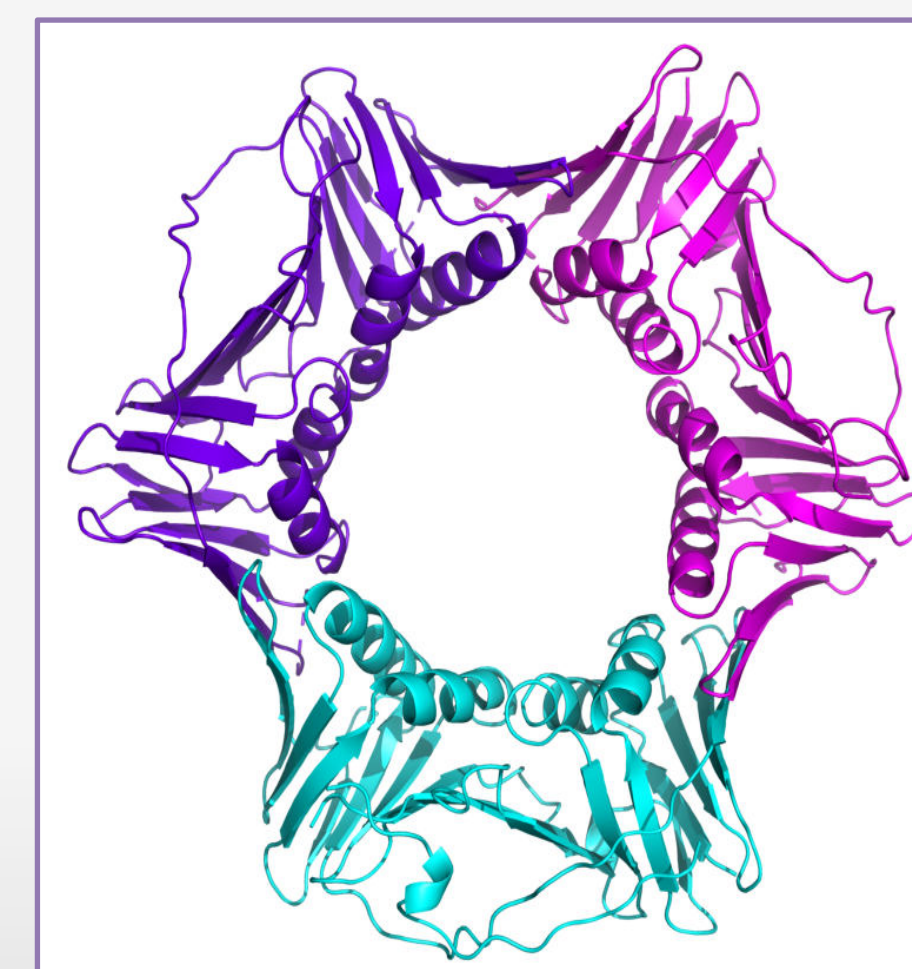


Introduction

- ❖ PCNA is a core protein of DNA replication process and has multiple interacting partner.
- ❖ PCNA proteins involved in DNA repair, recombination and cell cycle regulation
- ❖ There is no information of mutational effects of PCNA and its partner protein in human cancers
- ❖ Also no information how coevolving residues of PCNA and its interacting proteins formed the underlying networks
- ❖ Is there any key residues that holds a higher importance in those networks or there is no such clear information?



PCNA

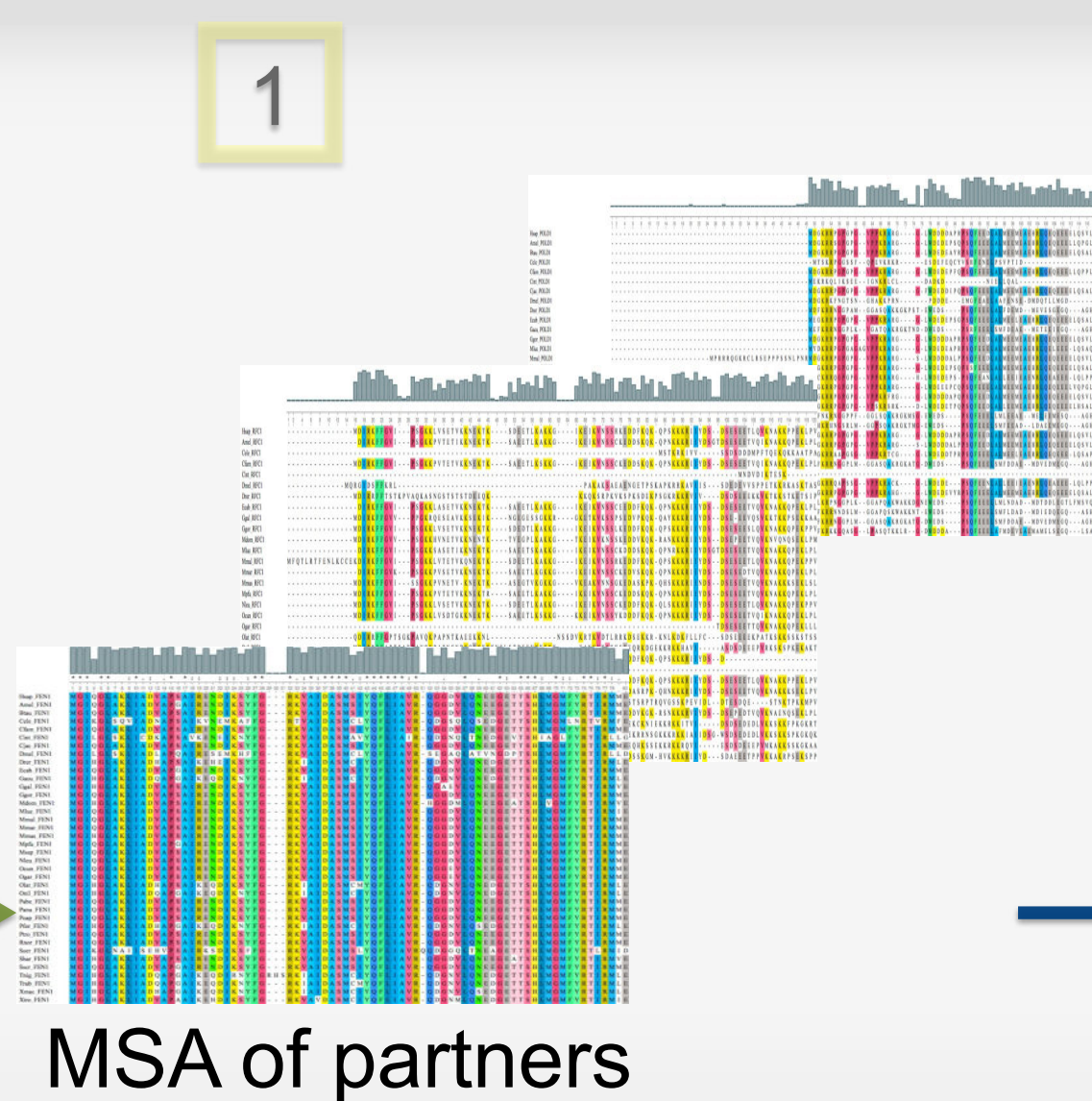
Objectives:

1. To investigate the evolutionary constraints in residue-residue interaction by network topology and other network properties like betweenness, degree distribution.
2. Mutational impact of coevolving residue on PCNA and its partner proteins at structural and functional levels.
3. The relationships of hub residues in context of cancer-associated mutations.

Materials and Methods

- 38 Eukaryotic PCNA protein sequences were collected from ensemble

PCNA



- Partner protein sequences were also collected from ensemble

FEN1
POLD1
RFC1

POLD2
POLD3
POLD4

RFC3
RFC4

- MSA of PCNA and partners were used in separate sets for determining coevolving residues

CA
PS
COEVOLUTION ANALYSIS
USING
PROTEIN SEQUENCES

Parameters

- Bootstrapped value 3000
- Correlation cut-off ≥ 0.8
- Alpha < 0.01

Col1	Col2
19	26
19	91
19	141
32	86
32	104
32	302
73	32
73	86
73	104
73	302
125	32
125	73
125	86
125	104
125	302
125	19
125	217
125	229
125	381
125	391
125	404
125	439
125	452
125	453
125	457
125	464
125	466
125	491
125	517
125	602

Coevolving residue lists

dbSNP	RefSeq	Gene	Protein	Position	Variant	Frequency
rs111000000	PCNA	PCNA	PCNA	125	G>A	0.000001
rs111000001	PCNA	PCNA	PCNA	125	G>T	0.000001
rs111000002	PCNA	PCNA	PCNA	125	G>C	0.000001
rs111000003	PCNA	PCNA	PCNA	125	G>G	0.000001
rs111000004	PCNA	PCNA	PCNA	125	G>A	0.000001
rs111000005	PCNA	PCNA	PCNA	125	G>T	0.000001
rs111000006	PCNA	PCNA	PCNA	125	G>C	0.000001
rs111000007	PCNA	PCNA	PCNA	125	G>G	0.000001
rs111000008	PCNA	PCNA	PCNA	125	G>A	0.000001
rs111000009	PCNA	PCNA	PCNA	125	G>T	0.000001
rs111000010	PCNA	PCNA	PCNA	125	G>C	0.000001
rs111000011	PCNA	PCNA	PCNA	125	G>G	0.000001
rs111000012	PCNA	PCNA	PCNA	125	G>A	0.000001
rs111000013	PCNA	PCNA	PCNA	125	G>T	0.000001
rs111000014	PCNA	PCNA	PCNA	125	G>C	0.000001
rs111000015	PCNA	PCNA	PCNA	125	G>G	0.000001
rs111000016	PCNA	PCNA	PCNA	125	G>A	0.000001
rs111000017	PCNA	PCNA	PCNA	125	G>T	0.000001
rs111000018	PCNA	PCNA	PCNA	125	G>C	0.000001
rs111000019	PCNA	PCNA	PCNA	125	G>G	0.000001
rs111000020	PCNA	PCNA	PCNA	125	G>A	0.000001

- Matching deleterious mutations from databases with Coevolving residue lists

Position	Mutation (EN)	Mutation (AA)	Wildtype (EC2AM)	Count	Mutation Type
7	T157C	P27S	COSM004105	1	1 Substitution - Missense
8	T157C	P27S	COSM004106	1	1 Substitution - Missense
11	T157C	L137M	COSM002634	1	1 Substitution - Missense
13	T157C	P27S	COSM004107	1	1 Substitution - Missense
13	T157C	P27S	COSM004108	1	1 Substitution - Missense
41	T157C	R207P	COSM004109	1	1 Substitution - Missense
70	T157C	P27S	COSM004110	1	1 Substitution - Missense
70	T157C	P27S	COSM004111	1	1 Substitution - Missense
72	T157C	P27S	COSM004112	1	1 Substitution - Missense
72	T157C	P27S	COSM004113	1	1 Substitution - Missense
72	T157C	P27S	COSM004114	1	1 Substitution - Missense
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