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Epithelial to Mesenchymal Transition induction with zfh-1

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Abstract: Epithelial to Mesenchymal Transition (EMT) is an important step in the metastasis of carcinomas, but it is not a well-understood process. Drosophila is an ideal model organism in which to study EMT, since individual cells within an intact in vivo epithelium can be genetically manipulated to investigate the genes involved in EMT. For this project we are developing a model system to induce and observe the process of EMT in the follicular epithelium of the Drosophila ovary. There are several genes, which have been identified as "master regulators" of EMT; these include snail, twist, ZEB1, and ZEB2. The gene zfh-1 is the sole Drosophila ortholog of the ZEB family of genes; however it has not been established whether zfh-1 has a similar role in EMT. To test if zfh-1 has a role in EMT expression of the gene zfh-1 was activated within individual cells in the epithelium using the "flip-on" method of mitotic recombination. The tissue was then evaluated using immunofluorescence to determine if the altered cells remained within the epithelial sheet, and to determine the state of epithelial differentiation. After zfh-1 activation, many zfh-1 positive cells had left the epithelial sheet, causing severe tissue disruption, as well as death of the neighboring germ cells. Cells with less extreme phenotypes (cells with zfh-1 activation that remained within the epithelium) were evaluated for expression of markers of differentiation such as E-cadherin and ß-catenin. Compared to neighboring wild-type cells, cells with zfh-1 expression showed normal accumulation of ß-catenin, but a significant decrease in the accumulation of E-cadherin in between zfh-1-expressing cells. This decrease in E-cadherin expression seen in zfh-1 expressing cells indicates that zfh-1 may have a role in the process of EMT.