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A Screen to Identify SAGA-activated Genes that are required for Proper Photoreceptor Axon Targeting in *Drosophila melanogaster*

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ABSTRACT

The inherited human genetic disease spinocerebellar ataxia type 7 (SCA7) is characterized by progressive neurodegeneration and visual impairment that ultimately leads to blindness. SCA7 results from a mutation in the human ATXN7 gene that causes an expansion of polyglutamine tracts in this gene's corresponding protein. Human ATXN7 protein serves as a component of the deubiquitylase (DUB) module of the large, multi-subunit complex Spt-Ada-Gcn acetyltransferase, or SAGA. SAGA is a transcriptional coactivator and histone modifier that functions to deubiquitylate histone H2B and allow for transcription of SAGA-mediated genes to occur. In *Drosophila*, mutations in SAGA DUB's Nonstop and sgf11 components compromise its deubiquitylase activity and result in mistargeting of photoreceptor axons R1-R6 within the developing eye-brain. Here, this work describes a screen to identify SAGA misregulated genes that are required for proper photoreceptor axon targeting in the developing visual system. Candidate genes were previously identified as targets of SAGA DUB by RNA-seq, and a previously optimized X-Gal staining protocol is used to visualize photoreceptor axon targeting in the *Drosophila* eye-brain upon candidate gene knockdown by RNAi. The results show that the transcriptional targets of SAGA are required cell-autonomously in glial cells for proper photoreceptor axon targeting. These data also suggest that genes involved in cell motility and photoreceptor axon targeting are pertinent players in proper visual and neurological development. By knowing the identity of these genes, it is possible to more clearly understand the pathogenesis of diseases such as spinocerebellar ataxia type 7.

KEYWORDS

SAGA, Spinocerebellar Ataxia Type 7, photoreceptor axons, histone modification