allied academies

2nd International Conference on

Hematology and Oncology

August 23-24, 2018 | London, UK

Imbalanced proportions of phospatidylinositol and phosphatidylcholine in plasma membranes of hematopoietic cells in patients with paroxysmal nocturnal hemoglobinuria

Jacek Nowak
Institute of Hematology and Transfusion Medicine, Poland

Paroxysmal nocturnal hemoglobinuria (PNH) is caused by somatic mutation in phosphatidylinositol glycan complementation group A (PIG-A) gene in single hematopoietic stem/progenitor cell (HSC). Pathomechanism of clonal domination of mutated HSCs over normal HSCs is not fully clear including autoimmune, pro-survival and/or anti-apoptotic background, among else. Phosphatidylinositol (PI) is important anti-apoptotic second messenger in cells and its conversion to glycosylated PI (GPI) is arrested in PIG-A mutated PNH cells. PI content in cells is fine regulated by highly specific enzyme, the phosphatidylinositol transfer protein that is able to deliver PI to plasma membranes at the expense of equimolar quantity of phosphatidylcholine (PC). In this study we assessed contents of PI and PC phospholipids in nucleated hematopoietic cells in patients with PNH (N=22) and healthy controls (N=6). Phospholipid fractions were isolated from plasma membranes using modified Folch-based lipid extraction protocol and evaluated using high performance liquid chromatography (HPLC) with charged aerosol detection (CAD). Phospholipid contents were expressed as nmoles/10^6 cells to show molecular proportions of PI and PC in cellular membranes. We found significantly higher PI/PC molar ratio in PNH patients than in controls both in polymorphonulear (PMN) (Mean±SE: 16.3±2.6 vs. 8.0±2.0 %mol/mol, p=0.020) and mononuclear cell (MNC) fractions (20.5±3.8 vs. 9.6±2.7 %mol/mol, p=0.024). This PI/PC imbalance was caused mainly by the fall of absolute content of PC in cellular membranes in PNH patients. FLAER(-) cell proportion in PNH patients correlated with PC content in PMN cells (R=0.53, p=0.020). In PNH patients we found highly significant correlation of platelet cell (PLT) counts with PC content in MNC subset (R=0.55, p<0.01). Both white blood cell (WBC) and PLT counts in patients show trend toward lower values with increasing PI/PC molar ratios (R>0.39, p<0.09). The results suggest that i) in PNH patients the proportions of PI to PC molecules in plasma membranes of hematopoietic cells are imbalanced. Higher relative proportions of PI may potentially increase anti-apoptotic capacity of certain PI-dependent enzymes in hematopoietic cells. ii) The results suggest a protective role of PC in platelet aggregation and turnover. In PNH patients PC deficiency in circulating blood cells may be associated with increased risk of thrombosis.

Speaker Biography

Jacek Nowak has completed his PhD from Military Medical Academy, Łodz, Poland and habilitation degree from Institute of Hematology and Transfusion Medicine, Warsaw, Poland. He is the tenure professor and head of Department of Immunogenetics at the Institute of Hematology and Transfusion Medicine. He has over 80 publications that have been cited over 470 times, and his publication H-index is 11 and has been serving as an editor at 2 books and has over 20 published chapters.

e: jnowak@ihit.waw.pl

Notes: