ImmunoTools *special* Award 2014

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MOLECULAR CARACTERIZATION OF CIRCULATING MICROPARTICLES AFTER AN ACUTE ISCHEMIC STROKE

Atherothrombosis is the major cause of cardiovascular disease and the main cause of morbimortality in the world. Platelets, endothelial cells and leukocytes are key players in the pathogenesis of atherothrombotic processes. Platelet adhesion and aggregation at sites of atherosclerotic plaque rupture or vessel injury lead to the development of either mural or occlusive thrombus triggering acute coronary syndromes, peripheral cardiovascular disease and ischaemic cerebrovascular events. However, the contributing factors beyond the underlying triggering atherosclerotic plaque rupture are still not fully identified.

Microparticles (MP) are small phospholipid microvesicles of 0.1 to 1 µm diameter, shed by activated endothelial or blood cells and defined by both size and expression of cell-specific antigens on their surface. Although the existence of shed membrane MP has been known from many years, recent studies have shed light on the pivotal role of these MP on several aspects of vascular biology such as thrombosis, inflammation or angiogenesis. Although present in plasma of healthy individuals, elevated numbers of specific subset of MPs have been reported in vascular disorders. Circulating MPs may originate from cells that are involved in the pathogenesis of atherothrombotic diseases, and that contain phosphatidylserine and distinct surface proteins depending on their parental cells. MPs can originate from platelets, endothelial cells, leukocytes, erythrocytes and smooth muscle cells, and are found in circulating blood at relative concentrations determined by the pathophysiological context. It is well known that they have strong procoagulant properties due to exposure of procoagulant anionic phospholipids as phosphatidylserine (PS) in a similar fashion as activated platelets and provide a catalytic surface that may promote coagulation since PS facilitates the binding of the coagulation factors and the assembly of the coagulation complexes, accelerating

the formation of thrombin. Besides, cMPs may also be bioactive molecular carriers that can activate other cells and contribute to inflammatory processes, triggering atherosclerotic progression. Indeed, it has been recently shown that circulating and platelet-derived microparticles enhance thrombosis on atherosclerotic plaques.

Whether individual circulating MP phenotypes, defined by parental cells biomarkers and cytokines and adhesion molecules expression, may be markers of clinical atherosclerotic lesion types remains unknown. In addition, whether the proinflammatory state defined by MP expression of cell activation molecules and MP shedding is associated with the appearance of cerebrovascular events remains unclear. Therefore, the aim of our proposal is to compare the phenotype of circulating MP between healthy controls and patients with a suspected ischemic stroke in order to identify new molecular pathways in the process of activation of stroke formation and to determine the relevance of circulating MPs as biomarkers of cerebral ischemia.

These results could have high translational value, because due to the etiological heterogeneity of the ischemic syndrome and the difficulty, in many cases, to identify their cause with current criteria, the possibility of using biomarkers as current MPs, which may be a reflection of what happens at the local vascular level, could be of great help in determining the type of vascular event, resulting in a better understanding of the specific pathophysiology of cerebrovascular stroke and consequently reduce the recurrence of this pathology by specific secondary prevention strategies.

Therefore, obtaining the ImmunoTools Award would contribute greatly to the execution of this proposal, as it will provide the necessary reagents to characterize circulating MPs.

ImmunoTools *special* AWARD for

Gemma Chiva-Blanch includes 25 reagents

FITC - conjugated anti-human CD3, CD11a, CD14, CD29, CD33, CD41a, CD54, CD56, CD58, CD62P, CD63, CD69, CD235ab,

PE - conjugated anti-human CD9, CD11b, CD11c, CD15, CD34, CD42b, CD45, CD50, CD61, CD62L, CD105,

APC - conjugated Annexin V

DETAILS more AWARDS