Control of Cell-to-Cell Adhesion to Facilitate Process Optimisation & Intensification

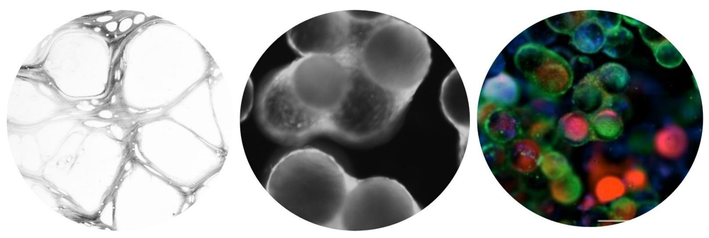
Azzeldin Madkour, William Morgan-Evans, Scott Kerridge, Esha Singh, Alvaro Yupanqui, Robert Smith, Elena Thomas, Laura Duffy, Martina Miotto, Chris Green & Francois Taute

The Problems caused by Cell-to-Cell Adhesion in bioprocessing

Cell death is a primary driver of process loss

Upstream

- Cells excrete extracellular matrix
- Cells stick to one another
- A lack of oxygen and nutrients causes cell death



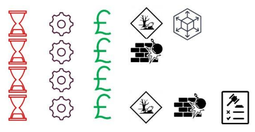
Consequences of MCs aggregation in the process

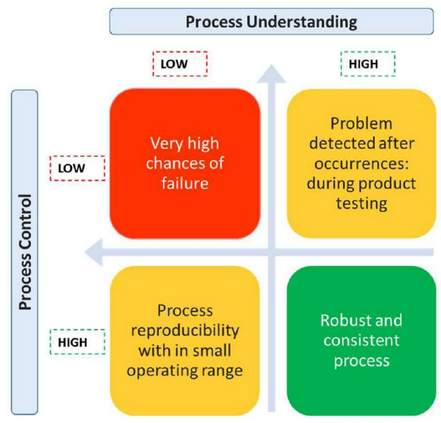
1. Upstream (USP)
   - ↓ Mass transfer efficiency = ↓ Cell culture homogeneity
   - ↓ ΔA for nutrient-waste and gas exchange
   - ↓ Cell viability = ↓ Productivity
   - Batch-2-batch variation = ↓ Productivity; ↓ Yield; ↓ Quality
   - Batch loss more likely (Process dependent: 15 – 60%)

2. Harvesting & Downstream (DSP)
   - ↑ Cell clumping = ↑ Complex cell harvesting = ↑ Cell / Product loss
   - ↑ Clogging: Spin filters, columns, etc.

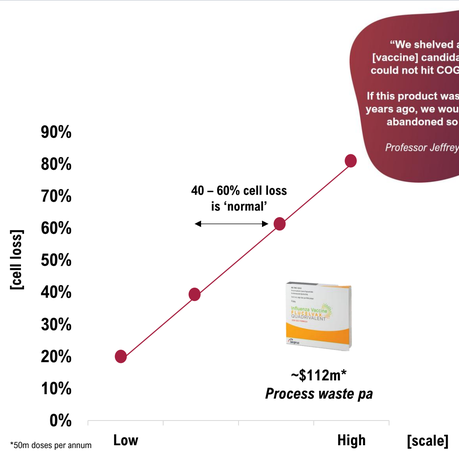
Current mitigations strategies:

a. Change the process design
b. Manipulate Cells & biochemistry
c. Alter the process parameters
d. Add anticlumping agents





Rathore et al, (2021), Life, 11:557



AggreGuard™ controls Cell-to-Cell Adhesion

How it works: AggreGuard™ is a wildtype bacterial enzyme cocktail capable of preventing and/or controlling cell-to-cell adhesion.

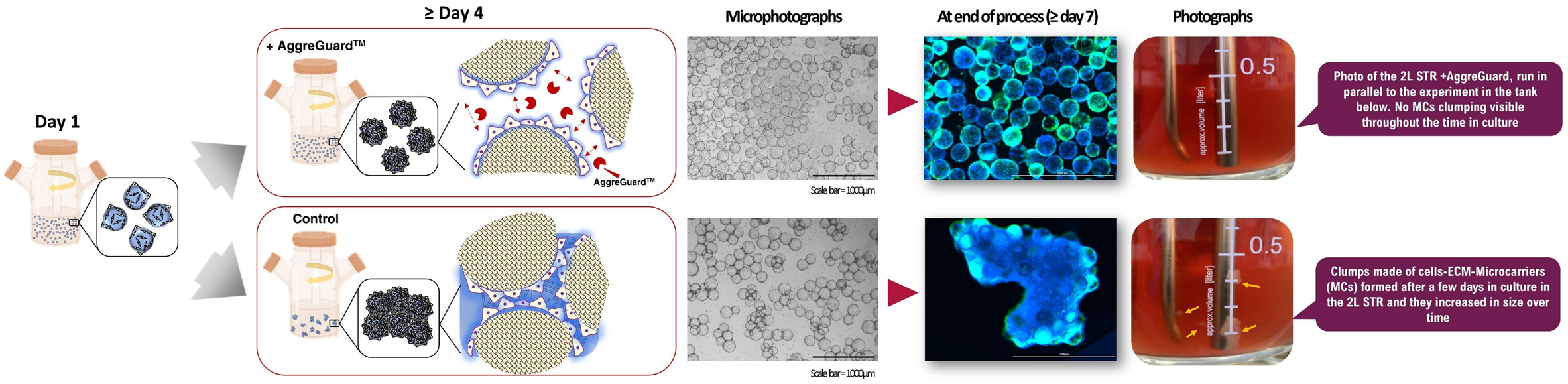


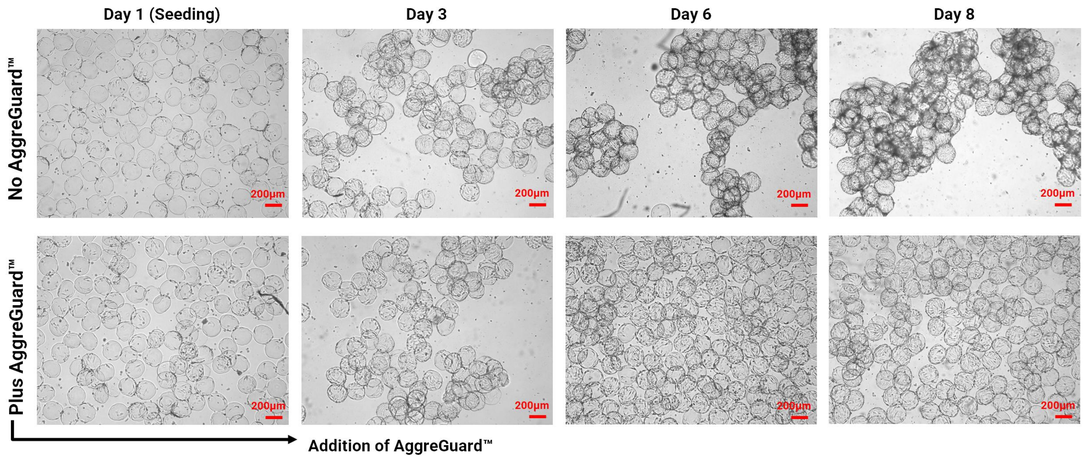
Photo of the 2L STR +AggreGuard, run in parallel to the experiment in the tank below. No MCs clumping visible throughout the time in culture

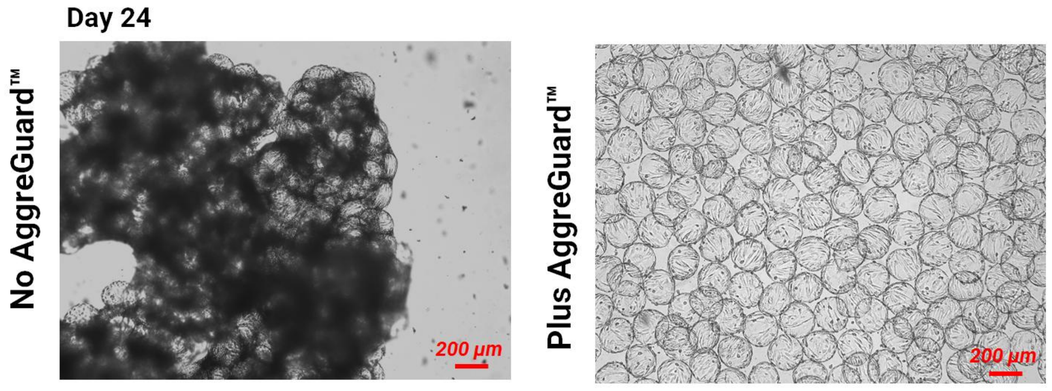
Clumps made of cells-ECM-Microcarriers (MCs) formed after a few days in culture in the 2L STR and they increased in size over time

Key data supporting the ability of AggreGuard™ in preventing and/or control cell-to-cell adhesion.

Fibroblasts

Used in vaccines, Interferon, RegenMed & CellAgri

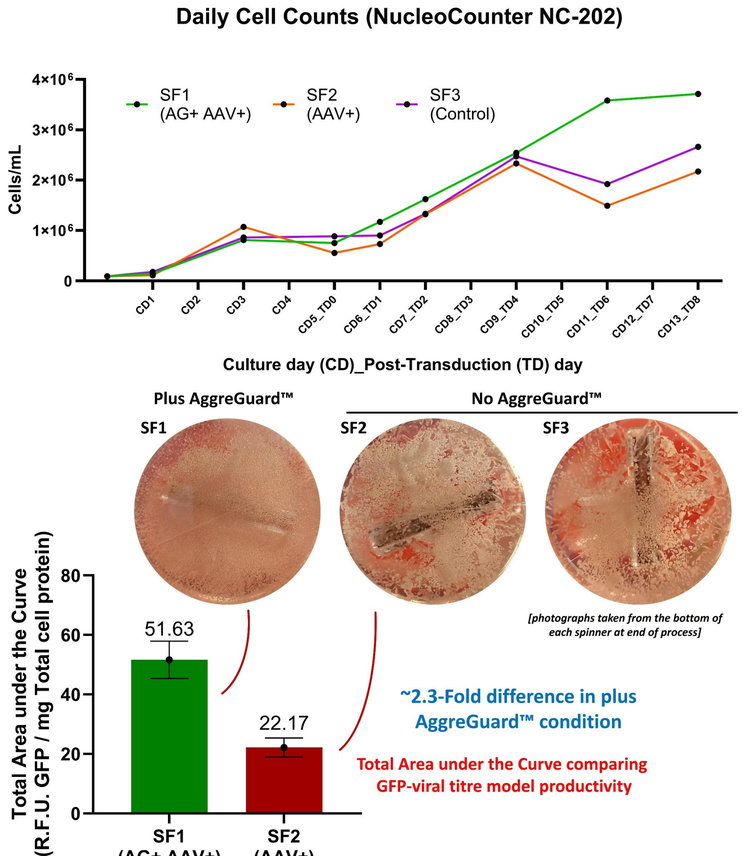




VERO

Work horse of the viral vaccine industry for viral vaccines (*i.e., polio, measles, HPV, COVID19, etc.*)

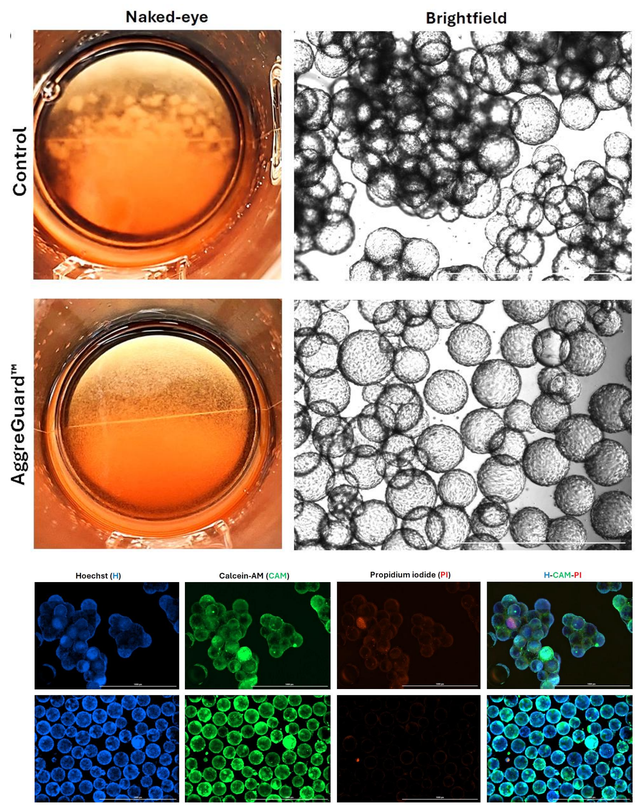
AggreGuard™ Improves Viral Titre
A GFP-Model using VERO cells on SoloHill® Plastic Plus MCs (Sartorius)



~2.3-Fold difference in plus AggreGuard™ condition

Total Area under the Curve comparing GFP-viral titre model productivity

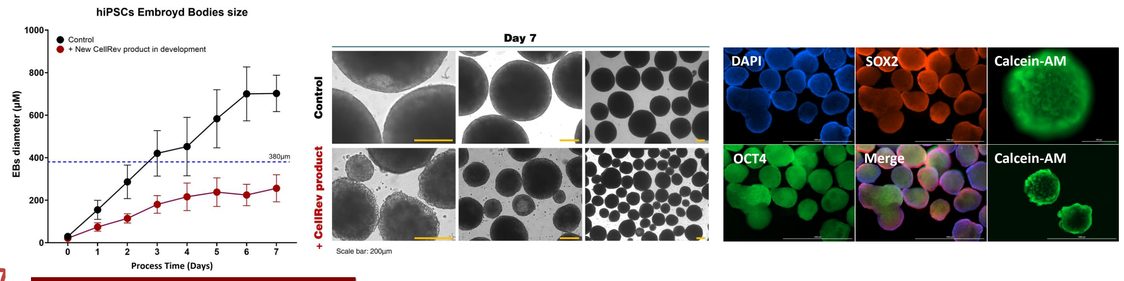
AggreGuard™ prevents aggregation of VERO cells grown Scapova™ CL MCs (Kuraray, Japan)



Products in development

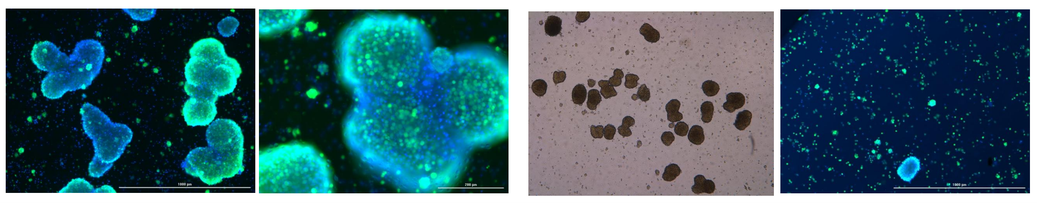
hiPSCs

Controlling spheroids size



HEK-293

Single Cell Suspension (AAV)



CellRev focus areas

Prevention / control of clumping and tissue aggregates

a. ↑ % microcarriers (% m/v) or ↑ cell density
b. "Old school" USP challenges, i.e., Bead-to-bead transfer
c. "Early" downstream interventions, i.e., spin filters
d. Viral titre yields
e. Cell yields and phenotype studies

Optimisation of bioprocess proof-of-concept work (*In progress*)

Partnering with biomanufacturing experts

a. Modernise old infrastructure with ↓ cost "upgrading"
b. Develop new biomanufacturing strategies
c. Capacity (in litres) need to ↑20-fold by 2040 or…

Live Cells. Lives Saved.

enquiry@cellrev.co.uk
info@cellrev.co.uk