

Compartmentalized Boolean modelling of the epithelial-mesenchymal transition

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Introduction: Cancer cells undergo epithelial-mesenchymal transition (EMT) to develop metastasis and drug-resistance in numerous cancerous diseases e.g., pancreatic cancer. Stimulating its reversal, the mesenchymal-epithelial transition (MET), is a potential therapeutic approach. To gain a systematic understanding of the regulation of EMT, Boolean modelling can be employed. The accuracy of these models could be improved by compartmentalization, which is the division of the network according to subcellular compartments (e.g., nucleus).

Aims: Our aims included the compartmentalization of a Boolean model of EMT and the comparison of the compartmentalized and original model's performance.

Methods: Dynamic simulations of perturbations were used with a readout that included node and signalling pathway activities. Attractor states were also characterized by stability and stable motif analysis.

Results: In 4 out of 5 simulations with differing outcomes, the outcome of the compartmentalized model was better compared to the original. With compartmentalization, the epithelial attractor was 4 times more stable and 2 fewer perturbations were needed to restore it from a mesenchymal state. Partial MET could only be achieved with the compartmentalized model.

Conclusions: Compartmentalization resulted in a more accurate modelling of EMT. It increased the stability of the epithelial attractor and facilitated the occurrence of MET.