

## Ronald Reagan High School SMART Team

C. Anderson, R. Bhatia, M. Ehlers, K. Ledger, H. Lentz, S. Marsh,  
B. Haralson, A. Puls, S. Sheikh, A. Smith, M. Spellecy, M. Sweeney, A. Ya

Ms. Schuld & Mr. Perez

Mentor: Edwin Antony, Ph.D. Marquette University

## ABCD – The Language of Replication Protein A (RPA)

**PDB:** 4GNX

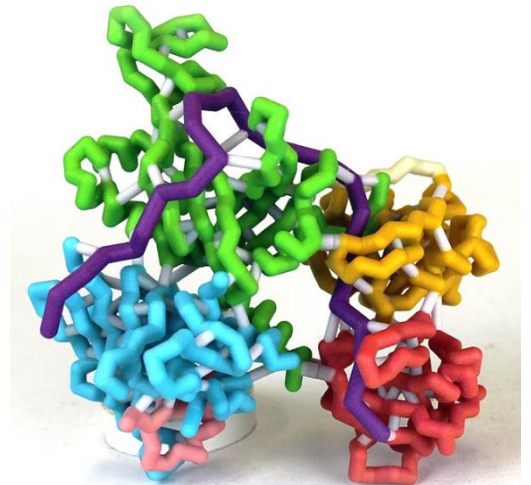
**Primary Citation:** Fan, J., Pavletich, N.P. (2012) Structure and conformational change of a replication protein A heterotrimer bound to ssDNA. *Genes Dev.* 26: 2337-2347

**Format:** Alpha carbon backbone

**RP:** Zcorp with plaster

### Description:

RPA is a ssDNA binding protein whose function is essential to DNA replication, recombination, and repair. RPA coordinates DNA repair processes responsible for maintaining genomic integrity, and hence is an attractive target for oncology. RPA interacts with ssDNA, and recruits other proteins onto ssDNA. RPA binds to ssDNA very tightly. Current research focuses on determining how an ssDNA-RPA complex is removed from the DNA by weaker DNA binding enzymes. Structurally, RPA is a heterotrimer made up of three subunits (RPA70, RPA32 and RPA14). The DNA binding function of RPA is carried out by four distinct DNA binding domains (DBDs), A (residues 182 - 305), B (residues 306 - 424), C (residues 425 - 623) and D (residues 46 - 175), that directly attach to the single stranded DNA (ssDNA). DBDs A, B and C reside in the RPA70 subunit and are connected by flexible linkers. DBD-D resides in the RPA32 subunit. The heterotrimer is held together as a complex through interactions between DBD-C (RPA70), DBD-D (RPA32) and the RPA14 subunit. Scientists use unnatural amino acids and chemical fluorophores to capture how each DBD binds and disconnects from ssDNA. This approach shows that DBD-A binds rapidly to ssDNA, but detaches quickly, while DBD-D binds more slowly to ssDNA, but is stable. Ronald Reagan High School's SMART (Students Modeling A Research Topic) Team has designed a model of RPA using 3D printing technology to investigate its structure and function. Additional research on RPA structure and mutations may prove helpful in determining cause and risk for cancer and developing potential treatments.



## Specific Model Information:

### Highlighted protein structures:

- DNA Binding Domains:
  - A – Tomato
  - B – Gold
  - C – Chartreuse
  - D – Cyan
  - E – Pink
- Ligand: Single Stranded DNA colored Purple
- Hydrogen bonds are colored Silver
- N-terminus is colored blue
- C-terminus is colored red

### Supporting Features:

- Struts are colored Ghostwhite

### CBM SMART Teams Website:

<http://cbm.msoe.edu/smartTeams/smartTeamsLocal.php>