Subtle transcriptomic signals in circulation after myocardial infarction might indicate the ventricular remodeling outcome

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Introduction

Prolonged duration of left ventricular remodeling (LVR) after myocardial infarction (MI) leads to progressive alteration in the structure, shape, size and function of the heart representing maladaptive LVR (MLVR) that precedes development of heart failure which is life threatening.

The aim of this study was to bioinformatically investigate the mechanisms that potentially protect from MLVR by analyzing transcriptome in MI patients with/without MLVR six months after the MI.

Methods

Sample: Peripheral blood mononuclear cells of 21 patients who suffered MI (12 without MLVR/9 with MLVR) were sampled 6 months after the insult.

MLVR was defined as progressive LV dilatation with LV diastolic volume increase (>20%) together with preserved or declined global LV ejection fraction at 6 months follow up.

Transcriptome was obtained by Illumina iScan microarray technology.

Gene Set Enrichment Analysis (GSEA) was used to detect concordant differences in a priori defined gene sets (Gene Ontology biological processes – GO:BP) between patients without MLVR and with MLVR. We adopted default GSEA settings and the significance of an enrichment score was evaluated by a 1000 permutation test with respect to phenotypes.

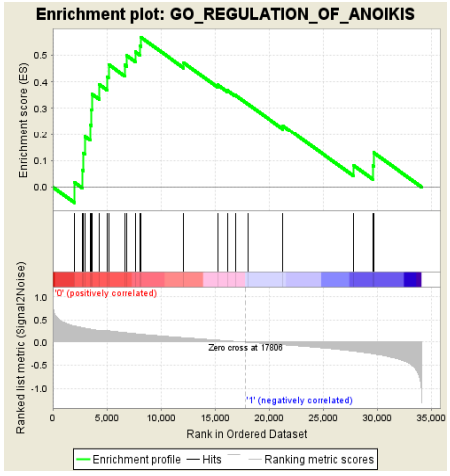

Fig 1. Top enriched process in phenotype without MLVR **(ES = 0.57, NES = 1.83, GSEA nominal p-value < 0.001)**

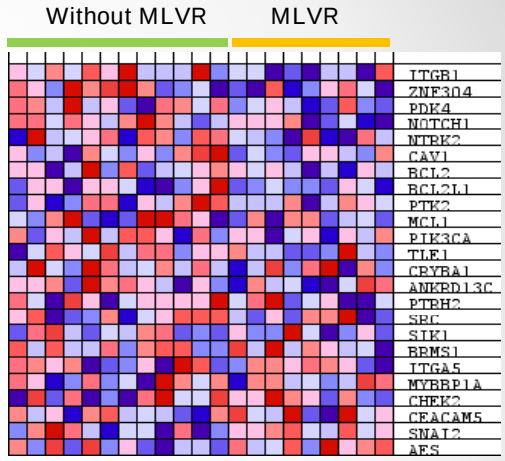

Fig 2. Leading edge subset of core genes that accounts for the gene set's enrichment score

Conclusions

Top regulated *ITGB1* gene is one of the major integrins that are responsible for cell-cell and cell-matrix interactions that acts in both cellular adhesion and signaling. Anoikis programmed cell death is induced by the loss of cell–matrix interactions, so *ITGB1* gene upregulation in patients without MLVR indicate that negative regulation of anoikis might be protective against MLVR.

Possibility to identify subtle transcriptomic signals in circulation makes this approach applicable in the research of new therapeutics for the protection of post MI heart failure development induced by MLVR.

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