Insights: Publications

A dual role for H2A.Z.1 in modulating the dynamics of RNA polymerase II initiation and elongation

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Written by Konstantinos Mylonas, Ph.D.

RNA polymerase II (RNAPII) pausing immediately downstream of the transcription start site is a critical rate-limiting step for the expression of most metazoan genes. During pause release, RNAPII encounters a highly conserved +1 H2A.Z nucleosome, yet how this histone variant contributes to transcription is poorly understood. Here, using an inducible protein degron system combined with genomic approaches and live cell super-resolution microscopy, we show that H2A.Z.1 modulates RNAPII dynamics across most genes in murine embryonic stem cells. Our quantitative analysis shows that H2A.Z.1 slows the rate of RNAPII pause release and consequently impacts negative elongation factor dynamics as well as nascent transcription. Consequently, H2A.Z.1 also impacts re-loading of the pre-initiation complex components TFIIB and TBP. Altogether, this work provides a critical mechanistic link between H2A.Z.1 and the proper induction of mammalian gene expression programs through the regulation of RNAPII dynamics and pause release.

Related People



Konstantinos Mylonas, Ph.D.

t 202.639.4729

cmylonas@ktslaw.com