AACR 2021: Single-cell technologies bring new insights to tumor cells

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April 13, 2021 -- Single-cell technologies have become important tools for cancer researchers and provide scientists with the ability to make measurements of individual cells to unveil heterogenicity among tissues. Recent developments in single-cell research have been a focus of the virtual American Association for Cancer Research (AACR) 2021 meeting held online April 9-14.

As part of the molecular and cellular biology/genetics track during the meeting, researchers from around the world explained how their work is helping to uncover important differences within tumors, to increase knowledge about the underlying biology of cancer evolution, and to tease out potential new targets for cancer therapeutics.

While some work focused on generating wide-encompassing atlases of tumor cells within a wide-range of cancer types, other work focused on bringing clarity to the composition of specific tumor microenvironments.

Single-cell technologies to explore many cancers

For instance, during a session titled "Single-Cell Analysis -- Changing the Landscape of Cancer Research," Zemin Zhang, PhD, from Peking University described his team's work in utilizing single-cell technology to understand the composition, special features, lineage, dynamics, cell-cell interactions, and clinical relevance of cells within tumor microenvironments.

The study built on previous work in which dendritic cell lysosomal associated membrane glycoprotein 3 (LAMP3) in liver cancer and tumor-associated macrophages (TAMs) with the phenotypes complement c1q c chain (C1QC) and osteopontin (SPP1) in colorectal cancer were found to be protumorigenic, meaning they promote cancer proliferation within the given tissue.

Using a pancancer transcriptome atlas of infiltrating immune cells, which included over 10 common cancer types, researchers discovered that LAMP3 dendritic cells were present in all cancer types -- pointing to their universal role in the tumor microenvironment. Alternatively, while C1QC macrophages were also very prevalent, SPP1 macrophages were only found in certain cancer types.

However, Zhang noted that where SPP1 cells were missing there were usually other types of suppressive macrophages present, representing the heterogeneity of tumor-infiltrating macrophages among various cancer types. Zhang closed by stating that these important differences are crucial and should be considered during the development of cancer-specific immunotherapies, such as monoclonal antibodies.

Single-cell technologies to further classify specific cancers

In a separate AACR session titled "Redefining the Tumor Microenvironmental Vulnerability with Single Cell Technologies," Alexander Swarbrick, PhD, professor at the Garvan Institute of Medical Research, gave a talk focused on an integrated multiomics approach to developing an atlas of breast cancer tissues.

The goal of the collaborative study that he detailed was to define the taxonomy of cell types within breast cancer tumors, determine the spatial distribution of cell types within the tumor environment, and elucidate how the cellular phenotype is influenced by the local tumor microenvironment.

Swarbrick's team focuses on the use of single-cell RNA-sequencing (scRNA-seq), in which researchers can generate full sequence transcriptomes from thousands of cells in each tumor. However, because they work with clinical samples, they take a more comprehensive approach to multidimensional cellular genomics to learn as much as they can from each sample.

In addition to scRNA-seq, they use cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq), which is a flow cytometry-based workflow where antibodies are labeled with DNA barcodes instead of fluorophores to enable the measurement of cell surface proteins. Importantly, Swarbrick explained that this data can be linked back to a library of data generated by flow cytometry and immunoassays.

The team has also created a new method called repertoire and gene expression by sequencing (RAGE-seq), which is capable of generating accurate full-length antigen receptor sequences at nucleotide resolution using the Oxford Nanopore sequencing platform. This platform allows the researchers to understand the evolution and variety of immune cells in a sample.

Lastly, the team conducted tissue-based analysis to provide spatial context to the analysis using the 10X Genomic Visium and Nanostring Digital Spatial Profiler (DSP) platforms. Ultimately, the researchers aim to tie the multiomics data to clinical and histopathological features of various breast cancers. The data generated from these analyses allow the researchers to begin to explore unique cells in the context of the specific location where they reside in tumors.

One of the main outcomes of Swarbrick's project was the development of a cellular taxonomy of breast cancer, which identified most of the cell types that make up breast cancer and defined their features and pure signatures for each tissue type.

Although it may go without mentioning, Swarbrick said that in the study, they identified all of the cell types that they expected to find. The additional multiomics data were able to then provide additional layers of information about each of the cell types.

For instance, the CITE-seq data allowed the team to characterize distinct populations of dendritic and macrophage cells, as well as monocytes within various breast cancer types. Overall, the team was able to identify recurring patterns across 14 types of breast cancers across the three main subsets of disease.