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Replication of hematopoietic stem cell niche: A genie to grant unlimited stem cells

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The bone marrow microenvironment maintains a stable balance between self-renewal and differentiation of hematopoietic stem/progenitor cells (HSPCs). This microenvironment, also termed the "hematopoietic niche", is primarily composed of stromal cells and their extracellular matrices (ECM) that jointly regulate HSPC functions. We have demonstrated that umbilical cord blood derived HSPCs can be maintained and expanded on stromal cell derived acellular matrices that mimic the complexity of the hematopoietic niche. The results indicated that matrices prepared at 20% O_2 with osteogenic medium (OGM), which were closer to vascular niche like conditions, were best suited for expanding committed HSPCs, whereas, matrices prepared at 5% O_2 without OGM and which mimic endosteal niche like conditions, were better for primitive progenitor expansion. Based upon these results, we proposed that individual constituents of these matrices could be responsible for regulation of specific HSPC functions. To explore this hypothesis, we have performed comparative transcriptome profiling of these matrix producing cells. We have identified differential expression of both known niche regulators, such as Wnt4, Angpt2, Vcam and Cxcl12, as well as genes not previously associated with HSPC regulation, such as Depp. MetaCore analysis of the differentially expressed genes suggests that several ECM related pathways are down-regulated while Ang-Tie2 and Wnt signaling pathways are up-regulated in OGM under high O_2 (20%). Thus, these findings could be helpful in understanding the biochemical organization of hematopoietic niches and may also suggest the possible design of bioactive and biomimetic scaffolds for hematopoietic stem-cell based tissue engineering there by increasing the availability of more transplantable HSPCs.

Biography

Abhilasha (Abhi) Tiwari is a postdoctoral fellow at Deakin University and is currently employed at Monash Institute of Medical Research, which is a centre dedicated to translation of research to clinical applications. Abhi's research is focused on developing a 'closed system stem cell expansion kit', which will be useful for medical and research applications. She completed her Ph.D. in 2012 in an Indo-Australian collaborative project between Centre for Cellular and Molecular Biology (CCMB), India and Deakin University, Australia and is continuing her current research in the same field of research.

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