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Inactivated Human Platelet Lysate is a new method to ensure safer GMP-compliant MSC production

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INTRODUCTION. Mesenchymal Stem Cells (MSCs) are ideal candidates in regenerative and immunomodulatory therapies. The use of xenogenic protein free GMP-compliant growth media, is a mandatory prerequisite for clinical-grade MSC isolation and expansion. Pooled Human Platelet Lysate (HPL) has been efficiently implemented into MSC clinical scale manufacturing as an animal serum substitute. In this study, we compared HPL as a supplement of MSC culture medium to Foetal Bovine Serum (FBS) usually used for MSC expansion. Moreover, to upgrade quality/safety we decided to test inactivated HPL (iHPL) compared to non-inactivated HPL for use in the clinical-scale expansion of MSCs.

METHODS. BM samples were directly plated at a density of 10000 cells/cm2 using 3 different culture mediums: 1) αMEM + 10 % HPL; 2) αMEM + 10 % HPL (iHPL) both with+ 2U/ml of heparin; 3) MSC medium (Stem Cell Technologies) containing 10% foetal bovine serum (FBS), usually used for MSC isolation and expansion. HPL was obtained from 10 to 15 Buffy-Coats derived platelet concentrates (BC-PCs) and iHPL was inactivated with INTERCEPT Blood System (Cerus).

At each passage, MSC morphology, cellular growth (cPD), immunophenotype (CD90, CD73, CD105, 45-34-14, CD271 and CD146), kariotype and sterility were analyzed. Statistical analyses were performed with Wilcoxon signed Rank Test-paired samples.

RESULTS. MSCs cultivated in αMEM+10% HPL (HPL group) appeared smaller and more numerous than MSCs in MSC medium (MSC medium group). Between the two groups, no differences were observed in the number of fibroblast colony-forming cells (CFU-F), but the CFU-F of HPL group are richer in the number of cells than those of MSC medium group. At the 3rd passage, the cPD of MSCs was 10% higher in the HPL cell group than in the MSC medium group, while no differences were observed in terms of immunophenotype, multipotent capacity or kariotype. The sterility was negative in all the samples analyzed. No statistical differences were found among iHPL and HPL in terms of MSC expansion efficiency.

CONCLUSION. HPL represents a good GMP-compliant alternative to animal serum for MSC clinical production and is more advantageous especially in terms of cellular growth. Moreover, the inactivation procedure improves HPL quality in terms of safety.