PROTEINS INVOLVED IN PLATELET ACTIVATION BY GPVI AND ALPHAIIBBETA3 RECEPTORS ARE DIFFERENTIALLY REGULATED IN ACUTE CORONARY SYNDROME: A PLATELET PROTEOMICS STUDY

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Platelets play a fundamental role in pathological events underlying acute coronary syndrome (ACS). We present an analysis of the platelet proteome of ACS patients compared to matched chronic controls. The objective was to identify differentially regulated proteins that could provide novel information on the molecular mechanisms associated with the onset of the acute episode.

In a first study, we compared the platelet proteome of 18 patients with non-ST segment elevation (NSTE)-ACS versus a control group consisting of 10 matched stable coronary artery disease (SCAD) patients. In a second study, platelets from a group of 11 patients with ST-segment elevation (STE)-ACS were compared with a matched control group of 15 SCAD patients. In both cases, samples were obtained at three time points: on admission to hospital, after 5 days and after 6 months. Proteins were separated by high-resolution-2-DE and identified by MALDI-TOF/TOF. Validations were carried out by 1D and 2-DE western blotting. Interactions among all proteins identified were investigated with the Ingenuity Pathways Analysis software.

Fluorescent staining with Sypro Ruby allowed the detection of over 2,300 spots per gel. After comparative analysis between ACS and SCAD controls, we found 40 differentially regulated protein features in the case of NSTE-ACS, and 56 in the case of STE-ACS patients. Significant differences decreased over time, supporting the idea of enhanced platelet activation during the acute event. Many of the differentially regulated proteins identified are involved in platelet activation by integrin αIIbβ3 and/or GPVI receptors (e.g. CrkL, GADS, ILK, SKAP-HOM, Src, talin-1). Most differences were due to post-translational modifications. Interestingly, the adapter protein CrkL was found to be up-regulated in STE-ACS patients compared to stable controls. In conclusion, the present study provides novel information on platelet proteome changes associated with platelet activation in ACS, highlighting the involvement of proteins implicated in αIIbβ3 and GPVI signalling.