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Dissertations-Kurzfassung

Adipogenic Differentiation Potential of Mesenchymal Stromal Cells from Cord Blood, Adipose Tissue and Bone Marrow

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MSC from bone marrow and adipose tissue in vitro undergo differentiation into mesodermal derivatives. CB-MSC behave differently, they fail to develop the mature adipocyte phenotype with perinuclear lipid droplets and inversion of the nuclear-cytoplasmic relation. This investigation follows specific protein markers and transcriptional factors during adipogenic induction of BM-, AT- and CB-derived MSC in order to identify a potential inhibitory pathway in CB-MSC.

Following adipogenic induction of BM-, AT- and CB-MSC, positive adipogenic phenotype and IF signals for perilipin, a specific lipid vacuole associated protein for mature adipocytes, were demonstrated in BM- and AT-MSC in contrast to CB-MSC. This was associated with increased RNA levels of perilipin, C/EBPα, PPARγ and adiponectin in BM- and AT-MSC. The expression level of this markers remained unchanged decreased in CB-MSCs. Pref-1, a transcriptional factor, associated with an undifferentiated state of preadipocytes, was downregulated in induced BM- and AT-MSC. In treated CB-MSC it remained elevated, supporting the notion that Pref-1 maintains CB-MSC in the proliferative state of undifferentiated cells. Inhibition of Pref-1 via si-RNA in CB-MSC did not result in a conversion of the undifferentiated state into mature adipocytes, consistent with missing upregulation of PPAR-γ and adiponectin mRNA in Pref-1 knocked down CB-MSC. The knocked down condition could however not be verified by Pref-1 protein expression analysis. Further protein analysis demonstrated that Pref-1 is present at high levels in CB plasma, underlining the specific function in CB-MSC. Finally in order to prove if further adipogenic stimulation is needed in order to achieve adipogenesis in CB-MSC, TZD were added to the cultivating media. Again this failed to induce adipogenesis.

This study suggests CB-MSC as a potent model to study modulatory pathways, with a focus on the inverse correlation between adipogenesis, osteogenesis and hematopoiesis, which are amongst others controlled by Pref-1 expression. Further there is a need to recognize the necessity to unify inducing protocols and culture conditions as they obviously influence MSC traits. Closer basic biological research on MSC will pave the way for optimized cell therapeutic applications.