Abstract:

Building molecular correlates of drug resistance in cancer and exploiting them for therapeutic intervention remains a pressing clinical need. To identify factors that impact drug resistance herein we built a model that couples inherent cell-based response toward drugs with transcriptomes of resistant/sensitive cells. To test this model, we focused on a group of genes called metastasis suppressor genes (MSGs) that influence aggressiveness and metastatic potential of cancers. Interestingly, modeling of 84 000 drug response transcriptome combinations predicted multiple MSGs to be associated with resistance of different cell types and drugs. As a case study, on inducing MSG levels in a drug resistant breast cancer line resistance to anticancer drugs caerulomycin, camptothecin and topotecan decreased by more than 50-60%, in both culture conditions and also in tumors generated in mice, in contrast to control un-induced cells. To our knowledge, this is the first demonstration of engineered reversal of drug resistance in cancer cells based on a model that exploits inherent cellular response profiles.