

W0307

The Crystal Structure of a Birnavirus RNA Polymerase Reveals a Distinct Active Site Topology and a Novel Protein-Priming Domain. Junhua Pan¹, Vikram N. Vakharia², Yizhi Jane Tao¹, ¹Dept. of Biochemistry & Cell Biology, Rice Univ., Houston, TX 77005, USA, ²Center for Biosystem Research, Univ. of Maryland, College Park, MD 20742, USA.

RNA-dependent RNA polymerases (RdRps) are often excellent targets for antiviral drug design because of their virus-specific functionalities. Birnavirus VP1 is a multifunctional protein that serves as both RdRp and protein-primer for initiation of RNA synthesis. Here we report the 2.5Å structure of a birnavirus VP1 determined by multiple isomorphous replacement and anomalous scattering (MIR-AS). Close inspection of this structure reveals that VP1 adopts a novel active site topology that has never been observed in other polymerase structures. Additionally, VP1 contains only two aspartate residues in the active site, another highly unusual feature for RNA-dependent polymerases. The putative guanylation site residue, which functions in initiating protein-primed RNA synthesis, resides in VP1 but is found 23Å away from the polymerase active site. Our results indicate that the novel topology in the active site may represent a dead-end product in evolution, and birnavirus VP1 is likely to be a descendant of polymerases from tetraviruses in the alphavirus superfamily, revealing the evolutionary relationship between dsRNA and +ssRNA viruses.