

Compartment-specific functions of proteins in a compartmentalized Boolean network model of epithelial-mesenchymal transition

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Introduction: Network modelling allows for the system-level investigation of complex biological processes, such as the epithelial-mesenchymal transition (EMT), which is associated with invasive cancer. Previously, we created a compartmentalized Boolean network model of transforming growth factor beta (TGF- β) mediated EMT, which can make predictions on the functions of proteins on a subcellular-compartment level.

Aims: As a proof of concept, we aimed to demonstrate compartment-specific functions of proteins in our compartmentalized model.

Methods: We used the BooleanNet software package to conduct dynamic simulations of our compartmentalized EMT model. At the beginning of the simulations, the model was perturbed by the activation (knock-in, KI) or deactivation (knock-out, KO) of a node.

Results: In the absence of the TGF- β signal, the KO perturbation of the cytoplasmic (and not the nuclear) node of glycogen synthase kinase-3 beta (GSK-3 β) and, separately, the KI perturbation of the nuclear (and not the cytoplasmic) node of glioma-associated oncogene (GLI) resulted in EMT. In the presence of the TGF- β signal, the KI perturbation of the nuclear node of GSK-3 β inhibited EMT more than its cytoplasmic KI. The results of these simulations were validated by experimental evidence from the literature.

Conclusions: By demonstrating the compartment-specific functions of GSK-3 β and GLI in EMT, we showed the possibility of gaining compartment-level information from signalling network models.