A Meta-analysis on the Use of Human Platelet Lysate as a Critical Ancillary Material for Cellular and Gene Therapy Products

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Introduction

With the rapid rise of cellular and gene therapy (CGT) product development, GMP cell culture supplements for safe and cost-effective cell expansion with good quality control are in high demand. Fetal bovine serum is a conventional supplement used for cell culture, however there are concerns about safety and ethical issues as well as heterogeneity between batches which can impact reliability and batch-to-batch reproducibility. Human platelet lysate (hPL) has been identified in numerous studies to be an effective, preferred xeno-free cell culture supplement to replace FBS. It contains abundant growth factors and cytokines necessary for cell proliferation and is increasingly used globally as an ancillary material in clinical protocols for CGT product production. GMP-compliant hPL products are manufactured from pooled human platelets collected from healthy donors at FDA-licensed blood centers, and each donor is tested in compliance with FDA guidance. Potency is highly consistent when pooling hundreds of platelet units for each lot, achieving minimal batch-to-batch variation. While hPL has been commonly used for MSC cell expansion over the past decade, this review highlights the extent of hPL applications across multiple cell types.

Objectives

A meta-analysis of published UltraGRO™ product R&D applications was conducted, to illustrate observations and insights into usage trends from both research and clinical perspectives.

Methods

This systematic review was performed by searching electronic databases, including PubMed, Embase, OVID, Cochrane Library, and Google Scholar. Study selection was collected on the published literature up to the end of December 2022. Keywords and similar words were used as follows: human platelet lysate (hPL), fibrinogen-depleted hPL (FD hPL), xenogenic-free culture supplement, UltraGRO™ (UG), UltraGRO™-Advanced (UGA), UltraGRO™-PURE (UGP), AventaCell, pathogen-inactivated UltraGRO™ (UGP GI), and cell expansion or regeneration, or cell-derived extracellular vesicle production. Patent searching was conducted by USPTO and EPO engine with the keywords of UltraGRO™ and AventaCell.

Results

Academic publications with UltraGRO™ product lines

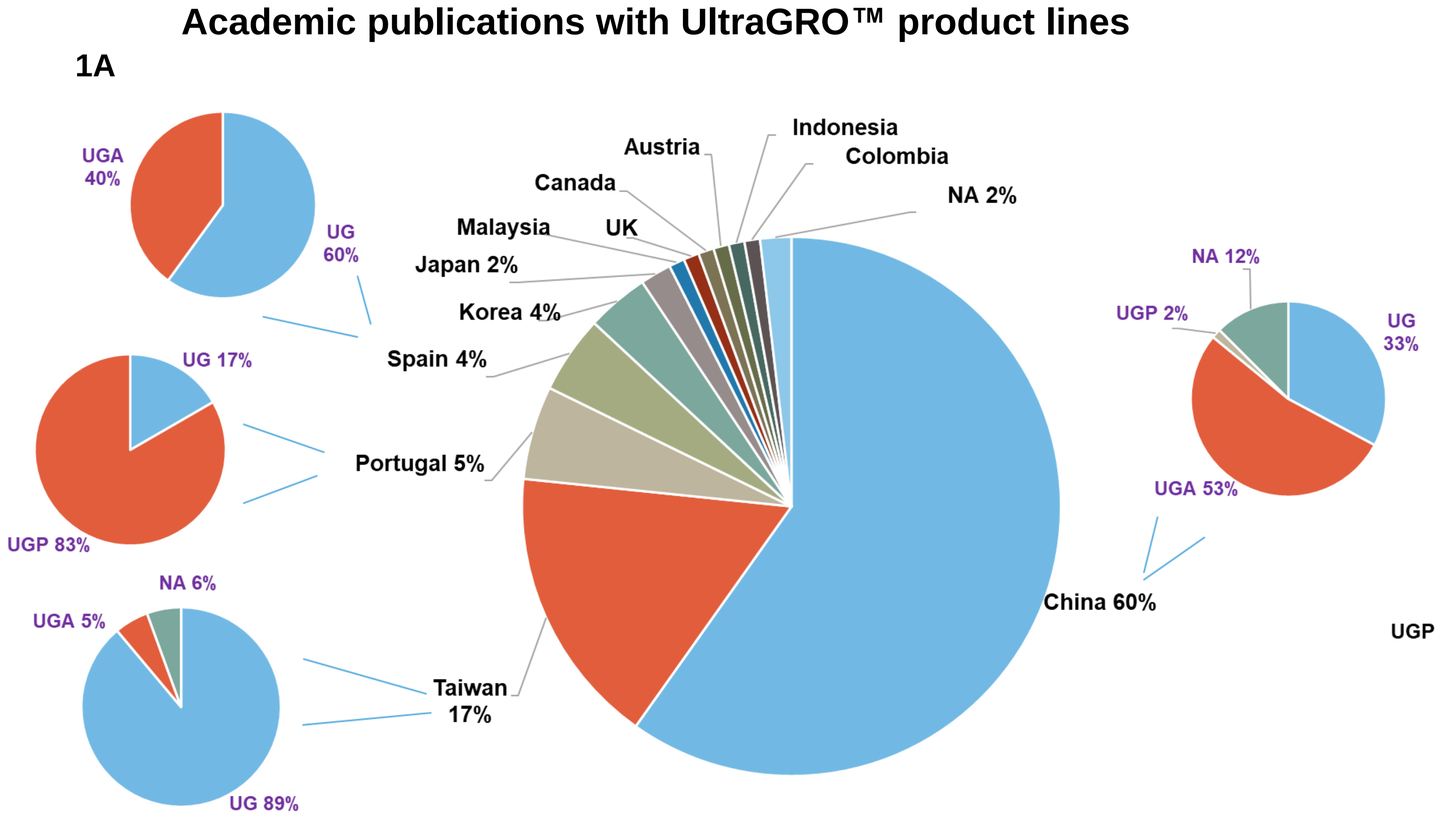


Fig 1. UltraGRO™ product lines have been used for various research projects in academic publication worldwide. (A) Most relevant publications using UltraGRO™ products as cell culture supplement were found in APAC region. (B) Total published number has reached 108 by the end of 2022, and the use of (C) fibrinogen-rich hPL (UG), fibrinogen-depleted hPL (UGA and UGP), and viral-inactivated hPL (UGP GI) in research studies were increasing over the period. (D) 41% academic publications conducted their studies with UG, 37%, 7%, and 2% with UGA, UGP, and UGP GI respectively. The rest of the references (13%) didn't mention what product was applied in the study. (E) 70% of the publications focused on the applications of human mesenchymal stem cells and 7% on human stem cells, leading a total 77% in stem cell topic with UltraGRO™ products. 13% were applied on the experiments with cancer cells, while 1-2% were on fibroblasts, epithelial cells, mouse cells, immune cells, red blood cells, and cat MSC.

MSC type	Publication
UC-MSC	56%
AD-MSC	21%
BM-MSC	11%
Amniotic-derived MSC	5%
Chorionic villous-derived MSC	4%
WJ-MSC	1%
Placenta-derived MSC	2%

Patent registration with UltraGRO™ product lines

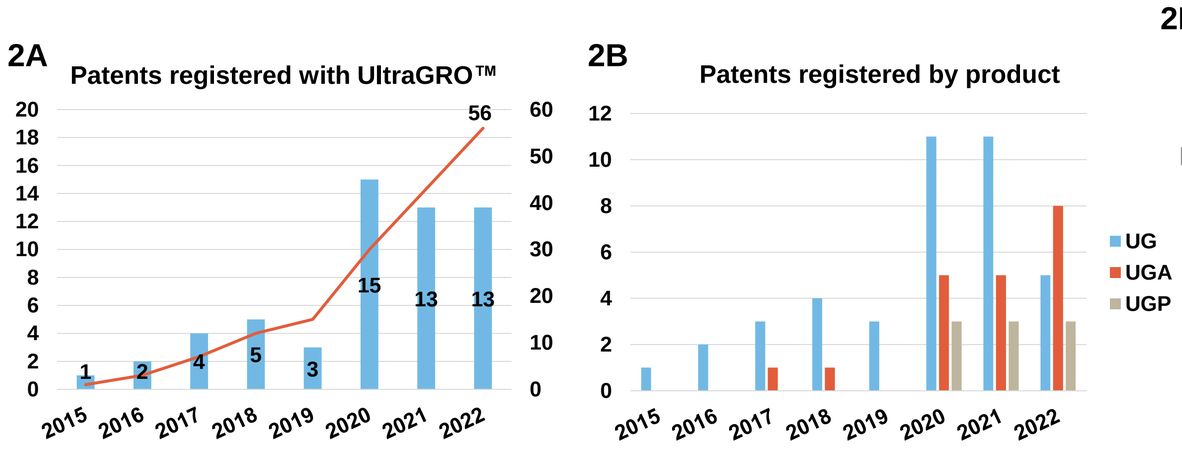
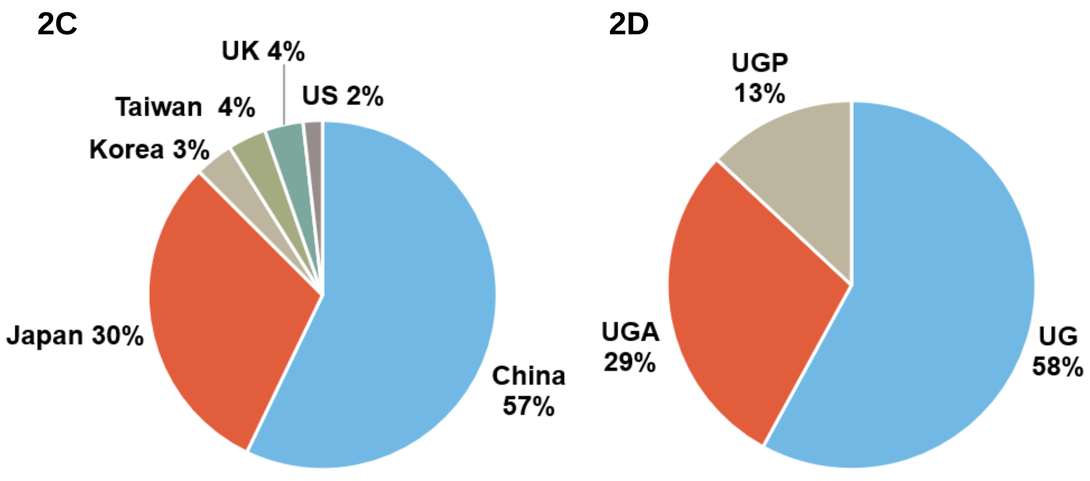


Fig 2. Case number of registered patent with (A) the use of UltraGRO™ product lines was significantly growing throughout the period, reaching 56 cases at the end of 2022. (B) fibrinogen-rich hPL (UG) and fibrinogen-depleted hPL (UGA and UGP) were increasingly used over the duration. (C) 57% of patents were filed from China and 30% from Japan, resulting a total 87% of patent registration from both countries. (D) Overall, there were 58% patents with UG, 29% with UGA, and 13% with UGP in the collected data. For the top 3 applied on target cells, 61% of patents are relative to MSC applications, 12% and 9% to NK and T cells respectively. (F) The use of UltraGRO™ product lines were applied on various innovative indications, including culture methods, cell-derived exosome related, cell isolation and storage, and composite materials and kits preparation.



Summary

Most publications (>75%) reported using hPL products (UltraGRO™) for expanding stem cells. However, extensive R&D has been emerging which offers new perspectives on broader applications in the future. Over 30 cell varieties were cultivated with UltraGRO™ products, including different stem cells, fibroblasts, epithelial and endothelial cells, immune cells, and even cancer cells. Interestingly, UltraGRO™ products were used not only for cell expansion but also for collecting extracellular vesicles for exosome research and therapeutic evaluation. In addition, enhanced tissue regeneration was established by applying biomaterials incorporated with UltraGRO™ products. Also, 56 registered patents were found related to the use of UltraGRO™ products for different purposes and innovations. Therefore, UltraGRO™ products (i.e. hPL), as ancillary materials, offer promising potential in producing a broad range of ATMPs and CGT products.