Cardiomyocytes derived small extracellular vesicles plays an important role in heart development

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Introduction: Neonatal rats have the capacity to regenerate their hearts in response to injury, but this potential is lost after the first week of life. Cardiac maturation lays the foundation for postnatal heart development and disease, yet little is known about the contributions of the microenvironment to cardiomyocyte maturation. Extracellular vesicles (EV) are bilayer-membrane nanoparticles released by all cell types, carrying proteins, lipids, and nucleic acids, which reflect the activation state of parental cells. Secreted small extracellular vesicles (sEV), prominently figure among extracellular signals that regulate cell function.

Purpose: We aim to determine whether cardiomyocyte (CM) derived sEV carried miRNA that has a role in heart development with specific regards to cardiomyocyte maturation.

Methods: sEV were isolated from rat cardiomyocyte at day 0 and 7 after birth by serial ultracentrifugation. sEV were characterized by NTA and analyzed by Western blot for the presence of classical EV markers (TSG101, Syntenin-1). The role of sEV in cardiomyocyte proliferation was assessed by analysis of EdU incorporation on neoantal rat CM treated with sEV_p0 or sEV_p7. miRNA content on sEV was assessed using a rat-miRNome MicroRNA Profiling Kit and the identified miRNA’s targets confirmed by RealTime-PCR and Western Blot.

Results: NTA and Western Blot analysis confirmed the presence of sEV in both the extracellular vesicles preparation. sEV_p0 showed to be able to slighty increase EdU incorporation in treated cardiomyocyte (1.15-Fold) while sEV_p7 significantly inhibit CM proliferation (0.78-Fold) toghether with a change in cardiomyocyte citoscheletal architecture. Data from miRNome analysis showed in sEV_p7 a significan increase in miRNA with cyclines as tagets. Downregulation of Cdk1, Cdk4, Cdk2; CcnB1 and CcnD1 was confirmed on CM trated with sEV_p7 compared to Ctrl. Down-regulation of CCND1 was aslo confrmed at the protein level by Western Blot analysis.

Conclusions: These preliminary resultes showed an important role in heart developpment of cardiomyocyte derived-sEV. A deeper investigation of the pathaway activated by sEV may have a potential interest for the identification of possible regulators for stimulating heart regeneration.