
**Stimulation of muscle regeneration by extracellular vesicles**

F. Magarotto[1], M. Grassi[1,2], A. Sgrò[2], M. Saggioro[1,2], M. Andretta[2], E Maghin[1,2], M Piccoli[3], M Jurga[4], G Perilongo[2], P Gamba[2], M Muraca[2] M Pozzobon[1,2]
Presenting Author: Michela Pozzobon, michela.pozzobon@unipd.it
[1]Stem Cells and Regenerative Medicine Lab, Institute of Pediatric Research Città della Speranza, Padova, Italy [2]Dept of Women and Children Health, University of Padova, Italy [3]Biomedical Sciences Dept, University of Padova,[4]The Cell Factory BVBA (Esperite NV), Italy

**INTRODUCTION:** The need of new biomaterials to replenish the loss of muscle mass is currently a challenge. While the implant of extracellular matrix (ECM) from decellularized tissues provide the best biocompatible scaffold, on the other hand ECM alone produce limited muscle recovery. We are now aware that several intercellular signals mediating tissue renewal, vascularization and immune regulation, are convoyed via extracellular vesicles (EVs), biologically active microparticles composed of a lipid bilayer produced by cells. The aim of this work is to analyze the muscle regeneration in a murine model of volume muscle loss after implant of ECM engineered with EVs.

**METHODS:** ECM samples were obtained using a detergent-enzymatic protocol and were embedded with EVs isolated from Wharton Jelly mesenchymal stromal cells (EV-MSC) and BJ fibroblast cell line (EV-BJ). EVs were obtained through ultrafiltration, characterized by citofluorimetric analysis, and quantified with MTA and qNano instruments. ECM-EVs were transplanted in mice after tibialis anterior damage (ECM-PBS and ECM alone were used as control). 72 hours post implant, EVs local injection was performed. After 7, 15 and 30 days, samples were analysed by histology, immunofluorescence and qPCR.

**RESULTS & DISCUSSION:** The macrophagic response in mice EV-MSC treated was clearly directed toward tissue rebuilding as confirmed by qPCR results on M2 and myogenic markers. 30 days post implant the fibrosis (collagen quantification) was significantly reduced in the same group of mice. vW+ cells -indicating neo-angiogenesis- and new born centrally nucleated fibers (CNFS) where present in a statistically higher percentage (***=$p<0.005$;****=$p<0.0001$.) again in EV-MSC treated mice in respect to the other experimental groups.

**CONCLUSIONS:** These preliminary results underlined the pro regenerative action of EV-MSC in a chronic model of volume muscle loss.

**ACKNOWLEDGEMENTS:** Financial support was received from University of Padova grant number BIRD 2016.

**REFERENCES**

[1] Sicari M et al. Sci Trans Med. 2014; 6, 234ra58
[2] Piccoli M et al et al. Methods Mol Biol. 2018; 1577:87-93
[3] Tkach M et al. Cell. 2016; 164(6):1226-1232