rythropoietin (Epo) Regulate Hematopoietic/ hymal Stem Cells Which Participates in Bone tion and Niche Activities

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ly we showed that HSCs isolated from stressed animals (an ced) regulates osteoblast (OBs) differentiation from bone stromal cells (BMSCs). An activity suggests that HSCs regulate lopment of their niche. The molecular basis for this activity is uction of BMP-2 and BMP-6 by HSCs. Yet what stimulates produce BMPs is unknown. We hypothesized that the production opoietin (Epo) may activate HSCs to produce BMPs or activate directly to form OBs. To test these possibilities, the Epo serum the bled vs non-bleed mice were determined and found to e time frame of HSC activation. Surprisingly, EpoR expression tified on the SLAM-family isolated HSCs, and its expression l in bled animals. To directly determine if Epo stimulates bone *in vivo,* newborn mice were treated with rhEpo or PTH (as a control), or vehicle for 4 weeks. rhEpo increased the levels of it and hemoglobin in a dose dependant manner. rhEpo s enhanced OB numbers in long bone sections, and micro-CT ments of the vertebra revealed an significant increase of the nation parameters. These data for the first time demonstrated regulates the formation of the HSC niche by both direct and pathways, and further demonstrate a coupling between esis and osteopoiesis in the marrow. These results also suggest eting the Epo/EpoR pathway may serve as a therapeutic to treat skeletal or mesenchymal abnormalities in humans.

ged Mesenchymal Stem Cell Display a Lower dative Power and Actin Cytoskeleton Dynamic

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rmal stem cells (MSCs) have elicited great hopes for c augmentation of physiological regeneration processes, e.g. acture healing. MSCs are the cellular component of various therapies including tissue engineering approaches. However, on potential decreases with age, which raises questions about ncy of autologous approaches in elderly patients. In order to he mechanisms and cellular consequences of aging, molecular onal changes in MSCs derived from young and old Sprague- ts were studied. High resolution 2D electrophoresis of the eome identified several age-dependent proteins, including f the calponin protein family as well as galectin-3. Functional clustering revealed that age-affected molecular functions are with cytoskeleton organization and antioxidant capacity. tioxidant power was shown to be reduced in old cells. Also, s seem to contain fewer actin filaments and displayed a lower ver. Our findings indicate that aging of MSCs is consistent nt models of cellular aging that suggest pivotal roles of rtoskeletal dynamics and increased levels of reactive oxygen hese data, along with the observed similar differentiation imply that MSC-based therapeutic approaches for the elderly us on attracting the cells to the site of injury and oxidative ection, rather than merely stimulating differentiation.

927 Maintenance of Hepatocellular Functions *In Vitro* Coculture with Mesenchymal Stem Cells

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Liver transplantation is the gold standard treatment for end-stage liver failure and for numerous liver based inborn errors of metabolism. However, organ shortage remains a major limiting factor and alternative solutions are being examined in the liver therapy field. Liver cell transplantation has become the most promising alternative. Increasing interest is carried to stem cells regarding the recent demonstration of their plasticity. Theoretical advantages of mesenchymal stem cells for tissue regenerative medicine are multiple: ease of harvest, proliferation capacity, efficiency of in vitro transfection and potential use of autologous cells. To identify the differentiation plasticity of adult bone marrow mesenchymal stem cells (MSCs) into hepatocyte-like phenotypes, we used a co-culture model with hepatocytes. Furthermore, we investigated whether MSCs can protect the acutely injured hepatocytes, stimulate regeneration and restore the functions of hepatocytes. This data have evidenced that the guided hepatic differentiation of MSCs is proportionate to the activity of co-cultured hepatocytes. The hepatogenic environment is crucial to MSCs differentiation. It evidenced the trans-differentiation potential of MSCs developing to the hepatocytes and restoration of the functions of acutely injured hepatocytes. Further future therapeutic application in hepatic regeneration will be focused on the created imitated niches for MSC to maintain the survival and functions of hepatocytes.

929 Characterization of Sphere-forming Cells in Umbilical Cord Blood Derived Multipotent Stem Cells

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Multipotent stem cells (MSCs) are relatively free from ethical problem and concerns of teratoma formation than embryonic stem cells (ESCs) or induced pluripotent stem (iPS) cells. Moreover, several recent reports evidenced that MSC possesses pluripotency that refers differentiation capability to form virtually all tissues of a body potentiating MSCs in cell-based clinical strategies. However, populations of MSCs relatively heterogenous compared with ESCs. We hypothesized that relatively homogenous cells with more stemness can be separated from MSCs pool by sorting sphere-forming cells like cancer stem cells. RT-PCR analysis shows sphere-forming cells, and secondary sphere cells have higher levels of *OCT4*, *SOX2* expression compared with control cells while *ZNF281* and *C-MYC* expression was not changed in either of primary, secondary sphere cells. CPDL was conducted after transfer of sphere cells to plastic dish. Four times of subsequent subculture, CPDL rate was 28.83 and 26.28 for sphere cells and control, respectively. Not only proliferation but also differentiation ability was superior in sphere-derived cells to plated cells. Adipogenesis was almost 2.3 times higher as visualized by oil red O staining and expression levels of adipogenic markers such as *PPARγ*,*AP2* ,*CEBPβ* were predominant in sphere-derived cells compared with control cells. Sphere-derived cells also showed slightly high levels of *OSTEOCALCIN* and *RUNX2* in osteogenesis and *MAP2, TUJ-1, PAX6* in neuronal induction. In the aspect of molecular signal transduction, AKT, GSK3β phosphorylation was increased in sphere cells. These pathways are crucial for cell proliferation and protection from apoptosis. These results suggest that sphere culture is a novel method for isolating homogenous cells with higher stemness from heterogenous MSCs pool and sphere-forming cells might be more potent cells since they show high ability of proliferation and differentiation.