O-18

Cryo-EM Structure of Rep68-ssDNA Complex

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Adeno-Associated Virus (AAV) Rep proteins are multifunctional proteins that carry out all the DNA transactions involved in essential biological processes such as initiation of DNA replication, transcriptional regulation and packaging of DNA into viral capsids. The large Rep proteins (Rep78/Rep68) share two domains with multiple DNA-interacting sites that confer them the ability to form different stoichiometric and functional complexes that are modulated by the type of DNA substrates. For instance, Rep68 forms double-octameric ring structures in presence of ssDNA. We have determined the structure of this complex using single-particle Cryo-EM. The structure reveals two octameric Rep68 rings that stack head-to-head using the N-terminal origin binding domains (OBD) as stacking units. The helicase domains form an 'inverted-dome' structure that sits on top of the octameric-OBD rings. The orientation of the OBD in the structure is such that the HUH motif is on the outside face of the ring. The structure illustrates the remarkable plasticity of Rep proteins to form different oligomeric complexes that may play diverse biological roles.