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Expressed Cellular Barcodes to enable simultaneous lineage tracing and single cell phenotypic measurements

Researchers at Stanford have developed a method using expressed genetic barcodes to enable simultaneous lineage tracing and single cell profiling. Intratumor heterogeneity fosters tumor evolution which is a key contributor to therapeutic failure and the lethality of cancer. To more effectively fight cancer, intratumor heterogeneity and tumor evolution need to be considered. Sequencing methods have been developed to help analyze and understand tumor evolution but they are not optimal. To help overcome the limitations of the existing methods the inventors have developed this technology. It is a sequencing-based ultra-high resolution lineage tracing and single cell phenotyping system for mammalian cells. It uses an expressed genetic barcode to capture subclone specific DNA, RNA or protein expression. This enables quantification of clonal dynamics and identification of functional determinants of this process. The technology can be used in therapeutic development and tumor diagnostics as it enables robust mapping of cellular identity to phenotype thereby allowing delineation of genotype to phenotype maps in cancer.

Stage of research
In vitro and *in vivo* proof-of-concept studies have been performed and show great promise. Additional development is ongoing.

Applications

- Research tool- barcoding for lineage tracing and single cell phenotyping
- Tumor diagnostics and therapeutic development:

    - Study clonal evolution
    - Delineate genotype to phenotype map in development and cancer
    - Identify functional determinants of clonal outgrowth
    - Quantify clonal dynamics
    - Quantify rare subclones
    - Monitor clonal dynamics of immune repertoires during immunotherapy

Advantages

- Enables simultaneous mapping of cellular lineage to functional determinants of clonal outgrowth
- Allows simultaneous lineage tracing and single cell profiling
- Provides functional information about subclones that is not obtainable using conventional barcoding methods
- Enables quantification of rare subclones
- Includes software to analyze barcodes at the DNA and RNA levels
- Compared to evolvable barcodes, this barcode does not suffer from inherent problem of expression of Cas9 and risk of identical barcodes being altered in multiple different lineages
- Method is tunable
- Method is cost effective

Innovators

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