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Mechanical induction of transitions into mesenchymal and amoeboid states

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One of the fundamental mysteries of biology lies in the ability of cells to convert from one phenotype to another in response to external control inputs. We have been studying the Epithelial-to-Mesenchymal Transition (EMT), which allows organized assemblies of epithelial cells to scatter into lone mesenchymal cells. EMT is critical for normal development and wound healing, and may be important for cancer metastasis. I'll present recent data on disorganizing mammary epithelial structures. We have used CRISPR to insert fluorescent tags directly into eight EMT-related genes (such as E-cadherin and Vimentin), which allows us to monitor the dynamics of the transition in real time, subject only to delays imposed by fluorophore folding/maturation times. With this information, we can begin to order events in time (temporal resolution ~ 30 minutes), starting with external signal inputs and proceeding through a succession of intracellular changes of gene expression on the path to the mesenchymal state.