

The Significance of Cell Functions in Acute Leukemia Single-Cell Evaluation

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DESCRIPTION

Acute Myeloid Leukemia (AML) is a genetically, epigenetically, and clinically heterogeneous disease that is characterized by proliferative, clonal, abnormally differentiated, and occasionally poorly differentiated cells of the hematopoietic system infiltrating the bone marrow, blood, and other tissues, failing to produce normal hematopoiesis. AML is more prevalent in older people, is linked to serious complications and high mortality, and is responsible for a disproportionately large number of fatalities from malignancy. With recent improvements in disease care, the cure rate has risen to 15% in individuals over 60 and to about 40% in patients under 60. Therefore, it is necessary to improve the prognosis for AML through the creation of customized treatment plans that consider the initial heterogeneity of AMLs and the potential for clonal drift over time (i.e., the spatio-temporal heterogeneity of AML blasts and leukemia stem cells). Treatment for hematological malignancies and acute leukemia's in particular, has advanced significantly through the molecular analysis techniques. Tumors can resist chemotherapy and immunotherapy for a variety of reasons. Identification of metabolic pathways for escape and total population expression of resistance markers are of interest. However, because it does not enable the identification of the cell populations affected by these expressions, the information offered by this total population analysis is incomplete. Even if it hasn't been shown, it is quite plausible that the expression of a particular resistance component has a distinct prognostic significance depending on whether it affects a terminally differentiated cell with low proliferation capacity or a leukemic stem cell with strong mitogenic potential.

Flow cytometry techniques have made it possible to analyze many markers on the same cell in order to get over this limitation, although not more than 50 markers and typically less than 20 on the cytometrics used in routine tests. Less than 100 parameters can be analyzed using mass spectrometry. Even while this number of markers already looks high, it is completely out

of proportion to the roughly 20,000 genes that a cell may express. Current single cell RNA analysis techniques support this strategy. In biological systems with cellular heterogeneity, single-cell RNA sequencing, or scRNA-seq, is a potent method for examining the complicated cellular transcriptome at single-cell resolution. The investigation of gene expression in many cell types within a tissue is made possible by the high-throughput sequencing and bioinformatics tools used in scRNA-seq. This technology also enables the discovery of uncommon and extremely heterogeneous cell populations. As this technique enables the investigation of intra- and inter-tumor heterogeneity and tumor microenvironment, the scRNA-seq has been extensively used in oncology, as well as in the fields of embryogenesis, developmental biology, immunology, and neurology. Even though traditional single cell RNA analysis is a very effective method, it still has a number of limitations. The expense of such an analysis, which is challenging to implement in routine analysis, is unquestionably the first. The second drawback, however, is the inability to compare two samples from distinct studies, despite the data having been standardized and normalized.

The cell hashing algorithm appears intriguing as a way to get around these two drawbacks. This is made possible by a step of cell labelling with antibodies specific to a protein expressed on all cell types, and this antibody is coupled to a hashtag oligonucleotide or HTO, which allows differentiating each sample after sequencing. One may see quickly comparing various chemotherapies in a single cell experiment. The therapeutic protocol could be modified in response to the single cell analysis in less than a week (delay considered reasonable in light of the protocol's adaptation to targeted therapies, aside from emergency situations like disseminated intravascular coagulation or leukostasis syndrome). By identifying chemo resistant cells (stem cells *versus* more differentiated populations), their escape mechanisms, and ways to get around them, this approach would also have the benefit of predicting tumor escape (re sensitization strategies).

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