ImmunoTools *special* Award 2016

Debora Kehl, PhD-student

Supervisor: PD Dr. Dr. Benedikt Weber

Institute for Regenerative Medicine, University of Zurich,
Moussonstrasse 13, 8044 Zurich, Switzerland

Comparative analysis of the pro-angiogenic potential of therapeutically relevant human mesenchymal stem cell sources

Human mesenchymal stem cells (hMSCs) represent a promising autologous cell source in the field of regenerative medicine. In the field of cardiovascular diseases hMSCs have been used clinically and experimentally for the regeneration of ischemic myocardial tissue as well as diseased cardiac valves and have shown to open up novel strategies with high potential for future therapeutic applications. In spite of these promising initial investigations clearly demonstrating the therapeutic value of this type of stem cells, the underlying mechanisms of the therapeutic effect of hMSCs have not been fully elucidated yet.

Interestingly, recent investigations suggest that not the hMSCs themselves but their **secretome** (respectively their paracrine mediators) are responsible for the therapeutic effects *in vivo*. In the case of myocardial infarction the paracrine factors have been shown to induce angiogenesis and support the remodeling of ischemic sites towards functional myocardium. Also in vascular bioengineered constructs, pre-seeded and pre-conditioned hMSCs have been shown to attract host cells to the transplant site and support the *in situ* tissue formation via an inflammation-mediated cellular cascade.

Given the proof of the significant role of paracrine factors in healing, remodeling and angiogenesis, the use of the cellular secretome for future therapeutic applications would overcome current limitations associated with cell-based therapies. However, so far the ideal composition of the secretome is lacking, also the most beneficial cell source secreting the ideal composition and concentration of paracrine factors has not been elucidated yet. Therefore, the aim of the presented project is the establishment of a systematic comparative analysis of the secretome of different therapeutically relevant hMSC sources, including cells isolated from the adipose tissue, bone marrow and umbilical cord.

The endogenous (in situ) remodeling initiated by the secretome is mediated through an inflammation-mediated process of host immune and vascular cell attraction. In this

regard, ImmunoTools would allow the characterization of the initially attracted immune cells, in particular monocytes and macrophages. Furthermore the activation and attraction of vascular endothelial cells after co-incubation with hMSC secretome could be analyzed by specific ImmunoTools markers for endothelial cells and angiogenesis. Selected ImmunoTools cytokines will be used as a direct comparison to hMSC derived secretoma.

Taken together ImmunoTools will allow to further characterize the underlying cellular cascade following secretome application. In addition this systematic comparison will create knowledge on the most beneficial cell source to be used for regenerative therapies and will guide decision making in the case of patients where multiple cell sources are available. Ultimately this knowledge may be used to mimic the pro-angiogenic effects of hMSC in the future and to create “synthetic, chemically-defined cocktails” that could directly be injected for cardiovascular diseases.

ImmunoTools *special* AWARD for **Debora Kehl**

includes 20 reagents

FITC - conjugated anti-human CD14, CD31, CD86, HLA-DR

PE - conjugated anti-human CD3, CD11b, CD105

PerCP - conjugated anti-human CD14

APC - conjugated anti-human CD3, CD16, CD20, CD62P

Multicolour combinations anti-human:

CD4 FITC / CD8 PE / CD45 PerCP

recombinant human cytokines: rh FGF-b / FGF-2, rh IFN-gamma, rh IL-6, rh MCP-1 / CCL2, rh SDF-1α / CXCL12a, rh TNFα, rh VEGF-A/VEGF-165

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