Identification of Combinations of Targets for Claudin-Low Triple Negative Breast Cancer Reversion

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Claudin-Low Triple Negative Breast Cancer (CL TNBC) has high relapse and low survival rates. One potential therapeutic strategy for this disease is tumor reversion, the biological process by which tumor cells lose a significant fraction of their malignant phenotype. This project aims to apply optimal control theory to identify *in silico* combinations of therapeutic targets for CL tumor reversion. An intracellular signaling network was constructed with multi-omics profile data for MDA-MB-231. Then a structure-based control method for nonlinear dynamic systems was applied to the network to identify driver nodes. The attractor landscape of the network was estimated using a topological signal flow analysis. This analysis was also used to run *in silico* screenings on perturbations of the driver nodes to predict the resulting attractors. Combinations of nodes whose concerted perturbation resulted in the system shifting from the tumorigenic basin of attraction to the normal-like basin of attraction were deemed putative concerted reversion targets. Through this methodology we have been able to identify several potential combinations of targets that will be validated in future work.