

**The histone demethylase UTX enables RB-dependent cell fate control.**

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**Public Summary:**

**Scientific Abstract:**

Trimethylation of histone H3 on Lys 27 (H3K27me3) is key for cell fate regulation. The H3K27me3 demethylase UTX functions in development and tumor suppression with undefined mechanisms. Here, genome-wide chromatin occupancy analysis of UTX and associated histone modifications reveals distinct classes of UTX target genes, including genes encoding Retinoblastoma (RB)-binding proteins. UTX removes H3K27me3 and maintains expression of several RB-binding proteins, enabling cell cycle arrest. Genetic interactions in mammalian cells and *Caenorhabditis elegans* show that UTX regulates cell fates via RB-dependent pathways. Thus, UTX defines an evolutionarily conserved mechanism to enable coordinate transcription of a RB network in cell fate control.

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