HELIOS® Exosome-Depleted UltraGRO™-PURE GI

For hMSC-derived EV production

Xeno-Free, Safe, Exosome-Depleted Supplement for EV Production

AventaCell BioMedical Corp. has developed an exosome depletion process to remove human platelet lysate (hPL)-derived exosomes from their FDhPL products. Exosome-Depleted UltraGRO™-PURE GI (**ED UG-P GI**) is able to support human MSC cell viability to secret abundant extracellular vesicles (EVs) without compromising phenotype over the culture period. Moreover, gamma irradiation processing of the product is used as a pathogen reduction treatment (PRT) for viral inactivation, to comply with regulatory guidance for clinical research and development.

Benefits of Exosome-Depleted UltraGRO™-PURE GI

- **Xeno-free with >95% nanoparticle removal from the hPL supplement**
- **Minimal hPL nanoparticle contamination**
- **MSCs cultured with the depleted supplement remain highly viable with stable phenotype markers throughout the culture period**
- **GMP Exosome-Depleted UltraGRO™-PURE GI to produce clinical grade hMSC-derived EVs**
- **Gamma irradiation processing is accepted by regulatory agencies as a validated PRT**

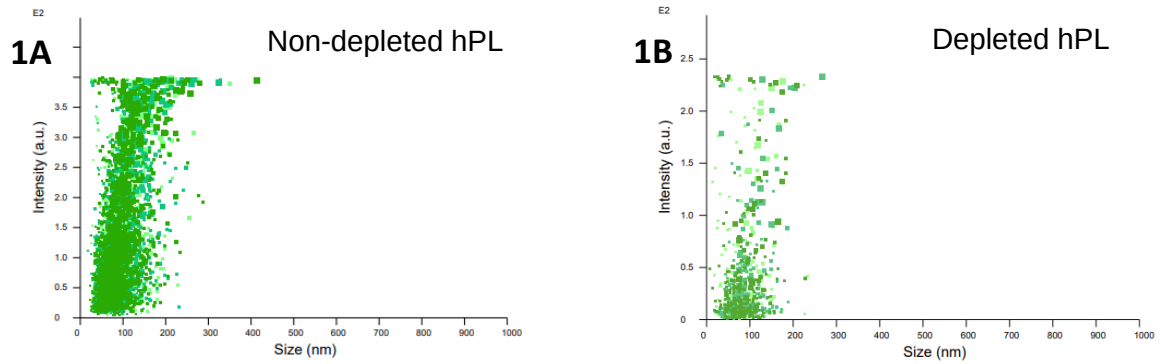

Fig. 1: Nanoparticles in human platelet lysate were analyzed by Nanoparticle Tracking Analysis (NTA). Nanoparticle size distribution in hPL product (A) before and (B) after the depletion process.

High depletion rate was performed in the manufacturing process

Particle count/mL	Non-depleted hPL	Depleted hPL	Depletion rate
Batch #1	$3.40 \times 10^{11} \pm 2.13 \times 10^{10}$	$5.17 \times 10^{8} \pm 5.25 \times 10^{7}$	99.85%
Batch #2	$2.43 \times 10^{11} \pm 6.63 \times 10^{9}$	$1.40 \times 10^{9} \pm 9.72 \times 10^{7}$	99.42%
Batch #3	$3.35 \times 10^{11} \pm 1.70 \times 10^{10}$	$1.73 \times 10^{9} \pm 2.34 \times 10^{8}$	99.48%
Average	**$3.06 \times 10^{11} \pm 5.46 \times 10^{10}$**	**$1.22 \times 10^{9} \pm 6.27 \times 10^{8}$**	**99.60%**

Table. 1: Particle concentration and depletion rate of each batch were shown in the table.

AventaCell BioMedical Corp

*AventaCell Internal Data 2021-2022

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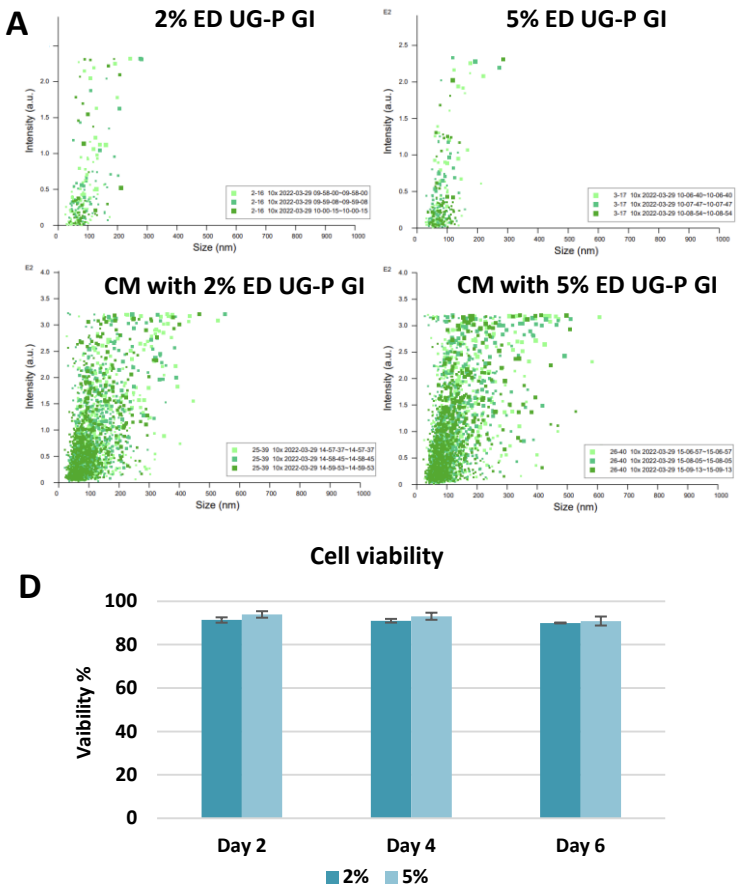

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MSC phenotype characterization

Culture period	CD73	CD90	CD105	CD34
Day 10	97.4%	99.4%	99.7%	1.2%
Day 14	97.9%	99.8%	97.6%	1.8%

Fig.2: After MSCs reached 60-70% confluency in a 6-well culture plate, the culture media was changed to ED UG-P GI supplemented culture media, and the media refresh was performed every 2 days as one culture cycle. (A) Nanoparticle distribution of culture media and conditioned media of MSCs after 2-day culture was analyzed by NTA as well as (B) the monitoring of secreted particles in each culture cycle, suggesting ~99% of the particle were from the cultured ADMSC cells, and (C) the accumulated secretion profile from day 0 to day 6, reaching billions of particle/mL throughout the culture period. Cultured MSCs remained great (D) cell viability from 90 – 93% , and (E) the specific phenotype was not altered throughout the culture period up to 14 days.

Specifications	Acceptance
Endotoxin	< 10 EU/mL
Sterility	No growth
Mycoplasma	Negative
Osmolarity	270-330
pH	6.5 – 8.5
Particle depletion rate	> 95%
Cell assay	Support MSC culture
Dosage of gamma irradiation exposure	40 – 50 kGy

Ordering Information

Product Number	Product	Bottle Size (mL)
HPCHEFRLI05	Exosome-Depleted UltraGRO™-PURE GI	50
HPCHEFRLI10		100
HPCHEFRLI50		500
HPCHEFGLI05	Exosome-Depleted UltraGRO™-PURE GI (GMP Grade)	50
HPCHEFGLI10		100
HPCHEFGLI50		500

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