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“Expansion of Hematopoietic Stem Cells ”

Technology Description

All mature cells in the blood and immune system are derived from hematopoietic stem cells (HSCs). This tremendous potential for reconstituting the hematopoietic system has allowed the development of bone marrow (or cord blood) transplantation as a clinical strategy. The use of cord blood for adult transplantation is greatly limited by the number of HSCs per unit of cord blood. Additionally, important clinical applications have been severely hampered by difficulties in ex vivo expansion of HSCs. Several years ago, the Lodish lab identified a novel fetal cell population that supports mouse HSC expansion in culture. From these they identified insulin- like growth factor 2 (IGF-2) and a group of Angiopoietin- like proteins (Angptls), in particular Angptl2 and Angptl3, as new growth factors for mouse HSCs. They subsequently developed and optimized a simple serum-free culture system - containing low but saturating levels of SCF, TPO, IGF-2, FGF-1, and Angptl2 - for mouse bone marrow HSCs. As measured by competitive repopulation analyses, there was a 24-30-fold increase in numbers of long-term repopulating HSCs after a 10 d culture of highly enriched mouse HSCs. In the last year they identified IGF binding protein 2 (IGFBP2) as another secreted protein that supports mouse HSC expansion.

Based on these results, they developed a serum-free medium for ex vivo expansion of human cord blood HSCs. HSCs were measured by transplantation into the nonobese diabetic severe combined immunodeficiency (NOD/SCID) mice; secondary transplantation was performed to evaluate the self-renewal potential of SRCs. The serum-free medium contains SCF, TPO, FGF-1, Angiopoietin-like 5, and IGFBP2. Culture in this new medium resulted in a ~20 fold net expansion of repopulating human cord blood HSCs, a number potentially applicable to several clinical processes including HSC transplantation.

Market and Application

This method for expansion of repopulating HSCs has the potential to deliver on the promise of cord blood in human transplantation.

Product Advantages

The major limitation of cord blood transplantation is that the cord blood does not contain sufficient amount of long term HSCs, which are multipotent and have the ability to self-renew. This application allows for the expansion of LT-HSCs.

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US 11/438,847 and EPO and Japan

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