

AggreGuard™

Improve Batch and Fed-batch Workflows



Microcarrier Aggregation: A Universal Bioprocess Challenge

Process Inefficiency due to Cell-to-Cell Induced Aggregation

Reduced Mass Transfer Efficiency

- Aggregates > 300µm have necrotic cores.
- ↓ ΔA for nutrient-waste and gas exchange.
- ↓ Cell viability.

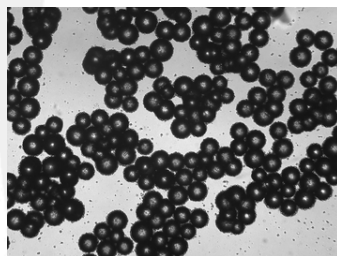
Upstream Process Reproducibility Challenge

- ↓ Mass transfer = ↑ Variability in cell proliferation, metabolism and gene expression.
- Aggregates reduce efficacy of infection and transfection workflows.
- Inconsistent productivity, yield and quality.

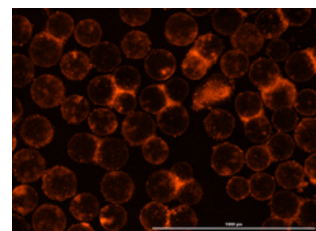
Challenges for Downstream Processing

- Large aggregates complicate filtration and separation methodologies.
- Workflow complication with added methodologies.
- Reduced cell product yields

VERO cells +
Corning®
Untreated
Microcarriers

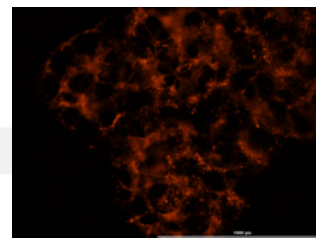
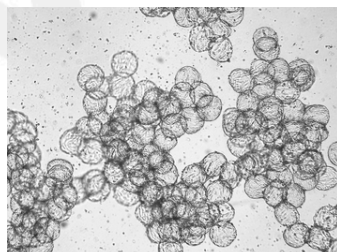


Process Day 4 - 7



Propidium iodide

Fibroblasts +
Corning®
SynthemaxII®
Microcarriers



What is AggreGuard?

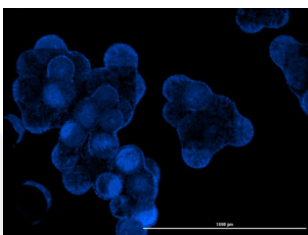


- Bacterial derived wildtype enzyme formulation
- Specific activity tailored to extracellular matrix proteins
- Prevents cell-to-cell adhesion induced microcarrier aggregation
- Activity is dose-dependent for gentle proteolytic manipulation and control of aggregation
- Rigorous external and internal QA/QC ensures minimal batch-to-batch variation
- AggreGuard™ is available in an affordable 100mg trial format

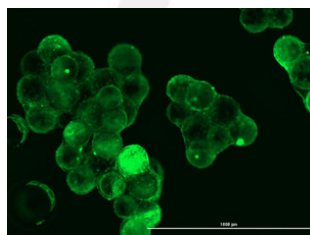
A solution for VERO cells

- Prevent cell-to-cell induced microcarrier aggregation
- Add to the process at the start as a preventative of mid-run (process day 3 - 5)

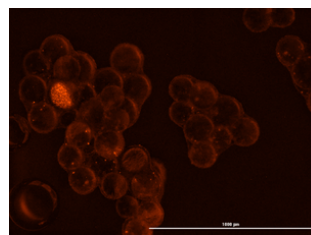
*No AggreGuard



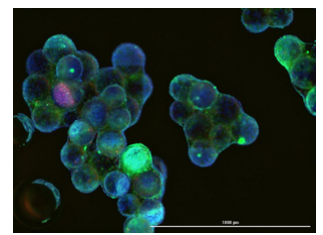
Hoechst



Calcein-AM

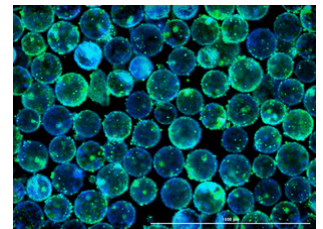
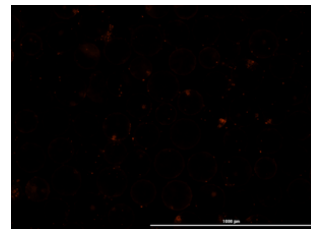
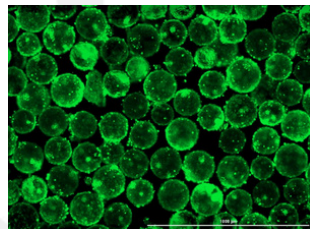
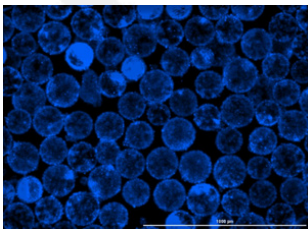


Propidium iodide



Overlay

*Plus AggreGuard

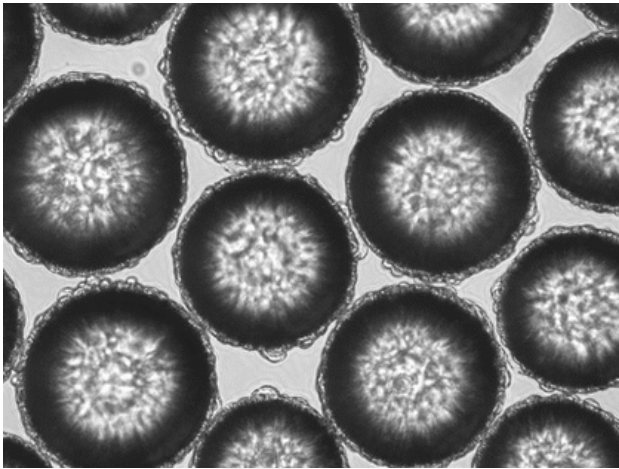


*Images are from the end of a batch process, total runtime = 10 days

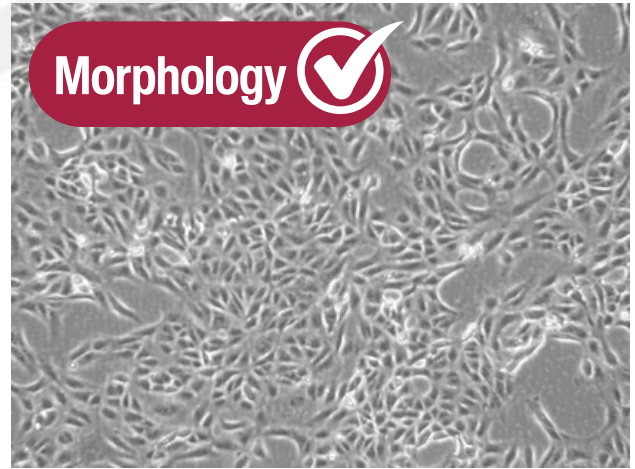


AggreGuard does not affect VERO cells adversely*

- VERO cells harvest end of process readily attach to standard culture surfaces
- No alteration observable in morphology of doubling time

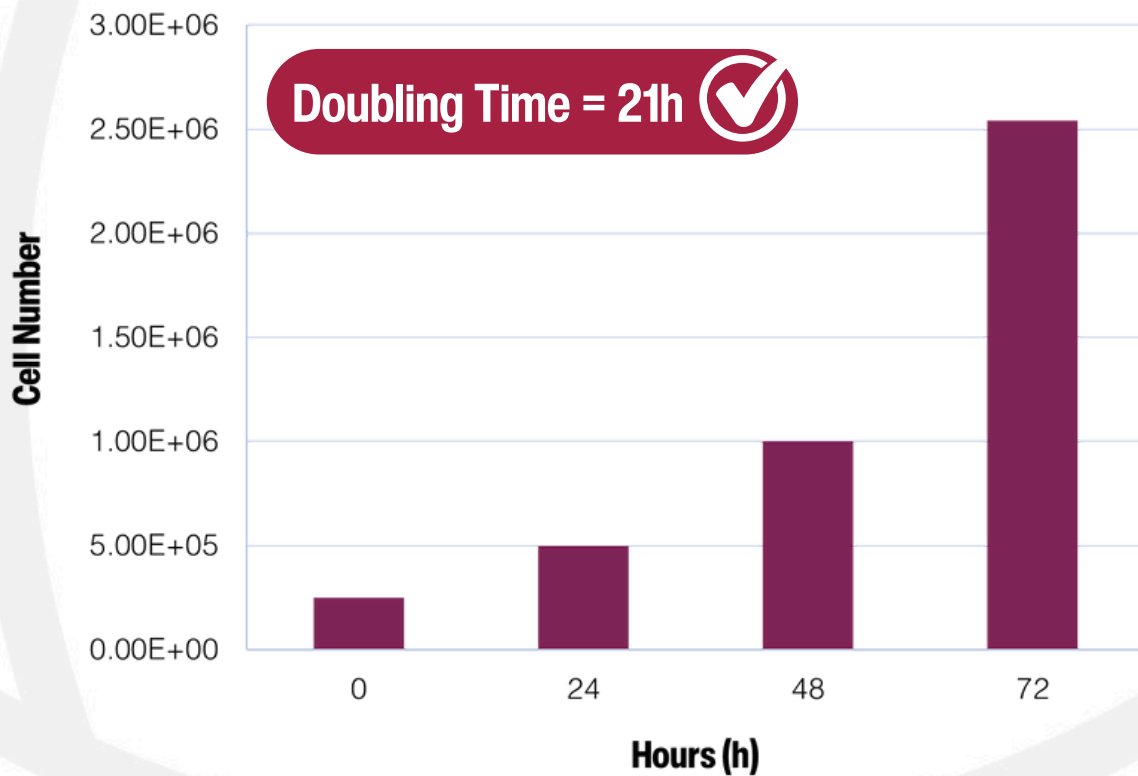


End of process (day 10)



Plated on standard T-flask

Daily cell counts on standard T-flask surface



*Qualitative assessment only

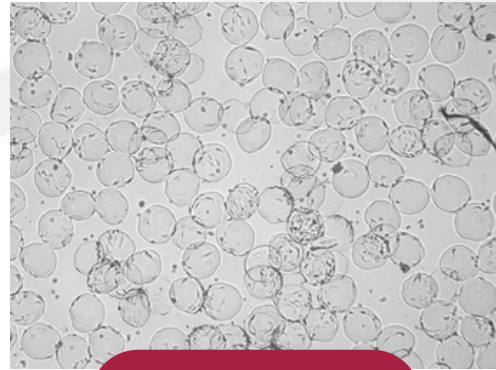
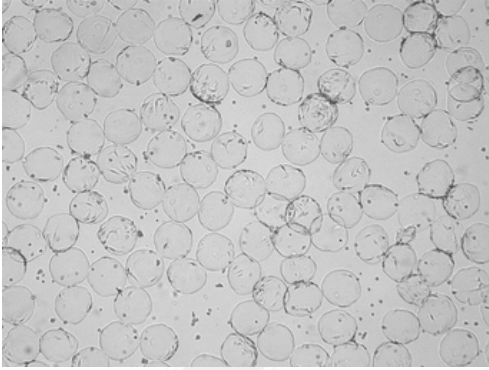


A solution for Fibroblast Culture

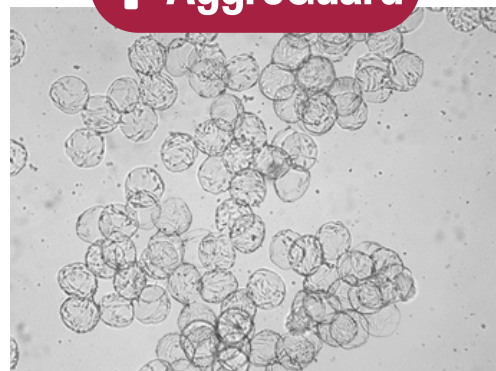
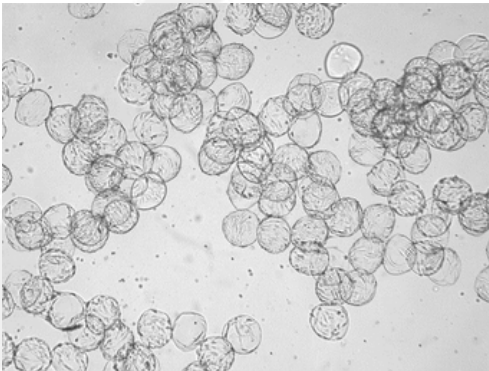
*No AggreGuard

*Plus AggreGuard

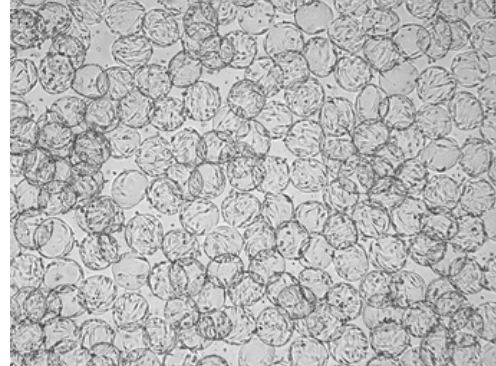
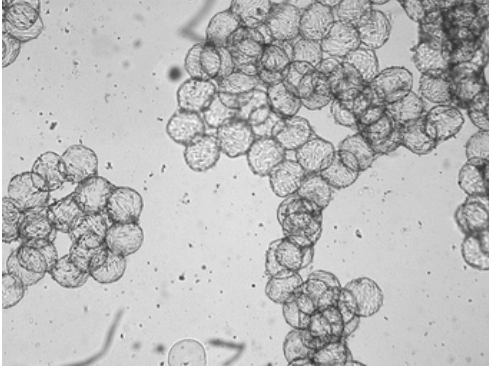
Day 1 (Seeding)



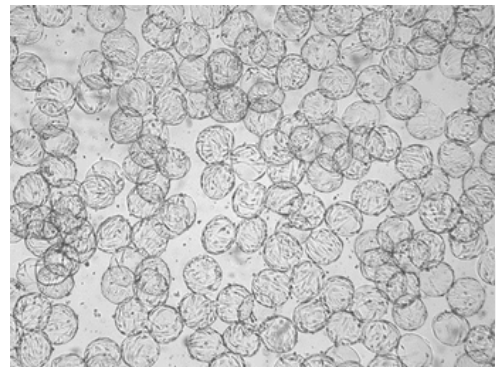
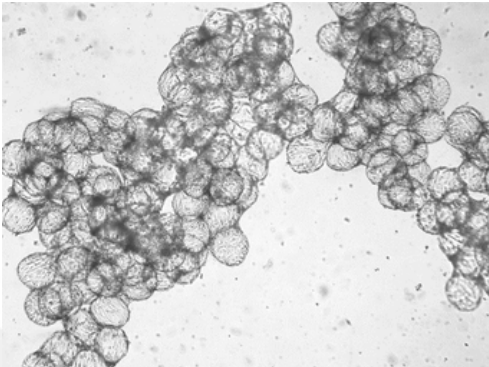
Day 3



Day 6



Day 8



+ AggreGuard

*Images are from spinner flask experiments with scale-up ongoing

Frequently Asked Questions

What is AggreGuard™?

A proprietary blend of bacterially derived wildtype enzymes, selected to facilitate extracellular matrix component digestion without affecting cells.

What is the purity of AggreGuard?

AggreGuard™ research grade is kept in stock and available. We do recommend you trial the research grade first to see if AggreGuard™ is suitable for your needs.

Will AggreGuard™ be available in GMP formats?

In the near-future, yes. [Contact us](#) for details.

What cell types and microcarriers are AggreGuard™ compatible with?

We have tested AggreGuard™ with VERO cells, muscle myoblasts and fibroblasts. We foresee that AggreGuard™ has a wide range of biocompatibility but the dose will be dependent on the cell type as well as the microcarrier pairing.

Is AggreGuard™ like bulk detachment enzyme formulations?

No. AggreGuard™ was not formulated to be used as a bulk detachment reagent.

Will AggreGuard damage our cells?

No. AggreGuard™ was formulated to be specifically active towards cell-to-cell adhesion extracellular matrix components. There is no trypsinolytic activity.

Does exposure to AggreGuard™ affect the phenotype of growth characteristics of our cells?

AggreGuard™ should not affect the phenotype of your cells or the doubling time. We tested VERO cells for 60-days continuously exposed to AggreGuard™ where no effect was seen on the phenotype, adhesion characteristics or doubling time of the cells.

Will this affect our infection/transfection workflow?

AggreGuard™ should not have any effect. The enzymatic cocktail half-life is ~18h, allowing for a window of low-to-null activity. We recommend testing dose-response based effects on infection/transfection experiments.



Frequently Asked Questions

Does AggreGuard™ effect the cell products?

The formulation of AggreGuard™ was specifically selected to only affect extracellular matrix components. A bioinformatics search indicates that AggreGuard™ has < 0.5% chance to show proteolytic activity to off-target proteins. Regardless, we recommend doing a dose-response evaluation on your cell products.

How do we add AggreGuard™ during a batch run?

A concentrated bolus addition at the experimental determined timepoints will suffice for batch runs. Fed-batch runs allow for AggreGuard™ integration during media feed/removal strategies.

How can I remove AggreGuard™ from my culture media or bioprocess?

Batch centrifugation with washing steps should remove the enzymes within a few washes. Alternatively, using size exclusion chromatography or other molecular weight selective filtration methods should also remove the enzymes (25kDa – 120kDa).

Can I use AggreGuard™ for bulk cell detachment, i.e. for bead-to-bead (intra/inter) transfer?

No, AggreGuard™ is not a bulk detachment or harvesting reagent and the formulation would not benefit such applications.

Does AggreGuard™ work for all cell types?

We do not know. We do have customers who are testing the applications with mesenchymal stem cells, inducible pluripotent stem cells and a wide range of immortalized primary cells line. [Contact us](#) to see if we could find a solution for you.

Is AggreGuard expensive? Does CellRev provide free samples?

We do not provide free samples, however AggreGuard™ is available in an affordable 100mg trial format to keep your experimental expenditure low to see if this is a solution for you.



Do you want to improve your existing process?

- Does your process suffer from microcarrier aggregation?
- Do you experience inefficiency due to unnecessary cell loss?
- Are you happy with your process, or are you open to continuously improve your protocols?
- Have you never worked with microcarriers before and want to understand how to scale from T-flasks?
- Would AggreGuard™ work for your existing process? Or do you want to develop a new process for scaling up?

If you answered YES to any of the above, contact CellRev at enquiry@cellrev.co.uk to discuss solutions



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