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10th World Congress and Expo on Cell & Stem Cell Research _Vascular niche signals in organotypic stem cell regeneration_ Shahin Rafii_ Ansary Stem Cell Institute_ USA

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Stem cell self-renewal and fret deamination are implicated in niche-derived signals. However, the source of niche cells and the mechanism by which these signals regulate regeneration are not fully defined. Stem cells are undifferentiated or partially differentiated cells that can differentiate into different cell types and proliferate indefinitely to produce more of the same stem cell. They are the earliest type of cell during cell lineage. They are found in both embryonic and adult organisms, but they each require slightly different properties. Tissue-specific endothelial cells (ECs) by the production of angiocrine factors establish an instructive vascular niche that choreographs somatic cell homeostasis and organ regeneration. During developmental and regenerative processes, vascular niche cells oscillate the availability of (excitatory) / (inhibitory) angiocrine factors et al. There are yet unknown factors. These angiocrine signals coordinate self-renewal and differentiation of organetic stem cells, like hematopoietic stem cells (HSCs). To uncover the mechanisms by which these angiocrine signals regulate somatic cell rearrangements, we designed an in-vivo tissue-specific vascular niche platform for HSC expansion and vascular heart, epithelial, liver, and neural 3D For the manufacture of organoids. Employing this vascular niche model, we point out that ECs deploy signals that are essential for specification, self-renewal, and differentiation of human, mouse, and non-human primate HSCs. Co-culture of adult marrow-derived hematopoietic cells with ECS results in 25 to 50-fold clonal HSC self-renewal, with the potential for long-term, multi-lineage incubation in mice and non-human prime hosts. Vascular niche cells are also required for pluripotent-independent conversion of easily accessible adult ECs into readily accessible HSCs. To prove this point, we performed phase-wise conversion of these ECs into long-term immunocampscent HSCs with vascular niche-induction of human or mouse adult mature ECs with Runx1 / Spi1 / Gfi1 / FosB transcription factors. The clonal population of transformed HSCs expanded over the vascular niche in-vitro, and fully reorganized multi-lineal hematopoiesis in rodents. Co-infusion of ECs as well as HSCs enhanced hematopoietic recovery, underscoring the importance of vascular niche-signaling in vivo in somatic cell reconstitution. To translate the ability of the vascular niche to the therapeutic setting, we have engineered generic ECs capable of vascularizing epithelial, liver, neural, and cardiac 3D organoid cultures. Cross talk about ECs with tissue-specific stem cells promotes proper patterning and remodeling in those tissues to functional tissues. Using an in vivo regenerative model, we demonstrated that transplantation of ECS stimulates hematopoietic, liver and lung repair, without degenerative fibrosis. These approaches have allowed us to uncover molecular determinants of vascular asymmetry; Bringing us closer to translating the regenerative capacity of ECs for organ repair in the clinic. Tissue-specific vascular-stem cell organoid cultures have facilities for gene-editing and identification of unknown vascular niche signals by small molecule libraries that coordinate differentiation to stem cell self-renewal and functional organ repair. Stem cell treatment can reduce the symptoms of the disease or condition that is being treated. Decreasing symptoms may allow patients to reduce medication intake for the disease or condition. Stem cell therapies can also provide somatic cell understanding and knowledge for future treatments for society.

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