World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:12, No:09, 2018

Large-Scale Screening for Membrane Protein Interactions Involved in Platelet-Monocyte Interactions

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Abstract : Background: Beyond the classical roles in haemostasis and thrombosis, platelets are important in the initiation and development of various thrombo-inflammatory diseases. In atherosclerosis and deep vein thrombosis, for example, platelets bridge monocytes with endothelium and form heterotypic aggregates with monocytes in the circulation. This can alter monocyte phenotype by inducing their activation, stimulating adhesion and migration. These interactions involve cell surface receptor-ligand pairs on both cells. This list is likely incomplete as new interactions of importance to platelet biology are continuing to be discovered as illustrated by our discovery of PEAR-1 binding to FcεR1α. Results: We have developed a highly sensitive avidity-based assay to identify novel extracellular interactions among 126 recombinantly-expressed platelet cell surface and secreted proteins involved in platelet aggregation. In this study, we will use this method to identify novel platelet-monocyte interactions. We aim to identify ligands for orphan receptors and novel partners of well-known proteins. Identified interactions will be studied in preliminary functional assays to demonstrate relevance to the inflammatory processes supporting atherogenesis. Conclusions: Platelet-monocyte interactions are essential for the development of thromboinflammatory disease. Up until relatively recently, technologies only allow us to limit our studies on each individual protein interaction at a single time. These studies propose for the first time to study the cell surface platelet-monocyte interactions in a systematic large-scale approach using a reliable screening method we have developed. If successful, this will likely to identify previously unknown ligands for important receptors that will be investigated in details and also provide a list of novel interactions for the field. This should stimulate studies on developing alternative therapeutic strategies to treat vascular inflammatory disorders such as atherosclerosis, DVT and sepsis and other clinically important inflammatory conditions.

Keywords : membrane proteins, large-scale screening, platelets, recombinant expression
Conference Title : ICPPI 2018 : International Conference on Protein-Protein Interactions
Conference Location : Rome, Italy
Conference Dates : September 17-18, 2018