Assembly of ssRNA viruses: The role(s) of the package during packaging.

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Previously we have been using the RNA bacteriophage MS2, a *T*=3 virus, as a model in which to answer fundamental questions about assembly mechanisms of ssRNA viruses. This has allowed us to define the molecular basis of genome sequence specific recognition by coat protein and in the past year this has been extended to an understanding of how discrimination between closely related viral RNAs is achieved. We have also shown for the first time in any system how the coat protein conformation is switched between quasi-equivalent conformers during the assembly process. *T*=3 capsid assembly is only efficient when two distinct conformers of the capsomer – a coat protein dimer in this case – are present. Binding the RNA stem-loop packaging signal leads to an allosteric conformational change forming a conformer of the CP_2 distinct from the one in the absence of RNA. We were also able to show that the unit of capsid growth is a coat protein (CP) dimer and that the initial higher order complexes formed are based around the particle three-fold axis rather than the five-fold. These data lead naturally to a model of assembly (Fig. 1) in which specific RNA binding causes a switch in quasi-equivalent conformer in the CP_2, thus providing both types of species needed for the final *T*=3 capsid. This begs the question of how quasi-equivalent switching is achieved beyond the initiation complex? Does the RNA folding present appropriately positioned stem-loop mimics that can function in this way, or is the initial conformational switch caused by the initiator stem loop binding sufficient to 'template' further coat protein dimers as they bind? Cryo-electron microscopy of wild-type phage particles is currently being used to address this question.

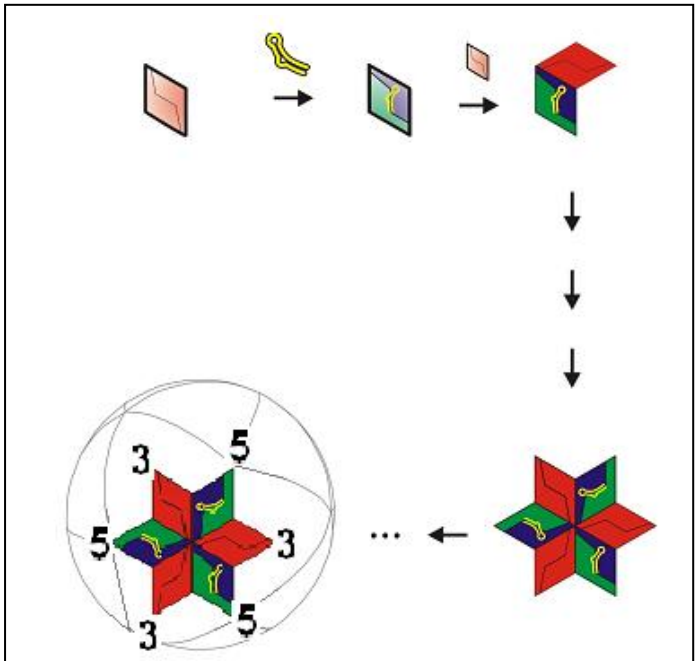

Figure 1 shows the model for MS2 assembly based on mass spectrometry and NMR spectroscopy; the allosteric RNA-CP interaction leads to formation of the initial three-fold axis in the particle, via CP dimer addition, ensuring that *T*=3 rather than *T*=1 shells are assembled.

Publications:

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