



**CELONIC**  
BEYOND BIOMANUFACTURING

Consistently delivering outperforming  
cell lines leveraging extensive CLD expertise  
and innovative seeding platform

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**Camille Evenou**  
**BPI Boston 2019**



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We are a  
Biologics  
Development  
and Manufacturing  
Organization  
specialized in  
Mammalian  
Cell Lines

## **From Discovery to Market Supply**

Comprehensive GMP development  
and manufacturing for New Biological Entities  
and Biosimilars

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## **Global Clientele**

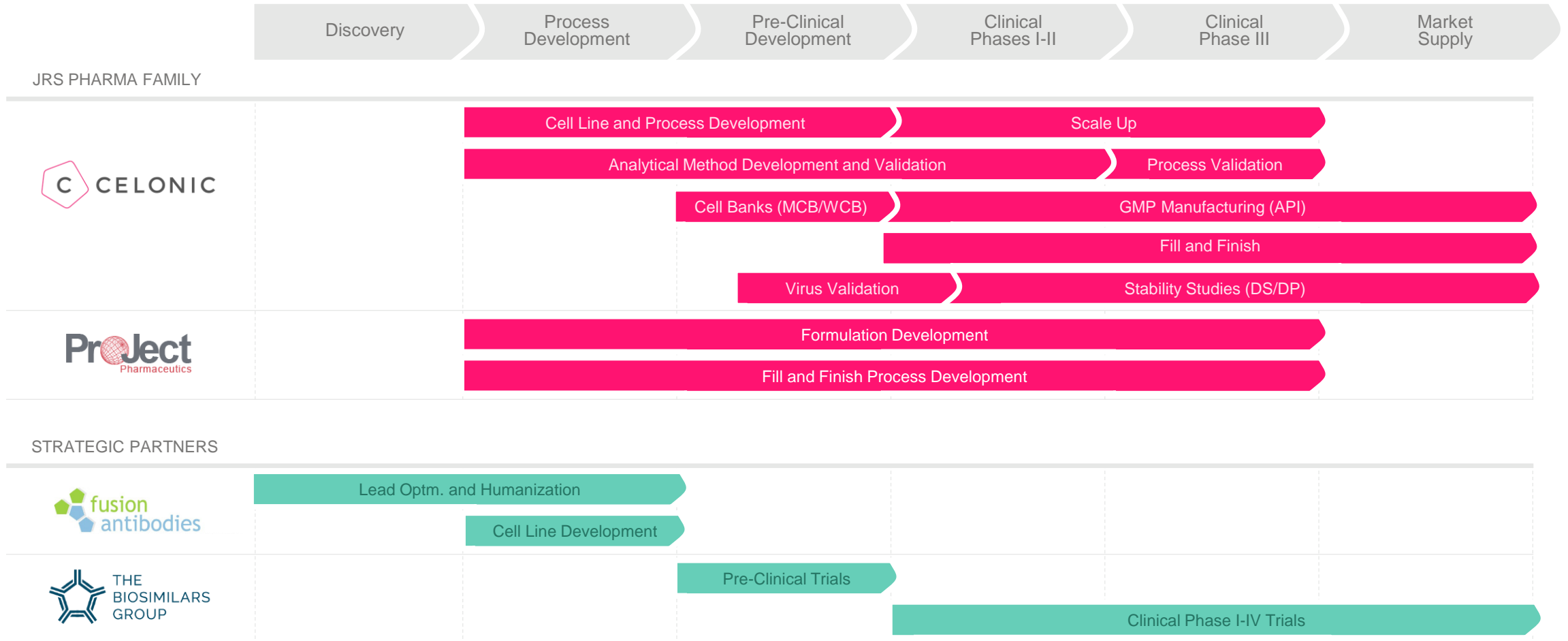
Innovative solutions that deliver commercial  
success for our customers

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## **Total Quality Commitment**

Empathy, Efficiency, Excellence

# YOUR TRUSTED PARTNER – FROM DISCOVERY TO MARKET SUPPLY



# ABOUT US

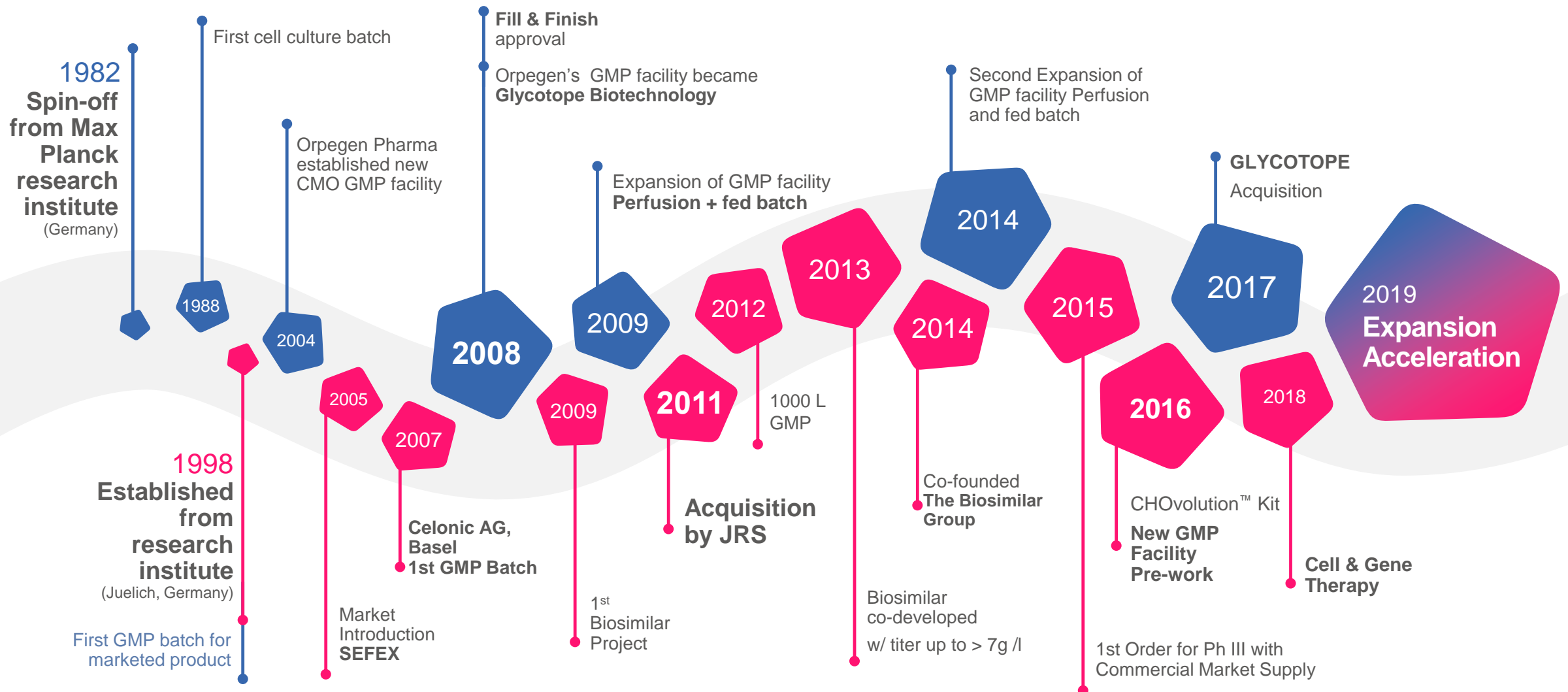
**Established** 1982  
**Employees** 290  
**CEO** Dr. Konstantin Matentzoglu  
**Ownership** Private, JRS Group, Germany

## LOCATIONS

- 1 **Basel**  
SWITZERLAND  
Development & GMP production  
**Employees: 117**
- 2 **Heidelberg**  
GERMANY  
GMP production  
**Employees: 173**



# OUR EVOLUTIONARY JOURNEY





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**HIGH  
PERFORMANCE  
CELL LINES**

# INNOVATIVE INDUSTRY-LEADING CELL EXPRESSION PLATFORMS

## CHOvolution™

Powered by Celonic's proprietary SEFEX® technology

Cell line based on CHO-K1 (non genetically modified CHO)

High productivity (up to > 7 g/l for mABs)

### SIMPLIFIED LICENSING MODEL

(e.g. no royalties from sales)

Cell line adapted to serum-free  
**EMA and FDA COMPLIANT MEDIA**

### HIGH SCALE-UP STABILITY

**GMP COMPLIANT**  
From R&D to market

Cell line in several  
**CLINICAL TRIALS in EU/US & Asia**

## GEX®

Human cells for fully-human glycosylation

Optimized for complex and sophisticated biopharmaceutical product

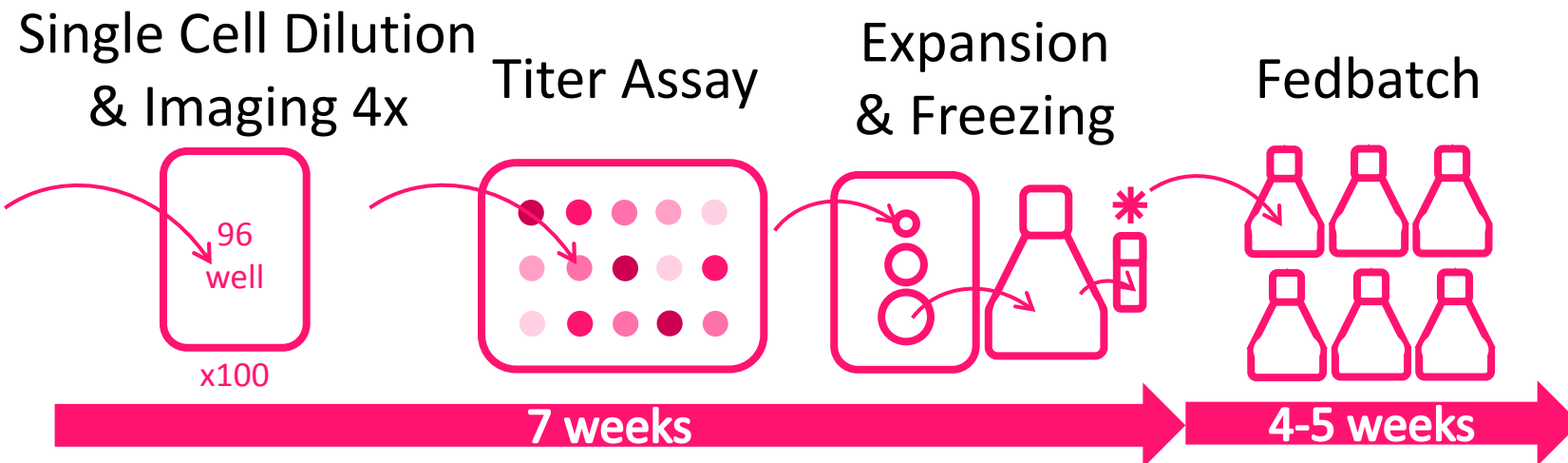
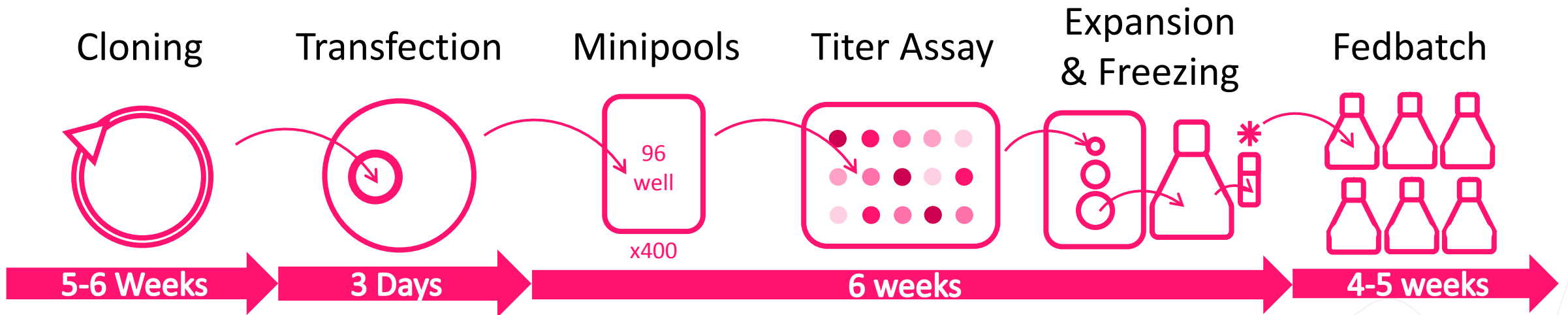
Stable product quality over full run time for R&D and/or GMP



**CLD CHO  
WORKFLOW  
OPTIMIZATION**

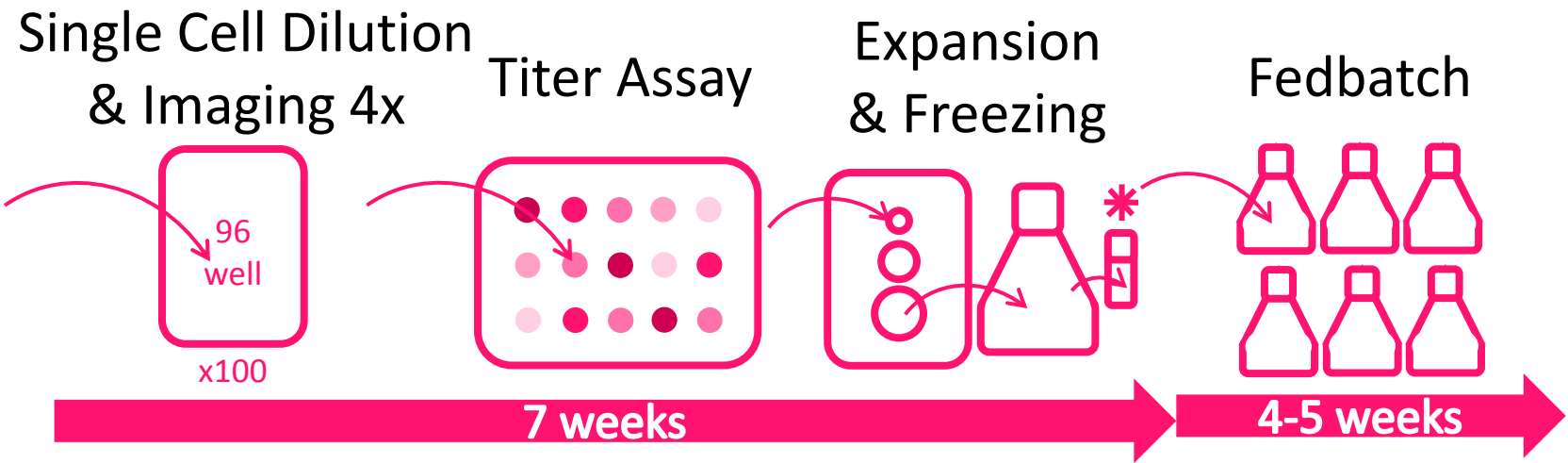
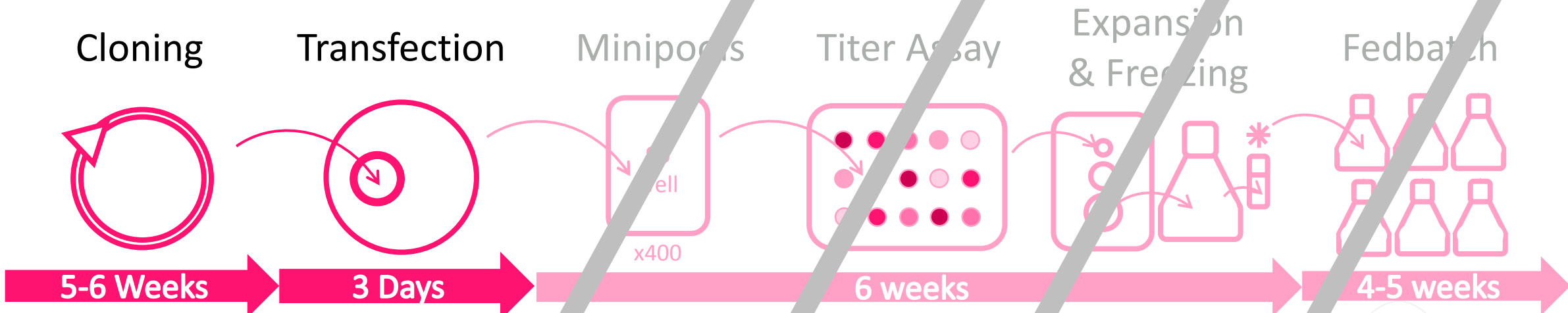


# Original CLD Minipool Workflow



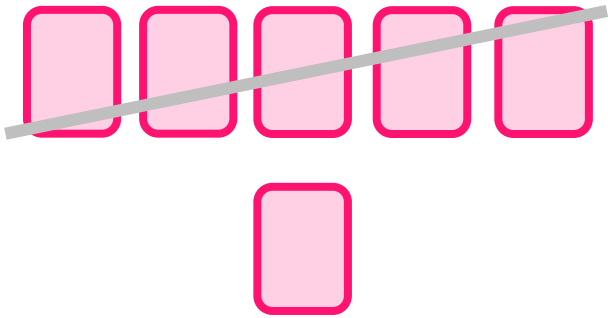
Up to 29 weeks  
Up to 500 plates

# Potential Improvement



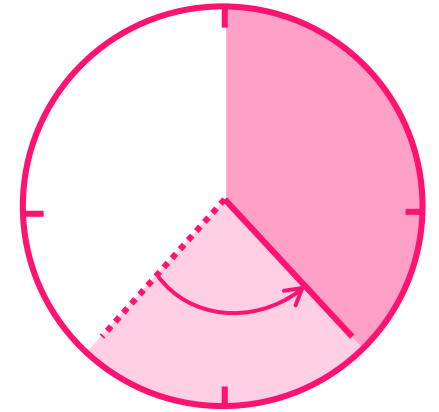
Could be 11 Weeks Faster!

# Improved Workflow Requirements



## Improved timelines for CLD

- More projects / year
- Streamlined CLD process
- Same enrichment properties

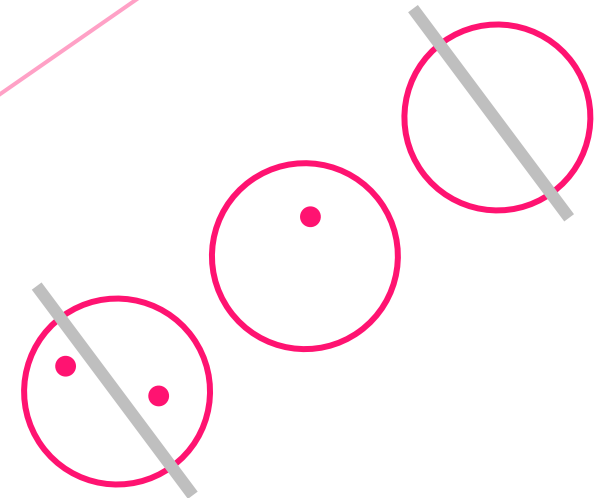


## Reduced amount of plates

- Same amount of clones
- Faster Handling
- More Imaging

## Proof of clonality

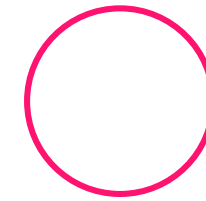
- Higher Quality Pictures
- Computer-assisted assessment of clonality
- Automated reports



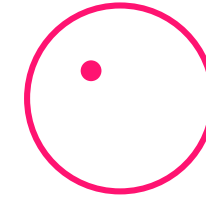
# Definitions

## Seeding Efficiency

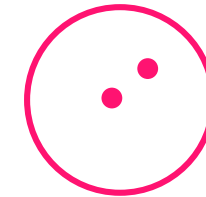
- %Wells seeded with a single cell per plate
- Depends on seeding method



Underseeded

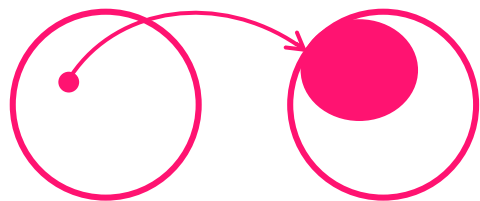


Clonal

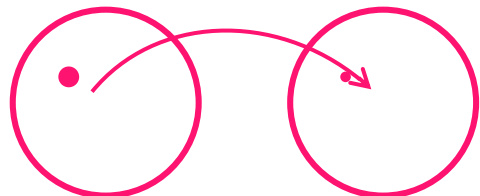


Overseeded

1 week after seeding



Outgrowth

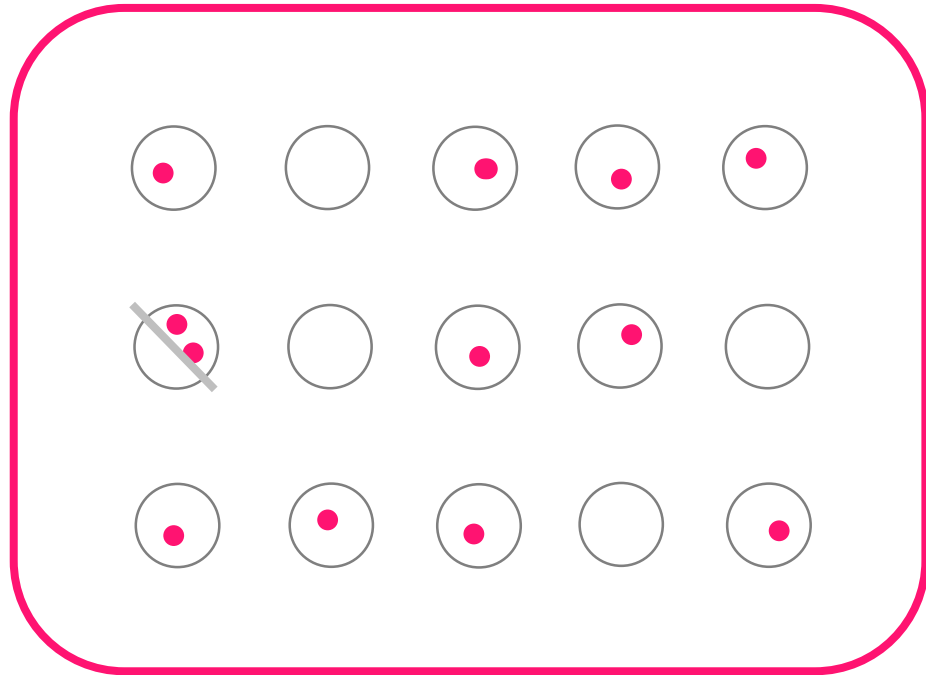


No outgrowth

## Outgrowth

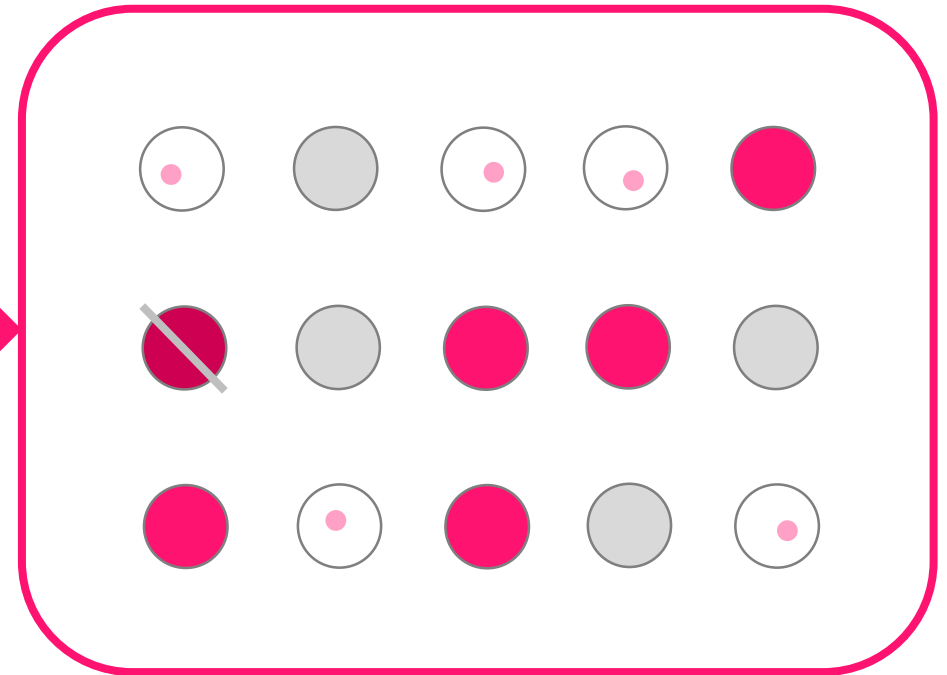
- %**Clonal** wells growing to colonies
- Depends on seeding method and medium

# Example



66% Seeding Efficiency  
10/15 wells seeded

2 weeks



50% Outgrowth  
5/10 potential clones

# Introducing FACS

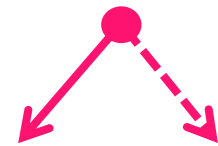
## Capabilities

- Analyse transfected pools
- Sort highest producers
- Single cell sorting

Analyse



Sort

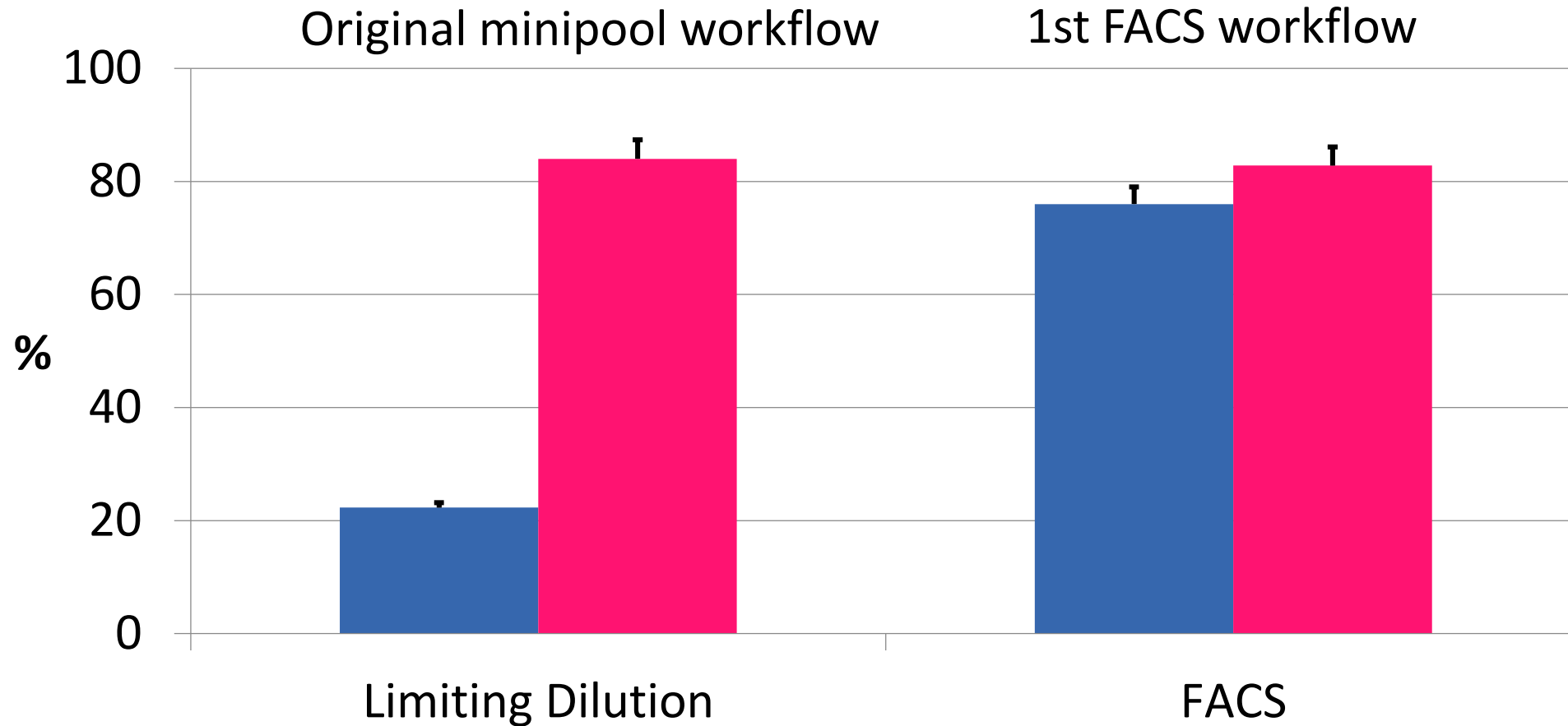


## Device

- FACS Aria™ Fusion
- Manufactured by Becton Dickinson



# FACS vs Limiting Dilution – GEX Cells (Human Perfusion Cell Line)



■ Seeding efficiency ■ Outgrowth

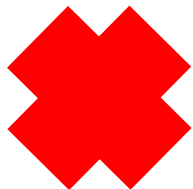
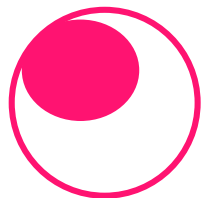
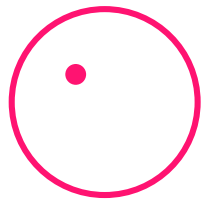
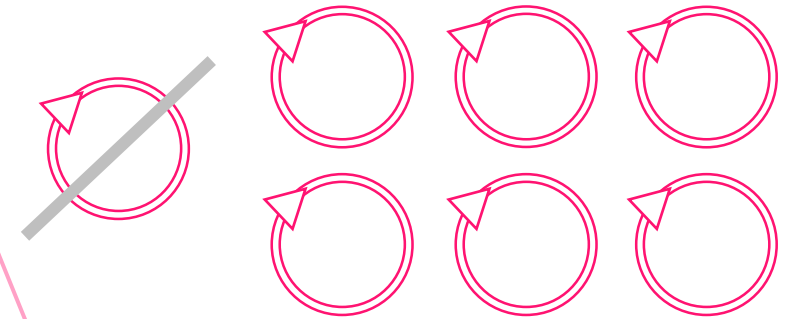
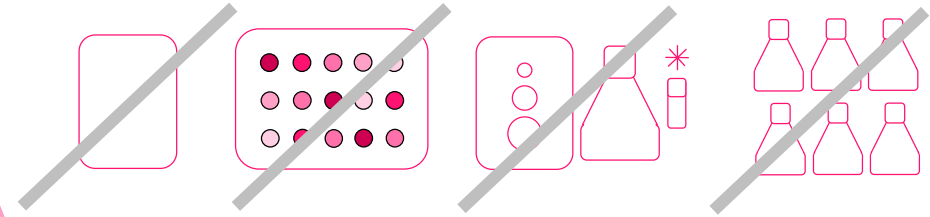
➔ Similar outgrowth, enhanced seeding efficiency

➔ Less plates needed for same amount of clones

# Introducing FACS

## Improvements

- No need for minipools
- Ability to screen several variations of the vector construct
- Works well with GEX cell line



## Shortcomings with CHO cells

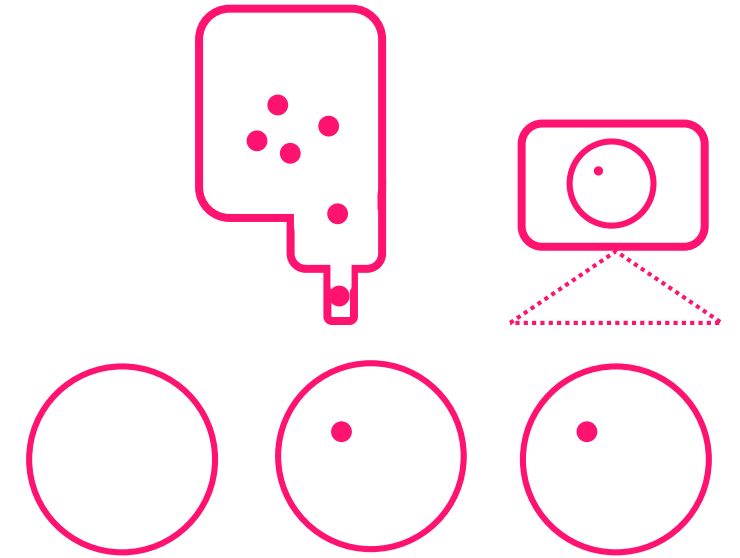
- Better seeding efficiency but lower outgrowth (much higher mortality than with Limiting Dilution)



# Introducing VIPS & Cell Metric

## Capabilities

- Gentle single cell seeding
- High resolution imaging
- Automated clonality reports

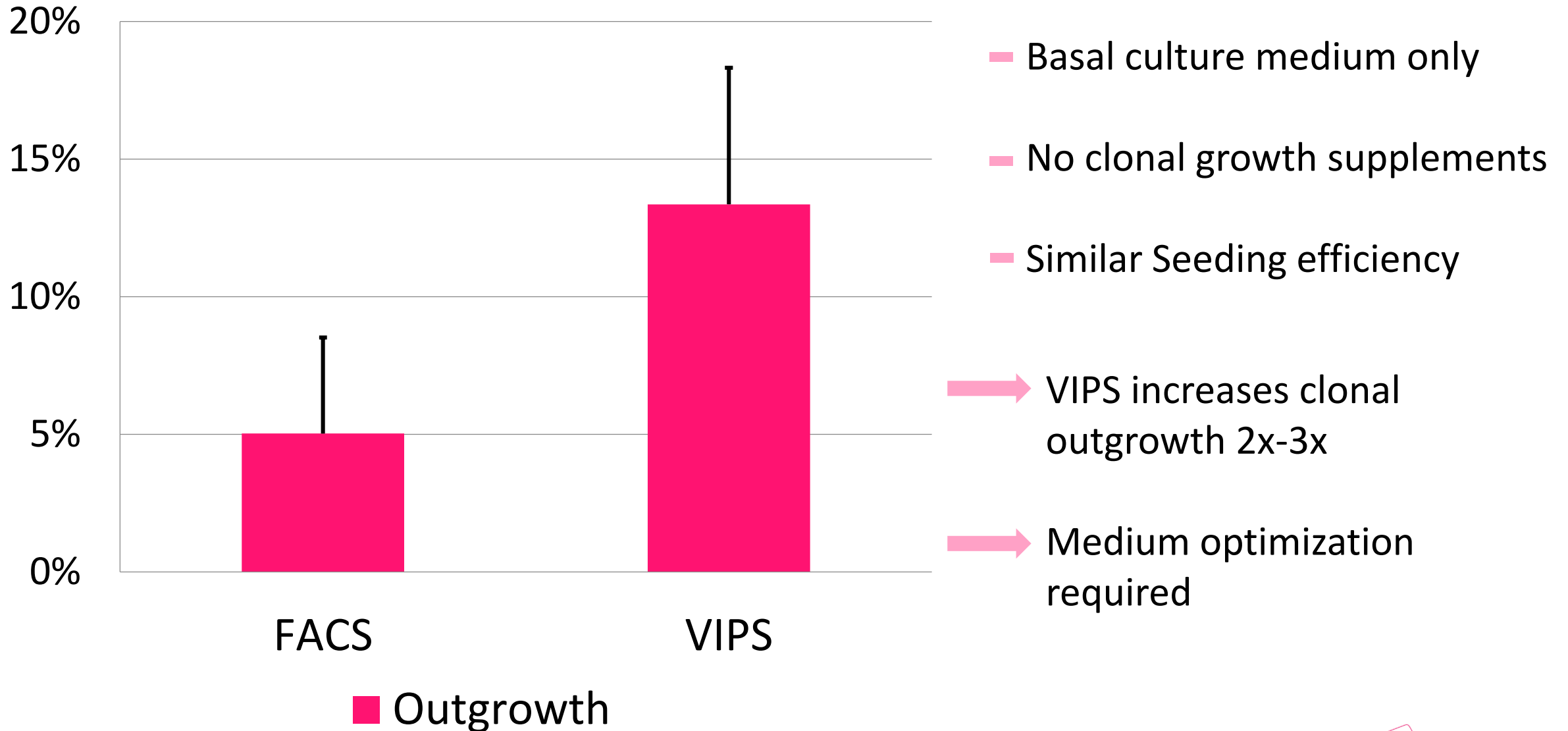


## Devices

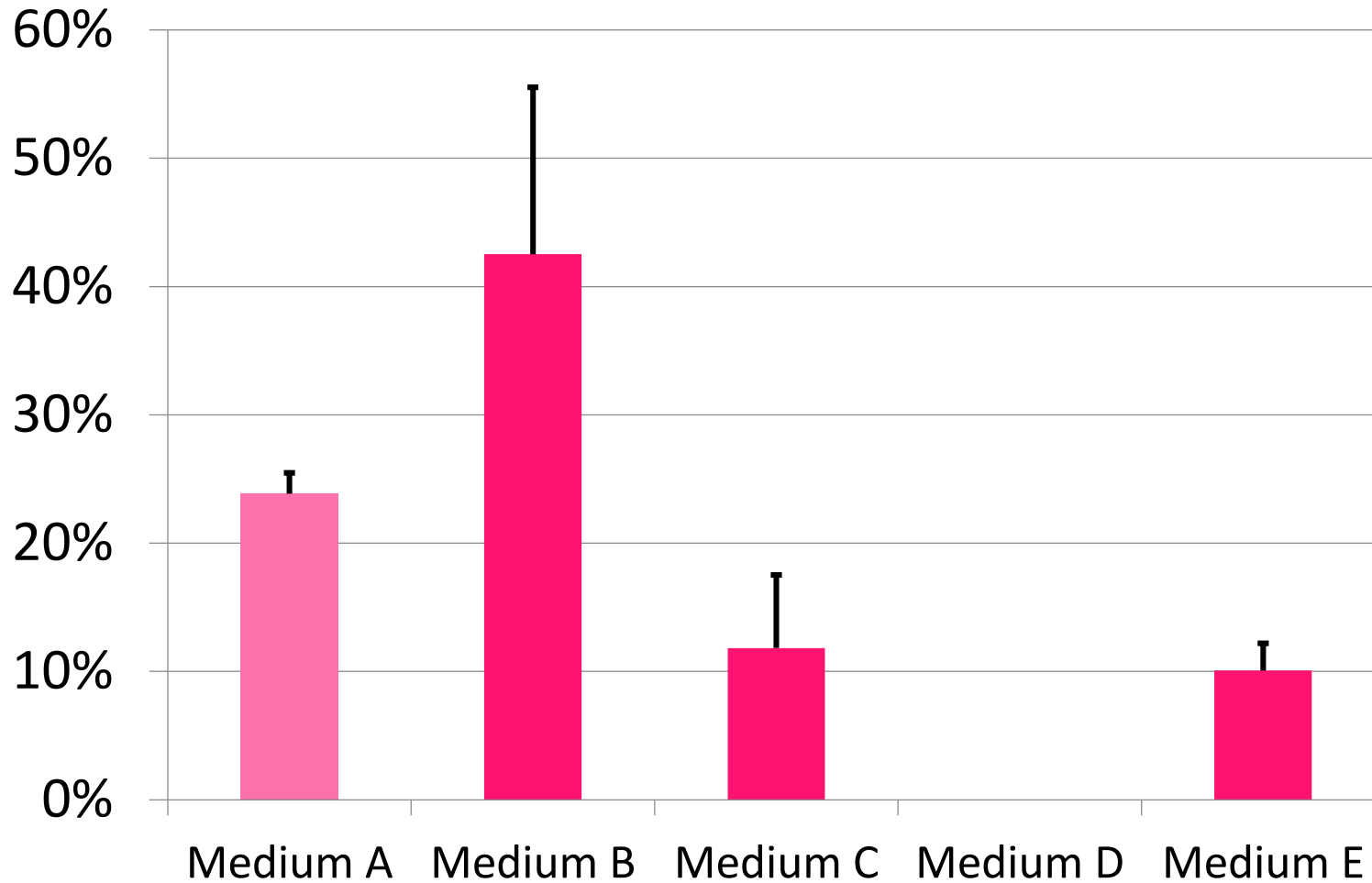
- VIPS™ – Verified In Situ Plate Seeding
- Cell Metric® Imager
- Manufactured by Solentim

**Solentim**  
Clarity in cell line development

# FACS Vs VIPS Outgrowth – CHO Cells



# Media Screening with VIPS– CHO Cells



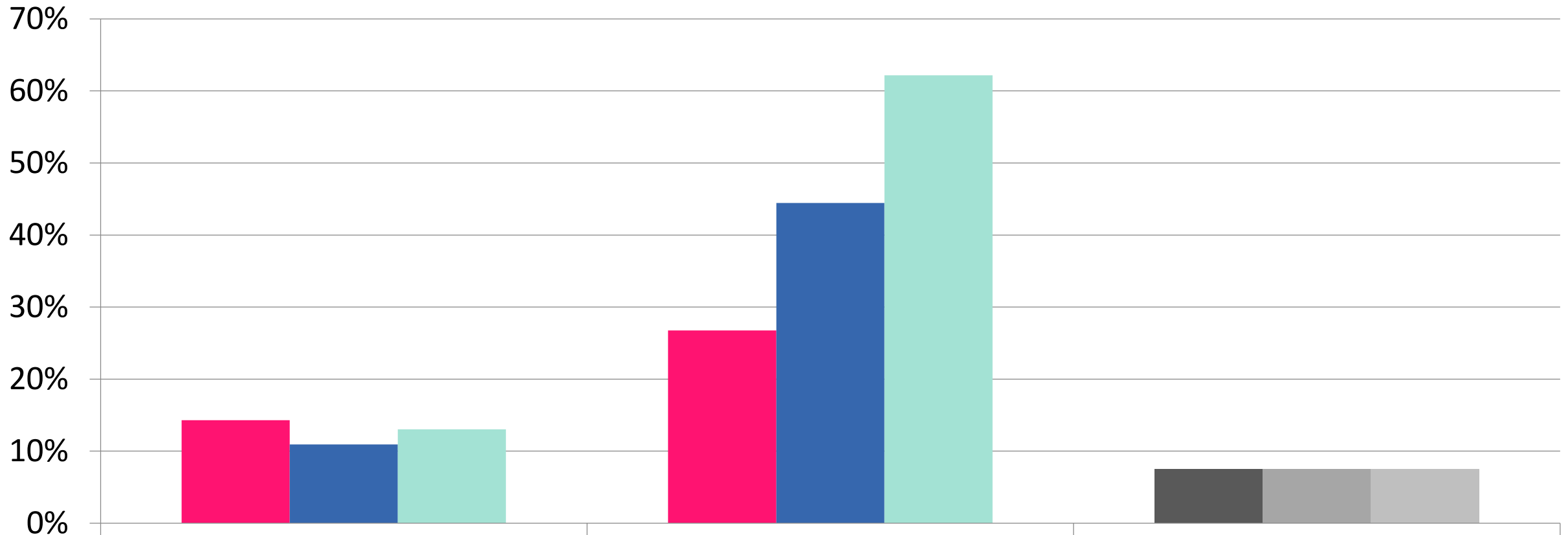
Original medium

Outgrowth

- Basal culture medium + 15 % conditioned medium
- No clonal growth supplements

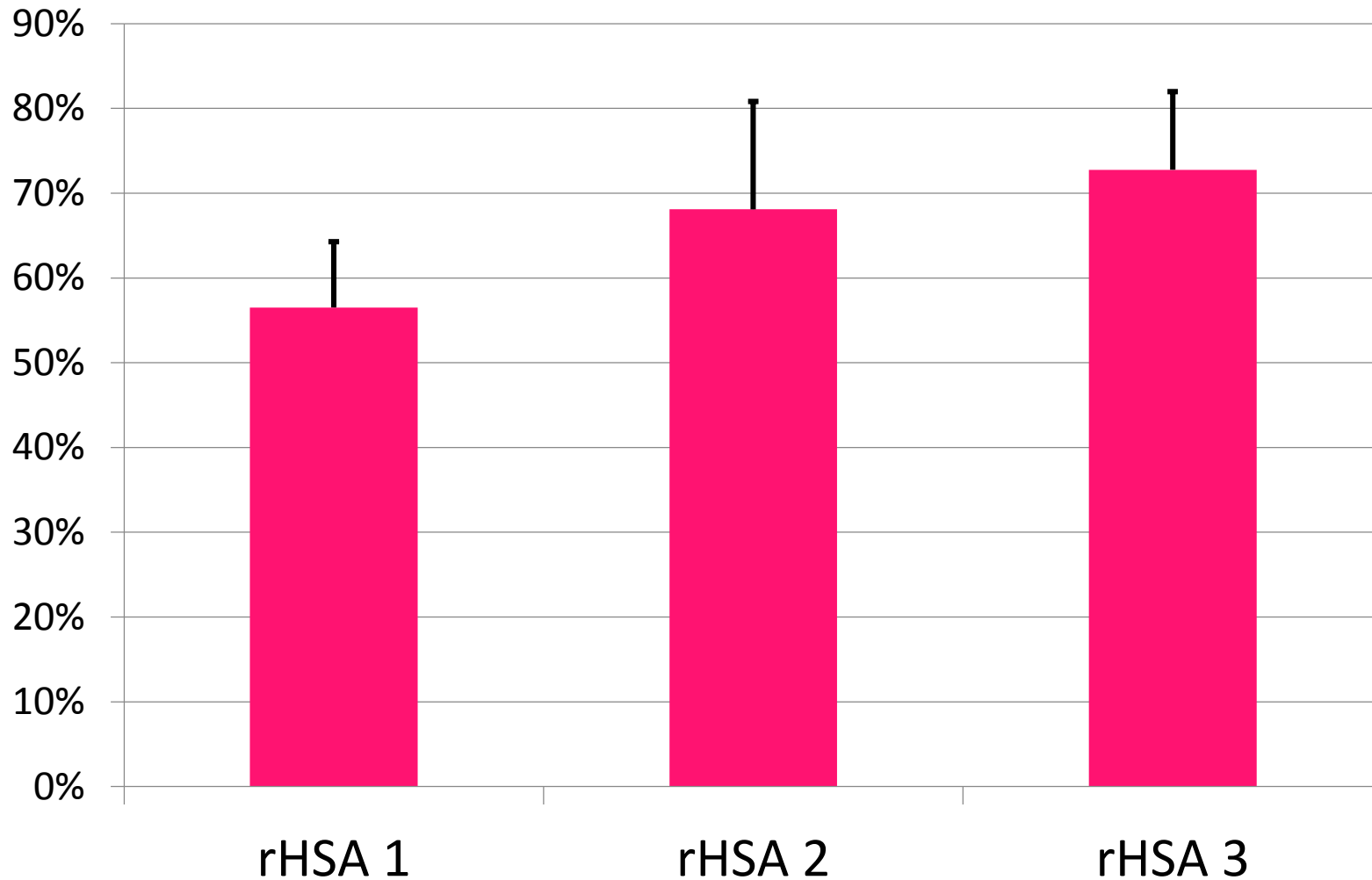
Medium B taken further

# Media Optimisation with VIPS – %HSA with CHO Cells



Outgrowth with ■ 0,5 ■ 1,5 ■ 2,5 g/L  
— No clonal growth supplements besides rHSA

# Media Optimisation – Different recombinant HSA

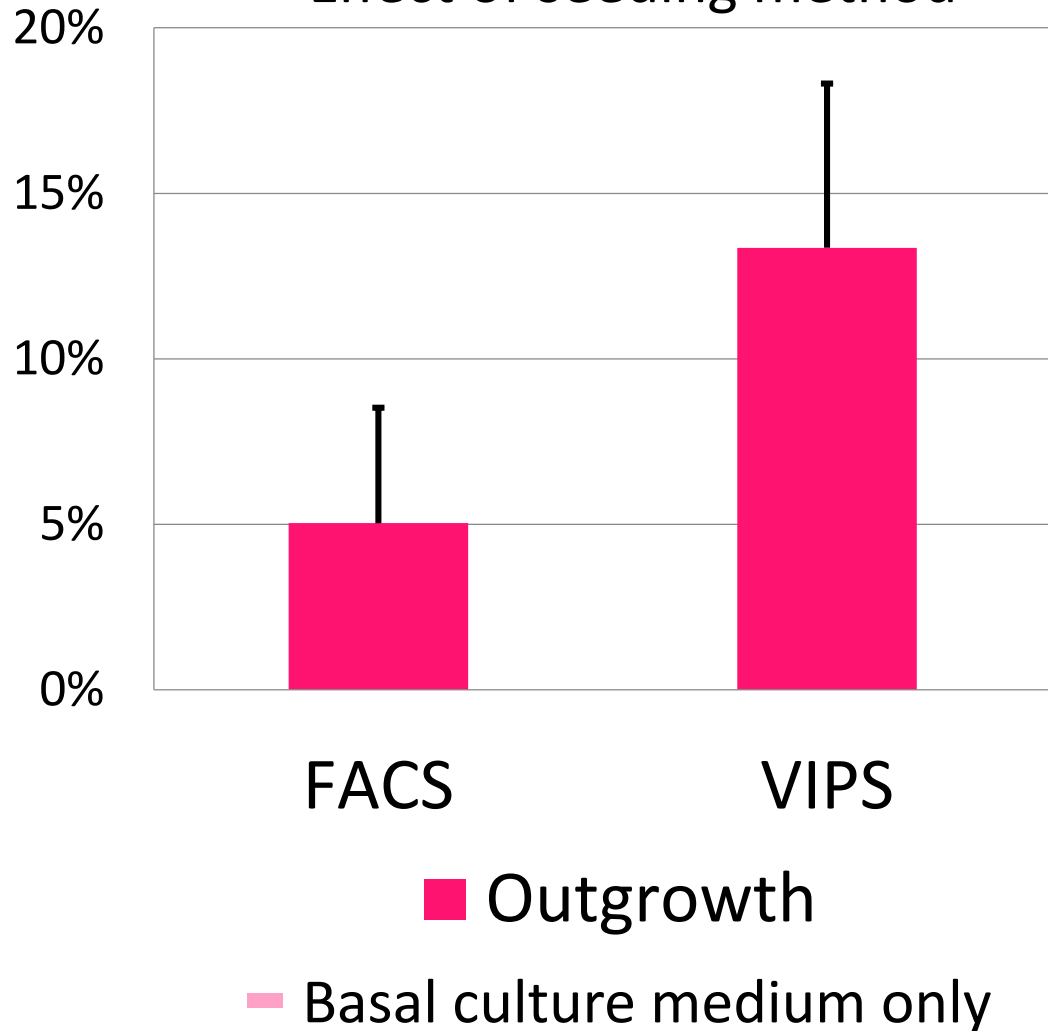


■ Outgrowth

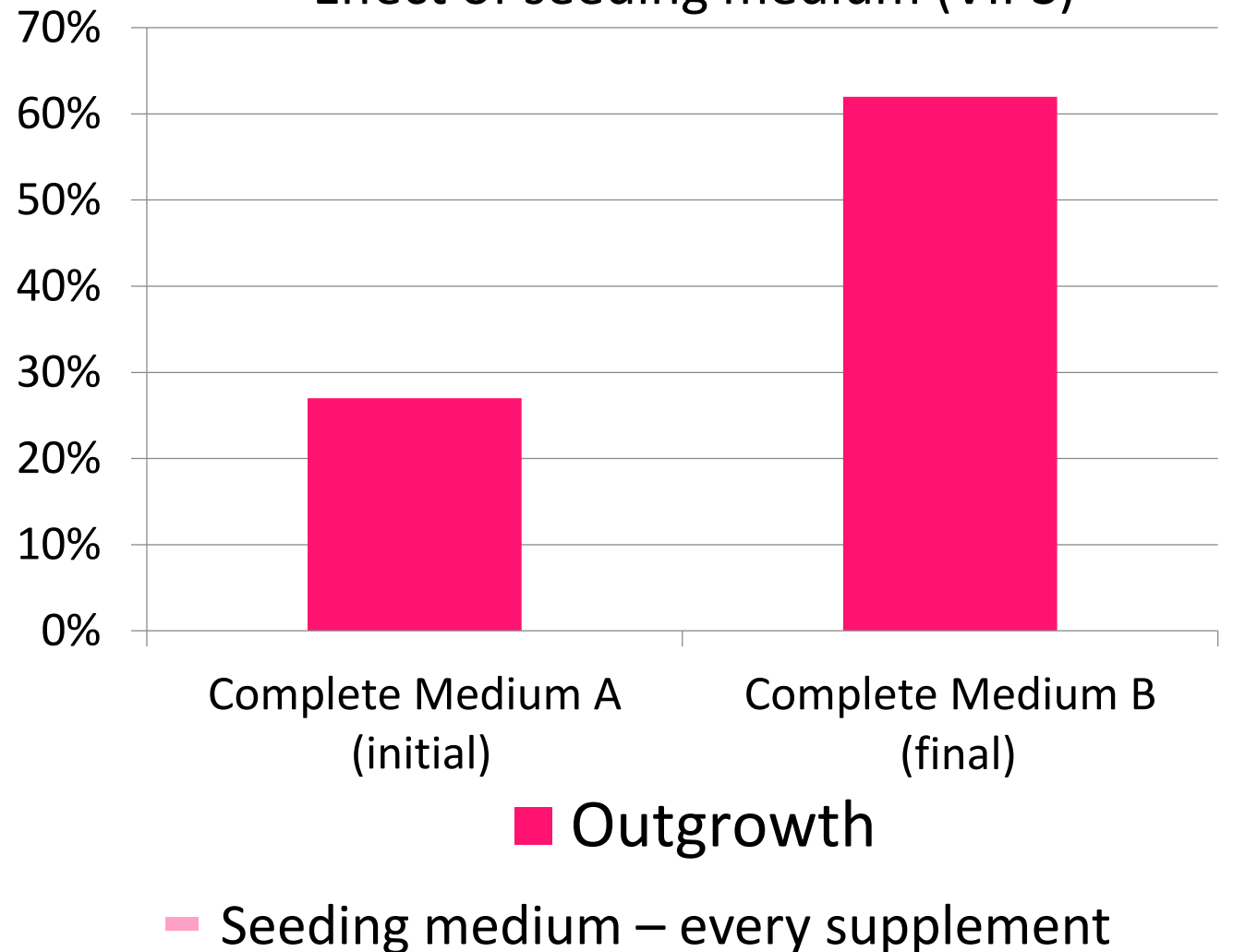
- Seeded via VIPS CHO cells
  - rHSA from different suppliers, different hosts
  - Full seeding medium
- Recombinant serums differ in their ability to support growth of clones

# Process Improvements – CHO Cells

Effect of seeding method



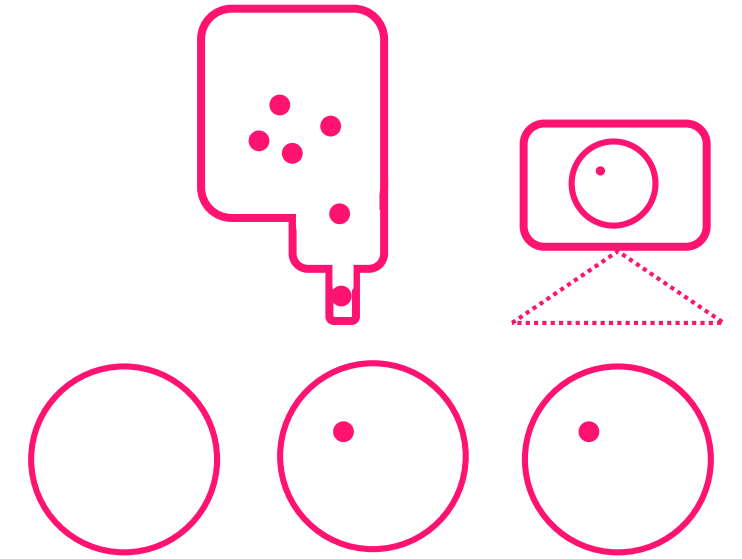
Effect of seeding medium (VIPS)



# Introducing VIPS & Cellmetric

## Capabilities

- Gentle single cell seeding
- High resolution imaging
- Automated clonality reports

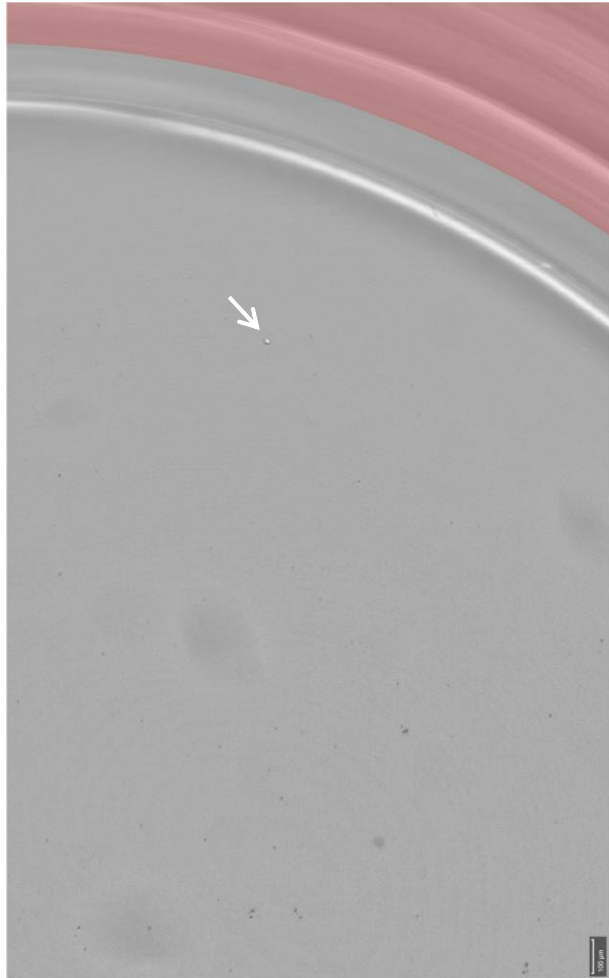


## Devices

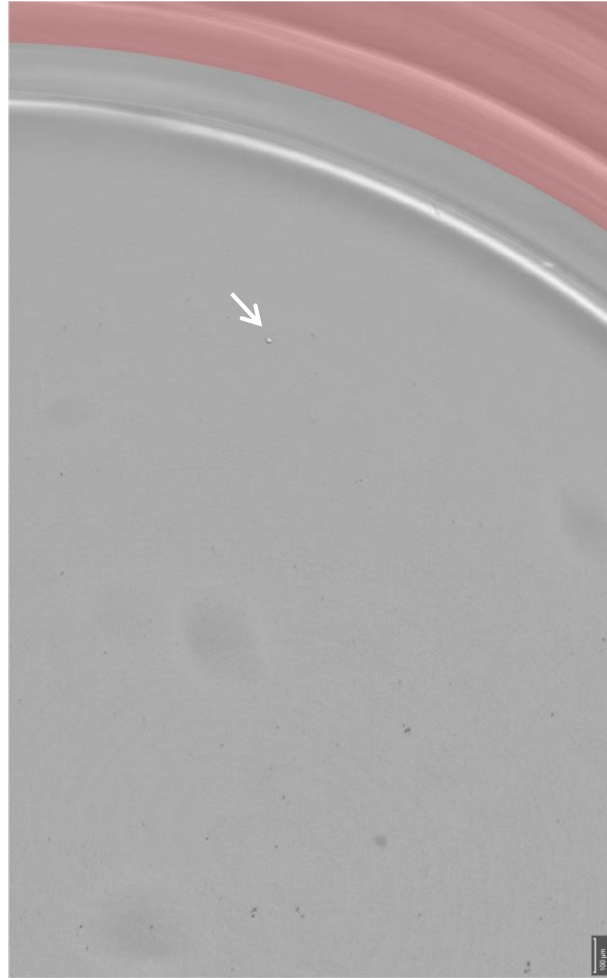
- VIPS – Verified In Situ Plate Seeding
- Cell Metric® Imager
- Manufactured by Solentim

**Solentim**  
Clarity in cell line development

# Assurance of Clonality – Previously (CSI)



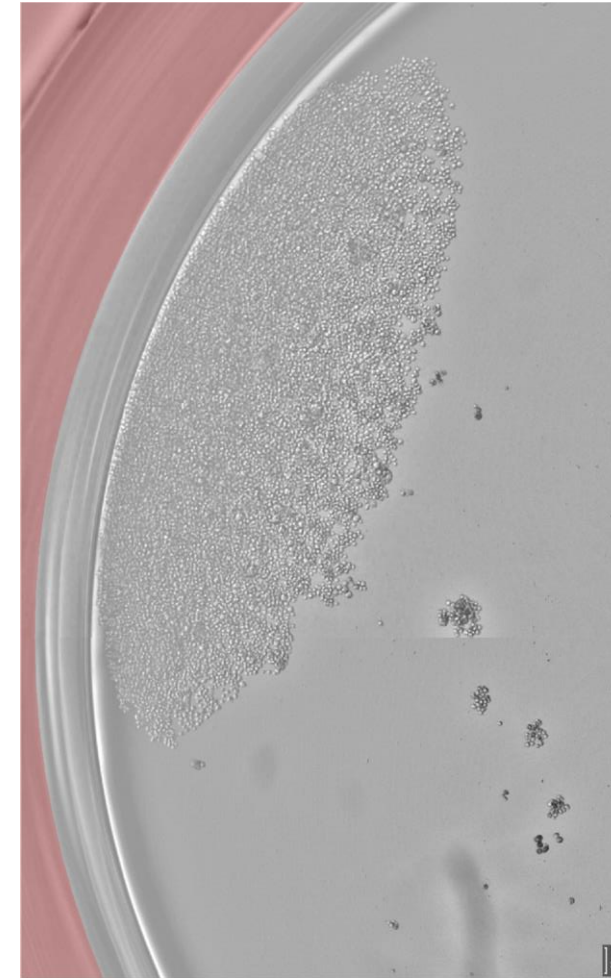
Day 0



Day 1



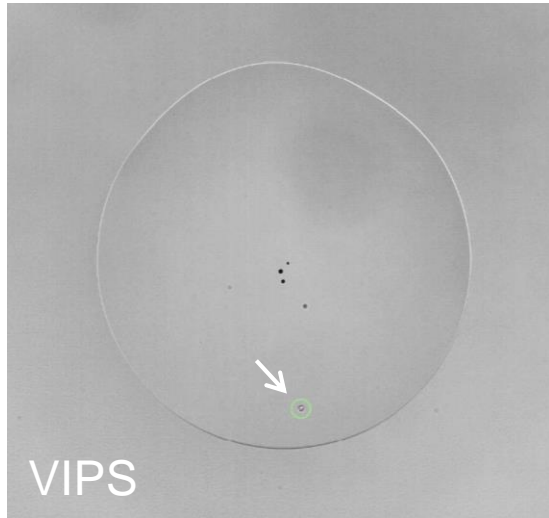
Day 7



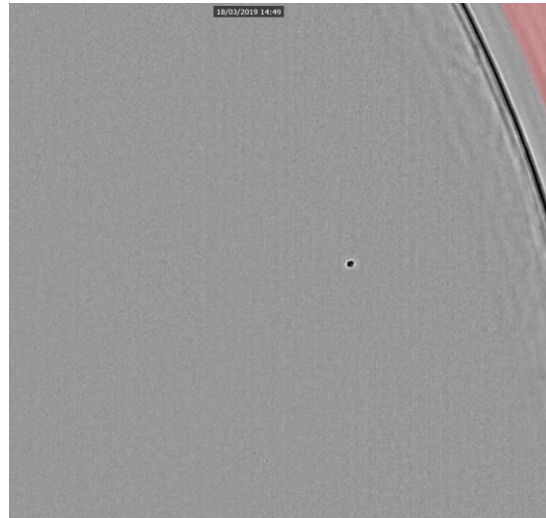
Day 12



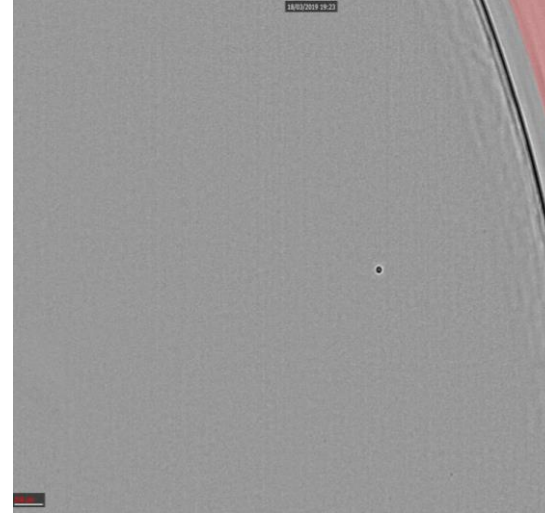
# Assurance of Clonality – Now (Solentim's Cell Metric<sup>®</sup>)



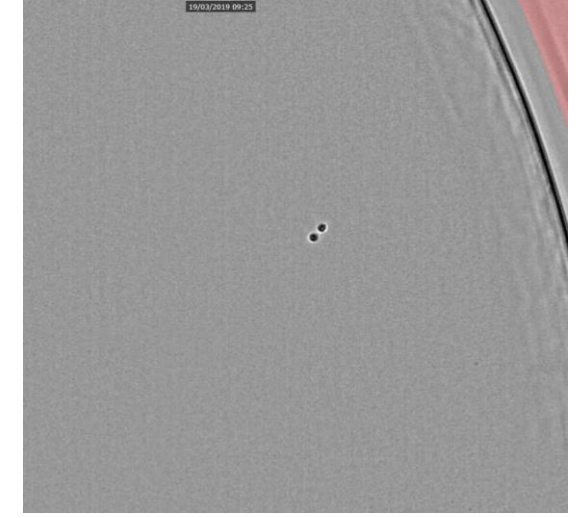
Day 0



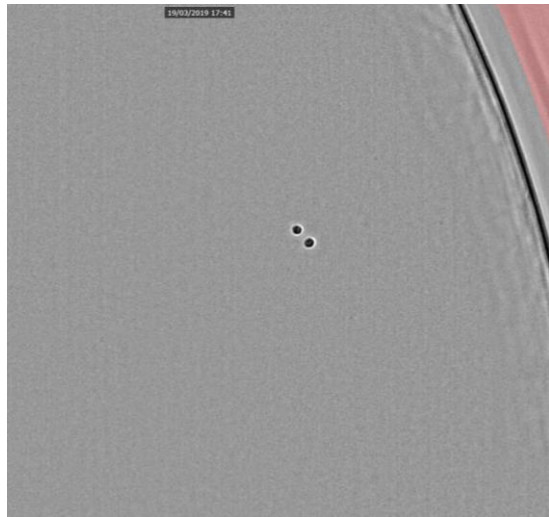
Day 0



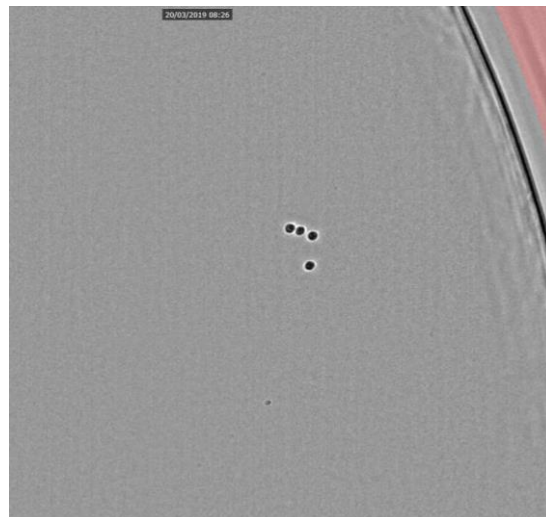
Day 0



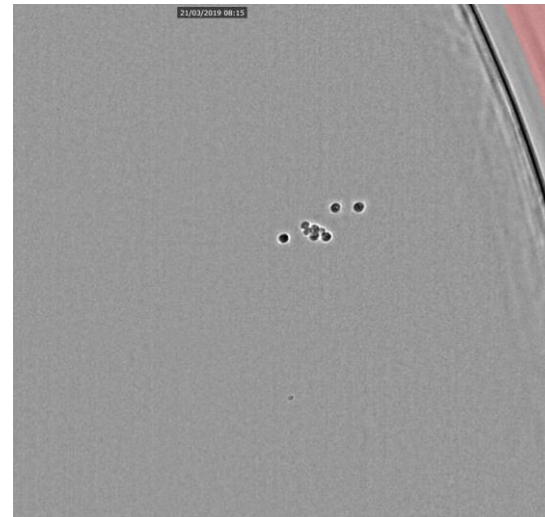
Day 1



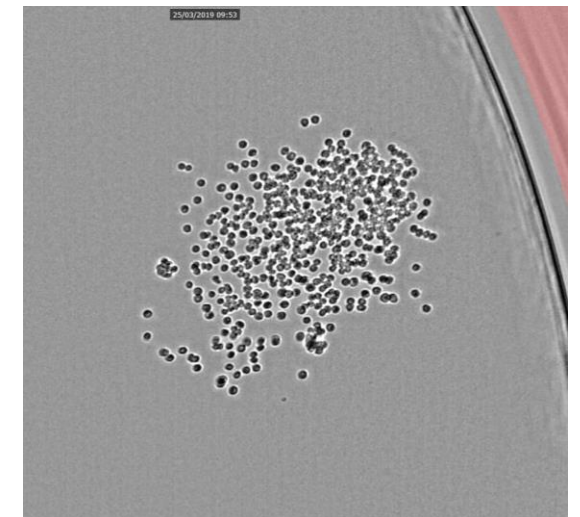
Day 1



Day 2

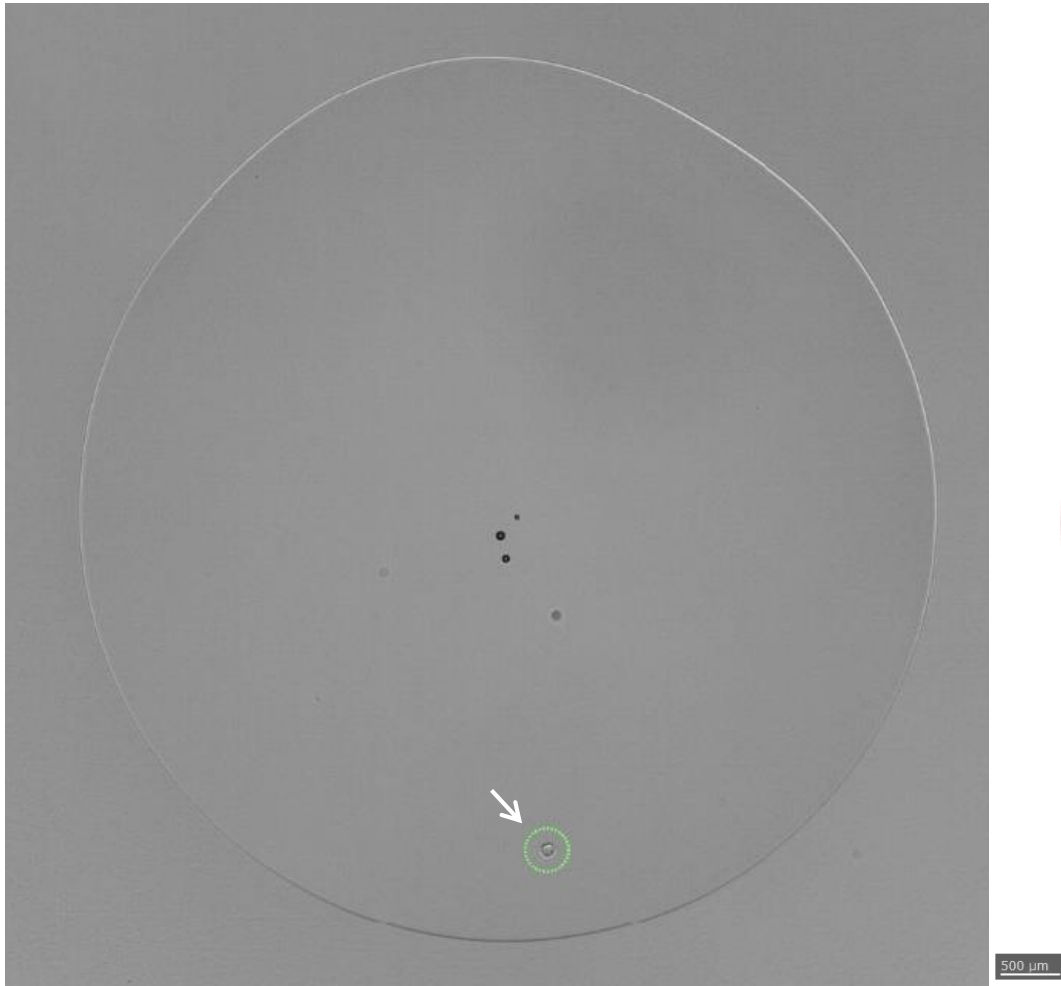


Day 3

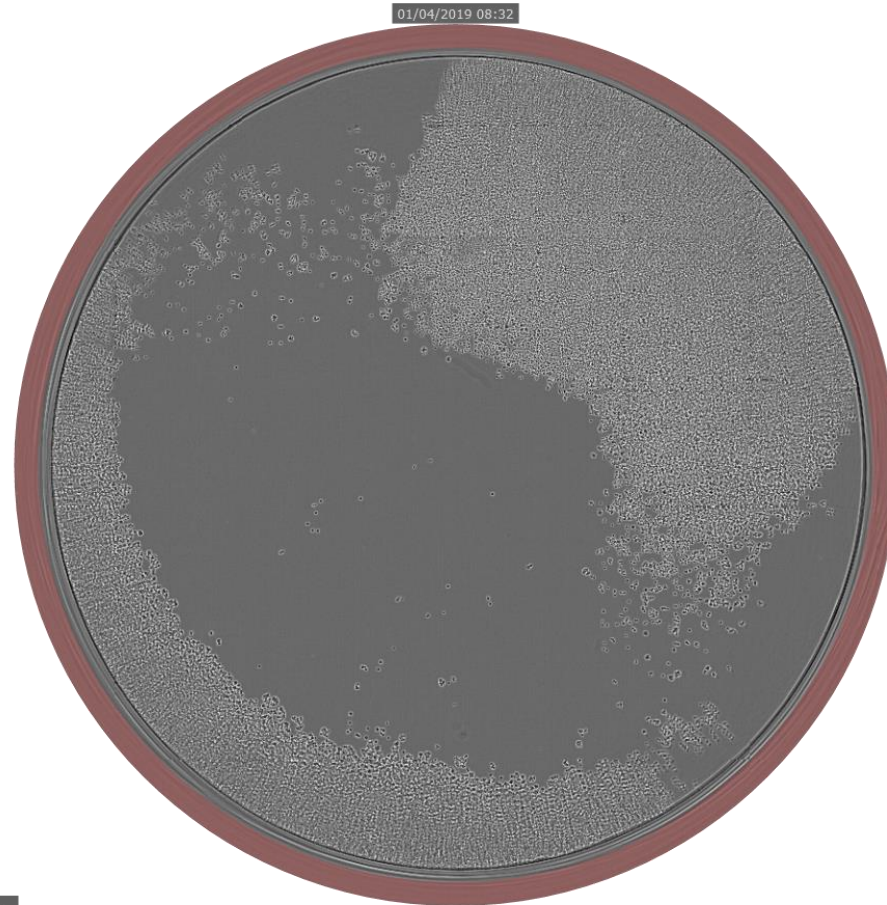


Day 7

# Assurance of Clonality – Now (via Solentim's Cell Metric®)



Day 0

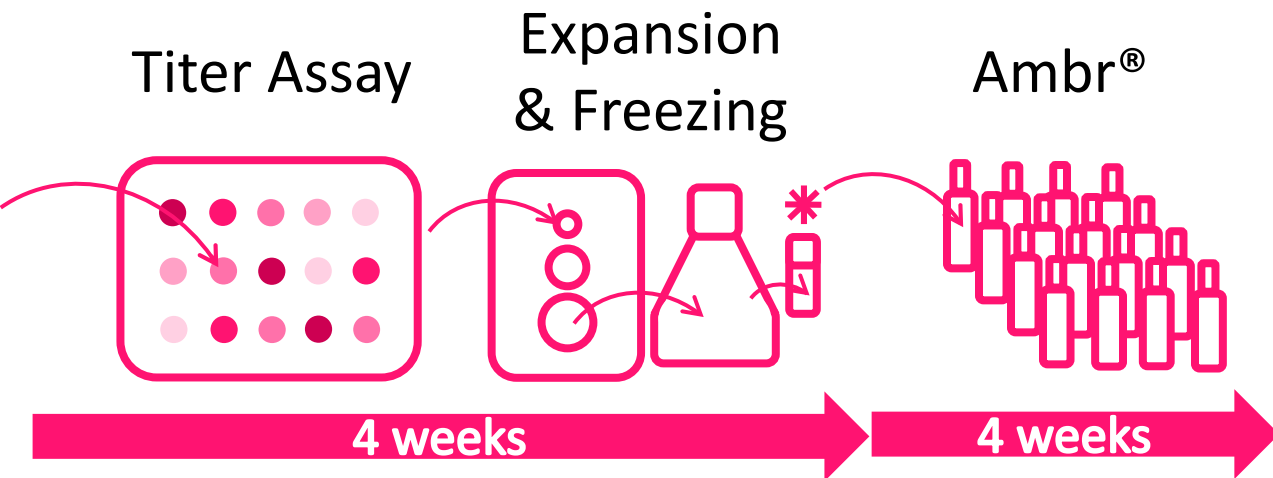
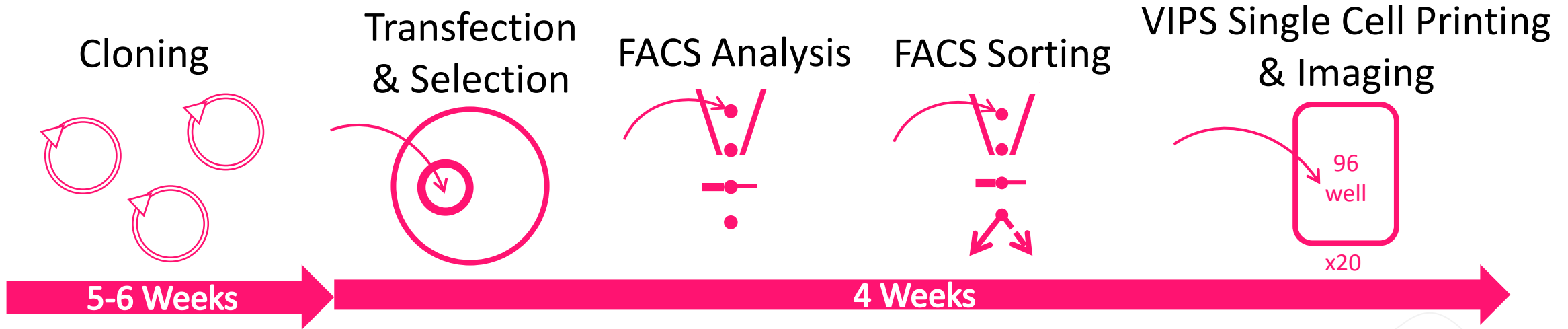


Day 12

- Automated report available
- Tracking of cells and particles/debris

➔ From single cell containing drop to full colony!

# Summary - New FACS & VIPS Workflow



From 29 to 17 weeks!  
From 500 to 20 plates!