Future Targeted Healthcare Manufacturing Hub: Next-generation biomanufacturing solutions to enable precision medicine

Suzanne S. Farid  PhD CEng FIChemE
Professor of Bioprocess Systems Engineering
Co-Director Future Targeted Healthcare Manufacturing Hub
UCL Biochemical Engineering  s.farid@ucl.ac.uk

16th Annual bioProcessUK Conference, Liverpool, Nov 26-28 2019
Suzy Farid: UCL Decisional Tools Research

- Professor of Bioprocess Systems Engineering CEng FIChemE
- Co-Director, Future Targeted Healthcare Manufacturing Hub
- Deputy Head of Department (Education)
- Leads research on “Bioprocess Decisional Tools”:
  - Cost-effective bioprocess design under uncertainty
  - Capacity planning, R&D portfolio management, risk-reward analysis
  - Predictive datamining, chemometrics
  - Applications to antibodies, cell/gene therapies, vaccines
- Director, UCL-AstraZeneca Centre of Excellence (2014 – present)
- Fellow of the Institution of Chemical Engineers (FIChemE)
- Member, BIA Manufacturing Advisory Committee
- Member, ISCT Business Models and Investment Committee
- Conference Chair, Recovery of Biological Products Conference (2020)
- Conference Chair, ECI Integrated Continuous Biomanufacturing (2015, 2017)
- Steering Committee, ECI Integrated Continuous Biomanufacturing (2019)
- Organizing Committee, ECI Advancing Manufacture of Cell & Gene Therapies (2019)

Industrial collaborators include: AstraZeneca/MedImmune, Pfizer, GSK, Bayer, Lilly, Lonza, UCB, CPI, Pall, GE, Ipsen, Allergan, Sutro Biopharma, Autolus, Oxford Biomedica
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, 2017-2024
Hub: UCL  Spokes: Imperial, Warwick, Manchester, Nottingham, Loughborough
User Steering Committee:


Industry/Govt Associations, Charities: ABB, BIA, Innovate UK, Invest NI, MMIP, NIBSC, Translational Spokes: CAPI, CPI
Targeted Healthcare Supply Challenges

Traditional One-Size-Fits-All Medicines

Targeted: Stratified Medicines

Targeted: Personalised Medicines

Stratified protein therapies
Manufacturing & Supply Chain challenges:
- Genomic screening of patients
- Diagnostic-driven administration
- Bespoke drug combinations
- Bespoke doses in future
- Make-to-order tailored therapeutics

Personalised cell therapies
Manufacturing & Supply Chain challenges:
- Cell source from patients – variability
- Single-use technologies essential
- Poorly automated, labour-intensive, open
- Inadequate characterisation methods
- Centralised v Point-of-care processing

Number of patients per group

Number of drug products

Moving from “one-size-fits-all” to “targeted” medicines...
How can stratified biologics and personalised cell therapies achieve success in manufacturing and business?
Spokes and Users for Collaboration

UCL Hub:
- UCL Biochemical Engineering decisional tools | CFS | formulation | microfluidics | CGT bioprocessing
- UCL Applied Health Research health economics
- UCL STEaPP regulatory strategies

Current Research Spokes:
- Imperial supply chain optimisation
- Warwick production planning
- Nottingham poly-formulations
- Manchester control strategies
- Loughborough cell culture process modelling
Hub Industry Users Shaping the Research Agenda

User Steering Committee
- x2 per y
- Decisional tools
- Cell free synthesis
- T-cell processing
- Formulation
- Healthcare: Regs & Reimbursement

User Feasibility Studies
- ~3 months Allocated PDRA time

Specialist Working Groups (SWGs)
- x2 per y per SWG

Further leveraging via:
- EngDs
- Innovate UK CR&D
- KTPs
Key Technology Focus

- **Aim**: Identify the technical innovation required for successful commercialisation of biological medicinal products with increasing patient stratification

- **Which disruptive technologies will enable targeted healthcare?**

<table>
<thead>
<tr>
<th>Disruptive technology</th>
<th>Stratified Proteins (e.g. ADCs)</th>
<th>Personalised Cell therapy (e.g. CAR T-cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell-free synthesis</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Companion diagnostics</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Co-formulation / Nanoencapsulation</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Bed-side v centralised supply chains</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Microfluidics</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Continuous / SUT</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>AI, ML, big data analytics</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Hub Grand Challenges - Interactions

**Grand Challenge 1 (Lead: Prof Suzanne Farid, UCL)**
Transforming supply chain management and economics for targeted medicines

- Manufacturing strategy
  - Optimal manufacturing technologies
  - Resource requirements
- Process development
  - Optimal scale and patient throughput
  - Performance observed. Variability in CQAs
- Clinical portfolio
  - Process intensification for end-to-end cycle times
  - Batch durations required to achieve yield targets
- Market supply
  - Supply chain robustness and pinch points
  - Operating window robustness observed
  - Ideal level of flexibility
- Cost-benefit of flexibility

**Grand Challenge 2 (Lead: Prof Paul Dalby, UCL)**
Sustainable manufacturing for future targeted medicines

- Novel manufacture, formulation, analytics and advanced control

---

New manufacturing technology features.

---

Interactions
Grand Challenge 1: Supply Chain Management & Economics

Aim: Identify the technical and supply chain innovation required for cost-effective commercialisation of biological medicinal products with increasing patient stratification

Key Hub research questions in GC1:

How can we create and use decisional tools to provide insights on:

- Which disruptive technologies will enable targeted healthcare?
- What performance targets are needed for new technologies to be competitive?
- Optimal route to commercialisation for targeted therapies?
  - In terms of feasible COG, business models & supply chains?
- Are current reg. pathways & reimb. models sustainable for personalised therapies?
- How can AI be used to enable feedback control, RTR, patient stratification?
Grand Challenge Research

**GC Focus**
- Decisional Tools
  - Techo-economic optimisation
  - Drug development pathway & Reimbursement
  - Clinical & commercial supply chain planning
  - Datamining

**Research themes**
- BIA, OXB
- UCL

**Stratified Protein Therapies (with CDx)**
- Modalities & Application
  - mAbs, ADCs
  - Cell-free synthesis v CHO
  - Batch v Continuous
  - CDx incentivisation
  - Biomarker stratification
  - Formulation datamining

**Autologous Gene-modified Cell Therapies & VVs**
- Modalities & Application
  - CAR T-cells, LV, AAV
  - All-in-one v segregated
  - Centralised v bedside
  - LV USP, DSP options
  - Process change economics
  - Supply chain optimisation

**User Feasibility Studies**

<table>
<thead>
<tr>
<th>Company Lead(s)</th>
<th>HEI partner</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIA, OXB</td>
<td>UCL</td>
<td>Economic consequences of switching to scalable GMP processes for viral vectors on drug devt &amp; commercialisation</td>
</tr>
<tr>
<td>Ipsen</td>
<td>UCL</td>
<td>Techno-economic evaluation of a cell-free synthesis (CFS) system for the expression of recombinant toxin</td>
</tr>
<tr>
<td>TrakCel</td>
<td>Imperial</td>
<td>Development of supply chain optimization models for autologous CAR T cells</td>
</tr>
</tbody>
</table>
Techno-economic & business modelling for targeted healthcare

Applications:

- Techno-economic
  - Data-mining
  - Decisional Tools
  - Portfolio Mgt
  - Supply Chain

1. **Drug Development**
   - FTHM Hub: UCL
     - Process economics evaluation of CFS for the commercial manufacture of ADCs

2. **Capacity Planning**
   - FTHM Hub: UCL & Ipsen
     - Process economics evaluation of CFS for the commercial manufacture of highly potent recombinant proteins

3. **Portfolio Mgt**
   - FTHM Hub: UCL & BIA
     - Economic consequences of process changes for viral vectors on drug development and commercialisation strategies

4. **Supply Chain**
   - FTHM Hub: UCL
     - Roadmap for commercialization of autologous CAR T-cell therapies: Needle-to-needle costs for centralized v bedside
UCL - BIA feasibility study – wider impact

- Discussions with various stakeholders
  - UK CDMOs (OXB – James Miskin, Cobra – Peter Coleman, Dan Smith)
  - UCL and Imperial clinical contacts (Pamela Tranter, Uta Griesenbach)
  - UK academic GMP facilities (KCL - Farzin Farzaneh)
  - US academic GMP facilities (CHOP, Philadelphia)
  - KTN (Sarah Goulding)
  - MMIP workstream on meeting academic vector needs (Chair: Ian McCubbin)

Fed into MMIP business case on

“A UK Strategy for the Manufacture of GMP Viral Vectors”
# User Feasibility Studies supported in 2019

Users can access up to 3 mo PDRA resource to test Hub tools in user environment

<table>
<thead>
<tr>
<th>Organisation &amp; HEI</th>
<th>Title/Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aglaris University of Manchester</td>
<td>Historical batch analysis and trajectory optimisation for T-cell expansion process control</td>
</tr>
<tr>
<td>Albumedix University of Nottingham</td>
<td>Formulating recombinant human albumin as nanoparticle scaffold and assessing the potential for drug delivery</td>
</tr>
<tr>
<td>AstraZeneca UCL</td>
<td>Real-time process analysis and control of continuous chromatography</td>
</tr>
<tr>
<td>BIA MAC, Oxford Biomedica UCL</td>
<td>Economic analysis to investigate the consequences of switching to scalable GMP processes for viral vectors on drug development lifecycle costs</td>
</tr>
<tr>
<td>Cell &amp; Gene Therapy Catapult Loughborough University</td>
<td>Mechanistic modelling for immunotherapy manufacture</td>
</tr>
<tr>
<td>Fujifilm Diosynth Biotechnologies UCL</td>
<td>Testing and developing established cell-free synthesis protocols for 3 classes of product</td>
</tr>
<tr>
<td>Ipsen UCL</td>
<td>Techno-economic evaluation of a cell-free synthesis system for the expression of recombinant toxin</td>
</tr>
<tr>
<td>TrakCel Imperial College</td>
<td>Development of supply chain optimization methods for autologous CAR T cells</td>
</tr>
<tr>
<td>West Pharmaceutical Services UCL</td>
<td>Comparing freeze-thaw performance of vials vs bags for the containment of T-cells</td>
</tr>
</tbody>
</table>
# User Feasibility Studies 2020 - Timeline

**CALL FOR PROPOSALS NOW OPEN!**

Call and Proposal Form can be downloaded from [Hub Documents](http://www.ucl.ac.uk/biochemeng/hub)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>User Feasibility Study Call for Proposals</td>
<td>June 2019</td>
</tr>
<tr>
<td>Specialist Working Groups – Networking</td>
<td>September, October 2019</td>
</tr>
<tr>
<td>User Steering Committee – Networking</td>
<td>November 2019</td>
</tr>
<tr>
<td><strong>Submission deadline for proposals</strong></td>
<td><strong>11 December 2019</strong></td>
</tr>
<tr>
<td>Review by Translation and Impact Committee</td>
<td>Late January 2020</td>
</tr>
<tr>
<td>Review of Decisions by Advisory Board</td>
<td>Early February 2020</td>
</tr>
<tr>
<td>Announcement of successful proposals</td>
<td>Mid February 2020</td>
</tr>
<tr>
<td>Earliest project start dates</td>
<td>Early March 2020</td>
</tr>
</tbody>
</table>
Ph2 Planning: Developing the Hub Agenda

- Mid-term review in early summer 2020
- We need to project our successes and describe a relevant vision for the future
- That vision must resonate with our community
- The outcomes must be relevant at least at a UK level, we intend it to be globally defining
Hub Impact

Research Excellence

- World-leading Expertise
- Multiple Disciplines
- Collaborative Consortium

Sector Influence

- Steer Research Agenda
- Business Aligned
- National Interest

Priority Access

- New Technologies and Decisional Tools
- Skilled Researchers & User Feasibility Studies
- Insights on stakeholder priorities

Contact: eleanor.bonnist@ucl.ac.uk

www.ucl.ac.uk/biochemeng/hub
Future Targeted Healthcare Manufacturing Hub:
Next-generation biomanufacturing solutions to enable precision medicine

Suzanne S. Farid  PhD CEng FIChemE
Professor of Bioprocess Systems Engineering
Co-Director Future Targeted Healthcare Manufacturing Hub
UCL Biochemical Engineering  s.farid@ucl.ac.uk

16th Annual bioProcessUK Conference, Liverpool, Nov 26-28 2019