Genetic Control of the Maintenance of the AIA Cell Fate

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Cell fate can be considered to involve two steps: establishment, in which an undifferentiated cell commits to a final, differentiated fate; and maintenance, in which a differentiated cell preserves the expression of its fate while precluding others. Cell-fate establishment has been well studied and is characterized by changes in cell morphology, gene expression and cellular function. Cell-fate maintenance has received comparatively little attention, and the mechanisms by which cell fate is maintained are poorly understood.

From a screen for *C. elegans* genes that specify cells for programmed cell death, we identified a gene, *ctbp-1*, that instead appears to be involved in maintaining one or more cell fates. *ctbp-1* encodes the worm homolog of the CtBP family of proteins, which in mice have been shown to act as transcriptional co-repressors that regulate gene expression during embryonic development. *ctbp-1* loss-of-function adult animals show ectopic gene expression in the AIA neurons, whereas L1 *ctbp-1* animals do not display this abnormality. Furthermore, adult but not L1 *ctbp-1* animals are defective in a turning behavior mediated by the AIAs. These observations indicate that AIA is normal in L1 but abnormal in adult animals, consistent with the hypothesis that *ctbp-1* mutants properly establish the AIA cell-fate establishment but fail to maintain this fate later.

We are currently attempting to test this hypothesis and to determine the mechanism by which *ctbp-1* might regulate cell-fate maintenance. We have performed a mutagenesis screen for suppressors of the misexpression phenotype of *ctbp-1* mutants to identify genetic interacting partners of *ctbp-1* and have identified 21 independent isolates that we are currently mapping. We have also performed RNA-seq to identify other genes misexpressed in *ctbp-1* mutants.

We hope to develop an understanding of the genetic control of cell-fate maintenance by specifically investigating how CTBP-1 promotes the maintenance of the AIA fate. This work might provide insight into diseases, such as cancer, in which perturbation of the maintenance of tumor cell fate might intervene with the oncogenic process.