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Commentary

Diagnostic Value of Plasma Proteins in Acute Leukemia and Lymphoma

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DESCRIPTION

Aiming to easily accessible biomarkers that focus on biological differences between hematologic diseases, the diagnostic value of plasma proteins in acute leukemia and lymphoma was investigated. A multiplex Proximity Extension Assay (PEA) was used to analyze 183 proteins in diagnostic plasma samples from 251 patients with acute leukemia and lymphoma and compared them with samples from 60 healthy controls. Multivariate modeling using partial least squares discriminant analysis revealed highly significant differences between various disease subgroups and controls. The model allowed us to clearly distinguish between leukemia and lymphoma, with few misclassified patients. Acute leukemia specimens had high levels of proteins associated with hemostasis, inflammation, cell differentiation, and cell-matrix integration, whereas lymphoma specimens had high levels of proteins known to be associated with the tumor microenvironment and lymphoma growth to level of protein. PEA technology can be used to screen large numbers of plasma protein biomarkers in low µL sample volumes to distinguish between controls, acute leukemias, and lymphomas. Plasma protein profiling may help provide insight into the pathophysiology of acute leukemia and lymphoma, and this technique may be a valuable tool in the diagnosis of these diseases.

Understanding disease biology and the interactions between host and tumor cells is critical for the development of diagnostic, prognostic, and predictive biomarkers. Identifying plasma protein patterns may add a new dimension to our knowledge and understanding of malignancies. The Proximity Extension Assay (PEA) measures many proteins simultaneously in a small amount of liquid tissue. Studies using this method have demonstrated clinical utility in various malignancies such as glioma, gastric cancer, and ovarian cancer. This study investigated three types of acute leukemia: Acute Myelogenous Leukemia (AML), Acute Promyelocytic Leukemia (APL), Acute Lymphoblastic Leukemia (ALL), and Diffuse Large B-Cell Lymphoma (DLBCL). Two common types of lymphoma were examined and Hodgkin Lymphoma (HL). Based on proteins detected in low µl range plasma samples from untreated leukemia and lymphoma patients and healthy controls, the aim was to distinguish these hematological malignancies using a well-developed protein detection panel. The pattern of these distinct proteins and the biological processes associated with them may indicate the biology of these malignancies.

With pancytopenia and maturation arrest as key features of the disease, leukemia patient's exhibit altered protein levels associated with hemostasis and stem cell differentiation, while AML, APL, and ALL are associated with lymphoid and myeloid development and expected the markers to be different. It has been hypothesized that lymphoma patients have elevated levels of inflammatory proteins and that protein profiles may reflect differences in the Tumor Microenvironment (TME) between HL and DLBCL in 107 patients aged 18 years or older with acute leukemia.

Clinical patient characteristics are displayed in plasma samples from 60 age and sex-matched healthy controls (30 males, 30 non-pregnant females) were obtained from the EpiHealth Biobank. High-quality longitudinal biobank that serially collects clinical data, blood and tissue samples from over 22,000 cancer patients. The EpiHealth cohort is a large population-based examination cohort investigating gene-lifestyle interactions with a total of 25,104 participants. For both cohorts, blood samples will be collected according to standardized schedules established in each study. At the U-CAN Biobank, the time from blood draw to freezing (usually less than 4 hours) was recorded for each sample. Samples are identified according to Standard Pre-Analytical Codes (SPREC). This study was approved by the Uppsala Erebro Regional Ethics Committee (EC) (2012/198, 210/198/1, 2014/233).

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