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Popular Article

Single Cell Proteomics (SCP): The Cell Analysis

Suruchi Sharma*1 And Sahil Sharma2
[1]M.V.Sc. Veterinary Biochemistry DGCN COVAS, CSKHPKV, Palampur,
[2]M.V.Sc. Animal Nutrition DGCN COVAS, CSKHPKV, Palampur
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Abstract

Cells from microbial cultures and mammalian cell cultures that have identical genomes and grow in the same environment do not have the same proteome. The distinctions Proteomes have important functional consequences. The proteome of each individual cell will be analysed using high throughput analytical platforms in Single Cell Proteomics; advanced isolation and sampling methods are required to minimize protein loss, and highly sensitive techniques are required for proteome analysis. Single Cell Proteomics can be used to create a proteome map of each type of cell in multicellular and single-cell organisms, interactions related to a biological process. This aids in the investigation of protein expression and modification under specific biological conditions, the characterization of protein functions in a genome, the identification of protein localization and compartmentalization at a given time, and the determination of protein-protein interactions related to a biological process.

Introduction

The body is composed of various organs and tissues that perform specific functions and processes to form the various body systems. Each system goes through a unique set of physiological and biochemical processes. Diseases can result from any deviation from these processes. These disease conditions can only be understood after a thorough understanding of normal physiological and biochemical processes. To comprehend and manipulate the key processes, comprehensive knowledge of all molecules expressed at a specific time under different conditions, as well as their interactions within subcellular levels and between different types of

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cells in an organism, is required. For the expression of molecules, the genes for the molecules must go through the central dogma, where the end product is proteins, and the various molecules are expressed through these proteins. As a result, understanding the physiological, biochemical, and even pathological processes in the body necessitates a thorough understanding of the protein expressed. Cells can be analysed at various levels of the central dogma: when done on DNA, it is known as Genomics, when done on mRNA, it is known as Transcriptomics, and when done on proteins, it is known as Proteomics. Although genomics and transcriptomics can be used to analyze cells, they have limitations in that they cannot open most of the cellular windows because proteins are the end product of central dogma and gene expression cannot fully predict the outcome protein molecule expression and modifications (Su et al. 2017).

Concept of Single Cell Proteomics

A new method for identifying proteins using varied throughput analytical platforms is single cell proteomics. Many cells with the same genome are found in some mammalian cell cultures and microbial cultures that are growing in a uniform environment. Although similar proteomes should be produced by these cells, this is not the case. When millions of cells are combined and their proteomes are lysed and analyzed by LC-MS/MS to determine the population average, significant similarities between the proteomes of cells from homogenous cultures can be found. Because population averages frequently overlook cellular heterogeneity, they are not representative of all cells. Proteome differences have significant functional implications. Such variations can only be detected by measuring protein levels in individual cells (Specht et al. 2018 and Lalhmangaihzuali et al. 2020).

Techniques in Single Cell Proteomics

Cell isolation, sample preparation, proteome map production utilizing high throughput analytical systems, and analysis using bioinformatic tools are all general procedures in single cell proteomics. These methods enable highly sensitive high-throughput protein loss prevention screening. Here are listed the many Single Cell Proteomics approaches with their method and principle: (Minakshi et al. 2019 and Lalhmangaihzuali et al. 2020).

Cell isolation

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- Fluorescence Activated Cell Sorter (FACS) - Cells are encapsulated in tiny liquid droplets, marked with an antibody that is fluorescing, and the marked cells are then separated using an electric field.
- Laser Capture Microdissection (LCM) - Application of a transparent thermoplastic coating over the target cell. Target cell sticks to the film with the focus of the laser beam. When the film is removed, the target cell that was attached to it is captured for isolation.
- Manual cell picking - Target cells are selected using a micropipette and pointed tungsten needles.
- Limiting dilution - On the basis of serial dilution. Samples are diluted to the point where single-cell separation is possible.
- Microfluidics - Pneumatic membrane valving, hydrodynamic cell traps, and droplet in oil-based separation

Sample preparation

- Cell lysis brought on by physical and mechanical pressure - Sonication, electrical field, and optical lasers can all be used.
- Lysis of cell by chemical, precipitation of protein and removal of contaminant – Solubilizing lipids and proteins in the membrane causes pores to develop and complete cell lysis when detergent lysis occurs and is incorporated into the cell membrane.

Analytical platforms

- Fluorescence flow cytometry – Based on the idea that data creation occurs when target proteins are bound to various types of labelled antibodies.
- Mass Cytometry – Based on the concept of target protein binding with variously labelled antibodies for data production, but fluorochrome is replaced with a pure heavy metal ion tag.
- ELISpot – Similar idea to the sandwich ELISA (i.e. it measures antigen between two layers of antibodies) but on a smaller scale.
- Single Molecule Array (SiMoA) – Based on the separation of individual immune-complexes using common ELISA reagents on paramagnetic beads.

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- Microfluidic antibody capture chip (MACS CHIP) – Combination of fluorescent antibody labeling, chip, software and contemporary microscopy.
- Single cell western blotting – Uses the same methodology as western blotting (i.e. to separate and identify proteins) but executes it on a typical histopathological microscope image.
- Capillary electrophoresis – Injection of samples into a capillary tube that is filled with a viscous polymer or gel. Samples segregated by applied voltage according to their electrophoresis mobility.
- Ultrathin layer gel electrophoresis – Utilizes two-dimensional electrophoresis.
- MALDI-TOF Mass Spectrometry – Based on measurements of the mass to charge (m/z) ratio of various analytes.
- SCoPE-Mass Spectrometry - Depends on liquid chromatography tandem mass spectrometry (LC-MS/MS).

Application of Single Cell Proteomics

In multicellular animals and single cell organisms, single cell proteomics can be used to create a proteome map of each type of cell. This assists in the research of disease development and its impact on various cell types, for diagnosis, therapy and treatment prognosis. Single cell proteomics aids in the creation of biomarkers. It also aids in the detection of cancer by revealing the characteristics of cancer cells, their progression and drug susceptibility, and how the immune system reacts to them (Mannello et al. 2012). It is used in the analysis of protein functions in a genome, the identification of protein localization and compartmentalization at a particular time, and the determination of protein-protein interactions linked to biological processes. Single cell proteomics can be used for lineage tracing of cellular phenotypes, for comparing the functioning of various immune cells in normal, deficient and excess, for cancer immunotherapies, for phosphoprotein signaling pathways, for analysis of cell motility, for response of targeted inhibitors on cancer cell, for response of cells to engineered molecular stipulations or different cells nearby, for cell-cell separation distance, for understanding of cellular functionality, high throughput screening, and for other purposes (Heath et al. 2016).

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Conclusion

An effective method for analyzing and collecting single cells from a heterogeneous pool is single cell proteomics. It can aid in understanding the diversity of various cells at each degree of central dogma. Single cell proteomics can assist in the study of various proteomes of cells at the individual level to understand both normal and pathological biological processes in the body because proteins are the end result of central dogma. With the development of high throughput and highly sensitive techniques, single cell proteomics has the potential to aid in the quicker and more accurate diagnosis of diseases, particularly cancer. It also has the potential to aid in the development of highly specific drugs that act on specific cells and to aid in the improvement of analysis and understanding of the life's developmental processes. Single cell proteomics will thus pave the way for the transformation of biology and medicine (Lalhmangaihzuali et al. 2020).

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