MS09 O4

Structure of the SARS coronavirus nucleocapsid protein dimerization domain suggests a novel mechanism for helical wrapping of viral RNA

Chwan-Deng Hsiao[a], Chun-Yuan Chen[a], Chung-ke Chang[b], Tai-huang Huang[b], [a]*Institute of Molecular Biology, Academia Sinica, Taipei, 115, Taiwan, ROC;* [b]*Institute of Biomedical Sciences, Academia Sinica, Taipei, 115, Taiwan, ROC.*
E-mail: hsiao@gate.sinica.edu.tw

Keywords: coronavirus, nucleocapsid protein, RNA-binding

The nucleocapsid protein of the severe acute respiratory syndrome (SARS) coronavirus contains two structural domains: the N-terminal putative RNA-binding domain (RBD, residues 45-181) and the C-terminal dimerization domain (DD, residues 248-365), flanked by disordered regions. Here we show that DD binds to ssRNA or ssDNA through its N-terminal positively charged region with an affinity higher than that of RBD. Moreover, the two domains show synergistic effect in binding to ssRNA and ssDNA. We further report the crystal structure of the DD to 2.5 Å resolution. In the crystal, the DD exists as dimers and four dimer molecules form a ring-like octameric structure of 90 Å in diameter with a central cavity of 30 Å in diameter in an asymmetric unit. Packaging of the octamers in the crystal forms a helical core with two parallel, positively charged grooves wound around each other as two left-handed helices. The crystal packing suggests a novel mechanism for fast and efficient helical packaging of viral RNA. In this model viral RNA wraps around the helical NP core with the phosphate backbone bound to the groove and the bases exposed. Stabilization of the helical RNP requires the synergistic interaction of both RBD and DD with RNA. The DD interacts with the RNA backbone through non-specific Coulomb interactions and the RBD stabilizes the exposed bases through stacking of the conserved aromatic groups with the RNA bases. This model constitutes the first rational description of helical viral RNA packaging at a molecular level.