Dynamics of the feedback loops required for the phenotypic stabilization in the epithelial-mesenchymal transition

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Abstract

The epithelial-mesenchymal transition (EMT) is a complex mechanism in which cells undergo a transition from epithelial to mesenchymal phenotypes (there is also an intermediary hybrid state) in response to microenvironmental alterations and aberrant stimuli triggered by molecules such as TGF-β. Recent studies in breast cancer progression reported new feedback loops and new participant molecules such as microRNAs 340 and 1199. In this work, we propose a logical model of EMT contemplating the influence of these new published molecules on the regulatory core of EMT. The model results were compared with theoretical and experimental data for the human breast epithelial cell line MCF10A presenting excellent agreement. We propose that the miRNAs 340 and 1199 should be considered phenotypic stability factors of the hybrid state based on the positive feedback loops they form with ZEB1. Our results highlight new mechanisms related to the EMT dynamics in response to TGF-β stimulus in epithelial breast cells and might help the design of therapeutic strategies for breast cancer.

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Link to Video: