

Tissue Niches for Stem Cell Differentiation: A Functional Concept

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We have carried out a series of experiments determining the capacity of whole or purified murine bone marrow to engraft into non-treated mice. We first determined total murine cellularity and then assessed competitive engraftment in the setting of infusing different levels of murine marrow cells into untreated mice. These experiments revealed that final engraftment in the non-marrow ablated mice was determined simply by ratio of infused donor to host cells. The final conclusion was that while niches certainly exist and specialized locations of cells occur, they are not limiting for engraftment. In other studies in the non-ablated mice, we showed that infusion of male Lin⁻ Rhodamine^{lo} Hoechst^{lo} stem cells into female mice resulted in accumulation of male cells in the peri-endosteal region 6 weeks after infusion.

Studies carried out using PKH 26 labeled whole marrow or lin⁻ Sca⁺ cells *in vitro* in the presence of green fluorescent protein positive (GFP⁺) Dexter stromal cells has shown a number of intriguing interactions with regard to bone marrow and stromal cells. We have observed cells overnight at 10-minute intervals or at shorter intervals down to 1 minute. With the longer observations, we have seen marrow cells taken up by stromal protopodia, and travel down the stalk of the protopodia into the body of the stromal cell. We also have seen extrusion of intracellular marrow cells from the stromal cells. At the shorter time frames, we observed a phenomena of stem cell rolling along a proteopod, and, perhaps most intriguingly, the collision of stem cells with stromal cells with an apparently transient intracytoplasmic residence of the stem cell in the stromal cell. These types of interactions offer an abundant, potentially unique opportunity for facilitating epigenetic change of interacting stem cell/stromal cell populations.