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Editorial on Single Cell Proteomics

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Editorial

Complex biological processes are based on dynamic interactions between individual cells, involving in many cases multiple cell types as well as different states and susceptibilities. Traditional bulk tissue analysis averages all of the differences in cell diversity found in most biological/biomedical samples, whereas single-cell analysis allows for the characterization of each individual cell, studying its genomics, transcriptomics, proteomics, metabolomics, and cell–cell interactions at the single cell level. This analysis allows for the discovery and classification of previously unknown cell states. The majority of single-cell research focuses on nucleic acids, particularly genes expressed at the cellular level. However, nucleic acid-based technologies ignore an important group of biological regulators in the cell: proteins. Proteins are the workhorses of the cell, impacting all aspects of cellular processes in all physiological situations. Nucleic acids behave predictably at the single-cell level, but the proteome has a diverse set of chemistries, interactions, dynamics, and abundances. Its acute state (i.e., the proteotype) is determined by the genotype as well as external perturbations and/or stimuli.

As a result, quantitative analysis of proteome dynamics, including Post-translational Modifications (PTMs) and their relationship to phenotypes and diseases, has become critical in biological and clinical research. Since there is a lack of an equivalent-at the protein level to DNA amplification by PCR, any protein detection technique must be sensitive enough to identify them, even at wide dynamic range of the protein concentration in the cell [1-3] .Proteomics seeks to identify, characterize, and quantify all protein isoforms in a given cell, tissue, organ, or organism.Global proteome measurements using Mass Spectrometry (MS) and/or tandem Mass Spectrometry (MS/MS, which is used to improve mass spectrometer specificity by coupling two analyzers using a collision cell) have been performed on biological samples containing thousands or millions of cells. This provides a quantitative protein expression profile but does not account for sample heterogeneity.

Novel Nano scale MS approaches that identify and quantify proteins in a more deep and accurate manner are promising tools in the development of single-cell protein analysis. These proteomics technologies will allow for high-throughput research into fundamental biological questions such as protein-binding signalling mechanisms and protein modifications. Researchers can now generate high-content data sets of single-cell genomic and transcriptomic data, and as Single-Cell Proteomics (SCP) emerges, they will be able to integrate single-cell mRNA and proteomic measurements. Many proteins' abundance and function are regulated by PTMs and degradation, which cannot be inferred from genomic or transcriptomic approaches, making proteomics essential for determining protein patterns relevant to disease diagnosis and/or drug response, among other things. Furthermore, genomic and transcriptomic sequencing cannot explain protein localization and protein–protein interactions [4-5], which are important in many signaling pathways.

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The abundance of proteins in a cell can differ between isogenic single cells, affecting regulatory roles and controlling cell fate during apoptosis and cell proliferation. Early studies of cellular heterogeneity concentrated on isogenic bacterial populations growing in the same culture, revealing that individual bacteria differed in terms of persistence; phage burst size, -galactosidase production, and chemotactic behavior. GFP measurements revealed unexpected variability in protein levels expressed from the same promoter, which was interpreted as biochemical noise made up of intrinsic (from the biochemical processes of transcription and translation) and extrinsic (from external environmental fluctuations) components. In many cases, protein abundance variability reflects different cellular states, which can result in a wide range of functional outcomes, whereas other studies have shown that gene expression heterogeneity can be used to respond to environmental changes in a dynamic manner. Several human health conditions are associated with immune system disturbances (autoimmune diseases, infectious diseases, or chronic inflammation) and other pathologies with varying ontogeny (e.g., cancer, neurodegenerative disorders). Infectious agents, such as Helicobacter pylori, hepatitis C virus, or Kaposi's sarcoma-associated herpesvirus, have been shown to cause approximately 20% of cancers (solid tumours and onco-hematological pathologies).

As a result of the close relationship between the immune system and various diseases, novel therapeutic approaches for tumour treatment have emerged. Vaccination, monoclonal antibodies, immune checkpoint inhibitors, adoptive T-cell transfer, and oncolytic virus therapy are among them. Understanding the cellular and molecular mechanisms underlying cancer allows researchers to identify potential targets for novel onco-immunotherapies based on immune response modulation and regulatory control. Tumor genomes are frequently disrupted by point mutations or more visible alterations, such as chromosomal complement changes. Thus, cancer cells have defects in signaling pathways that regulate normal cell proliferation and homeostasis, and tumor genotypes vary greatly.

Conflict of Interest

None.

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