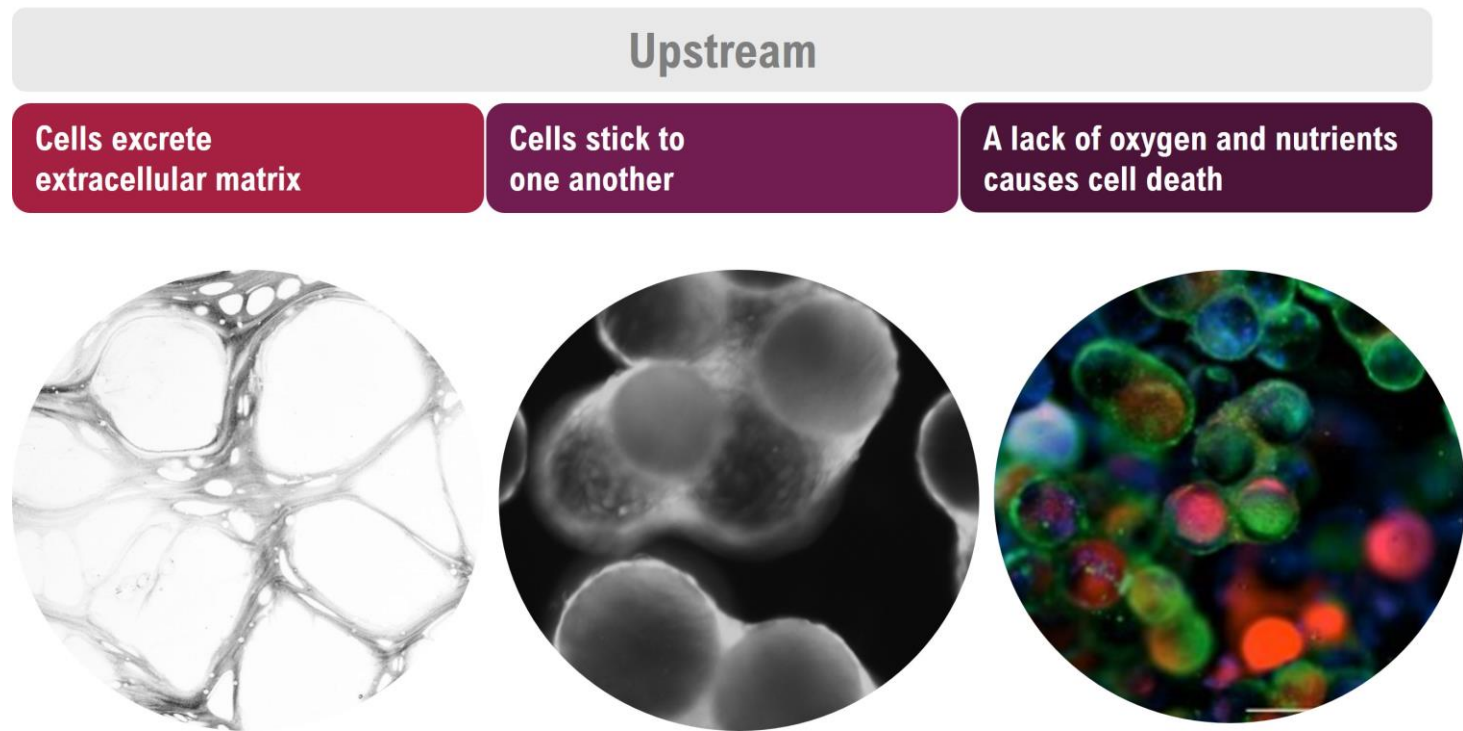


The Problems caused by Cell-to-Cell Adhesion in bioprocessing

Cell death is a primary driver of process loss

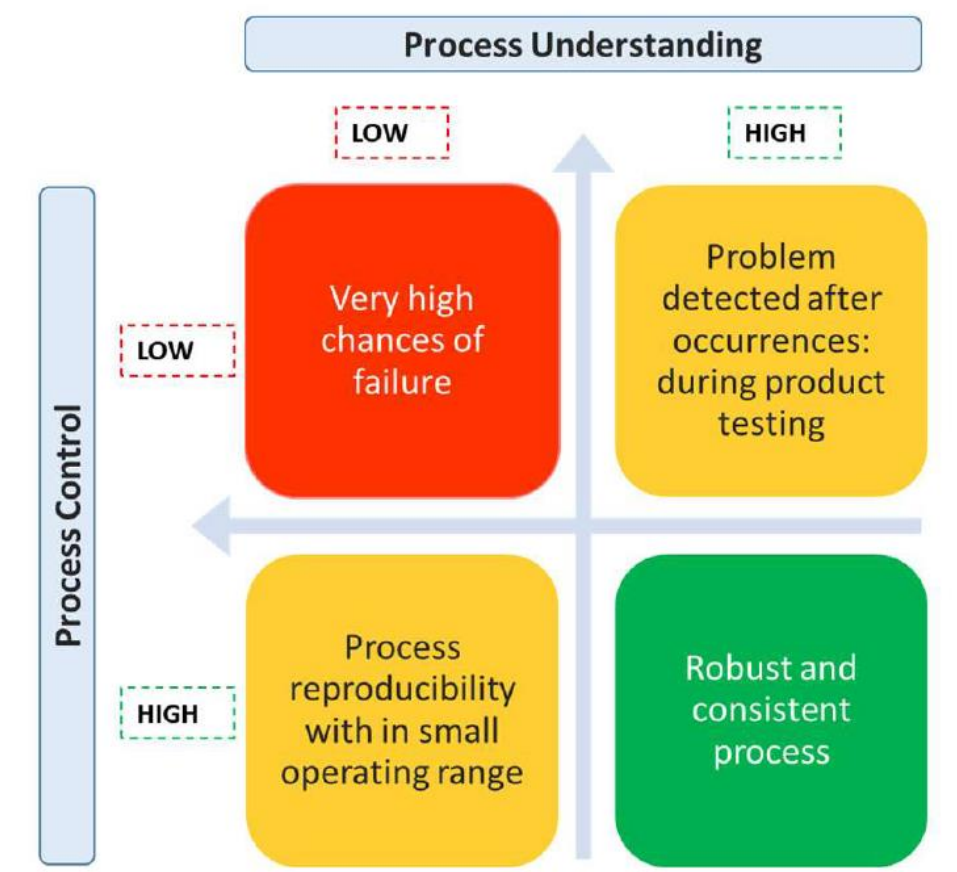
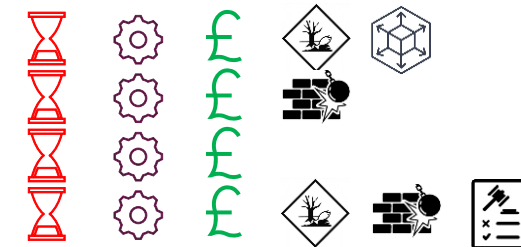


Consequences of MCs aggregation in the process

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

Current mitigations strategies:

- Change the process design
- Manipulate Cells & biochemistry
- Alter the process parameters
- 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.

Day 1

≥ Day 4

+ AggreGuard™

Control

Microphotographs

Photographs

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.

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

60-day Marathon experiment in spinner flasks

Stability Studies

Cryopreservation, Reattachment, Phenotype

Control Naked-eye, Brightfield

AggreGuard™ Naked-eye, Brightfield

With AggreGuard™ Without AggreGuard™

Phase contrast

Propidium iodide (PI)

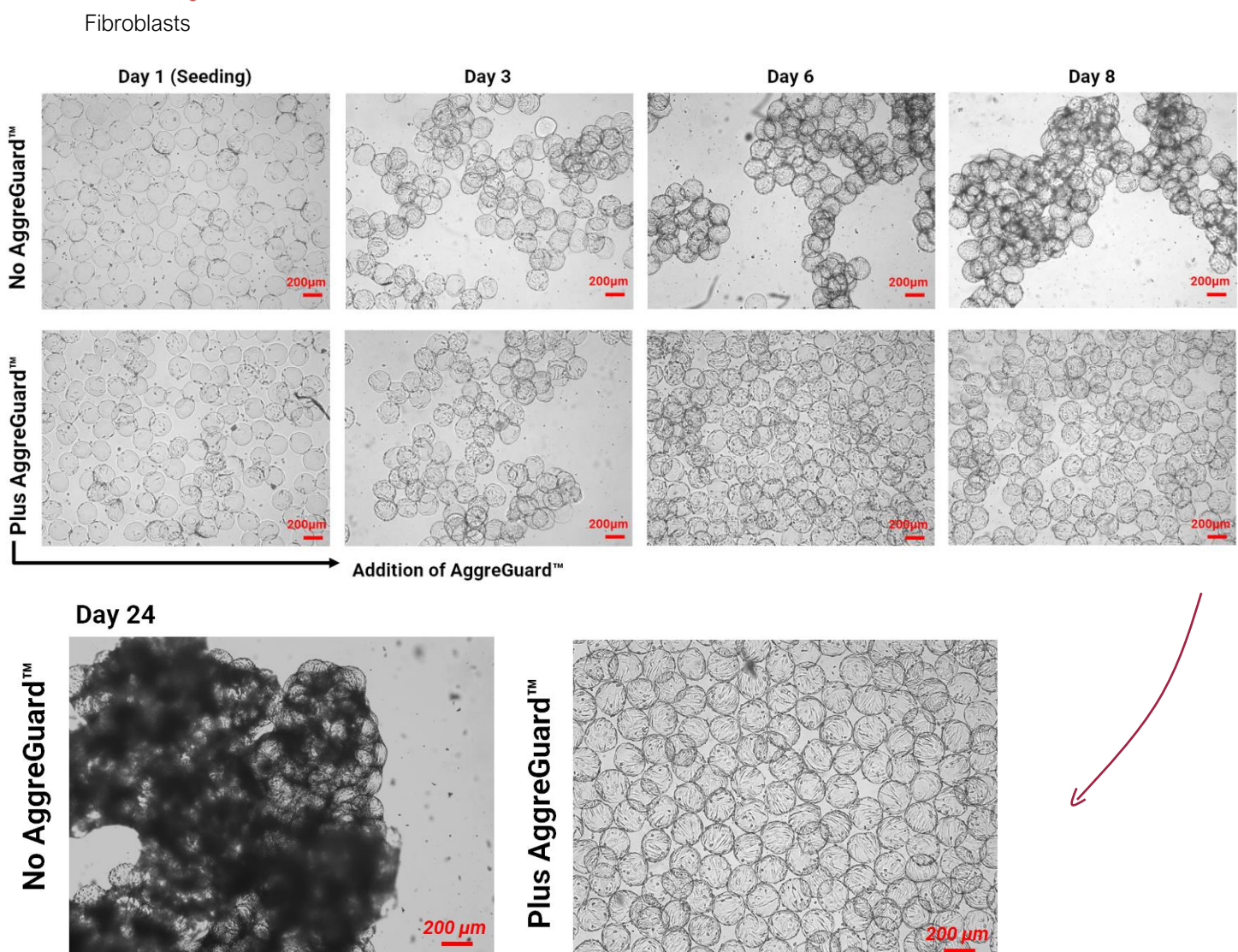
DAPI / Calcein-AM / PI

End of process cell yield (fold increase from day 0)

End of process cell yield (total cells harvested)

Hoechst (H) **Calcein-AM (CAM)** **Propidium iodide (PI)** **H-CAM-PI**

Used in vaccines, Interferon, RegenMed & CellAgri



Products in development

Single Cell Suspension (AAV)

HEK-293

Controlling spheroids size

hiPSCs

hiPSCs Embryoid Bodies size

EBs diameter (µm)

Process Time (Days)

Day 7

Control

+ CellRev product

CellRev focus areas

- Prevention / control of clumping and tissue aggregates
- Optimisation of bioprocess proof-of-concept work (*In progress*)
 - ↑ % microcarriers (% m/v) or ↑ cell density
 - "Old school" USP challenges, i.e., Bead-to-bead transfer
 - "Early" downstream interventions, i.e., spin filters
 - Viral titre yields
 - Cell yields and phenotype studies
- Partnering with biomanufacturing experts
 - Modernise old infrastructure with ↓ cost "upgrading"
 - Develop new biomanufacturing strategies
 - Capacity (in litres) need to ↑ 20-fold by 2040 or...

Live Cells. Lives Saved.

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