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

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Claudin-Low (CL) Triple Negative Breast Cancer 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. A topological signal flow analysis was used to estimate the attractor landscape of the network and to predict attractors resulting from driver node perturbations. Through this methodology, several combinations of nodes whose perturbation resulted in the system shifting from the tumorigenic to the normal-like basin of attraction have been identified. These putative concerted reversion targets will be validated in future work.