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Adult Stem Cells and Skeletal Repair and Regeneration

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Adult stem cells have generated great interest because of the potential they possess in regenerative medicine. The cells that have generated a great deal of attention are the stromal cells or mesenchymal stem cells (MSCs). These cells have been shown to exhibit potential to give rise to various cell lineages that include cartilage, bone, muscle and fat. Application of these cells in tissue engineering in scaffolding material to generated tissue engineered constructs for tissue replacement is currently an active area of investigation. Besides using the cells in engineered constructs, there is also an interest in use of the cells directly to repair and regenerated tissues or organs. Our research interest is focused on the use of these cells directly for bone repair and regeneration. An animal model of skeletal disease called osteogenesis imperfecta is used as amodel system to evaluate the potential of skeletal repair and regeneration when the stem cells are delivered via the circulatory system. Because the disease is genetic, stem cell application will require early intervention before manifestation of major skeletal abnormalities. To this end, our studies use bone marrow or adipose derived MSCs to test the hypothesis that MSCs delivered via circulatory system into developing mice will migrate, home to bone, differentiate into osteoblasts and deposit bone matrix. By using this approach we have been able to demonstrate that MSCs injected in developing mice will migrate and engraft in the bones of the developing mice. The number of cells that migrate to bone is however very small and may not be of clinical relevance. To overcome these obstacles, we have been focusing on devising means of generating cells that exhibit high potential for migrating to bone. One approach has been to precondition cells to bone microenvironment prior to cell delivery to the recipients. Using this approach we have been able to demonstrate that MSCs marked with GFP and pre-exposed to bone microenvironment by either direct injection into bone cavities with subsequent retrieval and expansion in vitro display predilection to migrate to bone when they are delivered systemically.

The strategy employed to deliver cells in developing mice is shown in **Fig. 1.** The cells are injected into the 2-day old mice via the superficial temporal vein. The cells migrate and engraft in the bones and differentiate into osteoblasts in vivo.

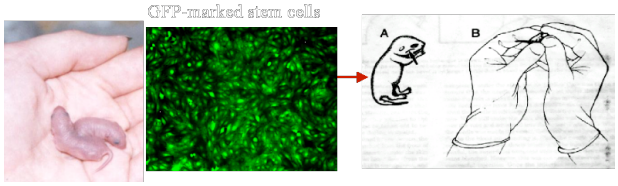

Figure 1 : The strategy employed to deliver cells in developing mice.

Because there are no specific markers available to identify adult stem cells, we are isolating single cells from bone marrow, expanding them in culture and testing their ability to migrate and engraft in the bones of the recipient animal models. Taken together, the data suggest that MSCs are transplantable and can be targeted to tissues of interest for possible repair and regeneration of specific tissues.

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