Transplantation of microencapsulated Sertoli cells in a mouse model of Duchenne muscular dystrophy (DMD) reduces inflammation and rescues muscle performance

Sara Chiappalupi^{1*}, Guglielmo Sorci^{1*}, <u>Giovanni Luca</u>^{1*}, Francesca Mancuso¹, Mario Calvitti¹, Luca Madaro³, Carmine Nicoletti³, Iva Arato¹, Giulia Falabella¹, Riccardo Calafiore^{2§} and Rosario Donato^{1§}

¹Department of Experimental Medicine & Biochemical Sciences, University of Perugia, Perugia, Italy

² Department of Internal Medicine, University of Perugia, Perugia, Italy

³ Unit of Histology and IIM, DAHFMO, Sapienza University, Rome, Italy

*These Authors contributed equally to this work

[§]Share senior authorship to this paper

Duchenne muscular dystrophy (DMD), a progressive muscle degenerative disease associated with chronic inflammation, necrosis and fibrosis, is currently treated with antiinflammatory steroids, despite their limited efficacy and undesired side effects. Testicular Sertoli cells (SCs) have been successfully implanted to treat many experimental diseases due to their ability to secrete trophic, antiinflammatory and immunomodulatory molecules (Mital et al., 2010). We transplanted microencapsulated SCs, within highly biocompatible microcapsules (Luca et al., 2007) into the peritoneal cavity of *mdx* mice, an animal model of DMD. Three weeks after transplantation, skeletal muscles from SC-treated mice, compared with muscles from mock-treated mice, showed: i) dramatically reduced number of infiltrated cells, including (MAC3+) macrophages; ii) a marked decrease in necrotic myofibers, and an increased number of regenerated (normally sized and centrally nucleated) myofibers; and, iii) a significant decrease in fibrous tissue infiltration. Moreover, SC-treated, but not mock-treated *mdx* mice showed recovery of muscle performance in treadmill endurance tests and a comparable resistance to exercise-induced muscle damage to that of untreated wildtype mice. These preliminary results suggest that our transplant product creates a suitable microenvironment for muscle regeneration and growth potentially applicable to DMD patients.

References

Mital et al. (2010) Immunoprotective Sertoli cells: making allogeneic and xenogeneic transplantation feasible. Reproduction 139: 495-504.

Luca et al. (2007) Encapsulation, in vitro characterization, and in vivo biocompatibility of Sertoli cells in alginate-based microcapsules. Tissue Eng 13: 641-648.

Keywords: Sertoli cells, Duchenne muscular dystrophy, transplantation, inflammation.