Normal circulating hematopoietic stem/progenitor cells spontaneously express high levels of anti-apoptotic protein kinase B (Akt)

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Proliferation and apoptosis of normal hematopoietic stem/progenitor cells (HSC) are tightly regulated so that steady-state kinetics is preserved. In contrast, in different hematological disorders disbalanced hematopoiesis can be explained by abnormal apoptosis. We adapted a flow cytometry (FC) and Phosflow method to determine main intracellular regulatory anti-apoptotic protein kinase B (Akt) in peripheral blood derived CD34+ HSCs. We found high levels of spontaneously expressed Akt in circulating CD34+ cells in normal subjects (N=7) as compared with mature mononuclear CD45+ cells (Mean±SE: 28.7±6.1% vs. 0.213±0.014%, OR=188.1; p<0.000001; 95% CI 154.3-229.4). Interestingly, in patients with paroxysmal nocturnal hemoglobinuria (PNH) (N=6) with no signs of aplastic anemia and high PNH clone in granulocytes (FLAER neg. >95%) in circulating CD34+ cells the level of Akt+ cells was significantly increased as compared with normal controls (50.1±12.9% vs. 28.7±6.1%, OR=2.50; p<0.000001, 95% CI 1.83-3.42). Our results have shown that the regulatory status of apoptosis in hematopoietic stem/progenitor cells can be monitored in peripheral blood using relatively simple FC/Phosflow method, avoiding bone marrow biopsy. Similar to leukemia stem cells, normal HSCs spontaneously express high levels of intracellular anti-apoptotic regulator, Akt. Highly increased Akt in HSC from PNH patients may suggest that clonal dominance of defective cells in PNH is caused by suppressed apoptosis. Proposed here method can serve as routine tool for the monitoring of different phases of hematological disorders with impaired apoptosis such as paroxysmal nocturnal hemoglobinuria, myelodysplastic syndromes and aplastic anemia.

Biography
Jacek Nowak has completed his PhD from Military Medical Institutes and Postdoctoral studies from Institute of Hematology and Transfusion Medicine, Warsaw, Poland where he is an Associate Professor and Head of the Department of Immunogenetics. He has published more than 55 papers in reputed journals, 21 chapters and has been serving as an Editor of three books.

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