

# CELL, GENE AND REGENERATIVE THERAPIES AT UCL AND NHS PARTNER TRUSTS

World leaders in the translation of advanced therapies

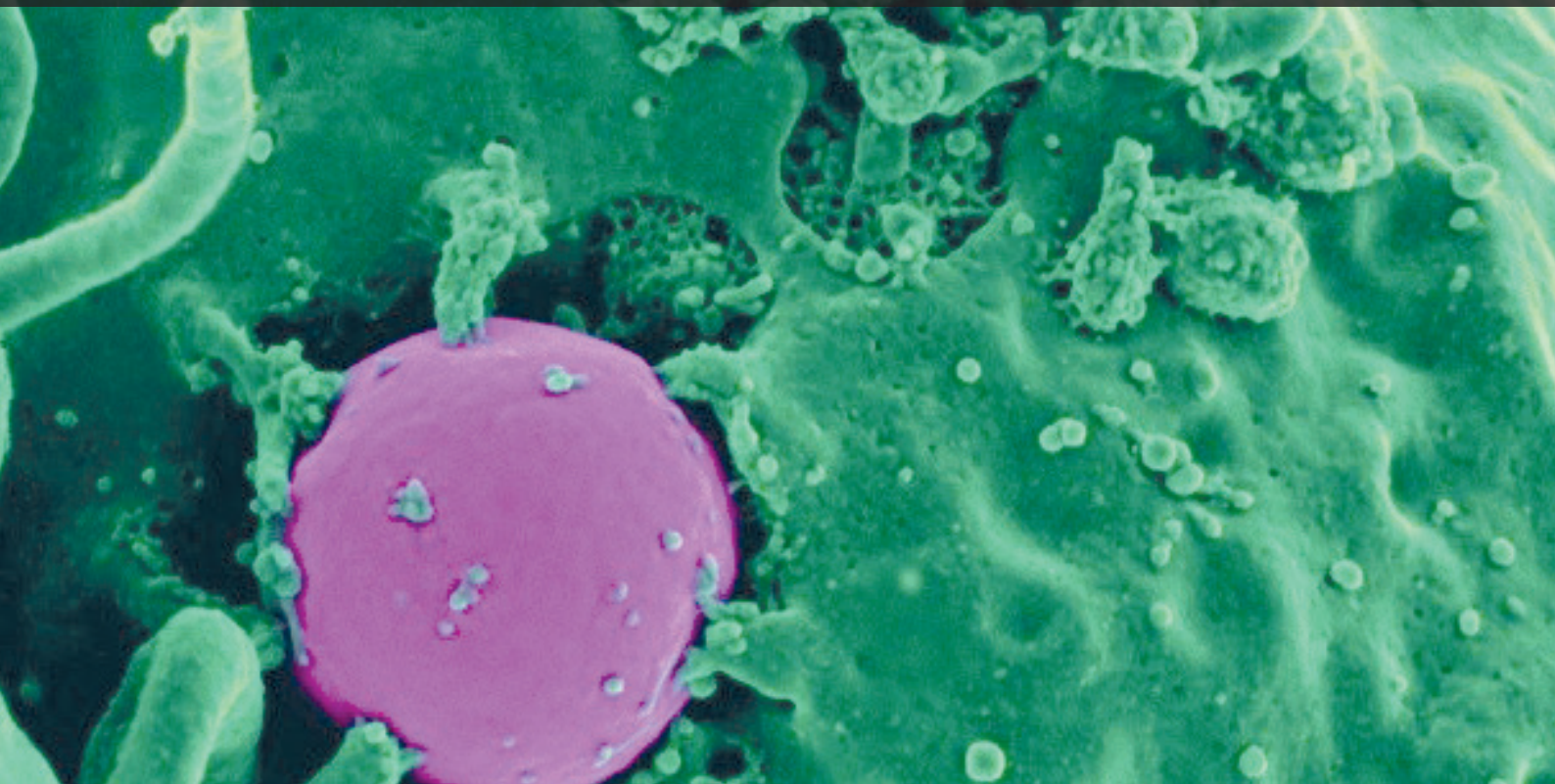


**NHS**  
Great Ormond Street  
Hospital for Children  
NHS Foundation Trust

**NHS**  
Moorfields  
Eye Hospital  
NHS Foundation Trust

**NHS**  
University College  
London Hospitals  
NHS Foundation Trust

**NHS**  
Royal Free London  
NHS Foundation Trust



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# PREFACE:

## FEBRUARY 2018

**We live in tremendously exciting times, with scientific breakthroughs seemingly reported on a near daily basis. One breakthrough area poised to deliver is the field of cell, gene and regenerative (advanced) therapies. The first FDA approval for a CAR T-cell therapy to treat children and young adults with B-cell acute lymphoblastic leukaemia was made in August 2017. Many more advanced therapy products are undergoing the transition from pre-clinical promise to clinical reality, offering the unprecedented potential for long-term management and even cure of disease. In the UK, the 2016 Advanced Therapies Manufacturing Taskforce Report recognised that “The UK has the opportunity to secure its position as a global hub for researching, developing, manufacturing and adopting advanced therapies”<sup>1</sup>. The academic sector, as exemplified by University College London (UCL), our NIHR Biomedical Research Centres (BRCs) and partner NHS Trust hospitals, is playing a pivotal role in advancing the field.**

UCL in partnership with our three NIHR BRCs at University College London Hospital (UCLH), Great Ormond Street Hospital for Children (GOSH) and Moorfields Eye Hospital (MEH) are **world leaders in:**

- the development and **delivery to patients** of novel cell, gene and regenerative therapies
- meeting the challenges associated with **manufacture**
- contributing to the **training** of the next generation of scientists in the field

Highlights in recent years include:

- Europe’s largest translational programme of CAR-T cell therapy in adults and children
- First-in-human (FIH) gene therapy for rare disease rolling out from children to adults (Wiskott Aldrich Syndrome, ADA-SCID)
- FIH gene-edited T-cells for acute leukaemia
- FIH embryonic stem cell-derived cell therapy for macular degeneration
- Five therapy and two technology spinout companies with a total investment of over £295 million

Our strength in cell, gene and regenerative therapies has been underpinned by over 30 years of research supported by research councils, the National Institute for Health Research, charities, government as well as by industry. This has enabled a community of in excess of 100 world class scientists at UCL to deliver on the promise of what is only now being recognised as the third pillar of pharmaceutical therapeutics.

We strongly believe that the advanced therapies hold the promise to transform healthcare for patients with some of the most severe and debilitating conditions, and that to do this requires partnership. Building partnerships is at the heart of UCL’s ethos of excellence, inclusivity and global outreach, values that are key to UCL’s strategy for the next 20 years (UCL 2034). Success will only come if we put the patient at the centre of all that we are trying to achieve. This central philosophy is one we share with all our partners.

If this is your philosophy we invite you to partner with us to deliver on the promise to the patient in this fast-moving and highly exciting area, as we cannot do this alone.

**Professor David Lomas, Vice Provost of Health University College London**  
**Professor Marcel Levi, Chief Executive University College London Hospital**  
**Dr Peter Steer, Chief Executive Great Ormond Street Hospital**  
**David Probert, Chief Executive Moorfields Hospital**  
**Sir David Sloman, Chief Executive Royal Free Hospital**

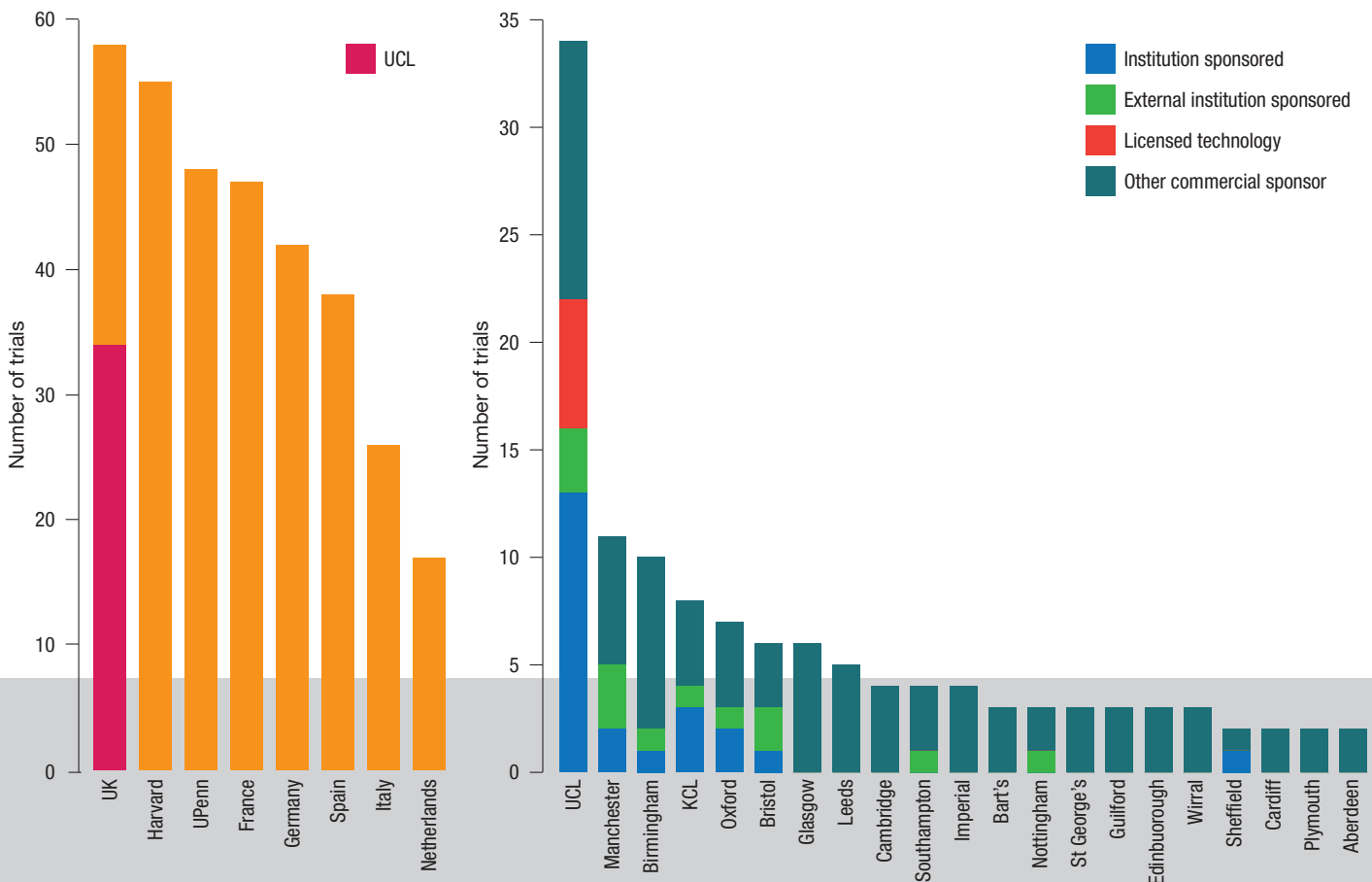
# DELIVERING THE PROMISE OF CELL, GENE AND REGENERATIVE THERAPIES

**UCL is a world-leader in the clinical translation of cell, gene and regenerative therapies. UCL and partner NHS Trusts participate in 59% of the UK's advanced therapy clinical trials, competing with US institutions such as Harvard and the University of Pennsylvania and with top European countries in terms of clinical activity<sup>2</sup> (Figure 1). In the UK, UCL is the lead participant in advanced therapies**

**clinical trials<sup>2</sup> (Figure 2).** Through our coordinated multidisciplinary network of researchers, engineers, clinicians, patients, health economists and professionals, the UCL Cell, Gene and Regenerative Medicine Therapeutic Innovation Network (CGRM TIN) has established a strong pipeline that is delivering to patients and to the UK's industrial ambitions.

UCL and partner NHS Trusts clinically deliver both in-house and commercial technologies: 38% of trials analysed were UCL-sponsored investigator technology, 9% external academic sponsored technology, 18% licensed UCL technology and 35% commercial partner technology.

**Figures 1 & 2. Participation in advanced therapy clinical trials September 2017.**  
Institutions participating in two or more trials are shown. Data source: clinicaltrials.gov.



**First-in-human gene-edited T-cells:** Layla Richards received gene-edited CAR-19 T-cells for relapsed acute lymphoblastic leukaemia at GOSH in 2015. The treatment was pioneered by GOSH BRC researchers led by Professors Waseem Qasim in collaboration with biotech company Collectis. Credit: Great Ormond Street Hospital.



**We are delivering multiple technologies, many first-in-human (FIH), across multiple disease areas in clinical trial and as specials.**

**UCL and partner NHS Trust clinical firsts**

- FIH gene therapy for Haemophilia B
- FIH optimised Factor VIII gene therapy for Haemophilia A
- FIH Haematopoietic stem cell gene therapy for Primary Immune Deficiencies
- FIH gene-edited T-cells
- FIH WT1-TCR engineered T-cells
- First UK CAR-T translational programme
- FIH embryonic stem cell-derived cells for macular degeneration
- Proof-of-concept gene therapy for retinal dystrophy
- FIH tissue engineered tracheal implant
- FIH novel TIPS biomaterial for tissue regeneration
- FIH maternal gene therapy for foetal growth restriction (in set-up)
- UK's first accredited GMP stem cell lab



**34**  
clinical trials  
active in 2017



**>50**  
clinical products released  
to patients in 2016

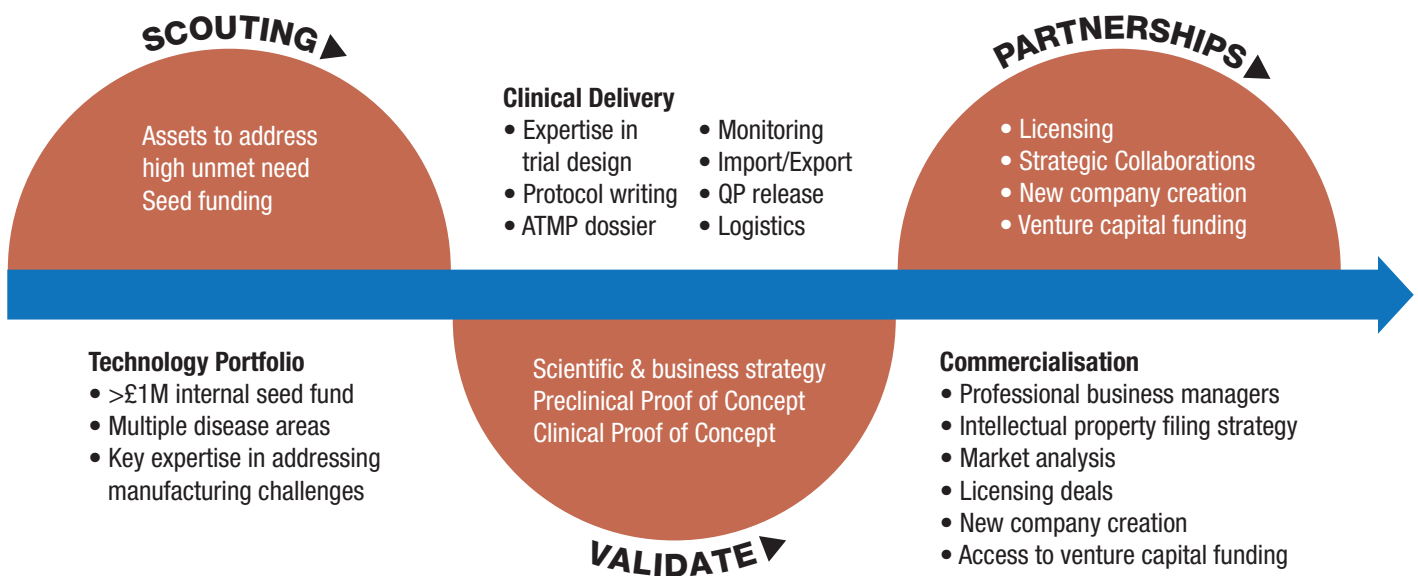


**4**  
GMP facilities

# OUR COLLECTIVE CAPABILITIES

UCL recognises that multiple stakeholders are needed to successfully deliver cell, gene and regenerative therapies with complex manufacturing and regulatory requirements. We offer end-to-end translation of advanced therapies through multi-disciplinary working, productive partnership with industry and access to extensive translational infrastructure encompassing three NIHR Biomedical Research Centres (BRCs). Our capabilities enable us to mature an idea from UCL's extensive science base, validate with pre-clinical and clinical proof-of-concept (POC) studies and to commercialise opportunities (Figure 3).

Figure 3: End-to-end translation of advanced therapies



# OUR COLLECTIVE CAPABILITIES: TRANSLATIONAL EXPERTISE

UCL's translational infrastructure is co-ordinated both within the university and at partner NHS Trust hospitals. UCL's three NIHR BRCs University College London Hospital (UCLH), Great Ormond Street Hospital for Children (GOSH) and Moorfields Eye Hospital (MEH) received over £167 million of renewed funding in 2016, the largest share of any UK university. BRCs and Partner NHS Trusts have made significant investments in the development of our cell, gene and regenerative therapies and

are critical in delivering our ambitions in the field. The Cell, Gene and Regenerative Medicine Therapeutic Innovation Network (CGRM TIN) brings together over 100 researchers across the university and partner hospitals to share expertise and maximise strategic opportunities. Key resources in pre-clinical development (Translational Research Office – TRO), industrialisation of manufacture (Faculty of Engineering, GMP facilities), regulatory expertise (TRO, Joint Research Offices – JROs), clinical

trial design (Institute of Clinical Trials and Methodology), sponsorship (JROs) and operations (Clinical Trials Units – CTUs, Clinical Research Facilities – CRFs), commercialisation (UCL Business), partner hospitals (NIHR BRCs) and NHS adoption (UCL Partners) align in order to accelerate delivery of advanced therapies to our patients (Figure 4).

**Figure 4: Extensive infrastructure accelerates the translation of advanced therapies**



# OUR COLLECTIVE CAPABILITIES: ADVANCED THERAPIES PORTFOLIO

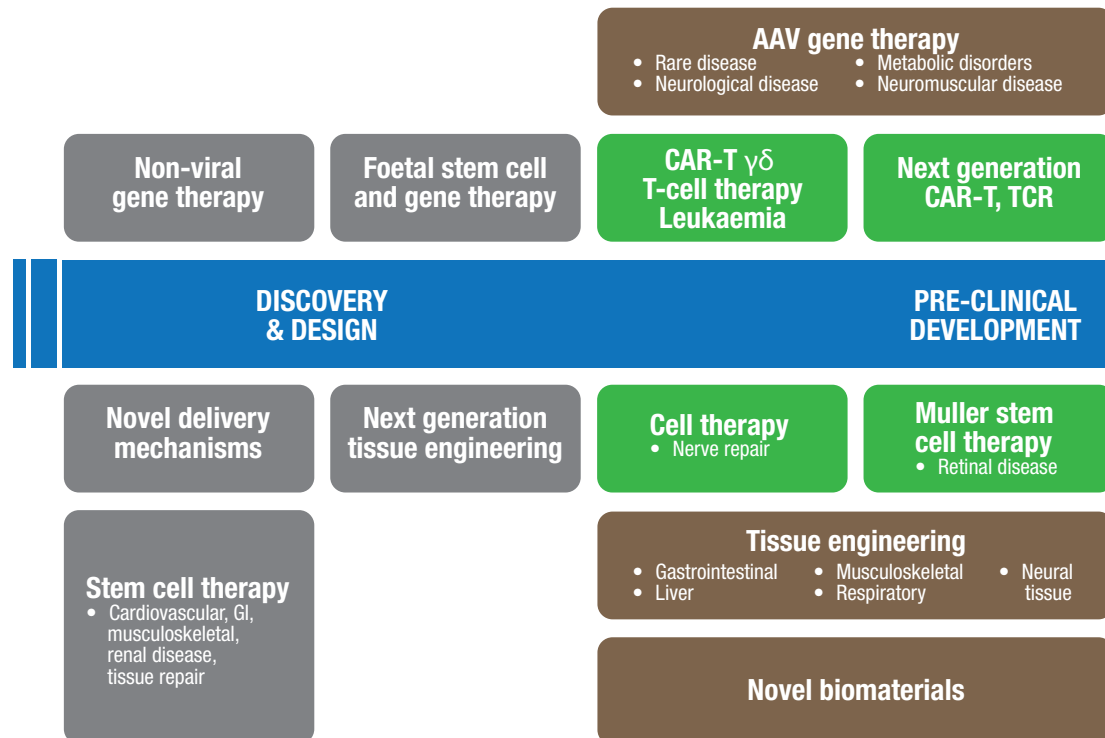
Our advanced therapies pipeline has breadth and depth across technologies and disease areas (Figure 5). High-profile technologies include gene-modified haematopoietic stem cells (HSCs) for primary immune deficiencies (PID), CAR-T (chimeric antibody receptor) and TCR (T-cell receptor) for haematology and oncology, gene-editing for haematology, adeno-associated virus (AAV) gene therapy

and embryonic stem (ES) cell therapy for retinal disease, tissue engineered products for respiratory disease and antisense therapy for Huntington's disease (HD) and Duchenne Muscular Dystrophy (DMD). Next generation constructs and application to new disease indications are in development for many of these therapies. The pipeline also includes a substantial translational portfolio of AAV gene

therapy products for rare neurological and metabolic disease and tissue engineered products including liver, musculoskeletal and neural tissue, as well as exciting new technologies such as foetal gene and stem cell therapies. Supportive technologies include extensive biomaterials science, novel delivery and imaging techniques, innovative human tissue models and big data capabilities.

## Figure 5: Key therapies in UCL's cell, gene and regenerative pipeline

Our advanced therapies pipeline is supported by extensive funding from Research Councils, NIHR, charities, government and industry, including but not limited to those listed on page 9. In a review of UCL's advanced therapies activity, over £165 million active funding was identified in a 14 month period (2014/15)<sup>3</sup>. Internal seed funding supported by the MRC, Wellcome Trust and our three NIHR BRCs accelerates the transition of discovery science to early stage therapeutic development.





Our funders include



Innovate UK



**NHS**  
National Institute for Health Research



CANCER RESEARCH UK

**Bloodwise**  
Beating blood cancer since 1960



Rosetrees Trust  
Supporting the best in medical research



**NHS**  
Blood and Transplant



Great Ormond Street Hospital Charity



Maternal gene therapy

Gene modified skin cells  
• Inherited skin disease

CAR-T, TCR  
• Cancer

Gene editing  
• Leukaemia

Next generation gene modified HSCs

AAV gene therapy  
• Haemophilia  
• Retinal disease

Gene modified MSCs  
• Lung cancer

Gene modified HSCs  
• PID

CLINICAL DELIVERY (OR SET-UP)

Next generation adoptive T-cells

MSCs  
• Tendinopathy

Adoptive T-cells  
• Post-HSCT

Corneal stem cells  
• Corneal & conjunctival disease

Novel devices

IPSC, ES-derived cells  
• Macular & retinal disease

TIPS novel biomaterial  
• Fistula

Tissue engineering  
• Respiratory organs

Automated gene-modified HSC & T-cell therapies

Antisense technology  
• DMD  
• HD

> 100 principal investigators

> £165M grants 2014/15

> 130 projects in discovery pipeline

# OUR COLLECTIVE CAPABILITIES: MANUFACTURING

**UCL's innovative Department of Biochemical Engineering provides key expertise in addressing the complex manufacturing challenges associated with the production of cell, gene and regenerative therapies.** With expertise in translation of manufacture to industrial scale, regulatory science and cost and reimbursement models, the department helps to bridge the gap between discovery science and routine patient care. In 2016 UCL Engineering was awarded the prestigious EPSRC Future Targeted Healthcare Manufacturing Hub, engaging academics across the UK as Spokes to drive a paradigm shift from one-size-fits-all

to personalised medicine manufacturing. The Hub will address the manufacturing, business and regulatory challenges to ensure that new targeted biological medicines including advanced therapies can be developed quickly and manufactured cost effectively to accelerate widespread clinical adoption. The world-class training offered by Biochemical Engineering in advanced therapies manufacturing is described on page 14.

**Advanced therapy medicinal product (ATMP) manufacture for clinical delivery is facilitated by four Good Manufacturing Practice (GMP) facilities with capabilities**

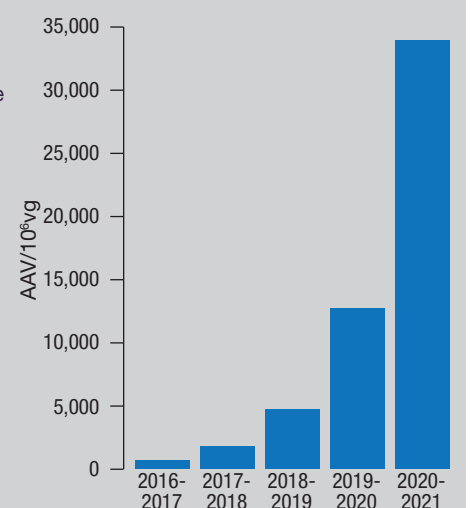
**in the production of gene therapy, cell therapy, gene-modified cell therapy and tissue engineered ATMP production, as well as QP (Qualified Person) expertise.**

- Centre for Cell, Gene and Tissue Therapeutics (CCGTT), Royal Free Hospital
- Cellular Therapies manufacturing unit, GOSH – pending expansion into Zayed building (2018)
- Cells for Sight Stem Cell Therapy Research Unit, MEH
- UCL Wolfson Gene Therapy Unit



**Figure 6. Projected demand for pan-London academic AAV GMP manufacture.**

Whilst industry requirements for ATMP manufacture have clearly been articulated<sup>1</sup>, UCL's CGRM TIN in collaboration with King's College London, Imperial College London and MedCity have quantified future GMP manufacturing requirements stemming from the academic base pan-London<sup>4</sup>. The report presented to the London Academic Health Science Centres/ Networks Executive Group in 2017 identified significant increases in demand for GMP manufacture of viral vectors (AAV shown here), cellular and tissue-engineered products by 2021 and is being used to support a London-wide dialogue around innovative capacity solutions.

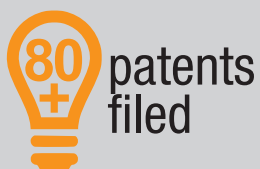


# OUR COLLECTIVE CAPABILITIES: COMMERCIALISATION

**UCL Business (UCLB) realises the commercial potential of research activity through patents, licensing deals, funding opportunities (UCL Technology Fund, Apollo Fund – a university-industry consortium) and the creation of spinout companies. In the field of academic cell, gene and regenerative therapies, UCLB have helped to forge the pathway to commercialisation by the creation of spinout companies including Puridify (now part of GE Healthcare) in 2014, Freeline Therapeutics, Athena Vision (now part of Meira GTx) and Autolus in 2015 and Orchard Therapeutics, Achilles Therapeutics and Engitix in 2016. Over £295 million in investment has been raised by these companies through sequential financing rounds. Projects continue to be licensed from the academic pipeline into these companies, as well as products licensed to other companies such as Cell Medica and Biomarin.**

Our spinouts continue to work with us, giving them access to the originators of the technology, insight into the cutting-edge technology leading to improvements of the products, as well as expert disease understanding and access to the clinical infrastructure and patient cohorts required for delivery. These industry relationships are set to continue and widen to other partners as our reputation continues to grow, allowing us to learn from one another and deliver these novel treatments to our patients.

## Spinout Companies



# OUR COLLECTIVE CAPABILITIES: PARTNERSHIPS

**Realising the promise of cell, gene and regenerative therapies cannot be done in isolation. Successful partnerships with the NHS, academia and industry underpin UCL's translational processes.**

This brochure highlights how UCL working in partnership with its three BRCs and partner NHS Trust hospitals has aligned to significantly drive forward the field of advanced therapies. This has been achieved in collaboration with Higher Education Institutions across the UK, Europe and worldwide. In addition, we have forged links with Industry and Contract Research Organisations (over 70 partnerships) to deliver in the areas of translational research, GMP manufacturing and testing, regulatory consultancy etc, making use of the very best expertise, advice and resource wherever it resides.

Industry and others are able to draw on the expertise of our advanced therapies community through the services of UCL Consultants. Key opinion leaders in the field have advised industry ranging from SME to large pharmaceutical companies. In addition, our close dialogue with regulators from an early stage in development helps to shape and inform the regulatory pathway.

Our collaborative approach has been recognised with the recent awards of:

- A £10 million EPSRC grant for the Future Targeted Healthcare Manufacturing Hub – driving the shift from one-size-fits-all manufacturing to personalised manufacturing.
- A prestigious 15 million Euro Horizon 2020 teaming grant (one of only 10 awarded) to establish the EU Discoveries Centre for Regenerative and Precision Medicine in Portugal, sharing our translational expertise in accelerating delivery of advanced therapies across Europe.
- Working across London Higher Education Institutes and NHS trusts via the Academic Health Science Centres to join up advanced therapy activity pan-London<sup>5</sup>, especially addressing the area of vector and cell manufacture capacity for the future<sup>4</sup>.

**Partnerships are pivotal to our success and we are continually seeking to create new, multidisciplinary alliances with patient-centric organisations from a variety of sectors. There are multiple reasons why you may wish to engage with ATMP research and development within our organisation:**

- To access world-class cutting edge science (novel targets, novel vector design, gene editing approaches, novel manufacturing solutions, novel imaging of cell and gene therapies etc)
- To access clinicians and patients to better understand/position your therapies for use
- To access expertise in clinical operations to deliver advanced therapy trials (UCL and its partner hospitals currently participate in 59% of active advanced therapy trials in the UK)<sup>2</sup>

**Partnership between Professors Emma Morris and Hans Stauss and cellular therapeutics company Cell Medica is accelerating UCL's novel TCR technology by generating leading-edge modified TCR products for the treatment of cancer.**



# OUR COLLECTIVE CAPABILITIES: PUBLIC & PATIENT INVOLVEMENT

**UCL and partner NHS Trusts hospitals/BRCs are keen for patients and the public to be actively involved in our research, not just as participants but in helping to design and conduct our work. Patient and public involvement (PPI) in research can lead to treatments that better meet the needs of users and the public, and to research results that are more likely to be put into practice.**

UCLH/UCLH BRC provides training, advice and support for researchers to enable them to better involve patients and the public in research. Groups of lay people meet on a regular basis and, together with patients, they can provide input into the strategic direction of research as well as advising on elements of a particular research study such as looking at grant or ethics applications, reviewing plain English summaries or advising on how best to recruit patients to trials. UCL and UCLH are also working hard to deal with the more challenging areas of PPI, including the input of patients and the public in early stage lab-based research.

GOSH/GOSH BRC engages patients and the public in research by actively consulting, involving and listening to their views on GOSH research, as well as aiming to raise awareness of research carried out by BRC and GOSH researchers. The Young Person's Advisory Group consists of children and young people aged between 8–21 that meet at GOSH and provide feedback to researchers to help them carry out research that is relevant to children and young people. The Parent/Carer Research Advisory Group consists of parents or carers who have a child with a health condition and provides advice on improving research into child health.

MEH/MEH BRC invites patients and staff to focus groups and patient panels, allowing the hospital to understand some of the issues facing the trust and to enabling patients and staff to work together to find solutions.



# OUR COLLECTIVE CAPABILITIES: TRAINING THE NEXT GENERATION – ADDRESSING THE SKILLS GAP

The potential for cell, gene and regenerative therapies to radically transform the life of patients is fast becoming a reality. Significant challenges remain however, not least:

- Educating patients and clinicians on the potential of advanced therapies
- Working with industry to upskill the existing workforce, as well as training the new workforce needed to manufacture these therapies
- Training more qualified persons (QPs)
- Increasing the number of regulatory advisors
- Enhancing the clinical infrastructure at hospitals to deliver these novel therapies

UCL is currently addressing the recognised skills gaps<sup>1</sup> by running accredited courses aimed both at students and at industry looking to up-skill their employees. We are working to expand our offering over the next five years. UCL's Department of Biochemical Engineering are pivotal in addressing training

around challenges in advanced therapies manufacturing.

## Education

- MSc/PGDip/PGCert programme in Cell and Gene Therapy
- BEng/MEng Regenerative Medicine Manufacturing Minor

## Training

- MBI<sup>®</sup> module: Cell and Gene Therapy Bioprocessing. This course is a component of UCL Biochemical Engineering's award-winning programme of Modular Training for the Bioprocess Industries.
- Human Pluripotent Stem Cells in Culture: Hands-on, basic cell culture training course focusing on induced pluripotent stem cells and human embryonic stem cells.
- Biochemical Engineering and Bioprocess Leadership EngD.

- Regulatory Science for Advanced Therapies – Bench to Medicine: Four day course in partnership with the British Society of Gene and Cell Therapy and the Cell and Gene Therapy Catapult
- Academic Careers Office skills training: MiniMD: Two-week clinical immersion programme for non-clinical biomedical scientists; Ignite: medical innovation summit for group leaders to engage with innovation from a variety of perspectives
- UCL Innovation and Enterprise: Entrepreneurship and business interaction are supported by training, funding and business services for staff, students and external entrepreneurs
- UCL partnership with the Centre for the Advancement of Sustainable Medical Innovation (CASMI): Building innovative solutions to barriers in the translation of the advanced therapies

UCL ADVANCED CENTRE FOR BIOCHEMICAL ENGINEERING

**UCL**

**Advancing Cell & Gene Therapy Bioprocessing & Manufacture**

Focusing on taking discoveries from lab to clinic and acquiring new skills sets to achieve this

09 – 11 JULY 2018

Held at the Department of Biochemical Engineering, UCL, London, UK

UCL LIFE LEARNING

mbi modular training for the bioprocess industries

UCL ADVANCED CENTRE FOR BIOCHEMICAL ENGINEERING

**UCL**

**Stem Cell Training Course: Human Pluripotent Stem Cells in Culture**

2016 – 2017\*

Held at the Department of Biochemical Engineering, UCL, UK

\*Course date is flexible, will run once cohort is confirmed – maximum 4 participants.

A 3-day hands-on course designed to equip life science and engineering graduates with the practical skills necessary to maintain pluripotent stem cell lines

Short Courses & Training in Biochemical Engineering



Professor  
Bobby Gaspar



Professor  
Adrian Thrasher

# CLINICAL CASE STUDY

## Gene-Modified Cell Therapy for Rare Disease

**A team led by clinician scientists Professors Bobby Gaspar and Adrian Thrasher at UCL's Great Ormond Street Institute of Child Health and partner hospital GOSH have pioneered the use of gene therapy for rare diseases in children.**

With a focus on primary immune deficiencies (PIDs), the team has developed the technique of *ex vivo* gene therapy of autologous (patient) haematopoietic stem cells in order to correct a disease's underlying genetic defect. The combination of GOS ICH's world-class academic environment, GOSH's unique patient population and GOSH BRC support has enabled the team to progress the innovative technology through *in vitro* and *in vivo* proof-of-concept (POC) studies and into clinical trial. The team have now led seven early phase clinical trials for PID including adenosine deaminase severe combined immune deficiency (ADA-SCID), X-linked SCID, Wiskott-Aldrich Syndrome and X-linked Chronic Granulomatous Disease, restoring immune function to patients with minimal side effects in the majority of cases. Therapies for PIDs including Fanconi Anaemia and *p47phox*-deficient CGD (with support from the UCL Technology Fund) and Mucopolysaccharidosis IIIA Sanfilippo

are in the clinical pipeline. In addition, extending the technology to gene-modify other cell types such as T-cells and fibroblasts has widened the scope to treat diseases including haematological disorders and skin disease.

*"We've made considerable progress in this field over the past decade. Gene therapy has been refined, trialled in patients and we've learnt a huge amount. Studies we have designed here are now open in Los Angeles, Boston, Paris and other international centres.*

Professor Adrian Thrasher

*"With support, we believe that a decade further on, gene therapy will be able to improve the life and health of many children with life-threatening diseases, where other treatment methods are either ineffective or non-existent. It's a very exciting time to be working in this field."*

Professor Bobby Gaspar

Professors Gaspar, Thrasher and Professor Waseem Qasim (also GOS ICH) founded spinout company Orchard Therapeutics in 2016 to advance and commercialise the group's *ex vivo* gene therapy platform. Orchard was created by UCL's technology transfer company UCL Business PLC and F-Prime Capital Partners, securing £21 million in Series A financing. The company has partnerships with UCL, GOSH, University of Manchester, University of California Los Angeles, and Boston Children's Hospital.



Dr Martin Pule

Professor  
Emma MorrisProfessor  
Hans Strauss

# CLINICAL CASE STUDY

## T-Cell Engineering

**T-cell engineering is changing the face of clinical haematology and has the potential to do likewise in areas such as oncology and autoimmune disease. UCL investigators strongly supported by the UCLH BRC are at the forefront of both CAR-T and TCR T-cell engineering technologies.**

### CAR-T

**Dr Martin Pule**, a clinician scientist at the UCL's Cancer Institute, has driven the evolution of CAR-T technology in the UK. CAR-T cells are genetically modified with a chimeric antigen receptor that re-directs the specificity of the patient's T-cells, allowing clonal killing of cells expressing the chosen surface antigen. Dr Pule has built a substantial translational CAR-T programme, establishing the largest portfolio of CAR-T clinical trials in Europe with eleven early phase trials open at UCL partner hospitals UCLH and GOSH in 2018.

Dr Pule is founder of the UCL spinout company Autolus, launched in 2015 to develop and commercialise a new generation of CAR-T cell therapies. Autolus was created by UCL Business PLC and healthcare investment company Syncona LLP, securing an initial £30 million in investment, followed by a further £40 million from Woodford Investment Management and Perceptive Bioscience Investments in 2016. Dr Pule was named BBSRC's Most Promising Innovator in 2016.

*"It is exciting to be involved in Autolus, where we have an opportunity to bring innovative new therapeutic approaches to patients who often have no alternative treatment path. The key will be to remain at the cutting-edge of T-cell engineering to create a new generation of programmed T-cells acting as autonomous agents to kill tumour cells. What we've seen so far in the CAR T-cell field is only the beginning."*

Dr Martin Pule

### TCR

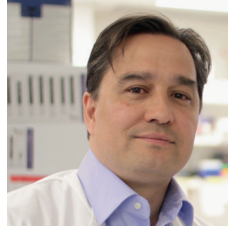
An alternative T-cell engineering strategy is being pioneered by **Professors Emma Morris and Hans Stauss** of UCL's Institute of Immunity and Transplantation. Expression of a recombinant T-cell receptor (TCR) re-directs the specificity of a patient's T-cells, facilitating recognition of the TCR's cognate epitope presented in the context of major histocompatibility antigens (MHC) on the cell surface. TCR strategies are MHC-restricted but have the advantage of recognizing intracellular antigens processed and expressed at the cell surface, a feature that may be advantageous for targeting solid tumours.

The team have developed a TCR that recognises the WT1 antigen, a protein over-expressed in a number of haematological malignancies and solid tumours. Following the demonstration of proof-of-concept (POC) *in vivo*, the team obtained MRC funding to test the safety of WT-1 TCR in AML and CML in a phase I/II clinical trial sponsored by the Cell Therapy Catapult. Results indicate excellent persistence of gene-modified T cells and ongoing cohorts are exploring the relationship between T cell dose and efficacy. Catapult Therapy TCR Ltd, a joint venture company set-up by the Cell and Gene Therapy Catapult, UCLB and Imperial Innovations to advance the WT-1 TCR technology, was acquired by cellular therapeutics company Cell Medica in June 2017. Collaboration with Cell Medica is driving the development of second generation TCR constructs.





Professor  
Amit Nathwani



Professor  
Robin Ali

# CLINICAL CASE STUDY

## AAV Gene Therapy

**UCL has a significant pipeline of adeno-associated virus (AAV) gene therapies including treatments for Haemophilia and inherited retinal disorders in clinical trial and treatments for rare neurological and metabolic disease in translation.**

### Haemophilia

In 2016, **Professor Amit Nathwani** of the UCL Cancer Institute and Director of the Katharine Dormandy Haemophilia Centre at the Royal Free Hospital, was awarded the European Society for Gene and Cell Therapy's Outstanding Achievement Award for his pioneering work on gene therapy for Haemophilia. In 2010, in collaboration with St. Jude Children's Research Hospital, a team led by Professor Nathwani was the first in the world to show correction of bleeding in patients with severe Haemophilia B by using AAV-based gene transfer to express Factor IX. Since demonstrating clinical POC, Prof Nathwani has extended this technology to other inherited bleeding disorders, working with the UCL TRO to develop translational pathways for Haemophilia A and for Factor VII deficiency. Partnership with biotechnology company Biomarin in the form of a licensing deal has enabled the progression of Haemophilia A gene therapy into phase I/II clinical trial in the UK; Biomarin has built its first gene therapy manufacturing facility to support GMP manufacture of the Factor VIII therapy for clinical trial and commercial production.

Professor Nathwani is founder, member and Chief Scientific Officer of Freeline Therapeutics, a spinout company launched in 2015 by UCL Business PLC and Syncona LLP with an initial investment of £33 million. Freeline Therapeutics builds on Professor Nathwani's AAV gene therapy platform technology to drive the clinical translation and commercialisation of treatments for bleeding disorders and other disorders that affect the liver.

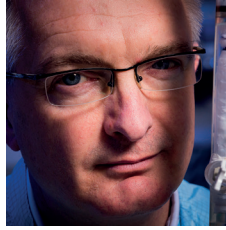
### Inherited retinal disorders

**Professor Robin Ali** of the UCL Institute for Ophthalmology (IoO) and theme leader for gene Therapy at MEH NIHR Biomedical Research Centre, has pioneered the development of AAV-based gene therapy for eye disease. His functional rescue of retinitis pigmentosa *in vivo* in 2000 established POC for ocular gene therapy and his team have since demonstrated *in vivo* POC for gene therapy of a wide range of ocular disorders, including retinal dystrophies, ocular angiogenesis and uveitis. In doing so, he has established a pipeline of therapies, supported by charities, UK National

Institute of Health Research, UK Medical Research Council and industry. As chief investigator, Prof Ali established one of the world's first clinical trials of gene therapy for retinopathy (Leber Congenital Amaurosis Type 2). The trial reported an improvement in vision and contributed to POC of gene therapy as a treatment for inherited retinal degeneration. Prof Ali has worked closely with the TRO to drive the pre-clinical development and clinical trial of optimised AAV vectors for LCA and achromatopsia type 3, with GMP manufacture of viral vectors at the UCL Wolfson Gene Therapy facility. These early phase clinical trials, now active, are supported through public and private funding, including from MeiraGTX, a company of which he is a Founder and Chief Scientific Officer.



Professor  
Julie Daniels



Professor  
Mark Lowdell

# CLINICAL CASE STUDY

## Cell Therapies

**Cell therapies developed at UCL and partner NHS Trust hospitals are being used to treat a range of diseases including eye diseases, tendinopathy and leukaemia. The expertise of the Cells for Sight (Director: Professor Julie Daniels) and CCGTT (Director: Professor Mark Lowdell) GMP facilities has been fundamental to the pre-clinical development and GMP manufacture of these therapies.**

### Stem cells

**Professor Julie Daniels** of the IoO has established a translational programme of research encompassing the use of stem cells and tissue engineering for diseases of the cornea and conjunctiva. Prof Daniels is founding director of the MEH Cells for Sight Stem Cell Therapy Research Unit, the UK's first accredited cultured stem cell facility. The Cells for Sight GMP facility manufactures cultured corneal stem cells on a compassionate basis for patients with blinding ocular surface disease.

**Professor Pete Coffey** of the IoO is director of the London Project to Cure Blindness, an MEH-NIHR collaboration aiming to bring pioneering stem cell therapy for retinal diseases to the clinic. In 2015 in a phase I clinical trial sponsored by Pfizer, patients with Acute Wet Age-Related Macular Degeneration were treated with human embryonic stem cell-derived retinal pigment epithelium cells manufactured at the Cells for Sight GMP facility. Prof Coffey's translational programme is now investigating alternative stem cell sources including induced pluripotent stem cells.

**Professors Astrid Limb and Sir Peng Khaw** are developing use of the Muller Stem cell, discovered at the IoO and named the Moorfields IO cell, for treatment of retinal degeneration. This therapy is being translated with support from Apollo Therapeutics.

**Mr Andrew Goldberg** of the Institute of Orthopaedics and Musculoskeletal Science and orthopaedic surgeon at the Royal National Orthopaedic Hospital, leads a phase II trial of autologous mesenchymal stem cells for repair of Achilles Tendinopathy. The cells are cultured from patient bone marrow at the CCGTT GMP facility. A second pilot study assessing the role of stem cells in ankle arthritis is in process which is also developing novel ways to assess a patient's regenerative capacity.

**Professor Sam Janes** of the Division of Medicine has developed a therapy for lung cancer using genetically-modified mesenchymal stem cells expressing the TNF-related apoptosis inducing ligand TRAIL. An MRC-funded phase I/II clinical trial has MHRA approval and is in set-up, with GMP cells being manufactured at the CCGTT facility.

### Adoptive T-cells

UCL investigators have been pivotal in the evolution of adoptive T-cell therapies in the field of haematopoietic stem cell transplantation (HSCT). **Professor Steven Mackinnon** and **Professor Karl Peggs** of the Cancer Institute developed the use of virus-specific donor T-cells for the reconstitution of recipient anti-viral responses post-allogeneic HSCT and demonstrated efficacy in the context of cytomegalovirus (CMV) in early clinical trials. Phase II clinical trials to assess pre-emptive efficacy in the matched sibling and unrelated donor settings have been sponsored in partnership with cellular therapeutics company Cell Medica. The use of alodepleted donor T-cell populations to safely reconstitute the immune system post-HSCT has been developed by **Professor Persis Amroliya** of ICH GOS and **Professor Ronjon Chakraverty** of the Cancer Institute. Prof Amroliya's technology, translated to phase I/II clinical trial with the support of the TRO and the Cancer Research UK and UCL Cancer Trials Centre, depletes alloreactive T-cells based on expression of cell surface markers CD25 and CD71; Prof Chakraverty's technology, currently in phase II clinical trial, removes CD8 T-cells from the donor T-cell infusion.



Professor  
Martin Birchall



Professor  
Paolo de Coppi



Richard Day

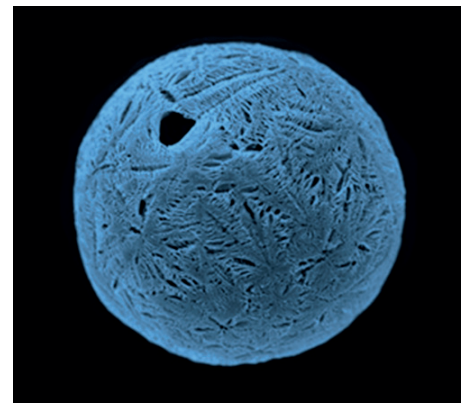
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## Tissue Engineering and Biomaterials

UCL's groundbreaking Tissue Engineering group comprises cell and developmental biologists, biomaterials scientists, biochemical engineers, clinician scientists and GMP manufacturers. **Professors Martin Birchall** of the Ear Institute, **Paolo de Coppi** of ICH GOS and **Mark Lowdell** of the Cancer Institute developed, manufactured and performed FIH tissue-engineered adult and paediatric tracheal tissue implants constructed from decellularized donor trachea seeded with recipient mesenchymal stromal cells. Phase I/II clinical trials for tissue engineered laryngeal, tracheal and oesophageal implants are active/in set-up. **Professor Massimo Pinzani** and team from the Division of Medicine have pioneered the development of tissue-engineered liver, and other tissue-engineered products in development at UCL include diaphragm, lung, liver, pancreas, small intestine, stomach, bladder, musculoskeletal and craniofacial tissue.

The UCL Centre of Nerve Engineering is another example of interdisciplinary working to achieve translational success. Launched in 2017 by cellular biologist **Dr James Phillips** from the School of Pharmacy and Mechanical Engineering's **Dr Rebecca Shipley**, the Centre's vision is "to create a multidisciplinary, inter-faculty research centre that translates diverse and complementary research in the physical and life sciences at UCL to clinical nerve repair". Dr Phillip's work developing tissue engineered neural tissue for nerve repair is supported by the UCL Technology Fund.

The first clinical trial of a UCL-developed biomaterial for tissue regeneration is the FIH phase I/II clinical trial of thermally-induced phase separation (TIPS) microparticles for the treatment of perianal fistulas. Developed by Division of Medicine's **Dr Richard Day**, TIPS provide a scaffold structure that cells can easily grow between and into. The clinical translation of TIPS technology, designated a class III medical device, has been supported by the UCLH BRC, UCL TRO and JRO. The knowledge gained in device regulations and manufacture will serve as a foundation for the translation of our significant biomaterials pipeline.



## HOW TO ENGAGE WITH US

In 2014 we established a team within the UCL Translational Research Office dedicated to the development and alliance management of strategic partnerships, working closely with our technology transfer office UCL Business and with Research Services to deliver a seamless package for engagement.

**If you would like to work with us to deliver on the promise of cell, gene and regenerative therapies, please contact Dr Chloe Marden (CGRM TIN Strategic Coordinator) at [chloe.marden@ucl.ac.uk](mailto:chloe.marden@ucl.ac.uk)**

**We very much look forward to working with you.**



**Dr Chloe Marden**

# CELL, GENE AND REGENERATIVE THERAPIES AT UCL AND PARTNER TRUSTS

World leaders in the translation of advanced therapies



## REFERENCES

1. Advanced Therapies Manufacturing Taskforce Report 2016
2. Clinical trials.gov analysis of cell, gene and regenerative medicine clinical trials open in September 2017
3. Advanced Therapies Scoping Review 2015, UCL Translational Research Office
4. Pan-London academic GMP requirements for cell, gene & regenerative therapies 2016-2021: UCL, King's College London, Imperial College London, MedCity, 2017.
5. £5M HEFCE Connecting Capabilities Fund award: King's College London, UCL, Imperial, MedCity

## LINKS

[www.ucl.ac.uk/translational-research](http://www.ucl.ac.uk/translational-research)  
[www.ucl.ac.uk/jro](http://www.ucl.ac.uk/jro)  
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