Platelet transcriptome profile in stable angina patients with type-2 diabetes mellitus

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Background- Type-2 diabetes mellitus (T2DM) is a major cardiovascular (CV) risk factor; diabetic patients show a higher incidence of CV events compared to non-diabetic patients, together with a platelet hyperreactive phenotype. Platelets contain megakaryocyte-derived mRNAs, which can be used to perform new protein synthesis in response to activation. Specific mRNAs may vary in different clinical conditions. We previously showed that platelet transcriptome is modified in coronary artery disease (CAD) patients compared to healthy subjects (HS). Whether T2DM may affect platelet transcriptome is currently still unknown.
Aim- Our aim is to compare platelet transcriptome profile of stable angina (SA) patients with or without T2DM in order to gain insights into the molecular pathways associated with and/or triggering persistent platelet activation, observed in T2DM to find new potential targets of pharmacological modulation.
Methods- We enrolled 32 SA $T2DM^+$ patients, 53 SA $T2DM^-$ patients and 16 HS matched for age and sex. Patients from both groups were treated with low-dose aspirin. Platelets were isolated from whole blood by centrifugation and filtration (using filter Pall Purecell^{TM}) and lysed in phenol/guanidine-based reagent. RNA was extracted, checked for its quality by using Bioanalyzer 2100 Agilent Technologies and hybridized on Illumina BeadChip Human HT-12 v4 microarrays.
Results- Microarray analysis showed that 319 unique mRNAs were differentially expressed between SA patients and HS: 156 of these genes were over-expressed, whereas 163 had a lower expression in healthy compared to SA (either T2DM-positive or not) platelets. When comparison of platelet gene profiling was performed between SA patients with or without T2DM, 35 genes were found differently expressed: 24 of them were over-expressed, whereas 11 showed a decreased expression in SA^+T2DM^+ compared to SA^+T2DM^- platelets. The most upregulated transcript in SA patients $T2DM^+$ was CD69, which was reported to be involved in thromboxane production and platelet aggregation. The most downregulated transcript was prothymosin alpha (ProT alpha), whose function in platelets is unknown.
Enrichment analysis of Gene Ontology (GO) categories identified biological processes and cellular components whose expression was significantly altered in SA in comparison with healthy platelets: gene involved in platelet degranulation and activation, cell adhesion, negative regulation of endocytosis, and integrin complex were up-regulated in SA patients; protein-DNA complex subunit organization, regulation of protein localization, transmembrane receptor protein tyrosine kinase signaling pathway, and extracellular structure organization were down-regulated in SA platelets. A similar analysis of GO identified transcripts involved in biological processes whose expression was significantly altered by T2DM in SA platelets: peptidyl-serine phosphorylation and nuclear-transcribed mRNA catabolic process appeared up-regulated in SA+T2DM+ platelets.
Conclusion- The differentially expressed transcripts in T2DM platelets provide insights, which warrant further investigations, into the mechanisms underlying the increased platelet reactivity and they may represent new potential biomarkers for thrombotic risk or targets of pharmacological modulation.