Poster Presentation

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Protein-Protein Interactions of Fanconi anemia proteins- FANCI, FANCD2 and BRCA2

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Fanconi anemia (FA), a cancer predisposition syndrome, exhibit hallmark feature of radial chromosome formation and hyper sensitivity to DNA crosslinking agents [1]. A set of FA pathway (DNA inter-crosslink repair pathway) proteins mainly FANCI, FANCD2 and BRCA2 were expressed to repair the covalent crosslink between the dsDNA [2]. We have performed the multimodal approach to evaluate the structure and protein-protein interactions (PPI) between the different regions present in FANCI, FANCD2 and BRCA2 proteins. It has been observed that FANCI ARM repeat interacts with FANCD2 Cue domain and BRCA2 central region. Interestingly, FANCD2 Cue domain forms strong interaction with BRCA2 central region. We also tested the interaction between BRCA2 and functionally relevant mutations present in FANCD2 Cue domain, Ser222Ala (cell cycle checkpoint mutant) and Leu231Arg (DNA ICL repair mutant), and observed that mutations abrogates the binding ability. These results suggest that (1) domain and regions present in FANCI, FANCD2 and BRCA2 play important role in PPI, (2) mutations cause the failure in the PPI of these proteins, that affect the cell cycle and DNA repair processes.

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