Antagonistic Roles of EED and Histone H3K36me2 in the Propagation of Histone H3K27me3

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Changes in chromatin state have been linked to developmental defects and diseases such as cancer. Thus it is important to understand how chromatin states are established and maintained. Modification of histone proteins that comprise the nucleosome plays a major role in regulating chromatin structure. Histone H3 protein modifications have been associated with both repressed and activated chromatin states. Polycomb repressive complex 2 (PRC2) is a protein complex that trimethylates lysine 27 on histone H3 (H3K27me3), a modification correlated with repressed chromatin. The MMSET/NSD2 protein dimethylates lysine 36 on histone H3 (H3K36me2), a modification correlated with activated chromatin. How these histone H3 modifications are regulated and propagated to either maintain or cause changes in chromatin structure is not well understood. This study provides in vitro evidence that H3K27me3-binding activity of the EED protein, a component of PRC2, is required for propagation of H3K27me3 at nearby chromatin sites. This study also provides in vitro evidence that presence of H3K36me2 leads to reduced propagation of H3K27me3, suggesting that the role of H3K36me2 in activating chromatin involves modulation of H3K27me3. Furthermore, creation of a novel cell line that will allow in vivo studies of the role of PRC2 in propagation and maintenance of repressed chromatin is described, enabling a new scope of research on PRC2 that was previously inaccessible. This work adds to our knowledge of how epigenetic marks like H3K27me3 are established and maintained and has important implications for understanding the role of chromatin structure in development and disease.