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Title:

Multiparameter single cell characterization of ovarian intratumor heterogeneity

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Objective:

Rapid advances in single-cell and deep sequencing technologies have revealed the genetic and functional complexity of bulk tumor tissue, particularly with regard to their heterogeneous and clonal composition. This is especially relevant to HGSOE patients, where existing analyses of these tumors have uncovered a high degree of intratumoral heterogeneity. In this work, we present methods for the isolation of single- and multi-cellular batches to better characterize clonal diversity from HGSOE patient-derived cells.

Materials and Methods:

We demonstrate single- and multi-cellular manipulation and sequencing using multiple technologies. Lysed genomic DNA from single or batched cells was characterized using the AmpliSeq 207-target HotSpot and more comprehensive 143-target OncoPrint cancer panels. Single cell, differential expression was conducted using Chromium high diversity mRNA sequencing.

Results:

We integrate phenotypic and genotypic profiling of single cells to characterize clonal heterogeneity in HGSOE tumors. Specifically, growth kinetics, differential expression, and clonal TP53 mutation profiling will be discussed in the context of pilot primary samples. Analysis of TP53 mutation demonstrated a clear sub-population (31%) of single cells exhibiting >75% mutation frequency, which is much higher than the 25-40% observed in bulk controls samples, indicating that a subset of cells likely drives downstream signaling effects. In addition to genetic data, single-cell real time cloning alongside CA125 and HE4 secretion assays will be discussed.

Conclusions:



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Collectively, this genomic data was used to identify cellular clonality and address the degree of clonal heterogeneity across HGSOC tumors when compared to bulk sequencing. We illustrate the potential for utilizing single cell sequencing data in the development of future therapeutic interventions.