Platelet omics

Alzheimer's disease biomarkers

Yu et al. performed platelet proteomics in T2DM patients with MCI (T2DM-MCI) and without MCI (T2DM-nMCI). Pearson analysis of the omics data with MMSE (mini-mental state examination), Aβ1-42/Aβ1-40 (β-amyloid), and rGSK-3β(T/S9) (total to Serine-9-phosphorylated glycogen synthase kinase-3β) revealed that mitophagy/autophagy-, insulin signaling-, and glycolysis/gluconeogenesis pathways-related proteins were most significantly involved. Among them, only the increase of optineurin, an autophagy-related protein, was simultaneously correlated with the reduced MMSE score, and the increased Aβ1-42/Aβ1-40 and rGSK-3β(T/S9), and the optineurin alone could discriminate T2DM-MCI from T2DM-nMCI. A combination of the elevated platelet optineurin and rGSK-3β(T/S9) enhanced the MCI-discriminating efficiency with AUC of 0.927, specificity of 86.7%, a sensitivity of 85.3%, an accuracy of 0.859, which is promising for predicting cognitive decline in T2DM patients. [1)].

Mantini et al. performed an integrative omics study investigating the biological processes of mRNAs and expressed MicroRNAs, as well as proteins in PDAC blood platelets, using benign disease as a reference for inflammatory noise. Gene ontology mining revealed enrichment of RNA splicing, mRNA processing, and translation initiation in MicroRNAs and proteins but depletion in RNA transcripts. Remarkably, correlation analyses revealed negative regulation of SPARC transcription by isomiRs involved in cancer signaling, suggesting a specific “education” in PDAC platelets. Platelets of benign patients were enriched for non-templated additions of G nucleotides (#ntaG) MicroRNAs, while PDAC presented length variation on 3' (lv3p) as the most frequent modification on MicroRNAs. Additionally, we provided an actionable repertoire of PDAC and benign platelet-ome to be exploited for future studies. In conclusion, our data show that platelets change their biological repertoire in patients with PDAC, through dysregulation of MicroRNAs and splicing factors, supporting the presence of de novo protein machinery that can “educate” the platelet. These novel findings could be further exploited for innovative liquid biopsies platforms as well as possible therapeutic targets. [2)].

As populations age, the number of patients sustaining traumatic brain injury (TBI) and concomitantly receiving preinjury antiplatelet therapy such as aspirin (ASA) and clopidogrel (CLOP) is rising. These drugs have been linked with unfavorable clinical outcomes following TBI, where the exact mechanism(s) involved are still unknown. In this novel work, we aimed to identify and compare the altered proteome profile imposed by ASA and CLOP when administered alone or in combination, prior to experimental TBI. Furthermore, we assessed differential glycosylation PTM patterns following an experimental controlled cortical impact model of TBI, ASA, CLOP, and ASA + CLOP. Ipsilateral cortical brain tissues were harvested 48 h postinjury and were analyzed using an advanced neuroproteomics LC-MS/MS platform to assess proteomic and glycoproteins alterations. Of interest, differential proteins pertaining to each group (22 in TBI, 41 in TBI + ASA, 44 in TBI + CLOP, and 34 in TBI + ASA + CLOP) were revealed. Advanced bioinformatics/systems biology and clustering analyses were performed to evaluate biological networks and protein interaction maps illustrating molecular pathways involved in the experimental conditions. Results have indicated that proteins involved in neuroprotective cellular

pathways were upregulated in the ASA and CLOP groups when given separately. However, ASA + CLOP administration revealed enrichment in biological pathways relevant to inflammation and proinjury mechanisms. Moreover, results showed differential upregulation of glycoproteins levels in the sialylated N-glycans PTMs that can be implicated in pathological changes. Omics data obtained have provided molecular insights of the underlying mechanisms that can be translated into clinical bedside settings [3)].

1)
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