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Federica Di Scipio

PhD Supervisor: Prof. Dr. Giovanni Nicolao Berta

Department of Clinical and Biological Sciences,
Hospital San Luigi Gonzaga, Regione Gonzole 10,
10043 Orbassano (Turin)

DENTAL PULP AS A SOURCE OF MULTIPOTENT MESENCHYMAL STEM CELLS CHARACTERIZED BY UNCOMMON BEHAVIOR AND PROPERTIES EXPLOITABLE IN REGENERATIVE MEDICINE

Cell therapy is based on the concept that stem cells (SCs) can proliferate and differentiate into specialized cells in order to replace the dead ones and to allow the functional recovery of damaged tissues or organs. Among SCs, adult mesenchymal stem cells (MSCs) are a promising source of cells for regenerative medicine due to their self-renewal capability and multilineage mesenchymal differentiation potential: they are able to differentiate into at least three cell lineages (osteogenic, chondrogenic, adipogenic) and also into other ones when grown in defined microenvironment. Bone marrow represents the primary, historical, classical source of MSCs, but these cells are also present in many other tissues, including peripheral and cord blood, muscle, brain, adipose tissue, skin or gut. Because of MSCs extraction techniques from these anatomical sites require difficult and invasive maneuvers, the search for more accessible sources has propelled interest in dental tissues, such as dental pulp. The main fate of dental pulp mesenchymal stem cells (DP-MSCs) consists in their differentiation into dental cells, but they can differentiate into mesenchymal and non-mesenchymal lineages. In fact, during my PhD experience, we extracted and characterized DP-MSC lines (murine and human ones) and showed that they are able to both proliferate and differentiate *in vitro* into many histotype precursors (1,2). Moreover, since several studies reported a clinical benefit by MSCs injection after myocardial infarction and since we demonstrated that DP-MSCs are able to differentiate into cardiomyocytes when are in cocolture with neonatal cardiomyocytes, a part of my PhD project has been dedicated to assess the early homing behavior of DP-MSCs in an *ex vivo* infarcted heart model. While in normal hearts DP-MSCs remain in the site of injection forming round-shaped cell clusters, in infarcted ones they migrate very early towards the injured areas. In lesioned hearts, they start to elongate side by side with cardiomyocytes and gap junction CX43 is localized between resident cardiomyocytes and transplanted DP-MSCs, otherwise in the control ones CX43 is less expressed and mainly among DP-MSCs. Next step will be to understand the factors involved in DP-MSCs migration. In this context, the most important factors involved could be e.g. SCF, G-CSF, SDF-1α, FGF-1. Here, we would like to test a large array of different growth factors and cytokines to better comprehend

the migration phenomenon. ImmunoTools reagents might be an important option to complete our studies.

(1) Sprio AE, **Di Scipio** F, Raimondo S, Salamone P, Pagliari F, Pagliari S, Folino A, Forte G, Geuna S, Di Nardo P, Berta GN. *"Self-Renewal and Multipotency Coexist in a Long-Term Cultured Adult Rat Dental Pulp Stem Cell Line: An Exception to the Rule?"*. Stem Cells Dev. 2012 Jun 25. doi: 10.1089/scd.2012.0141.

(2) Testa G, Gamba P, **Di Scipio** F, Sprio AE, Salamone P, Gargiulo S, Sottero B, Biasi F, Berta GN, Poli G, Leonarduzzi G. *"Potentiation of amyloid-β peptide neurotoxicity in human dental-pulp neuron-like cells by the membrane lipid peroxidation product 4-hydroxynonenal"*. Free Radic Biol Med. 2012 Sep 3;53(9):1708-1717. doi: 10.1016/j.freeradbiomed.2012.08.581.