

## **Molecular Mechanisms of Breast Cancer Progression**

### **Faculty:**

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### **Project for Student Scholars:**

**Background:** Our work focuses upon two helix-loop-helix transcriptional regulatory factors, Id (Inhibitor of DNA binding) and TWIST, and how their expression might affect the progression of breast cancer. We want to know whether the levels of these two factors present in breast cancer cells may be related to the spread or metastasis of cells from localized tumors to other locations in the body. The cells that line the ducts of normal breast tissue are epithelial cells, and originally derived from mesenchymal stem cells (MSC). MSCs and epithelial cells can be differentiated from each other on the basis of which genes they express. MSCs express TWIST, which serves to inhibit the expression of genes that should be turned on only when MSCs transition from being stem cells to being differentiated breast tissue. When this transition occurs, Id2 is expressed and inhibits twist, allowing the genes that twist inhibits to be expressed. It has been observed that as breast cancer progresses, the cancer cells look more like MSC cells and less like epithelial cells.

**Hypothesis:** One way the cancer may occur is that TWIST somehow becomes active again, perhaps by decreased expression of Id2, causing epithelial cells to revert to a more MSC-like character. If the hypothesis is correct, then medical intervention in which twist is inactivated, or Id2 is activated, might stop the progression of breast cancer.

**Experimental Approach:** The student scholar would participate in experiments designed answer the following questions:

- 1) How do the levels of Id2 and TWIST affect the epithelial to mesenchymal stem cell transition?

The scholar will use gene transfer to manipulate the levels of Id2 and TWIST expressed in breast epithelial and MSC cell lines and observe for intracellular molecular changes that indicate a transition from one cell type into the other.

- 2) What are the DNA/protein interactions that regulate expression of the Id2 and TWIST genes in epithelial, MSC, and breast cancer cells?

The scholar will perform gene transfer assays in which wild type and mutated regulatory regions of the Id2 and TWIST genes are tested for their ability to drive expression of a reporter gene in the three types of cells.

**Scholar Requirements:**

Experiments will be performed at CSULA and COH. The student should commit about 10 - 15 hours per week during an academic year quarter and ~30 hours per week during summer quarter. He or she should be able to travel easily between the two institutions, although specific projects will be carried out primarily at one institution or the other. The scholar should have the ability to communicate effectively and to work well as a member of a team. He or she will be expected to assume increasing independence as he or she becomes more familiar with the project and more adept in the lab.

**Contact Information:**

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