into large, helical superstructures formed by the nucleoprotein (N) that assembles on the RNA genome. Although a vital step in viral replication, the assembly process of N into nucleocapsids (NC) has largely remained obscure since overexpression of N in eukaryotic and prokaryotic expression systems leads to NC formation within the expression host. We show how the presence of a short 50 residue, intrinsically disordered, peptide from the measles phosphoprotein (P) can prevent premature assembly during expression by forming a monomeric N^0P construct that self-assembles into NC-like particles upon addition of RNA in vitro. This approach allowed us, for the first time, to study NC assembly and its kinetics by NMR and fluorescence spectroscopies, and revealed a remarkable dependence on RNA sequence despite the fact that N has to encapsidate the entire viral genome [1]. A structural analysis of N^0P comprising the full intrinsically disordered tails of P and N of more than 400 residues in length allowed us now to delineate the importance of the full P_{TAIL}. Since other negative strand RNA viruses share similar protein architectures, these results promise to have implications on a large number of important human pathogens.

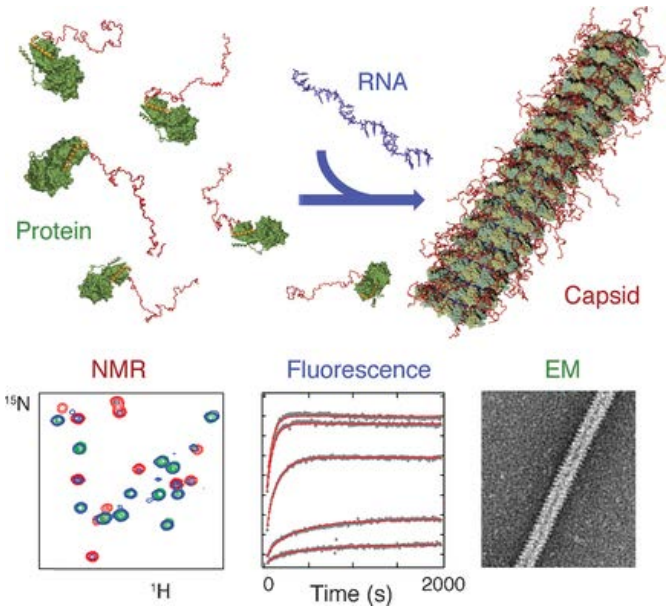

Figure 1: Measles virus nucleocapsid assembly from chaperoned N^0P complexes by NMR, fluorescence and electron microscopy.

References

[1] - Self-Assembly of Measles Virus Nucleocapsid-like Particles: Kinetics and RNA Sequence Dependence. S. Milles, M.R. Jensen, G. Communie, D. Maurin, G. Schoehn, R.W. Ruigrok, M. Blackledge, Angew Chem Int Ed Engl. 2016 Aug 1;55(32):9356-60.