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**Structural Unity among Viral Origin Binding Proteins: Crystal Structure**

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Adeno-associated virus (AAV), unique among animal viruses in its ability to integrate into a specific chromosomal location, is a promising vector for human gene therapy. AAV Replication (Rep) protein is essential for viral replication and integration, and its amino terminal domain possesses site-specific DNA binding and endonuclease activities required for replication initiation and integration. This domain displays a novel endonuclease fold and demonstrates an unexpected structural relationship to other viral origin binding proteins such as the papillomavirus E1 protein and the SV40 T antigen. The active site, located at the bottom of a positively charged cleft, is formed by the spatial convergence of a divalent metal ion and two conserved sequence motifs that define the rolling circle replication superfamily.

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