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The Importance of Niches-Dimensionality in Regulating the Bone Marrow Hematopoietic Stem Progenitor Cells Pool

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Abstract: Research in stem cell biology relies on the knowledge of the cell microenvironment *in vivo*, known as "stem cell niche", where stem cells are nurtured by the niche signals. Hematopoietic stem cells (HSCs) are capable of continuously generating and maintaining the body's full immune and hematopoietic systems. In adult, a pool of hematopoietic cells, including HSCs, primarily reside in the bone marrow (BM) niches that plays critical roles on cell fate. Niche supporting cells, cytokines, extracellular matrix proteins and other biochemical cues associated with HSCs behaviors (quiescence, self-renewal, proliferation, differentiation, mobilization, homing, and apoptosis) has been revealed in quantity. Recently the understanding of BM niche biophysical characteristics is expected to accelerate novel remarkable advance on not cell fate regulation *in vitro*-systems but, moreover, also on clinical applications. Here we presented that matrices stiffness and dimensionality are important biophysical signals regulating the growth of hematopoietic progenitor cells in the bone marrow stem cell pool. Mice bone marrow derived progenitor cells (BMPCs) were cultured within the 3-dimension(3D) collagen hydrogel matrices. We found stiffer hydrogel with higher collagen concentration promote the expansion of lineage negative (Lin^-) progenitor cells and $Lin^-Sca\text{-}1^+c\text{-}kit^+$ (LSK) HSCs compared to soft hydrogel. Moreover, 3D embedded construct were favorable to promote the expansion of Lin^- cells and LSK HSCs, compared with the cells cultured on the hydrogel top(2D). Gene expression analysis indicated the bright changes on HSCs behaviors including differentiation and mobilization induced by niches-dimensionality. Our study showed that the 3D niche microenvironment provides necessary information to maintain the hematopoietic stem progenitor cells proliferation. In addition, the connection of external physical signals and internal molecular mechanism were demonstrated, which may offer critical reference for artificial HSC niches according to clinical needs.

Keywords: Hematopoietic stem cells; bone marrow niches; niche-dimensionality; 3D hydrogel matrices