BIOGRAPHICAL SKETCH

Cesare Gargioli

A. Personal Statement

Associate Professor at Department of Biology, Rome University Tor Vergata. He published 80 publications in peer reviewed journal (35 as first or last/corresponding author) among which several in high impact journal likewise Nature Medicine, EMBO Mol Med and Biomaterials. Total H index 28. He directs the laboratory of Comparative Anatomy and Tissue Engineering focusing on tissue regeneration and skeletal muscle reconstruction employing biomimetic matrices and 3D printing novel technology. His research has been financed by MIUR (PRIN Program) and Italian Defense Ministry (PNRM).

B. Positions, Scientific Appointments and Honors

Education, training and academic career

2000: Degree in Biological Sciences (summa cum laude), University of Rome Tor Vergata, IT.
2000-01: Research Assistant, Department of Biochemistry, IRBM (P. Angeletti), IT.
2001-04: PhD student in Developmental Biology, Centre of Regenerative Medicine, University of Bath, UK.
2004-05: Post-doctoral fellow Institute of Cell Biology and Tissue Engineering, S. Raffaele Biomedical Park Foundation, Rome, IT.
2005-09: Senior Research Associate, Institute of Cell Biology and Tissue Engineering, S. Raffaele Biomedical Park Foundation, Rome, IT.
2010-12: Assistant Professor, Department of Biology, Rome University Tor Vergata, IT.
2012-14: Researcher, IRCCS Multimedica, Milan, IT.
2014-19: Fixed Term Researcher, Department of Biology, Rome University Tor Vergata, IT.
2019-22 Tenure track Researcher, Department of Biology, Rome University Tor Vergata, IT.
2022- present: Associate Professor, Department of Biology, Rome University Tor Vergata, IT.

C. Contributions to Science

His research interests during his professional life have been fascinated by regenerative phenomena. Muscle satellite cells were originally described in amphibians, but just as bystander cells without regenerative potential; in fact, amphibians muscle regeneration was ascribed to budding myoblasts (reentering cell cycle) from undamaged myofibers. During his PhD training (in the Prof. Slack laboratory) by exploiting a transgenic *X. laevis* model, he revealed the ability of resident stem cells (muscle satellite cells) to regenerate tail muscles, getting the basis for muscle satellite cells dependent myofiber regeneration in amphibians and thus demonstrating previously unappreciated analogy between amphibian and mammalian muscle regeneration (Gargioli and Slack, 2004). During his PostDoc research period, his interest has been attracted by muscle modifications in a dystrophic mouse model (alpha Sarcoglycan KO) at advanced stages of the disease (12 months old). So, he used tendon fibroblasts, engineered to produce angiogenic factors (Placental derived Growth Factor, PlGF and metalloproteases (MMP9) to rescue old dystrophic muscle, succeeding in ameliorating muscle environment, reducing sclerosis and restoring microcirculation. These modifications allowed efficient cell therapy in old dystrophic mice, thus opening the possibility to extend new therapies to currently untreatable patients (Gargioli et al., 2008). More recently being part of Angioscaff FP7 large scale European Project scheme, he focused the attention on skeletal muscle tissue engineering in order to promote muscle regeneration and engineered artificial muscle construction exploiting biomaterial technology. Thus, using vessel associated muscle progenitor cells, so called mesonagioblast (Mabs,

in combination with biomimetic matrix (PEG-Fibrinogen PF, he investigated artificial muscle construction carrying out tissue engineering approaches:

1) *in vivo* experiments conducted in a muscle injury mouse model (cardiotoxin crushed) using PF as carrier for Mabs injection demonstrated increasing of transplanted cell survival, an ameliorated cell engraftment into injected muscles and overall PF showed a remarkable influence to improve integration and fusion of injected cells with host muscle forming hybrid regenerating and mature fibers (Fuoco et al., 2012);

2) Further above cited results he poured one's energies into skeletal muscle reconstruction, thus employing the same technology he was able to reconstruct a normal, complete and functional TA after massive ablation (90% of muscle dislodged) (Fuoco et al., 2015).

Recently, increasingly the attention about tissue engineering, he began to investigate new myogenic stem cell populations and new technologies in order to enhance architectural and cellular complexity of artificial tissue. Thus, in collaboration with Prof. Madeddu at Bristol University he settled the isolation and characterization of perivascular myogenic precursor, namely pericytes, showing amazing capabilities in terms of proliferation and over all muscle differentiation. Furthermore, revealing a considerable role in supporting endothelial cells during angiogenesis (Fuoco et al., 2014; Vono et al., 2016). Besides collaborating with Dr. Costantini group at Institute of Physical Chemistry, Polish Academy of Science at Warsaw, he started to explore the possibility to exploit new technologies to ameliorate tendon tissue engineering (Testa et al.,2017) and skeletal muscle tissue engineering employing 3D printing techniques (Costantini et al., 2017).

Key publications

1. Gargioli C. and Slack J.M.W. **Cell lineage tracing during *Xenopus* tail regeneration.** Development 2004 Jun; 131 (11): 2669-79

2. Gargioli C, Coletta M, De Grandis F, Cannata SM, and Cossu G. **PlGF-MMP9 expressing cells restore microcirculation and efficacy of cell therapy in old dystrophic muscle.** Nat Med. 2008 Sep 14(9):97

3. Fuoco C, Biondo A, Salvatori ML, Shapira-Schweitzer K, Santoleri S, Bernardini S, Cannata S, Seliktar D, Cossu G and Gargioli C. **Injectable PEG-fibrinogen improves survival and differentiation of transplanted myogenic progenitors in acute and chronic skeletal muscle degeneration.** Skelet Muscle 2012; 26;2(1):24.

4. Fuoco C, Sangalli E, Vono R, Testa S, Sacchetti B, Bernardini S, Madeddu P, Cesareni G, Seliktar D, Rizzi R, Bearzi C, Cannata S M, Spinetti G and Gargioli C. **3D hydrogel environment rejuvenates aged pericytes for skeletal muscle tissue engineering.** Front Physiol. 2014 May 30;5:203.

5. Fuoco C, Biondo A, Longa E, Mascaro A, Shapira-Schweitzer K, Salvatori M L, Santoleri S, Testa S, Bernardini S, Cannata S M, Bottinelli R, Seliktar D, Cossu G and Gargioli C. ***In vivo* generation of an entire, functional skeletal muscle.** EMBO Mol Med. 2015 Feb 25. pii: e201404062

6. Vono R, Fuoco C, Testa S, Pirrò S, Maselli D, Mc Collough DF, Sangalli E, Pintus G, Giordo R, Finzi G, Sessa F, Cardani R, Gotti A, Losa S, Cesareni G, Rizzi R, Bearzi C, Cannata S, Spinetti G, Gargioli C, Madeddu P. **Activation of the Pro-Oxidant PKCβII-p66Shc Signaling Pathway Contributes to Pericyte Dysfunction in Skeletal Muscles of Diabetic Patients with Critical Limb Ischemia.** Diabetes. 2016 Sep 6. pii: db160248.

7. Testa S, Costantini M, Bernardini S, Trombetta M, Seliktar D, Cannata S, Rainer A and Gargioli C. **Combination of biochemical and mechanical cues for tendon tissue engineering.** J Cell Mol Med. 2017 May 4.

8. Costantini M, Testa S, Mozetic P, Barbetta A, Fornaretti E, Tamiro F, Jaroszewicz J, Święszkowski W, Trombetta M, Seliktar D, Garstecki P, Cesareni G, Cannata S, Rainer A and Gargioli C. **Microfluidically enhanced 3D bioprinting of highly aligned hydrogel structures for *in vitro* and *in vivo* fabrication of artificial muscle tissue.** Biomaterials. 2017 Jul;131:98-110.

9. Errico V, Arrabito G, Fornetti E, Fuoco C, Testa S, Saggio G, Rufini S, Cannata S, Desideri A, Falconi C, Gargioli C. **High-Density ZnO Nanowires as a Reversible Myogenic-Differentiation Switch.** ACS Appl Mater Interfaces. 2018 Apr 25;10(16):14097-14107.

10. Testa S, Riera CS, Fornetti E, Riccio F, Fuoco C, Bernardini S, Baldi J, Costantini M, Foddai ML, Cannata S, Gargioli C. **Skeletal Muscle-Derived Human Mesenchymal Stem Cells: Influence of Different Culture Conditions on Proliferative and Myogenic Capabilities.** Front Physiol. 2020 Sep 16;11:553198.

11. Costantini M, Testa S, Fornetti E, Fuoco C, Sanchez Riera C, Nie M, Bernardini S, Rainer A, Baldi J, Zoccali C, Biagini R, Castagnoli L, Vitiello L, Blaauw B, Seliktar D, Święszkowski W, Garstecki P, Takeuchi S, Cesareni G, Cannata S, Gargioli C. **Biofabricating murine and human myo-substitutes for rapid volumetric muscle loss restoration.** EMBO Mol Med. 2021 Feb 15:e12778.

12. Fornetti E, Testa S, De Paolis F, Fuoco C, Bernardini S, Pozo Devoto V, Stokin G B, Giannitelli S M, Rainer A, Bigot A, Zoccali C, Baldi J, Sandonà D, Rizzi R, Bearzi C, Forte G, Cannata S, Gargioli C. **Dystrophic Muscle Affects Motoneuron Axon Outgrowth and NMJ Assembly.** Advanced Materials Technologies, 2022, 7(7), 2101216.