

## Extracellular Vesicles and Cardiovascular Diseases

M. Camera<sup>1,2</sup>, M Brambilla<sup>2</sup>, P. Canzano<sup>2</sup>, L. Rossetti<sup>2</sup>, A. Parolari<sup>2</sup>, E. Tremoli<sup>1,2</sup>

<sup>1</sup>Dept. of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy

<sup>2</sup>Centro Cardiologico Monzino IRCCS, Milan, Italy

Within the past decade cell-derived microvesicles (MVs), which are heterogeneous in nature, varying in size and content (proteins, lipids and mRNA), have been recognized as important mediators of intercellular communications, being vectors of biological messages, and playing different roles on target cells depending on the cell of origin and the stimulus responsible for their generation. MVs are now appreciated as relevant players in different pathophysiological conditions, including cardiovascular disease (CVD). MVs are indeed increased in patients suffering from CVD, and different subtype profiles of circulating MVs between patients with stable disease and those with acute coronary syndrome or myocardial infarction have been reported. *Ex vivo* studies on human carotid endoarterectomy specimens have provided detailed information about the cellular origin, composition, inflammatory and thrombogenic activity of MVs present in the atherosclerotic plaque, supporting the rationale for MV involvement in atherosclerosis. Based on the accumulated data, circulating MVs have been also considered as biomarkers of vascular injury and inflammation in several CVD. Graft patency and completeness of revascularization are major determinants of long-term outcome following coronary artery bypass graft (CABG). Occlusion rates can be as high as 28% (per graft) or 45% (per patient) 12-18 months thereafter. The issue of identifying predictors of graft patency after CABG has been addressed by several studies, which mainly focused on the presence of conventional risk factors for atherosclerosis, genetic markers, features of coronary targets, or technical aspects concerning the handling of the conduits during harvest. We recently investigated whether the profile of circulating MVs (sampled before surgery) could predict graft patency comparing patients with patent and closed graft assessed with a 64-rows CT scan evaluation of graft patency 18-24 months after surgery. Multiparametric flow cytometry analysis of plasma MVs revealed that patients with occluded graft showed a significantly higher number of total and of procoagulant platelet-derived (Annexin V-, CD41-, CD62P-, Tissue Factor-positive) MVs in patients with occluded graft compared to those with patent graft. These promising results suggest the use of the molecular signature of MVs as informative biomarker of graft patency in CABG. Considering the complex role of MVs in vascular and cardiovascular diseases, this is an area of immense interest, that promises to yield important advances into diagnosis and therapy.