Abstract

Leukemia cell signaling

Acute leukemia (AL) is the most common pediatric cancer. Approximately 90 - 100 children is diagnosed every year in the Czech Republic. Acute leukemia is a complex disease that is pathologically manifested at the DNA, mRNA, protein and cellular level. Leukemic cells aberrantly express molecules that are found in other cell types under physiological conditions and their functional involvement in leukemic cells is unknow. We found that aberrantly expressed CEACAM6 increases the expression and affinity of integrins, increases the phosphorylation of intracellular kinases Akt, p38MAPK and p44/42 MAPK and triggers apoptosis in B-cell precursor acute lymphoblastic leukemia cells. Adaptor molecule NTAL, aberrantly expressed in T-cell acute lymphoblastic leukemia, signals through intracellular kinase p44/42 MAPK and potentiates corticosteroid induced apoptosis. Current leukemia research is focused mainly on monitoring of mutations at the DNA level, however, the functional consequences of these changes on cellular machineries are not straightforward. Since proteome analysis can provide link between gene sequence and cellular physiology, proteomics will contribute to elucidate mechanism of disease, prognosis and response to treatment. Protein microarrays technology is of major interest for basic proteomic research as well as for diagnostic applications. It can be used for fast and easy quantitative detection of fusion proteins (e.g. PML-RARα in acute promyelocytic leukemia) or for detection of proteomic changes after targeted therapeuticals.

Signaling of non-malignant B-cells

Common variable immunodeficiency (CVID) is a heterogeneous group of diseases characterized by decreased production of antibodies. Changes in the proteome, altered signaling, impaired maturation of B-lymphocytes or defective B-cell / T-cell interactions are possible causes of this immune system failure. Patients with CVID typically present with less memory B-cells and more naive B-cells. Subgroup of patients also presents with CD27neg CD21neg CD38neg B-lymphocytes that are rare in healthy humans. We divided these CD21neg B-lymphocytes into two populations according to CD24 and IgM expression. Focusing on the expression of IgM and CD24 and on *in vitro* functional tests, these two populations correspond to follicular (FO) I and FOII cells previously described in mice. CD27neg CD21neg CD38neg B-lymphocytes probably originate from the two FO subsets after loss of CD21 expression.