High-resolution Antibody Array Analysis of Childhood Acute Leukemia Cells.

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Abstract

Acute leukemia is a disease pathologically manifested at both genomic and proteomic levels. Molecular genetic technologies are currently widely used in clinical research. In contrast, sensitive and high-throughput proteomic techniques for performing protein analyses in patient samples are still lacking. Here, we used a technology based on size exclusion chromatography followed by immunoprecipitation of target proteins with an antibody bead array (Size Exclusion Chromatography-Microsphere-based Affinity Proteomics, SEC-MAP) to detect hundreds of proteins from a single sample. In addition, we developed semi-automatic bioinformatics tools to adapt this technology for high-content proteomic screening of paediatric acute leukemia patients. To confirm the utility of SEC-MAP in leukemia immunophenotyping, we tested 31 leukemia diagnostic markers in parallel by SEC-MAP and flow cytometry. We identified 28 antibodies suitable for both techniques. Eighteen of them provided excellent quantitative correlation between SEC-MAP and flow cytometry (p< 0.05). Next, SEC-MAP was applied to examine 57
diagnostic samples from patients with acute leukemia. In this assay, we used 632 different antibodies and detected 501 targets. Of those, 47 targets were differentially expressed between at least two of the three acute leukemia subgroups. The CD markers correlated with immunophenotypic categories as expected. From non-CD markers, we found DBN1, PAX5, or PTK2 overexpressed in B-cell precursor acute lymphoblastic leukemias, LAT, SH2D1A, or STAT5A overexpressed in T-cell acute lymphoblastic leukemias, and HCK, GLUD1, or SYK overexpressed in acute myeloid leukemias. In addition, OPAL1 overexpression corresponded to ETV6-RUNX1 chromosomal translocation. In summary, we demonstrated that SEC-MAP technology is a powerful tool for detecting hundreds of proteins in clinical samples obtained from paediatric acute leukemia patients. It provides information about protein size and reveals differences in protein expression between particular leukemia subgroups. Forty-seven of SEC-MAP identified targets were validated by other conventional method in this study.


Published: 17. 10. 2016 / Responsible person: Mgr. Ing. Tereza Kůstková

Source URL (retrieved on 30. 10. 2018 - 16:31):