CARBON NANOTUBES INSTRUCT PHYSIOLOGICAL GROWTH AND FUNCTIONALLY MATURE SYNCYTIA: NON-GENETIC ENGINEERING OF CARDIAC MYOCYTES

Oral Contributions
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Authors: Luisa Mestroni, Valentina Martinelli, Giada Cellot, Francesca M. Toma, Carlin Long, John Caldwell, Lorena Zentilin, Mauro Giacca, Antonio Turco, Maurizio Prato, Laura Ballerini, University of Colorado, Aurora, CO, USA, University of Trieste, Trieste, Italy

Rationale: Myocardial tissue engineering currently represents one of the most appealing strategies for cardiac repair. We have recently discovered the ability of carbon nanotube scaffolds to promote cell division and maturation in neonatal rat ventricular myocytes (NRVM). However, a mechanistic understanding of these changes is still needed.

Objective: We tested the hypothesis that carbon nanotube scaffolds promote cardiomyocyte growth and maturation by altering the gene expression program, implementing the cell electrophysiological properties and improving function and maturation of functional syncytia.

Methods and Results: We combined microscopy, biological and electrophysiological methodologies, and calcium imaging, to verify whether NRVM cultured on substrates of multi-wall carbon nanotubes (MWCNT) acquire a physiologically more mature phenotype compared to control (gelatin). The MWCNT substrate stimulated the induction of a gene expression profile characteristic of terminal differentiation and physiological growth, with a 2-fold increase of α-myosin heavy chain (P<0.001) and upregulation of sarcoplasmic reticulum Ca2+ ATPase 2a (SERCA2a). In contrast, markers of pathological hypertrophy remained unchanged (β-myosin heavy chain, skeletal α-actin, ANP). These modifications were paralleled by an increase of connexin-43 gene expression, gap junctions and functional syncytia, and protection against the toxic effect of phenylephrine. Finally, NRVMs on MWCNTs demonstrated a more mature electrophysiological phenotype of syncytia and intracellular calcium signaling.

Conclusions: Our study demonstrates that carbon nanotubes interacting with cardiac myocytes have the ability to promote physiological growth and functional maturation. These properties are unique in the current vexing field of tissue engineering, and offer unprecedented perspectives in the development of innovative therapies for cardiac repair.