Kaitlyn E Johnson* (k.john@utexas.edu), k.john@utexas.edu, and Aziz Al’Khafaji, Eric Brenner, Grant Howard, Daylin Morgan, Andrea L Gardner, Angela Jarrett, Thomas E Yankeelov and Amy Brock. Integration of multimodal experimental data sets for parameter inference of a mathematical model of therapy-induced resistance in cancer.

The ability to quantify the dynamics of drug resistance from data has direct consequences for the optimization of cancer treatments. Recent technological advances have enabled the ability to capture high-throughput “omics” data and longitudinal population dynamics, which can in theory be used to disentangle the role of differential growth and death rates from the effects of directed transitions. However, integrating these data types into a comprehensive mathematical modeling framework has remained a challenge in the field. In this work, we develop a mathematical-experimental approach to calibrate and validate a model of drug-induced resistance from multimodal data sets. We utilize single cell RNA sequencing and lineage tracing to characterize gene expression states associated with chemotherapy resistance and quantify the phenotypic composition. We combine the phenotypic frequencies with longitudinal drug response data to jointly calibrate a mathematical model of drug-induced resistance. The inferred parameters are then used to make predictions about the effect of different treatment regimens. This is the first work to our knowledge that combines single cell RNA sequencing with longitudinal data into a mathematical model to reveal the dynamics of drug-induced resistance. (Received September 17, 2019)