Epigenetic modifications are deposited, interpreted, and removed by catalytic enzymes. One such enzyme, SETD2, is responsible for trimethylation of lysine 36 of histone H3 (H3K36Me3). This serves as a chemical tag that recruits a series of protein effectors that promote processes such as RNA splicing, DNA repair, and preventing spurious transcription.[1] SETD2 is widely appreciated as an important tumor suppressor gene. SETD2 loss of function mutations are most commonly associated with clear cell renal cell carcinoma, where SETD2 is reported to be the third most commonly mutated gene.[2] However, little is known about the precise mechanism by which SETD2 loss contributes to tumorigenesis. Here we describe a novel, H3 methylation-independent function for SETD2 that we believe underlies SETD2's role in tumor suppression. We first uncovered a previously unrecognized interaction between SETD2 and proteins of the nuclear lamina, including lamin A/C, lamin B1, and emerin. We found that this interaction is mediated by SETD2's 1322 amino acid N-terminus and is crucial for maintaining the integrity of the nuclear lamina. Through its extended N-terminal region, SETD2 interacts with the master regulator of mitosis, CDK1, to ensure sufficient phosphorylation of lamins prior to the mitotic breakdown of the nuclear envelope. Our results suggest that SETD2's N-terminus serves as a molecular platform for CDK1-mediated lamin phosphorylation during G2/M. These results expand the knowledge of SETD2's role in the cell and present an alternative way by which SETD2 loss contributes to tumor progression.