THE INFLUENCE OF MICROENVIRONMENTAL CUES ON BONE MARROW MESENCHYMAL STROMAL CELLS

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Since the 1970s, Mesenchymal stromal cells (MSC) in the bone marrow are known as skeletal progenitor cells, later immunomodulatory properties have been suggested. Nevertheless, the translational success of MSC-based cell therapies and tissue engineering is limited. Among other reasons, this is related to a still incomplete understanding of the interactions of MSC with their environment.

We were interested to study interactions of MSC in the skeletal niche in steady state as well as during bone healing and regeneration. Human decellularized bone scaffolds were established as an in vitro model of the extracellular matrix environment in the skeletal niche. The early phase of bone healing was studied in an in vitro model utilizing platelet-rich plasma gel to mimic the platelet content in the fracture hematoma and in a murine segmental bone defect model in vivo. Functional characteristics of MSC, including lineage commitment, senescence and immunomodulatory properties have been studied in the different experimental setting.

Both in vitro models have been successfully established and validated. Results suggest that the natural bone extracellular matrix supports MSC attachment and viability. In vitro exposure of MSC to platelet-released factors induces immunomodulatory functions as indicated by increased gene expression of Ptgs2 and HIF-1α, pronounced inhibition of lymphocyte proliferation and induction of regulatory T cells. In line with this, MSC isolated from mouse bone and bone marrow from femoral bone defects showed declined clonogenicity along with immunomodulatory potential in vitro.

We here established tools to study the influence of various microenvironmental cues on MSC in vitro and in vivo. Results suggest that MSC behaviour is affected by the extracellular matrix environment as well as soluble factors released in the course of tissue healing. This indicates that the regenerative potential of MSC is critically influenced by their microenvironment and needs to be considered for therapeutic application of MSC.

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