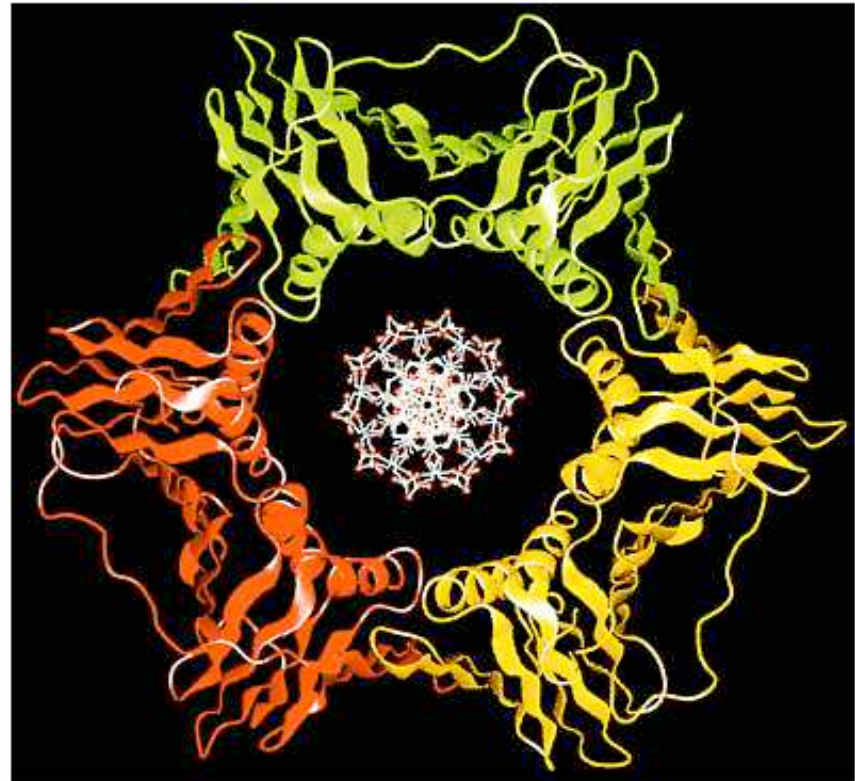


PCNA

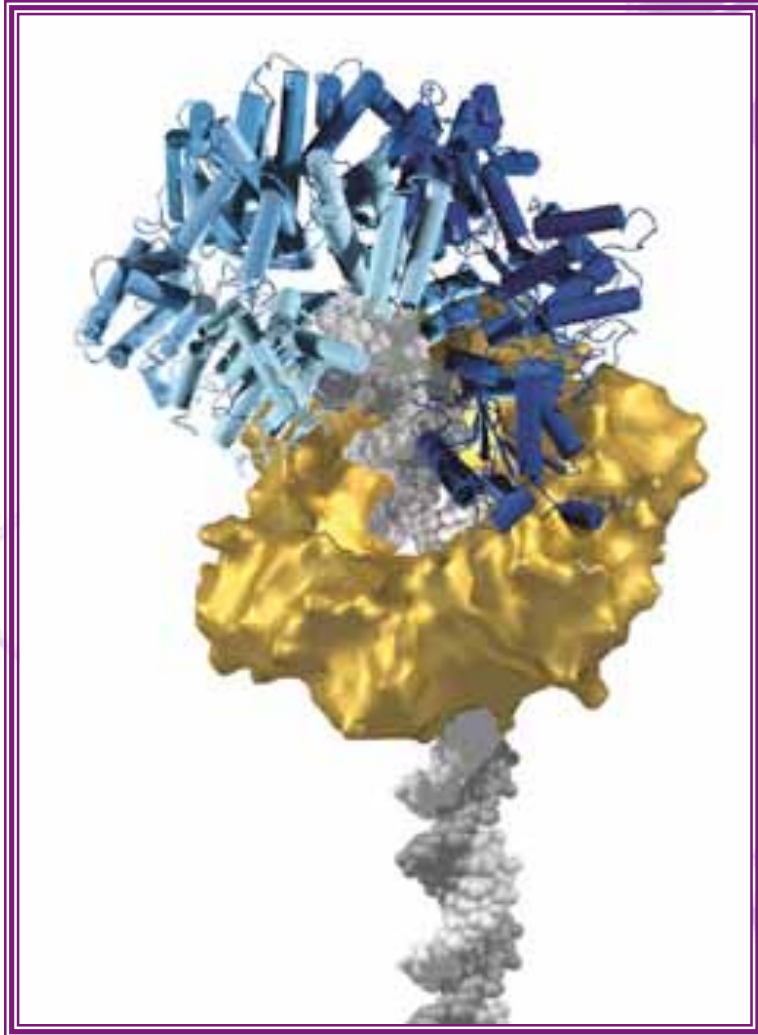
Proliferating Cell Nuclear Antigen

- ❖ Discovered as an antigen in the autoimmune disease systemic lupus erythematosus
- ❖ Co-localized with incorporated bromodeoxyuridine in S-phase
- ❖ 1987 Prelich et al. provided proof of PCNA's role in DNA replication
- ❖ Subsequent research = processivity factor
 - ❖ -PCNA ~10nt incorporation
 - ❖ +PCNA ~thousands



Courtesy of John Kuriyan, The Rockefeller University.

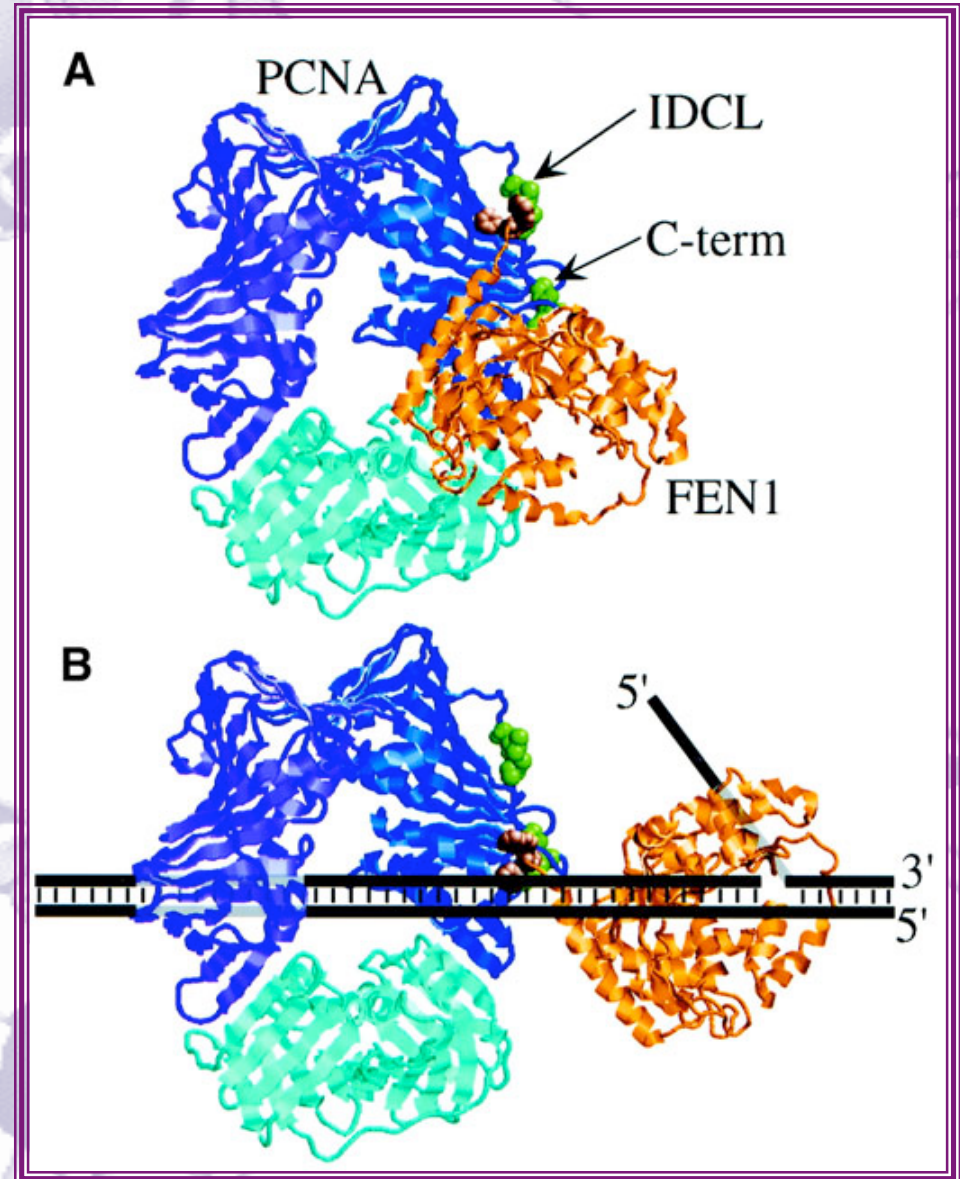
Known Binding Partners



- ❖ DNA
- ❖ Pol δ and ϵ
- ❖ Replication Factor C (RFC)
- ❖ FEN1 (flap endonuclease)
- ❖ P21 WAF1/CIP1 (CDK inhibitor)
- ❖ DNA Ligase
- ❖ XP-G
- ❖ UNG2
- ❖ MSH2, MLH1
- ❖ Et cetera

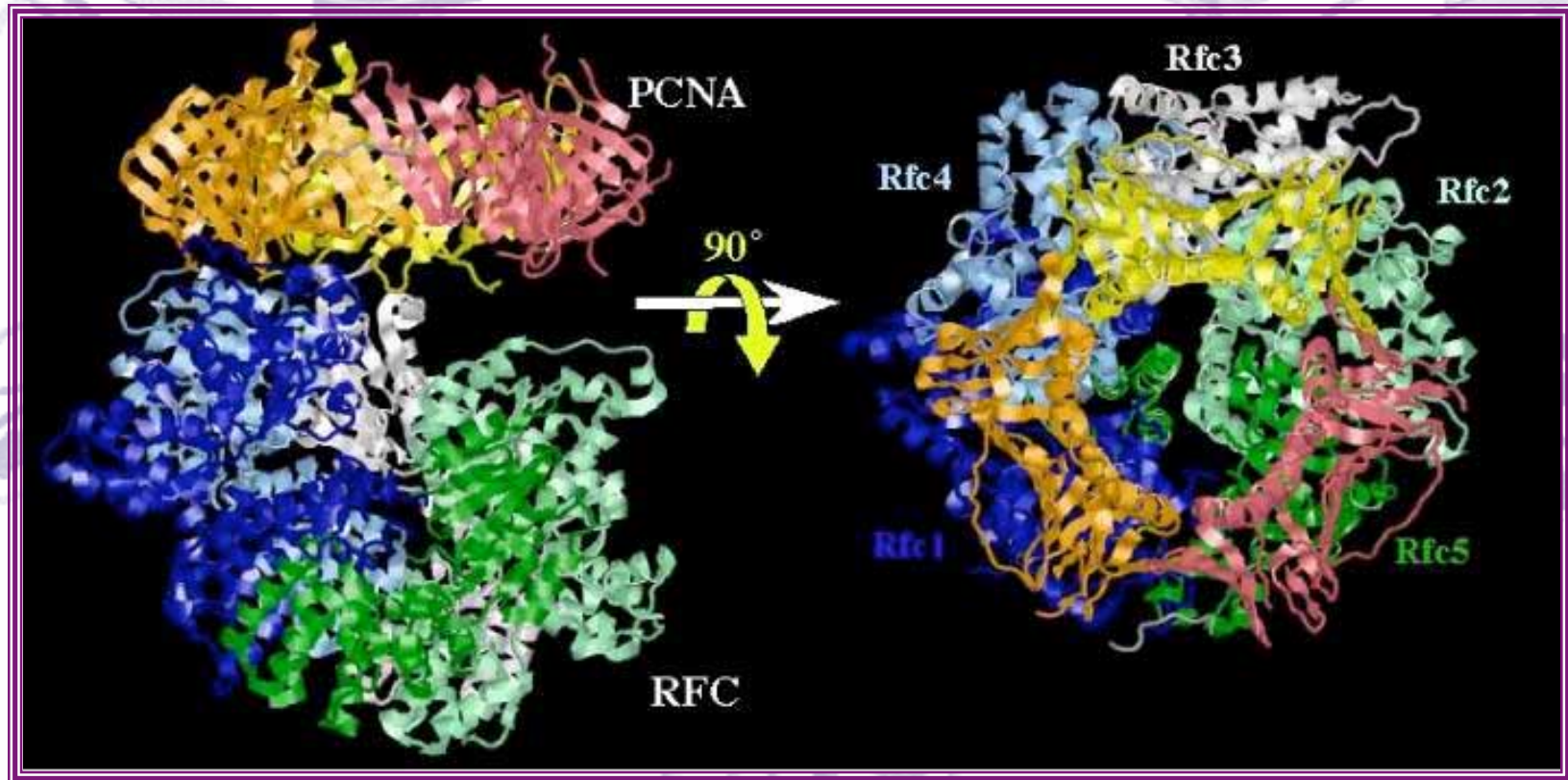
Functions

- ❖ Docking partner
- ❖ DNA polymerase accessory factor
- ❖ Role in Okazaki Fragment joining
- ❖ MMR
- ❖ Chromatin Reorganization
- ❖ Cell cycle control



PCNA/RFC Interactions

- ❖ RFC is the clamp loader
- ❖ Head to tail interactions through hydrophobic residues
- ❖ Ring must open to accept DNA – ATP hydrolysis
- ❖ C-side loop (asp41-his44) and c-term tail (lys254-glu256)



PCNA Points of Interests

- ❖ Homologous to beta subunit in prokaryotes, similar structure/function, virtually no sequence identity
- ❖ Down regulation of PCNA is a marker for some proliferative diseases
- ❖ Various malignant tumors are related to expression levels
- ❖ Antisense experiments have shown that inhibition can halt certain cancers
- ❖ Under proliferative cellular conditions removal of PCNA appears to trigger apoptotic activity
- ❖ Many binding partners have a conserved region, -Q--I/L--FF-
- ❖ If yours doesn't work right, you are in trouble!

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