

Proceedings of German Society for Stem Cell Research (PGSSCR)

GMP-Compliant Manufacturing of Autologous Stem and Progenitor Cells For Tissue Repair

Prante C¹, Gastens MH¹, Prohaska W¹, Stratmann B², Lammers D², Kirana S²,
Tschopev D², Kleesiek K¹

¹Institut für Laboratoriums- und Transfusionsmedizin, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinik der Ruhr-Universität Bochum, 32545 Bad Oeynhausen

²Diabeteszentrum, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinik der Ruhr-Universität Bochum, 32545 Bad Oeynhausen

Published on 16 May 2007

Many regenerative medicine research efforts focus on the treatment of severe medical conditions with cells derived from the patient's own bone marrow (BM). The effectiveness of these autologous BM cell therapies is often limited by the number of stem and progenitor cells in the final product that contain tissue regenerating potential. One strategy to address the issue of stem and progenitor cell number is to culture the patient's BM cells, prior to implantation, in a standardized and reproducible cell manufacturing process. Here we describe a closed, automated Good Manufacturing Practice (GMP)-compliant process that begins with a small bone marrow aspirate from the patient and through a series of process steps generates a patient-specific dose of Tissue Repair Cells (TRCs) that contains a higher number and higher percentage of stem and progenitor cells than the original BM.

Bone marrow mononuclear cells (MNCs) from a small sample of the patient's BM (30-50 ml) are isolated by Ficoll gradient centrifugation using an automated device to

deplete the erythrocyte and granulocyte components of the BM. The resulting MNCs are then inoculated into a cell culture cassette and cultivated for 12 days in a completely closed automated cell manufacturing system that provides a completely computer-controlled culture environment through the regulation of temperature and gas and media exchange. This cell environmental control together with the single-pass perfusion technology, enables the replication of early-stage stem and progenitor cells while preventing their differentiation into mature cells. The resulting cell product shows significantly increased populations of stem and progenitor cells and decreased populations of mature cells. CD90+ mesenchymal stem cells, represent a key cell population that undergoes significant expansion under this perfusion culture and has been observed to increase up to 48-fold in cell number and up to 200-fold in CFU-F forming capability during the manufacturing process. The stem cell content of the product has been proved through the ability of specific sub-populations to differentiate into adipocytes, osteoblasts or cells with endothelial characteristics.

In conclusion the combination of closed and automated technologies can be used to support the production of a validated and GMP-compliant cellular product for therapeutic use.

JSRM
www.pubstemcell.com