A standardized and characterized clinical grade human platelet lysate for efficient expansion of human bone marrow mesenchymal stem cells

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Introduction: Human platelet lysate (hPL) is rich in growth factors and nutritive elements and represents an advantageous xeno-free alternative to fetal bovine serum (FBS) for human mesenchymal stem cell (hMSC) proliferation. However, there is a great variability in hPL sources and production protocols, resulting in discrepancies in product quality, low management of product safety and poor batch-to-batch standardization.

Material and Methods: We describe here the development and the characterization of a standardized hPL prepared from outdated screened normal human donor platelet concentrates (PCs), manufactured on an industrial scale (batch sizes of 10 L; 240 donors) and based on GMP standards (clean room, trained operators and validated industrial process). PCs were frozen at -80°C and thawed at +4°C to lyse platelets. The number of freeze-thaw cycle was optimized. Cell debris were removed by centrifugation and the supernatant (hPL) was recovered. In order to ensure final aseptic filtration of hPL, we tested 5 different filter sequences and selected a 0.22μm size pore membrane allowing optimal growth factor recovery (EGF, VEGF, bFGF, TGF-β1, PDGF-AB and IGF-1). Clinical grade 10L batches of aseptic filtered hPL were characterized.

Results: We showed a robust standardization between batches in terms of reproducible growth factor contents, biochemical analyses and efficacy on bone marrow (BM) hMSC proliferation. Finally, we compared expansion and functional characteristics of BM-MSCs grown in clinical grade hPL versus MSC-screened FBS batch. We showed a reproducible increase in cell growth kinetics using hPL, a maintenance of BM-MSC membrane marker expression and clonogenic potential and a similar adipogenic and osteogenic differentiation potential.

Conclusion: We demonstrated the feasibility to use a standardized, efficient and clinical grade hPL for research and cell therapy applications.