

## A NEW PROTEIN INTERACTION OF THE SETD1A METHYLTRANSFERASE COMPLEX: LINKING EPIGENETIC REGULATION TO THE DNA DAMAGE RESPONSE

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**S**ETD1A is a component of an histone methyltransferase assembly, analogous to the *S. cerevisiae* Set1/COMPASS complex. In mammalian cells, SET1/MLL histone methyltransferase (HMT) complexes methylate H3K4, resulting in an epigenetic mark generally associated with increased transcription. While the SET domain-containing proteins are believed to be non-redundant, the SET1/MLL complexes contain shared subunits such as WDR5 (WD repeat domain 5), RBBP5 (Retinoblastoma-binding protein 5), ASH2L (Absent, small or homeotic)-like), and HCF1 (host cell factor 1), as well as factors that may be unique to specific complex isoforms. Defects in SETD1A have been linked to a number of human diseases, including cancer and schizophrenia. To further investigate the role of SETD1A, we mapped the physical interactions of the protein under endogenous conditions in two cell lines (HEK and NT2). We were able to confirm the identity of known interactors within the SETD1A-complex and validated the interaction of a new interactor, Rad18. Rad18 is a ubiquitin ligase involved in DNA repair pathways. Size exclusion chromatography was used to confirm that the interaction with Rad18 occurs in a distinct complex to SETD1A-complex. Depletion of both SETD1A & RAD18 lead to reduce the expression of both proteins, suggesting that SETD1A regulates RAD18 expression. Notably, depletion of both SETD1A and RAD18 shows a defect in the monoubiquitylation of PCNA (Ub-PCNA) in the presence of DNA damage agent (MMC). This newly defined function for SETD1A could be a novel therapeutic target for cancer drug development and therefore detailed structural analysis of the SETD1A domain and its interaction with RAD18 will be illuminating and potentially important for future drug development.

### Biography

Manal has completed her Master on 2014 from California State University Dominguez Hills and currently she is enrolled for Ph.D programme at University College Dublin (UCD). She will graduate on April 2019. She was awarded a prize for the best oral presentation on May 2016 on the Research Day at UCD. She is planning to publish her thesis soon.

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