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Title: Emergent cellular ecosystems in melanoma revealed by single cell analysis

Abstract: Anti-cancer therapies can often kill the vast majority of tumor cells but a few rare cells remain and grow despite treatment. Non-genetic variability has emerged as a potential contributor to this behavior. However, it remains unclear what drives this variability, and what the ultimate phenotypic consequences are. We have developed a set of new single cell barcoding technologies (Rewind and FateMap) that have enabled us to show how different types of variability can translate into different drug-resistant outcomes upon treatment with drug. In particular, we found that even a genetically and epigenetically clonal population harbors enough latent variability to produce an entire ecosystem of different resistant cell types, and show preliminary evidence suggesting that these cell types can contribute to tumor development in distinct ways.