SHED MEMBRANE PARTICLES FROM T LYMPHOCYTES IMPAIR ENDOTHELIAL FUNCTION AND REGULATE ENDOTHELIAL PROTEIN EXPRESSION.

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Microparticles (MPs) are vesicles released from the plasma membrane of various cell types, such as platelets, T and B cells, monocytes, and endothelial cells during activation by agonists, shear stress or apoptosis. MPs bear surface cell proteins and cytoplasmic component of the original cell and exhibit negatively charged phospholipids, mainly phosphatidylserine at their surface conferring their procoagulant and proinflammatory properties.
Under pathological states, such as acute coronary syndrome, atherosclerosis, diabetes, or after cardiac surgery, elevated levels of MPs have been detected in blood from patients.
Because MPs usually accumulate in areas of disordered blood flow, the enhanced level of MPs may have pathological consequences. To date, little is know about the effects of MPs on function of cells forming the vessel wall.
The present study was designed in dissecting the effects evoked by T lymphocytes-derived MPs on vascular wall particularly, the endothelium known to play a crucial role in the regulation of vasomotricity. T lymphocytes-derived MPs, at concentrations that can be reached in circulating blood (i.e. 30 nmol/L phosphatidylserine), impair endothelium-dependent relaxation both in conductance, aorta, and resistance, small mesenteric, arteries of the mice. MPs treatment affect relaxation in response to both chemical stimuli (acetylcholine, Figure A) and physical stimuli (shear stress Figure B). MPs treatment reduce nitric oxide (NO)- and prostacyclin- but not endothelium derived hyperpolarizing factor (EDHF)-mediated dilatation. In endothelial cells from human umbilical vein and in mice aorta, the effect of MPs results in a decrease in expression of endothelial NO synthase, an overexpression of endothelial caveolin-1 but not in alteration of the increase calcium evoked either by thrombin or histamine. Reduced expression of cyclo-oxygenase 1 does not account for the impairment of prostacyclin component of endothelial response. These results provide evidence that MPs from T cells induce endothelial dysfunction both in conductance and resistance arteries. MPs regulate endothelial protein expression for endothelial NO synthase and caveolin-1. These data contribute to a better comprehension of the deleterious effects of enhanced circulating MPs observed in cardiovascular diseases.

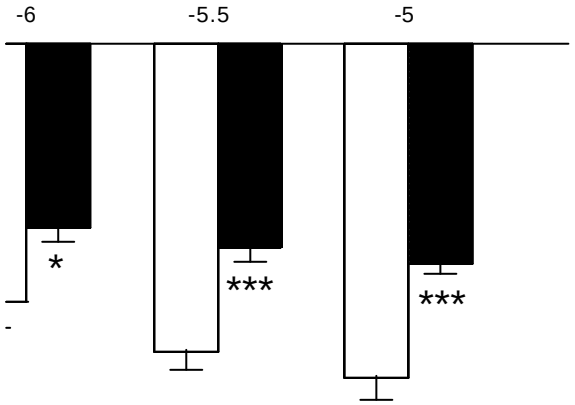

Figure A

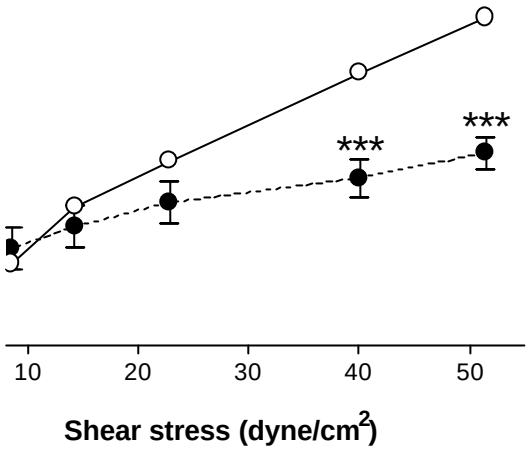

Figure B