

**Core promoter factor TAF9B regulates neuronal gene expression.**

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**Public Summary:**

Gene regulation in multicellular organisms involves coordinate interaction of many different proteins. Among these is the "preinitiation complex," a group of >85 proteins that until recently was considered invariant among different cell types. Emerging evidence points to an unexpected diversification of preinitiation complex components that can serve as important regulators of cell-type specific gene transcription. Here, we report that one such factor, TAF9B, is selectively up-regulated upon in vitro motor neuron differentiation, and is required for expression of specific neuronal genes. TAF9B binds to both promoters and distal enhancers of neuronal genes, partially co-localizing at binding sites of OLIG2, a key activator of motor neuron differentiation. Analysis of dissected spinal column from Taf9b KO mice confirmed that TAF9B also regulates neuronal gene transcription in vivo. Our findings suggest that alternative preinitiation complex components may provide a key mechanism to lock in and maintain specific transcriptional programs in terminally differentiated cell types.

**Scientific Abstract:**

Emerging evidence points to an unexpected diversification of core promoter recognition complexes that serve as important regulators of cell-type specific gene transcription. Here, we report that the orphan TBP-associated factor TAF9B is selectively up-regulated upon in vitro motor neuron differentiation, and is required for the transcriptional induction of specific neuronal genes, while dispensable for global gene expression in murine ES cells. TAF9B binds to both promoters and distal enhancers of neuronal genes, partially co-localizing at binding sites of OLIG2, a key activator of motor neuron differentiation. Surprisingly, in this neuronal context TAF9B becomes preferentially associated with PCAF rather than the canonical TFIID complex. Analysis of dissected spinal column from Taf9b KO mice confirmed that TAF9B also regulates neuronal gene transcription in vivo. Our findings suggest that alternative core promoter complexes may provide a key mechanism to lock in and maintain specific transcriptional programs in terminally differentiated cell types. DOI: <http://dx.doi.org/10.7554/eLife.02559.001>.

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