SCIENTIFIC REPORT

Project title: Impact of high glucose in valvular endothelial cells-monocyte crosstalk: molecular signatures and role in early valvular dysfunction
Acronym: VALDYSIGN
Phase 1: Characterization of the molecular profile induced by short-term exposure to diabetic conditions in the VEC-monocyte interaction (part I)
Implementation period: 01.04.2022-31.12.2022

Activity 1.1: Sequencing the entire transcriptome to identify molecules involved in the early changes induced in VEC-monocyte interactions under diabetic conditions.
Activity 1.2: Validation of key molecules through Real Time PCR.

SUMMARY OF PHASE 1: Aortic valve disease (AVD) and diabetes are progressive diseases that represent global health problems. Diabetes is a risk factor for AVD, predicts a faster disease progression, and accelerates AVD. The early mechanisms of aortic valve dysfunction are still unclear, but valvular endothelial cells (VEC) and monocytes (Mo) play key roles in this process. The mechanisms by which diabetes contributes to early valve dysfunction are not yet well known, so our hypothesis is that high glucose alters the normal interaction of valvular endothelial cells with monocytes, inducing progressive molecular changes, phenotypic changes, and functional alterations in both cell types. The aim of the VALDYSIGN project is to highlight the modified molecules in VEC and Mo in their communication under HG conditions, to evaluate the role of key molecules in cell dysfunction, and to propose new mechanisms of early valvular dysfunction in diabetes.
In the first phase of the VALDYSIGN project, the molecular profile induced by short-term exposure to high glucose in the VEC-Mo interaction was characterized by sequencing the entire transcriptome of both cell types. Differentially expressed genes (DEGs) in different experimental conditions were functionally analyzed by association with available KEGG maps in databases. In VEC interacting with Mo under conditions of high glucose, molecules involved in focal adhesions, tight junctions, adherens junctions, cellular adhesion molecules, matrix-receptor interactions, cytoskeleton regulation and endothelial transmigration were identified, suggesting changes in endothelial permeability and cellular cytoskeleton changes. In addition, molecules involved in matrix-receptor interactions, transendothelial migration, cellular adhesion molecules, and signaling pathways TLR, NF-kB, JAK-STAT, TNFα and chemokines, suggesting increased monocytic adhesion and transmigration to the endothelium and an inflammatory phenotype, were identified in Mo interacting with VEC under high glucose conditions. These data suggest that early exposure to high glucose induces progressive molecular and phenotypic changes in both cell types, contributing to valvular dysfunction in diabetes.

DISSEMINATION: Participation at the XXXIX Annual Scientific Session of the Romanian Society of Cell Biology, October 21-23, 2022, Cluj-Napoca, Romania – MOLECULAR SIGNATURES OF

VALVULAR ENDOTHELIAL CELLS AND MONOCYTES CROSS-TALK IN EARLY DIABETIC CONDITIONS.
Monica Tucureanu, Letitia Ciortan, Ileana Manduteanu – poster.