J Blood Disord Transfus 2016, 7:2(Suppl)
http://dx.doi.org/10.4172/2155-9864.C1.014

Role of protease-activated receptors (PARs) and G-proteins in thrombin induced monocyte/macrophage migration

Ravisekhar Gadepalli
All India Institute of Medical Sciences, Jodhpur, India

The recruitment of monocytes/macrophages to the sites of dysfunctional endothelium and transformation of these cells into foam cells by the uptake of oxidized lipoproteins in the sub endothelium are the major pathophysiological features of atherosclerosis. Since thrombin is produced at the sites of vascular injury, and in order to understand its involvement in atherosclerosis, we tested its role in the modulation of THP-1 cell migration. Thrombin induced THP-1 cell migration in a dose dependent manner. Thrombin induced sequentially the tyrosine phosphorylation of Pyk2, Gab1 and p115 RhoGEF leading to Rac1 and RhoA-dependent Pak2 activation. Downstream to Pyk2, Gab1 formed a complex with p115 RhoGEF involving their PH domains. Furthermore, depletion of Pyk2, Gab1, p115 RhoGEF, Rac1, RhoA or Pak2 levels using their respective antisenseoligos substantially attenuated thrombin-induced THP-1 cell cytoskeleton formation and migration. In addition, SCH79797, a selective PAR1 antagonist, inhibited thrombin-induced Pyk2, Gab1 and p115 RhoGEF tyrosine phosphorylation and Rac1-RhoA-depenedent Pak2 activation resulting in diminished THP-1 cell cytoskeleton formation and migration. Together, these observations reveal that thrombin induces THP-1 cell migration via PAR1-dependent Pyk2-mediated Gab1 and p115 RhoGEF interactions leading to Rac1-RhoA-Pak2 activation. Based on these findings, we envision a role for thrombin and its receptor PAR1 in atherosclerosis.

gadepallirs@gmail.com
gadepallir@aiimsjodhpur.edu.in

Comprehensive approach vs. NGS

Jianxiang (Jason) Chi
Karaiskakio Foundation, Cyprus

The recent discovery of frame shift mutations in Calreticulin (CALR) in approximately 70% of myeloproliferative neoplasms (MPN) patients lacking the Janus Kinase 2 (JAK2) and myeloproliferative leukemia (MPL) mutations offer a reliable diagnostic marker for the diagnosis of MPN. Different approaches can be applied for the detection of CALR mutation in diagnosis laboratory. E.g., Sanger sequencing, RT-QPCR, High resolution of melting curve, fragment analysis or classic gel documentation. However, we still lack certain knowledge of "triple negative" case which usually leads to a poor prognosis. A universal approach for the mutation detection of MPN is needed for MPN mutation. With the next generation sequencing method becoming more and more popular in diagnosis laboratory, the developing a next generation sequencing based gene panel of MPN might be a solution for this.

jason.chi@karaiskakio.org.cy