Elucidating the Roles of the REST C-Terminus and CoREST1 in Zebrafish Neural Development and Behavior

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The RE-1 Silencing Transcription Factor (REST) is a central transcriptional repressor that regulates a wide range of neural genes. REST is highly conserved among vertebrates and modulates processes including neurogenesis, development, and behavior. Misregulation of REST activity has been implicated in various neurological diseases including Huntington's, Down syndrome, and Alzheimer's. The lethality of the REST knockout in mice has impeded understanding of REST's role in development and behavior. However, zebrafish (Danio rerio) REST mutants are viable, providing a unique opportunity to uncover REST's role. Similarly, the CoREST protein is primarily known as a REST corepressor that binds to the REST C-terminus, yet recent studies show that CoREST also interacts with the Notch signaling pathway in regulating neurogenesis. To investigate the roles of REST and CoREST in development and behavior, I utilized zebrafish Rest C-Terminal and Rcor1 (CoREST1) mutant lines, which are both viable as I demonstrate here. Rest C-Terminal mutant larvae are behaviorally hypoactive, and adult Rest C-Terminal mutants are recovered at diminished rates and display irregular spinal curvature. Rcor1 mutant larvae show significantly increased levels of neurogenesis marker HuC, suggesting that CoREST1 regulates early neurogenesis. Given REST's and CoREST's prominent implications in neurological diseases, this study offers novel and unique insight into their contributions to development, behavior, and neurogenesis.

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