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**Title: EPIGENETIC REGULATION OF THE 7SK SNRNP IN POLYMERASE PAUSE CONTROL**

**Abstract**

Plasticity associated with the epithelial to mesenchymal transition (EMT) is a driver of cancer progression and allows for the acquisition of invasive and metastatic traits. Our lab and others have shown that the inhibition of the histone methyltransferase SUV420H2 and depletion of its product H4K20me3 promotes EMT plasticity and increases invasion of breast cancer cells. Previous work in our lab has established that SUV420H2-mediated H4K20me3 enforces RNA polymerase 'pausing' to attenuate transcription. However, the mechanisms by which SUV420H2-mediated H4K20me3 regulates pausing to control EMT plasticity is unclear. The 7SK ribonucleoprotein complex (7SK snRNP) plays a critical role in RNA polymerase pausing by sequestering pTEFb and precluding the release of paused RNA polymerase into elongation. Here, we examined the regulation of the 7SK complex by H4K20me3. Using CUT&Tag, we found that the 7SK snRNP component HEXIM1 co-localizes with H4K20me3 at a subset of active gene promoters, and that the depletion of H4K20me3 results in an altered distribution of HEXIM1. An in vitro pull-down approach was used to examine H4 tail interactions. We found that histone H4 tail peptides bearing differently-methylated H4K20 modifications co-precipitated HEXIM1 as well as other 7SK components LARP7 and MePCE from breast cancer cell nuclear extracts in a methylation state-specific manner. Taken together, these data suggest that the methylation state of H4K20 may regulate pausing by selectively interacting with the 7SK complex. These ongoing studies will provide insight into fundamental mechanisms of transcriptional control and the cell plasticity that underlies cancer-associated EMT.