# Role of Academia in Building Effective R&D Partnerships to Accelerate ATMPs

**Advanced Therapies – Opportunities and Challenges**
**14th November 2017**


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Athena SWAN Silver Award

UCL ENGINEERING
Change the world

The Queen's Anniversary Prizes for Higher and Further Education 2013

# UCL Biochemical Engineering

## Who we are

- **Founding** lab, 1st UK Department
- **Research excellence** in accelerating bioprocess design
  → 20 academic staff, 35 postdocs, 110 doctorate students, >80 UGs & MScs
- **90% staff** rated as **"World Leading (4*)" or "Internationally Excellent (3*)"** (REF2014)
- Attracted **>£85M research income** (research councils, TSB, industry)
- Raised **> £40M over** past 15 years for infrastructure and new facilities
- **Extensive industrial collaborations –** Centres of Excellence with GSK & Medimmune
- **3 spin-out companies** from the department
- **Pioneered education for industry**: MBI® training for industrialists and VISION Leadership programme
- **Awards**
  → **Athena SWAN Silver award** for gender equality
  → **Queens Anniversary Trust Award (2013)** for pioneering studies bioprocessing industry.

Athena SWAN Silver Award

The Queen's Anniversary Prizes for Higher and Further Education 2013

# Global Industrial Collaborations

Collaborated with >100 companies worldwide ranging from the international majors such as GSK, Eli Lilly and Merck through to new enterprises where our engineering input has often been key to the development of the business.

## Unparalleled industrial collaboration:

- > 25 partners for EPSRC Centre for Innovative Manufacturing
- 13 partners for Industrial Biotechnology programme
- > 40 partners for Industrial Doctoral Training Centre in Bioprocess Leadership
- **Centres of Excellence (CoE)** set-up with GSK and Medimmune
- Gates funding for Innovation in Vaccine Manufacturing for Global Markets - £14m over 5y
- > 35 partners for NEW **EPSRC Future Targeted Healthcare Manufacturing Hub** - £10M over 7y focusing on personalised and stratified medicines

# Role of academia in accelerating ATMPs

1. Creating academic and industrial partnerships for effective R&D platforms

2. Novel, translational research activities to:
   - Address fundamental biological/engineering challenges
   - De-risk industrial development and expedite commercial manufacture

3. Addressing the skills gap – undergraduate, postgraduate and industrial-level training programmes

# 1. Creating partnerships for effective R&D platforms

# Case study 1: ambr250® for production of adherent cells

- £250k InnovateUK KTP Project with Sartorius Stedim
- Identified need for effective small-scale models and enabling tools and technologies for ATMPs
- Develop a platform process for the production of anchorage-dependent cells in the ambr250® automated bioreactor platform

List and characteristics of investigated impellers

| Impellers | Power number |
|---|---|
| Elephant ear A | 2.069 |
| Elephant ear B | 0.811 |
| Elephant ear C | 1.370 |
| Elephant ear D | 0.613 |
| Naval propeller | 0.680 |
| Hydrofoil A | 0.376 |
| Hydrofoil B | 0.434 |
| Paddle | 5.325 |


**Physical Characterization**

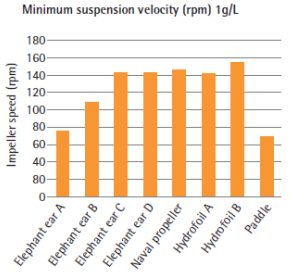
Experimental rig with DC motor and multi-meters

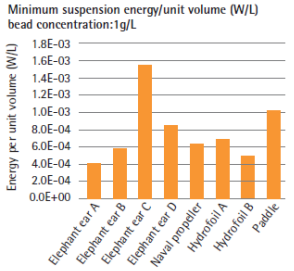
Special R&D ambr 250 high throughtput vessels

Determination of the impeller power number (Po)

Determination of NJS (minimum suspension speed) with Cytodex 1 microcarriers at different solid concentrations (1 to 5 g/L)

Microcarriers dyed with blue dye



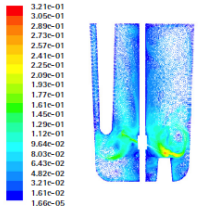




ambr ® 250 high throughput vessel

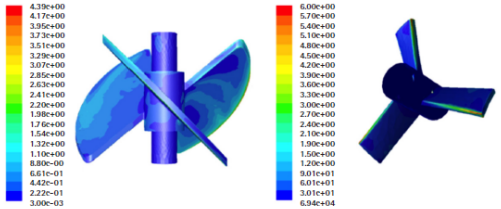
**Computational Characterization**

Eulerian-Eulerian CFD simulation, steady state, single liquid phase, various impellers, unbaffled and baffled vessel.

Analysing flow pattern, poor mixed zones and shear stress around the vessel.



Velocity flow pattern (m/s) from a CFD analysis of a Elephant ear vessel



Shear stress (Pa) on Elephant ear and Hydrofoil impellers at NJS

ambr ® 250 high throughput

**Biological Characterization**

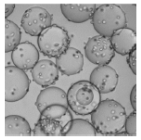
Elephant ear impeller at 115 rpm (1.5 W $m^{-3}$)

Vero cells

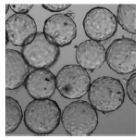
Cytodex 1 at 1 g/L concentration

ambr 250 high throughput 12 vessel system

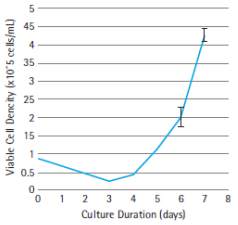
DO control, pH control, 5% $CO_2$ added, no sparging



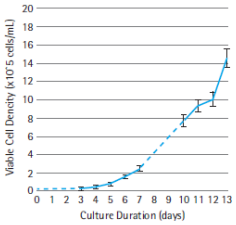
Vero cells on microcarriers, 2h after inoculation



Vero cells on microcarriers, day 7, reaching confluency




Vero cell D0 0.5 M/mL, cytodex 1 1g/L, batch culture, N=12

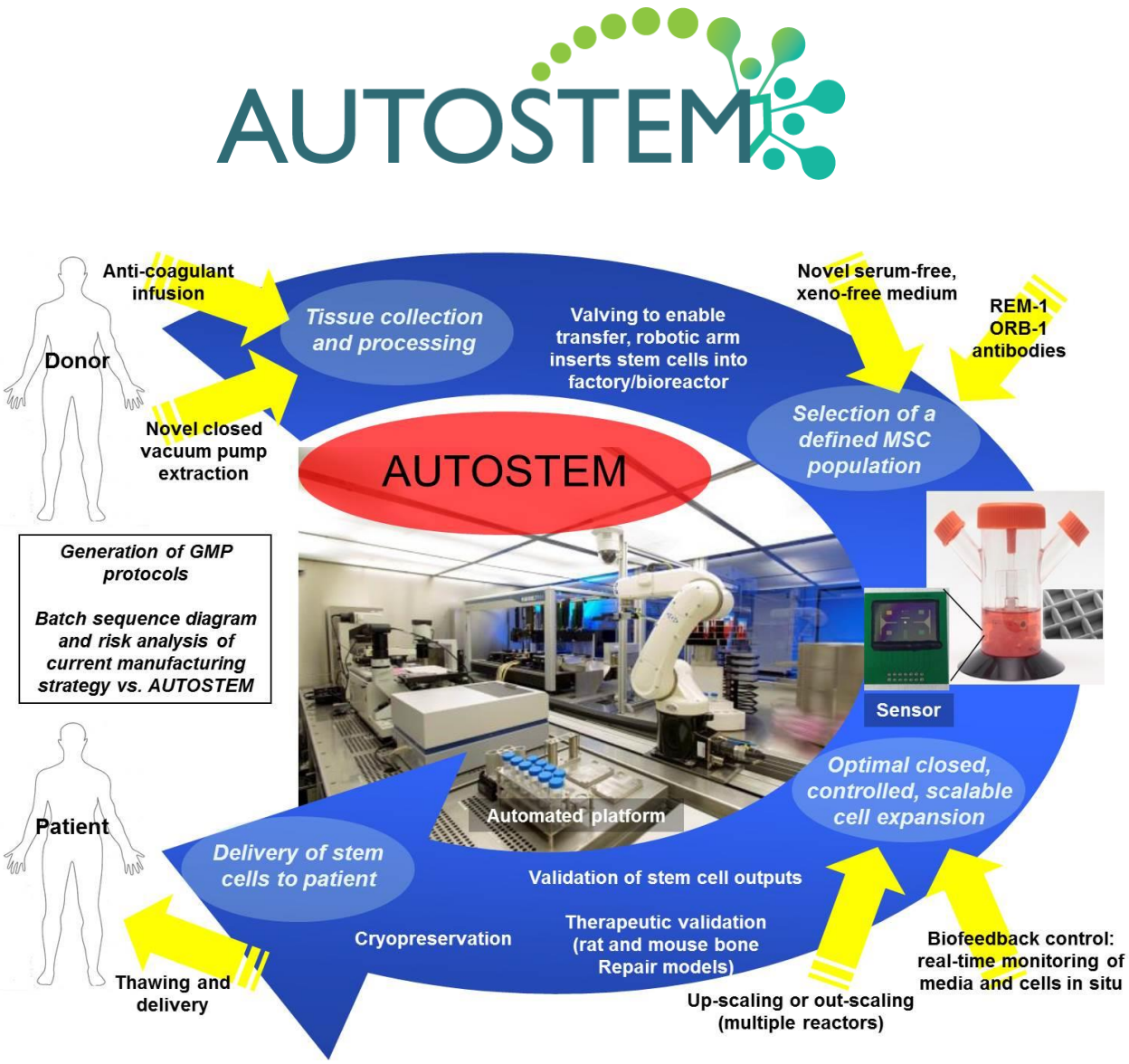



Vero cell D0 0.5 M/mL, cytodex 1: D0 1g/L, D4 2g/L, D8 4g/L, fed-batch culture, N=12

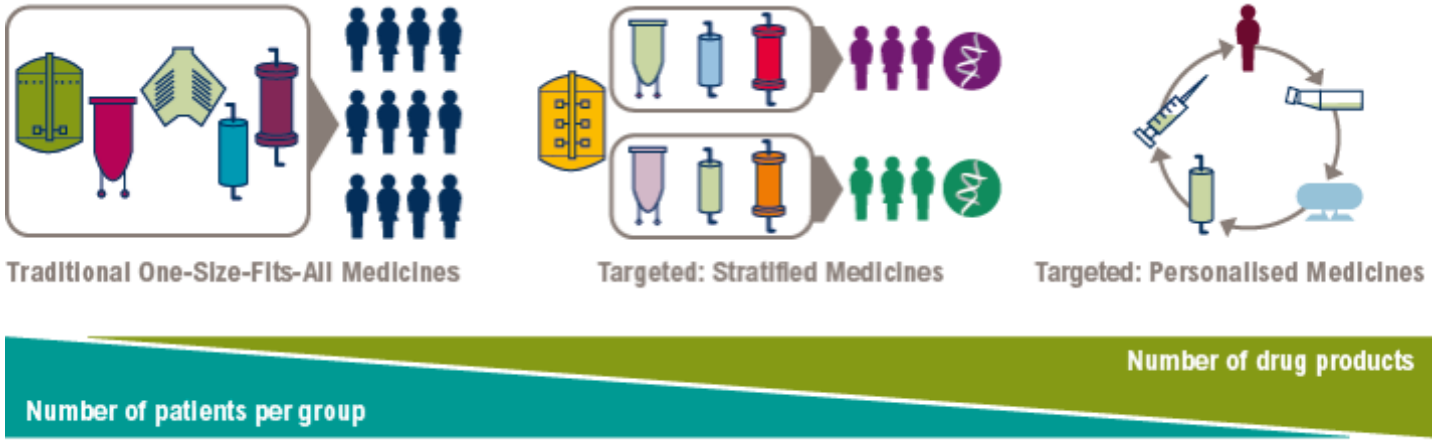
- Project led to development of a 'microcarrier vessel' which is now being produced and marketed by Sartorius alongside the traditional 'suspension vessel'

Innovate UK sartorius

# Case study 2: EU H2020: €6M AUTOSTEM Project



# Case study 3: Future Targeted Healthcare Manufacturing Hub




**Moving from "one-size-fits-all" to "targeted" medicines…**

**How can stratified biologics and personalised cell therapies achieve success in manufacturing and business?**

Director: Prof Nigel Titchener-Hooker Co-Directors: Profs Suzy Farid & Paul Dalby
Grant: £10m, 7 years
Hub: UCL Spokes: Imperial, Warwick, Manchester, Nottingham, Loughborough

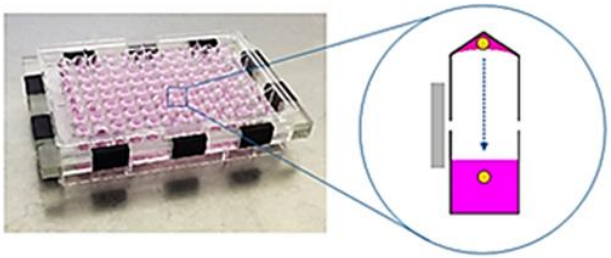
User Group. Companies: Albumedix, Allergan, AstraZeneca/MedImmune, Autolus, BIA Separations, BiologicB, BioPharm Services, DeltaDot, Eli Lilly, FloDesignSonics, Francis BioPharm Consulting, Fujifilm Diosynth, GSK, Lonza, Merck & Co., Merck KGaA, Novo Nordisk, Oxford BioMedica, Perceptive, Pall, Pfizer, Puridify, Purolite, Reneuron, Roche, Sartorius, Sutro Biopharma, Tillingbourne Consulting, TrakCel, UCB, Wyatt. Industry/Govt Associations: ABPI, BIA, KTN, LGC, MMIP, NIBSC. Translational Spokes: CGTC, CPI/NBMC

# 2. Novel translational research activities

# Novel Translational Research Activity – Process Development

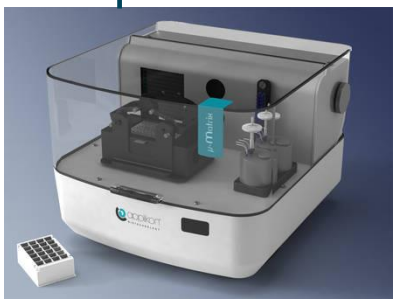
## Ultra-scale down cell culture platforms:

### Aggregates



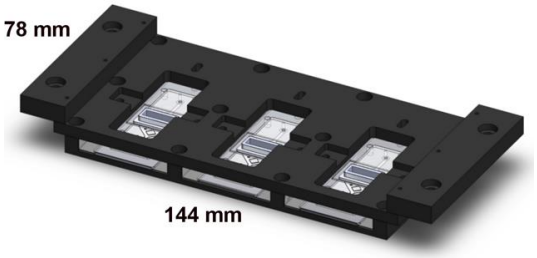
*Tang et al., Under review*

### Suspension



*Sharma et al., 2016*

### Attached




*Super et al., 2016; Jaccard et al., 2014a and 2014b; Macown et al., 2014; Reichen et al., 2013 and 2012*

## Cell culture environment improvements:

### Forces

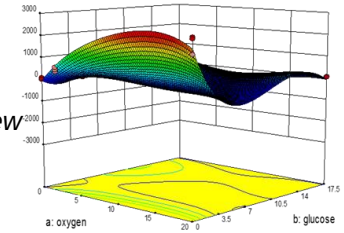
*Ali et al., 2015; Papantoniou et al., 2011; Hemsley et al., 2011; Veraitch et al., 2008; Pelling et al., 2007*

### Metabolic factors

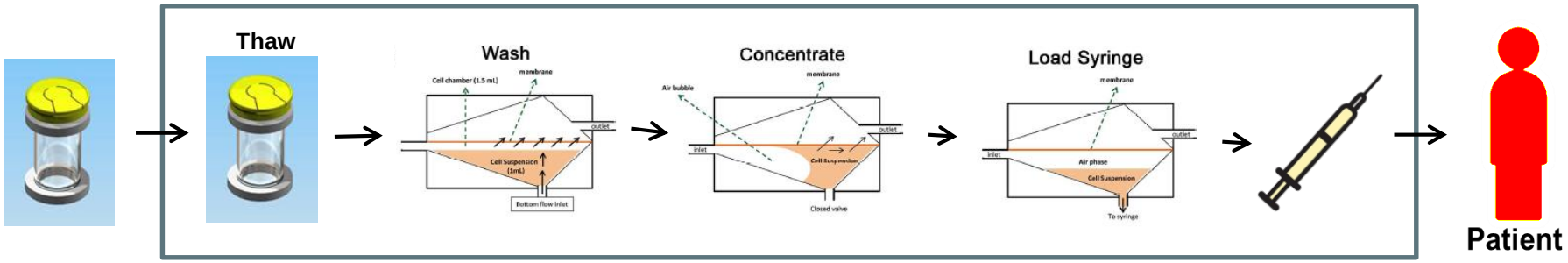
*Fynes et al., 2014; Mondragon-Teran et al., 2013, 2011 and 2009; Bae et al., 2012*

### Multivariate

*Khalife at al., Under Review*




## Closed point of care processing:




*Tostoes et al., 2016*

# Novel Translation Research Activity – Decisional Tools

- Systems approach to valuing biotech / cell therapy opportunities – process to enterprise
  - Cost-effective process and facility design
  - Capacity planning and factory floor scheduling
  - Portfolio management and process change management
  - Chemometrics for predicting root cause analysis and process control


- Typical questions addressed:
  - Most cost-effective cell culture and purification kits?
  - How do rankings change from clinical to commercial prodn?
  - Key process economic drivers?
  - Current technology gaps?
  - Process performance targets for desired reimbursement?
  - Process change impact on lifecycle costs?
  - Root cause of CQA deviations?
  - Predicting facility fit issues?

- Cell therapy case studies explored:
  - 2D v 3D culture for allogeneic MSC therapies (Simaria et al, 2014, P Chilima et al, 2016)
  - TFF v kSep for allogeneic MSC therapies (Hassan et al, 2015)
  - Process change costs switching to 3D culture (Hassan et al, 2016)
  - Autologous v allogenic CAR T-cell therapies (P Chilima et al, in prep)
  - Spontaneous v directed differentiation for RPE therapies (Jenkins et al, in prep)
  - Manual v automated processes for iPSCs for drug discovery (Jenkins et al, 2015)
  - Centralised v decentralised manufacture v GMP-in-a-box (P Chilima et al, in prep)

Industrial collaborators include: Pfizer, GSK, Lonza, Pall, Celgene, Autolus, eXmoor

# 3. Addressing the skills gap

# Addressing the skills gap

- Biochemical Engineering BEng, MEng and MSc programmes offered with a distinct focus on ATMPs

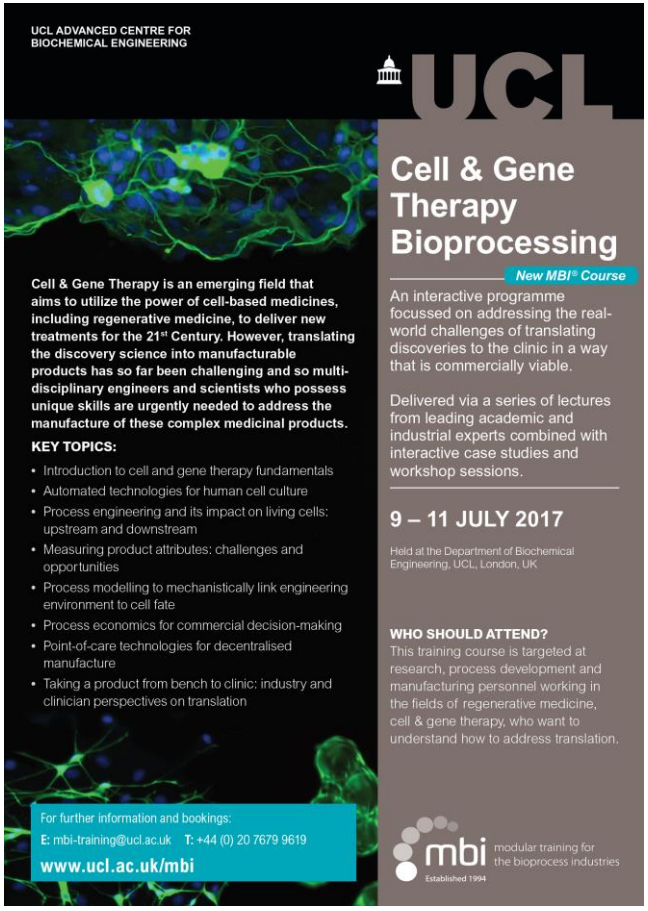
- Doctorate-level training
  - EngD Bioprocess Engineering Leadership


- Modular training for the bioprocess industries (MBI)
  - 700 individuals from 200 companies since the start of the programme in 1994

mbi modular training for the bioprocess industries

# UCL MBI® Cell & Gene Therapy Bioprocessing Course

## NEW Cell and Gene Therapy Bioprocessing MBI®
## 9 – 11 July 2018




- **MBI Course on Cell and Gene Therapy Bioprocessing**
- **Key Topics:**
  - Automated technologies for human cell culture
  - Process engineering and modelling
  - Point-of-care technologies for decentralised manufacture
  - Taking a product from bench to clinic: industry and clinical perspectives on translation
- **Who should attend?**
  - Targeted at Executive Personnel as well as those in research, process development and manufacturing activities for regenerative medicine, cell & gene therapies
- **Course overview:**
  - Translationally-focused, interactive workshops & case-studies

mbi modular training for the bioprocess industries
Established 1994

**www.ucl.ac.uk/mbi**

2014 UCL Life Learning Enterprise Award for CPD & Short Courses
2012 IChemE Award for Training Innovation

Thank you…

# ANY QUESTIONS?

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