SCRATCH-seq: Capturing Dynamic Genetic Changes in Lymphocytes

A platform that allows the combined profiling of chromatin accessibility, transcription analysis with parallel analysis of B and T lymphocytes antigen repertoire.

Technology

Researchers at NYU have developed a novel workflow that allows the sequencing of the immune repertoire in parallel with transcriptomic profiling, surface epitope identification, and chromatin accessibility at the single-cell resolution. This technology provides a comprehensive approach that determines the clonality of lymphocytes and provides further insight into the molecular changes that occur during disease.

Background

Lymphocytes are defined by their unique genetic signatures, notably the rearrangements of T-cell receptors (TCR) or B-cell receptors (BCR). Sequencing the repertoire of B and T cell receptors enables confident identification of clonal populations of the lymphocytes that expand in response to cancer or an infection. In hematological malignancies like lymphoma and leukemia, assessing clonality is vital for the detection of malignant cells. Furthermore, in both hematologic malignancies and in solid cancers, progression is influenced by the dynamic interactions within the tumor microenvironment (TME). Comprehensive insights into these interactions require understanding of transcriptional state, chromatin accessibility, and surface phenotype of individual states. Such a multi-dimensional analysis not only improves our understanding of the tumor and inflammatory microenvironments but also enhances our ability to monitor therapeutic responses and discover new therapeutic targets. Current sequencing technologies such as ECCITE-seq and TEA-seq are lacking in certain modalities, resulting in an incomplete picture of the immune landscape. SCRATCH-seq (Single-Cell Immune Repertoire, Antigen, Transcription, Chromatin accessibility by sequencing) aims to bridge this gap by delivering a more complete view, thus enhancing our ability to design targeted interventions in oncology.

Applications

- Tracking lymphocyte states in the tumor microenvironment or site of infection, and in response to drugs or vaccination.
- Tracking the development of antigen-specific B and T cells to provide a more accurate characterization of immune response in cancer, autoimmunity, and infection.
- Identifying new biomarkers or epigenetic changes that reflect cancer progression and response to immunotherapies.
- Simultaneously defining transcriptional and chromatin accessibility changes in clonally-defined lymphocytes and bystander cells following therapy.

Advantages

Category

Life Sciences/Platform Technology

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Life Sciences/Research tools/Oncology

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Learn more

Faster and Cheaper: Parallel multiple sequencing modalities.

Compatible with 10x Genomics: Can be combined with tetramer staining for increased specificity and identification.

Intellectual Property

NYU has filed a U.S. provisional patent application.

References

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3. Zavitsanou et al , https://www.cell.com/cell-reports/pdf/S2211-1247(23)01307-4.pdf