

SETD5

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SET domain-containing 5 (SETD5) is an uncharacterized member of the protein lysine methyltransferase family and is best known for its transcription machinery by methylating histone H3 on lysine 36 (H3K36). These well-characterized functions of SETD5 are transcription regulation, euchromatin formation, and RNA elongation and splicing. SETD5 is frequently mutated and hyperactive in both human neurodevelopmental disorders and cancer, and could be down-regulated by degradation through the ubiquitin-proteasome pathway, but the biochemical mechanisms underlying such dysregulation are rarely understood. Herein, we provide an update on the particularities of SETD5 enzymatic activity and substrate specificity concerning its biological importance, as well as its molecular and cellular impact on normal physiology and disease, with potential therapeutic options.