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Genotypic Determinants of metastatic fitness: a delicate balance of passenger and driver mutations

The transformation of cancer from localized to metastatic is a highly lethal and poorly understood process. Evolutionary dynamics drive the primary tumor population, but also are important in the selection of successful metastases. A gene-centric mathematical model derived from population genetics was developed by which stochastically accrued mutations could either strongly benefit (driver mutation) or weakly detriment (passenger) a cancer cells reproductive fitness. We modeled cells starting at the initial site of tumorigenesis and followed them to the site of metastasis and observed metastatic deposits in silico. We found that, on average, greater mutational load correlates with lesser metastatic fitness and endeavored to test this hypothesis experimentally.

I will present the mathematical model, in silico results and initial biological validation, both in vitro and in vivo.