7SK-BAF axis controls pervasive transcription at enhancers.

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Public Summary:
Many long noncoding RNAs emanate from active gene switches called enhancers. We found that one noncoding RNA named 7SK is needed to limit the production of enhancer RNAs, especially in human and mouse embryonic stem cells. The 7SK brake is needed to prevent excess enhancer RNA production that damages the enhancer DNA. Thus, we discovered a system that ensures genome integrity in embryonic stem cells and likely other cell types.

Scientific Abstract:
RNA functions at enhancers remain mysterious. Here we show that the 7SK small nuclear RNA (snRNA) inhibits enhancer transcription by modulating nucleosome position. 7SK occupies enhancers and super enhancers genome wide in mouse and human cells, and it is required to limit enhancer-RNA initiation and synthesis in a manner distinct from promoter pausing. Clustered elements at super enhancers uniquely require 7SK to prevent convergent transcription and DNA-damage signaling. 7SK physically interacts with the BAF chromatin-remodeling complex, recruits BAF to enhancers and inhibits enhancer transcription by modulating chromatin structure. In turn, 7SK occupancy at enhancers coincides with that of Brd4 and is exquisitely sensitive to the bromodomain inhibitor JQ1. Thus, 7SK uses distinct mechanisms to counteract the diverse consequences of pervasive transcription that distinguish super enhancers, enhancers and promoters.