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Perspective

Importance of Peripheral Blood Mononuclear Cells (PBMCs) in Clinical Immunology

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DESCRIPTION

Human Peripheral Blood Mononuclear Cells (PBMCs) are immune cells with a single round nucleus that are derived from the bone marrow and secreted into the peripheral circulation. These cells are important components of the immune system and are involved in both humoral and cellular immunity. Peripheral Blood Mononuclear Cells (PBMCs) are readily accessible cellular parts of blood organs along with platelets. PBMCs contain several types of cells such as lymphocytes, monocytes and macrophages. It represents the only site of active gene expression in the blood. These cells undergo immune phenotypic changes in a variety of diseases and represent a peripheral source for monitoring gene expression and post-translational modifications associated with many diseases. It is hypothesized that blood proteins released from PBMCs by active and passive method can contain an important part of the plasma proteome. Using state-of-the-art proteomics profiling techniques in PBMCs enable minimally invasive monitoring of disease progression, response to therapy, and biomarker discovery. Detailed mapping of the PBMC proteome using a sensitive, robust and quantitative methodological setup is required to achieve the goal of disease diagnosis and prognosis. PBMC are relatively easy to obtain from the blood samples which are used for routine check-up. They provide direct access to physiologically relevant (immune) proteins. Most omics research till date using PBMCs were transcriptional profiling experiments in the context of inflammatory (pre-eclampsia, rheumatoid arthritis, chronic pancreatitis, etc.) and malignant (chronic lymphocytic leukemia and renal cell carcinoma) diseases. These studies have revealed many differentially regulated genes at the mRNA level. Post-translational modifications and protein processing plays an important role in regulation and they can control cellular response pathways to disease and can have profound effects on protein function and activity in specific samples. To expand the range of proteomics biomarker discovery, technical and systematic need of improvements needed to get more detailed images of proteomics pattern of PBMC. This will greatly improve the prospects for discovering effective biomarkers in PBMC. This is especially true when PBMC-derived proteins occur only in very low concentrations in serum or plasma. PBMC have very great potential in the field of clinical proteomics, compared with its other usage like its involvement as proteins in biochemical pathways from the KEGG database and many others. Some of the researchers used 2D-PAGE and MS-shotgun analysis to identify the proteomic profile of T cells, monocytes, and PBMCs. proteomic approach is excellently suited for the study of PBMCs and the attached physiological roles like activation studies and immune phenotyping. By using a TMT-based quantitative workflow, biomarker discovery projects for quantification of up to 10 samples in parallel are enabled till now. The method setup is thus suited to significantly extend the range of molecular markers defined for specific activation states of all cell types contained in PBMCs, which then may be exploited for focused activation studies where a complete panel of activation markers will be measurable in a multiplex manner. Methodologically this can also be achieved by transferring newly identified or already established protein markers into a TMT-Selected Reaction Monitoring (SRM) based approach. A similar approach is often used to check protein regulation discovered during discovery studies. PBMCs are often targeted for toxic responses and therefore act as important tool for researchers exploring new and exciting horizons in pharmacogenomics. PBMCs can be cultured in 24- or 96-well plates supplemented with RPMI-1640 medium for 5-7 days and incubated at 37℃ in a humidified atmosphere of 5% CO_2. Proteomic profiling of PBMC is the method of choice for identifying marker proteins whose expression may be characteristic of a particular disease. The formation of such marker proteins results from disease-related pathophysiological processes. In healthy individuals, Peripheral Blood Mononuclear Cells (PBMCs) circulate in a quiescent cellular state and monitor potential immune-related events, but respond to potential pathogen invasion in an inflammatory manner rapidly and efficiently it should have the ability to respond. Activation of these cells is most likely accompanied by characteristic proteomic changes. Human PBMCs proteomic profiling is carried out by top-down 2D-PAGE approach or bottom-up LC-MS/MS-based shotgun approach. In addition, primary human T cells and monocytes were purified and activated separately. The

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involvement of inflammation-activated PBMCs in specific diseases and the responsiveness of these cells to anti-inflammatory drugs can be assessed by quantifying these marker proteins. As PBMCs were inflammatory activated *in vitro* with the help of lipopolysaccharide (LPS) and phytohemagglutinin (PHA) followed by 2D-PAGE (top-down) and LC-MS/MS-based shotgun approach (bottom-up) are basic topic for current studies. PBMCs are composed of several different cell types, and proteomic analysis of these cells is highly data complex, especially considering their different functional states. Furthermore, the heterogeneity of biological samples and methodological challenges can hinder direct interpretation of the data from PBMCs cells. Proteomic characterization of PBMCs and their functional cellular state reveals and assesses the contribution of these cells to specific diseases that are the focus of current proteomic research, such as cancer, Alzheimer's disease, and chronic inflammatory diseases. Studying the proteomic profile of PBMCs can provide a better understanding of immune processes and the potential to monitor the health status of the host organism. Proteomic analysis of PBMCs achieves stated goals because important immune-related biomarkers are readily and easily accessible for analysis.