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Meghan C Ferrall-Fairbanks, Tampa, FL 33612, and **Gregory J. Kimmel** and **Philipp M. Altrock*** (philipp.altrock@moffitt.org), Tampa, FL 33612. *Uncovering time-dependence of intra-tumor heterogeneity*. Preliminary report.

We have developed a pipeline to quantify intra-tumor heterogeneity at the transcriptomic level using a generalized diversity index (GDI). We here ask at which time points in a tumor's evolutionary trajectory GDI can be used prognostically. We can show that an order of diversity parameter, q , allows us to control for different population properties. Richness emerges at low values of q , while high q shifts the emphasis to the phenotypic drivers of the adapting tumor population. We then use an evolutionary game theoretic approach to understand how GDI changes over time. Using replicator-mutator dynamics, we explore the effects of constant and frequency-dependent selection. Our analyses suggest that GDI undergoes non-monotonic changes as the population evolves. We explore these dynamic features further in sequential single-cell RNA sequencing samples of fused breast cancer cells, where at earlier passages after fusion, GDI approaches a maximum, and later returns to levels similar to the initial state. Overall, GDI as a means to quantify intra-tumor heterogeneity is a powerful tool to understand eco-evolutionary dynamics in cancer under uncertainty of the precise adaptive forces. (Received September 10, 2020)