ABSTRACT

Hematopoietic stem/progenitor cells (HSPCs) are responsible for the generation of blood cells throughout life. It is believed that, in addition to soluble cytokines and niche cells, biophysical cues like elasticity and oxygen tension are responsible for the orchestration of stem cell fate. Although several studies have examined the effects of bone marrow (BM) niche elasticity on HSPC behavior, no study has yet investigated the effects of the elasticity of other niche sites like the fetal liver (FL), where HSPCs expand more extensively. In this study, we evaluated the effect of matrix stiffness values similar to those of the FL on BM-derived HSPC expansion. We first characterized the elastic modulus of murine FL tissue at embryonic day E14.5. Fibrin hydrogels with similar stiffness values as the FL (soft hydrogels) were compared with stiffer fibrin hydrogels (hard hydrogels) and with suspension culture. We evaluated the expansion of total nucleated cells (TNCs), Lin−/cKit+ cells, HSPCs (Lin−/Sca+/cKit+ (LSK) cells), and hematopoietic stem cells (HSCs: LSK- Signaling Lymphocyte Activated Molecule (LSK-SLAM) cells) when cultured in 5% O2 (hypoxia) or in normoxia. After 10 days, there was a significant expansion of TNCs and LSK cells in all culture conditions at both levels of oxygen tension. LSK cells expanded more in suspension culture than in both fibrin hydrogels, whereas TNCs expanded more in suspension culture and in soft hydrogels than in hard hydrogels, particularly in normoxia. The number of LSK-SLAM cells was maintained in suspension culture and in the soft hydrogels but not in the hard hydrogels. Our results indicate that both suspension culture and fibrin hydrogels allow for the expansion of HSPCs and more differentiated progeny whereas stiff environments may compromise LSK-SLAM cell expansion. This suggests that further research using softer hydrogels with stiffness values closer to the FL niche is warranted.