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PhD Dissertation Defense

Entitled

INVESTIGATING THE ROLE OF FUN30, A CHROMATIN REMODELER, IN DNA REPAIR

By

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Date & Venue

At 4 PM

Thursday, 28th of April 2022

Conducted Online

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Abstract:

The repair of DNA double-strand breaks (DSBs) is crucial for maintaining genome stability. DSB repair needs to take place within the complex organization of the chromatin, and this requires changes in the chromatin structure adjacent to DSB sites. These changes occur through covalent histone modifications that alter histone-DNA contacts as well as by the actions of ATP-dependent chromatin remodelers. Many chromatin remodelers, including Fun30, are involved in DSB repair. Fun30 facilitates DNA end resection at DSB site during the homologous recombination repair pathway. Apart from its role in DNA repair, Fun30 promotes gene silencing at the heterochromatic loci such as telomeres, rDNA regions, and the mating-type locus *HML*α and *HMR*a, which are known to be clustered at the nuclear periphery. In this study, using mass spectrometry analysis of pulled down TAP-tagged Fun30, we observe co-purification of Fun30 with several nuclear pore proteins. Moreover, we also observed a reduced level of Mps3 and Nup84 at a single irreparable DSB in *fun30*Δ mutant suggesting that Fun30 helps to translocate irreparable DSBs towards the nuclear periphery. In addition, we observed that Fun30 supports histone H2A variant Htz1 recruitment at DSB. Thus, Fun30 favors the relocation of DSB by controlling the levels of histone variant Htz1 and by favoring DNA end resection at the DSB site.

Keywords: DNA Repair, Chromatin Remodeling, Nuclear Envelope, Fun30, Resection