107306

Plasma exosomes after PCI in non-diabetic STEMI patients fed barley beta-D-glucan-enriched pasta reduce oxidative stress-induced endothelial cell senescence

Valentina Casieri[a], Hakim Karim Chabane[a], Vincenzo Lionetti[a,b]

[a]*Unit of Translational Critical Care, Laboratory of Basic and Applied Medical Sciences, Interdisciplinary Center of Research "Health Science", Scuola Superiore Sant'Anna, Pisa, Italy*
[b]*UOSVD Anesthesia and Intensive Care, Fondazione Toscana G. Monasterio, Pisa, Italy*

Senescent endothelial cells delay endothelialization, which increases restenosis risk in acute coronary syndrome with ST segment elevation (STEMI) patients following primary percutaneous coronary intervention (PCI). Normocaloric diet supplemented with barley beta-D-glucan (BBG)-enriched pasta protects the heart, but it is not yet clear whether this is due to the ability of this dietary combination to release exosomes that prevent endothelial aging following PCI.

In non-diabetic anterior STEMI patients (mean age 57 years, 8 women) who underwent PCI, we isolated plasma exosomes (pEXOs) before (T0) and after 3 months (T1) of normocaloric diet supplemented with 100 g of pasta containing 3 g of BBG (STEMI-BBG, $n = 19$) or without supplementation (STEMI-C, $n = 18$). Nanoparticle tracking analysis (NTA) determined pEXOs size and levels. Senescence-associated β-galactosidase activity was used to identify senescent human umbilical vein endothelial cells (HUVECs) induced by hydrogen peroxide (H2O2; 100 μmol/L for 24 h). HUVECs were treated with pEXOs (10^7particles/mL) for 24 h without and with H2O2. Dihydroethidium staining was used to detect oxygen free radicals (ROS) in HUVECs.

Significantly increased levels of pEXOs were observed at T1 in the STEMI-BBG group, but not in the STEMI-C group. NTA revealed that large pEXOs contribute to this increase, but not the other exosomal subpopulations. T0 and T1 pEXOs isolated from all patients promoted premature endothelial senescence in the absence of ROS elevation. In contrast, T1 pEXOs isolated from STEMI-BBG patients significantly prevented worsening of endothelial senescence induced by exogenous H2O2 via reducing oxidative stress ($p < 0.05$), but not T1 pEXOs from STEMI-C group.

Our findings suggest that pEXOs derived from reperfused non-diabetic STEMI patients exert pro-senescent signaling on HUVECs. However, pEXOs isolated from reperfused STEMI patients consuming BBG-enriched pasta exhibit a unique ability to mitigate the endothelial senescence induced by H2O2. This differential impact could be attributed to distinct transcriptional landscapes associated with the respective microenvironments.

doi:10.1016/j.vph.2024.107306

107307

Dynamic co-culture of endothelial and smooth muscle cells as a platform for pathophysiological investigations of vascular calcifications

Elisa Ceccherini[a], Manuela Cabiati[a], Elisa Persiani[a], Ilaria Gisone[a], Letizia Guiducci[a], Maria Aurora Morales[a], Silvia Del Ry[a], Antonella Cecchettini[b], Federico Vozzi[a]

[a]*Institute of Clinical Physiology, National Research Council, 56124 Pisa, Italy*
[b]*Department of Clinical and Experimental Medicine, University of Pisa, 56126 Pisa, Italy*

Vascular calcification (VC) is a cardiovascular condition where calcium salt deposits occur within the vessel wall by vascular smooth muscle cells (VSMCs). In vitro models used for investigating vascular calcification typically involve VSMC monocultures under static conditions. However, given the significant role that endothelial cells (ECs) and VSMCs play in vascular function, both in physiological and pathological conditions, the aim of the current study was to create a dynamic co-culture of ECs and VSMCs that could better replicate the in vivo vascular microenvironment.

The presented work utilized a double-flow bioreactor to facilitate cellular interactions and emulate blood flow dynamics. To induce VSMC calcification, the cells were placed in a calcification medium composed of high glucose DMEM supplemented with 1.9 mM NaH_2PO_4/Na_2HPO_4 (1:1) for 7 days. The study assessed calcification, cell viability, inflammation, and molecular markers (SIRT-1, mTOR-1, TGFβ1, and Elastin IV). Results revealed that the dynamic model could replicate VSMC calcification and an inflammatory environment. Additionally, the regulation of effectors responsible for VSMC calcified phenotypic displayed an opposing trend to that seen in static monoculture, highlighting the significance of ECs-VSMCs communication in controlling cell behavior. Therefore, this model provided information that was not obtainable with standard cell monoculture, demonstrating its usefulness in exploring the pathophysiologic mechanisms behind vascular calcification because of its enhanced ability to imitate human vascular tissue.

doi:10.1016/j.vph.2024.107307

107308

The new role of Tryptophan 2,3- dioxygenase in modulating human endothelial cell and endothelial precursor functions

Marta Cecchi[a], Cecilia Anceschi[b], Angela Silvano[c], Anna Laurenzana[b], Astrid Parenti[c]

[a]*Department of Neuroscience, Psychology, Drug Research and Child Health, Neurofarba, University of Florence, 50139 Florence, Italy*
[b]*Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, 50139 Florence, Italy*
[c]*Department of Health Science, University of Florence, 50139 Florence, Italy*

Tryptophan-2,3-dioxygenase (TDO) and Indoleamine-2,3-dioxygenase (IDO1) are the main enzymes involved in tryptophan (Trp) catabolism to kynurenine (Kyn) via the kynurenine pathway (KP), which is known to have a role in the immune regulation. An increased plasma Kyn/Trp ratio has been found in numerous diseases, including cardiovascular diseases. Most Trp is catabolized by IDO1 and its activity has been associated with worse cardiovascular outcomes in patients with coronary artery disease. TDO is mainly expressed in the liver in physiological conditions and recently, TDO-expressing cells were identified as pericytes in numerous types of tumors and in inflammatory pulmonary lesions, suggesting its pro-angiogenic role. Since TDO and IDO1 involvement in angiogenesis is still unknown, we aimed to characterize their role in human umbilical venular endothelial cells (HUVECs) and in human endothelial colony-forming cell function (ECFCs). TDO and IDO1 expression was evaluated by real-time PCR and immunofluorescence. ELISA assay was performed to assess KP activity. Cell proliferation was evaluated by MTT test and in vitro angiogenesis was studied by Geltrex 3D capillary morphogenesis. TDO and IDO1 were expressed by both HUVECs and ECFCs. To