Innovation Hubs for Gene Therapies

Addressing the Skills Gap in Cell & Gene Therapies

UKRI Medical Research Council

UKRI Biotechnology and Biological Sciences Research Council

LifeArc

Contents

Foreword

In 2021, the three Innovation Hubs for Gene Therapies were established with £18m of funding from the Medical Research Council, the Biotechnology and Biological Sciences Research Council, and the medical research charity LifeArc. These world-class facilities offer manufacturing of commonly used vectors including both lentiviral and adeno-associated viral vectors that are needed for gene therapy trials.

Gene therapies offer huge therapeutic potential for a wide range of conditions and could enable patients to live without the need for ongoing medication or the burden of daily disease management. In the UK, we have a world-class research base and a well organised translational and clinical environment that will enable us to advance promising research into new genetic treatments for patients, including those with rare and life-threatening genetic diseases.

However, as with any emerging sector, there are barriers that must be overcome before this potential can be fully realised. The need for talented and skilled workers has intensified as more therapies are moving towards commercialisation. To continue to build on the UK's great strengths in this area, the Innovation Hubs will deliver an extensive training and skills programme to address the shortage of skills in GMP manufacturing.

Dr Sven Kili
CEO, Antion Biosciences

Chair of the Innovation Hubs for Gene Therapies Coordinating Committee

As GMP-accredited sites based in academic and healthcare centres of excellence, the Innovation Hubs for Gene Therapies are in a unique position to offer a wide range of training opportunities to support the UK sector and ensure that it remains at the forefront of delivering revolutionary gene therapies to patients. The Hubs will offer apprenticeships, short courses and Master's programmes in gene therapies and viral vector manufacture and bioprocessing, along with distance and self-paced learning opportunties.

To ensure the training and skills programme offered by the Hubs is complementary to the activities of other key stakeholders in the sector, the team have built strong links to the Cell and Gene Therapy Catapult, who operate the Advanced Therapies Apprenticeship Community and the Advanced Therapies Skills and Training Network, as well as the Bioindustry Association's Cell and Gene Therapy Advisory Committee.

It is imperative that the UK advanced therapies sector continues to attract new and upskill existing talent, to ensure the UK remains a global leader in clinical gene therapy research. I am delighted to present this report showcasing the contribution from the Innovation Hubs to address this vital need.

Professor Uta Griesenbach
Professor of Molecular Medicine, National Heart & Lung Institute, Imperial College London

Chair of the Innovation Hubs for Gene Therapies Skills and Training Group

Summary

The Cell and Gene Therapy (CGT) industry is one of the fastest growing areas in the life sciences, tackling diseases such as rare genetic disorders, cardiovascular and neuromuscular diseases, and cancer. Despite the growing interest and global investment in this sector, the demand for skilled workforce in this industry has become an obstacle for CGT companies in the UK. A core challenge for many of these companies is the recruitment and retention of skilled staff, particularly when it comes to bioprocessing and manufacturing of advanced therapies.

The Innovation Hubs for Gene Therapies (IHfGT) is a UK initiative designed to advance the clinical development of new genetic treatments. The Innovation Hubs are located in Sheffield, Bristol, and London, and based in academic and healthcare centres of excellence. The Hubs manufacture GMP-grade plasmids, lentiviral vector and adeno-associated viral vector (AAV) to support academics in translating their gene therapies to clinical trial, ensuring these novel treatments reach patients.

One of the Hubs' core ambitions is to support translational research and provide training opportunities to address the skills shortage. This report provides our perspective on the skills gap in the UK cell and gene therapy sector. There is an urgent need to ensure that the employment and recruitment of scientists meets the demand of this rapidly expanding area. To this end, we consulted with experts in the cell and gene therapy field from across academia, research institutes, and industry, and they provided insight and recommendations on how the Innovation Hubs could expand our training programmes. The findings of this consultation are presented in this report. In addition, we share the training activities offered by the Innovation Hubs, as well as those under development, to address the needs of the sector and to help maintain and expand the UK workforce.

Introduction to the Innovation Hubs for Gene Therapies

The Innovation Hubs for Gene Therapies (IHfGT) are helping academic researchers across the UK to take their gene therapy research into clinical trials by providing access to high-quality, clinical grade viral vectors and essential translational support and regulatory advice.

The Innovation Hubs were established in 2021 with £18m funding from the medical research charity LifeArc, the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC), in response to a request by academic researchers, service providers and stakeholders in the advanced therapies sector for support in translating viral gene technologies. The Innovation Hubs produce high quality lentiviral vector, help source plasmids and reagents, and will commence adeno-associated viral vector (AAV) production in 2023.

The Hubs, located in Sheffield, Bristol, and London, bring together staff with high-level expertise and work flexibly to meet the needs of researchers and gene therapy developers (see Annex 1).

Our vision is to accelerate academic-led development of novel gene therapies throughout the UK to bring new treatments closer to patients. We will achieve this by:

- **Increasing the volume of high-quality gene therapy research in the UK**
- **Increasing the number of gene therapies bridging the gap between early research, Phase I trials and beyond**
- **Supporting and improving the UK infrastructure for gene therapy research, enabling more scientists to work within the field**
- **Working closely with academics to advise, support and advance their research for the benefit of patients.**
- **Ensuring the skills and training needs of the sector are supported through the provision of training resources and materials.**

Skills and Training Committee

The network has a dedicated Skills and Training Committee with an ambition to address the skills gap in the advanced therapies sector. With a focus on manufacturing and bioprocessing, the network aims to build the UK's capacity and infrastructure in gene therapies through its training activities. The Hubs will upskill existing staff and bring new people into the sector through courses and apprenticeships, as well as offering training to academic groups developing gene therapies to share their expertise in manufacturing and support the translational pathway.

Each Hub brings unique strengths to the network, offering a variety of expertise delivered through a range of training programmes (Figure 1). Furthermore, the Skills and Training Committee has excellent links to other groups working to address the skills gap, for example the Cell & Gene Therapy Catapult and BIA Cell & Gene Advisory Committee, to ensure a joined-up approach across the advanced therapies community.

IHfGT Skills Consultation

A comprehensive skills consultation was conducted by the Innovation Hubs Skills and Training Committee. This was achieved through a series of interviews and discussions with academic (14 academics; 4 clinicians) and industry experts (17 manufacturing; 3 regulatory; 2 public bodies), to review the needs across the sector and ensure the Hubs deliver training packages that directly address the key skills gaps. The information provided in this report was gathered through a series of unstructured interviews, taking place between September 2022 – March 2023. A set of questions used during the consultation can be found in Annex 2. Given that several consultations and surveys focused on the advanced therapies skills gap have been published in recent years, this consultation focused on the remit of the Hubs and was intended to align with existing reports. The survey was used to inform any further gaps that the Innovation Hubs have the expertise and resources to address. The results of this survey are summarised in this report, along with the IHfGT Skills Strategy and an overview of the training packages available from the network.

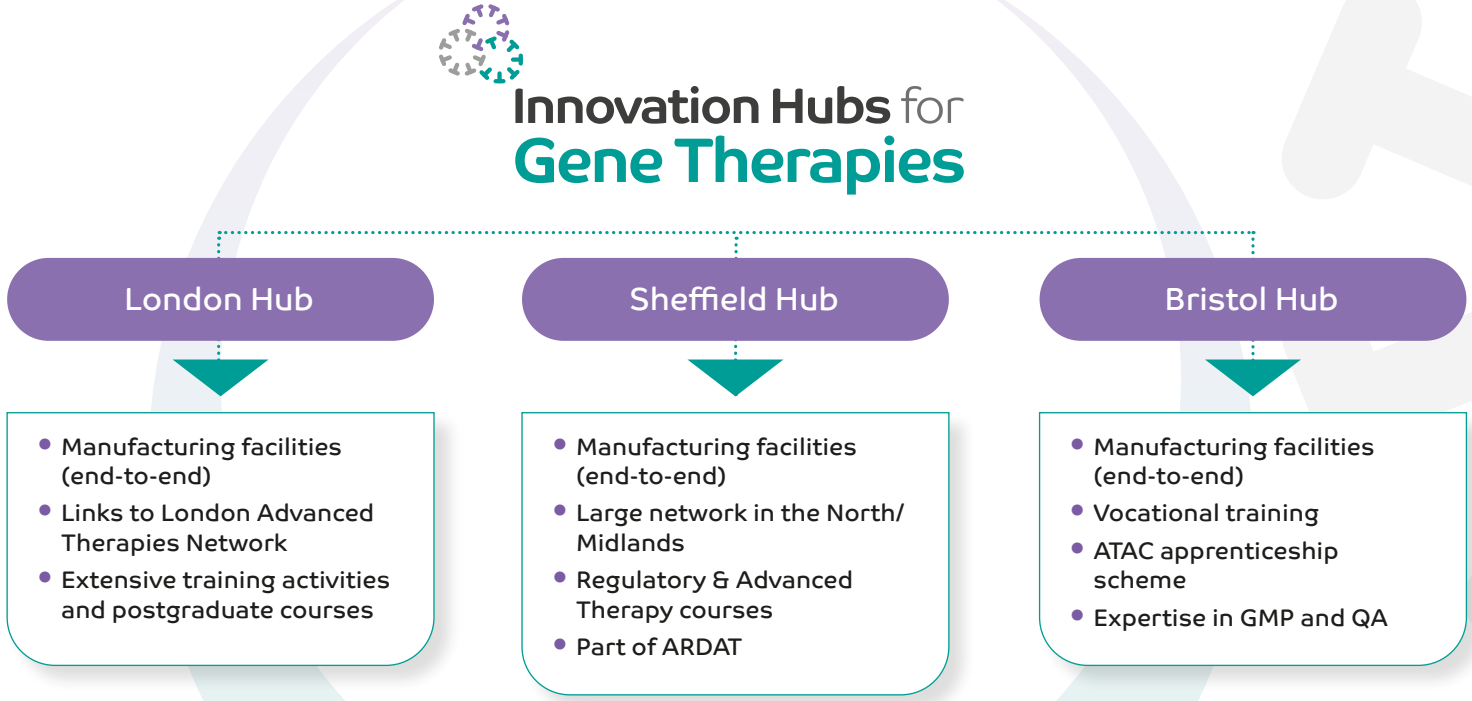


Figure 1: Each Innovation Hub brings unique expertise and training programmes to offer a comprehensive platform for addressing the skills shortage.

Meet the Team

Prof Uta Griesenbach
Imperial College London
Skills & Training
Committee Chair

Prof Qasim Rafiq
University College London

Prof Janine Kirby
University of Sheffield

Prof Laura Ferraiuolo
University of Sheffield[1]

Dr Joanna Przysowa
King's College London

Dr Anji Miller
LifeArc

Dr Ceri Roberts
NHS Blood & Transplant

Dr Suhair Salman
NHS Blood & Transplant

Dr Sujith Sebastian
NHS Blood & Transplant

Dr Sophie Mountcastle
Medical Research Council

Dr Mohammad Jaffar
University College London

Prof Francesca Gliubich
King's College London[2]

[1] Prof Ferraiuolo left the University of Sheffield as of April 2023.
[2] Prof Gliubich left King's College London as of May 2023.

Background

The Cell and Gene Therapy (CGT) landscape is emerging as one of the most transformative and fastest growing sectors in the biopharmaceutical industries. Globally, there are currently more than 1000 firms focused on the development of advanced cell and gene therapies and, as of 2022, there are over 300 clinical trials taking place[3]. The clinical potential of these therapies to provide personalised treatments with long-lasting therapeutic effects has resulted in significant investment to try and bring CGTs to patients. It is estimated that there will be over 60 new, approved CGTs in the next 10 years. Nevertheless, there are still challenges that CGT developers are facing, including patient access, manufacturing operations, regulatory hurdles, and the growing skills gap that need to be addressed to realise the potential of these therapies and to impact the healthcare system globally.

As a consequence of the growing interest in the area, the Cell & Gene Therapy Catapult was set up as one of a number of initiatives financed by the government and supported by UK Research & Innovation (UKRI) – a non-departmental body responsible for supporting scientific development across the UK. The CGT Catapult provides funding for the expansion and strengthening of the UK's highly skilled workforce in cell and gene therapies. The group said that, in 2022, around 5,000 people in the UK have been "up-skilled and supported through CGT Catapult-led initiatives." Since 2019, there has been a doubling in the levels of employment in this sector, with the CGT Catapult playing an important role in establishing the UK as a centre of technological innovation. One major accomplishment has been the establishment of the world's third largest cluster of cell and gene therapy companies, based around Stevenage, where collaborators have raised over half a billion dollars in the last twelve months. In 2022, 32% of European advanced therapy companies had operations within the UK, and 9% of all clinical trials in this therapy area were taking place in the UK[4].

The rapid growth and remarkable capital investment from governments and industry in CGT in the last few years has increased the need for skilled and experienced people to promote and stimulate development in the field. According to a recent Cell and Gene Therapy Catapult report,[5] the workforce in the CGT sector has increased 6-fold in the past decade. The recorded UK figure a decade ago was around 500, and by 2019 the headcount for CGT workforce was around 3000. This figure is predicted to double to 6000+ by 2024.

Financially, the CGT sector has grown exponentially in recent years and as of 2020, the investment into the sector was in the region of $20 bn. This is predicted to rise significantly in the near future and consequently, this has resulted in a skills gap bottleneck that needs to be urgently addressed in order to ensure these revolutionary treatments reach patients.

[3] https://clinicaltrials.gov/
[4] https://ct.catapult.org.uk/
[5] UK Cell & Gene Therapy Skills Demand Survey Report, 2021

Expert consultation results

In general, the stakeholders interviewed by the IHfGT Skills and Training Committee agreed that there was a skill shortage across the whole CGT space, with particular emphasis on the topics of manufacturing and regulation. More was needed to promote and tempt scientists into the area.

> *Skills is an issue that needs to be addressed*

The experts noted that many of the workforce interested in a career in the CGT sector would have transferable skills from their undergraduate (UG) and postgraduate (PG) degrees and / or post-doctoral experience gained in the general scientific fields. As in most industries, internal training and upskilling was available for new employees (for example, for clinical trial managers, production staff and QA/QC personnel). However, there were certain areas of expertise in the CGT sector that required specific attention due to the ever-evolving innovations and challenges in these areas. The experts indicated that the main shortage was in the manufacturing space.

Manufacturing

Due to the complexities of scale-up in the manufacturing process, a substantial team with specific skills and extensive facilities is required to deliver a product, especially if that product is patient personalised. Additionally, the manufacturing process is often largely manual and labour-intensive. Therefore, the processes are challenging and require a great level of control and monitoring.

Because the CGT area is young when compared to other scientific disciplines, there is a shortage of experienced laboratory managers and technicians that are available to provide 'in-house' training to new employees. This issue needs to be urgently addressed as the headcount is predicted to increase exponentially in the coming years – a striking and poignant example where demand outstrips supply.

> *Demand is outstripping supply*

This may be addressed, to some extent, by providing focused training opportunities and activities coupled with a clear career path for employees. It was indicated that there has to be a pleasant and gratifying working environment with a dedicated career path and financial incentive to keep new and experienced employees loyal to the sector. These proposed recommendations can also be applied to entice clinical trials managers, analytics and QA/QC personnel into the sector. In addition, the experts indicated that there should be a healthy collaboration between academia and industry, and this may be achieved through collaborative grants and the creation of a networking forum (Figure 2).

> *Competition of the workforce within the sector, instead of enticing personnel from other sectors*

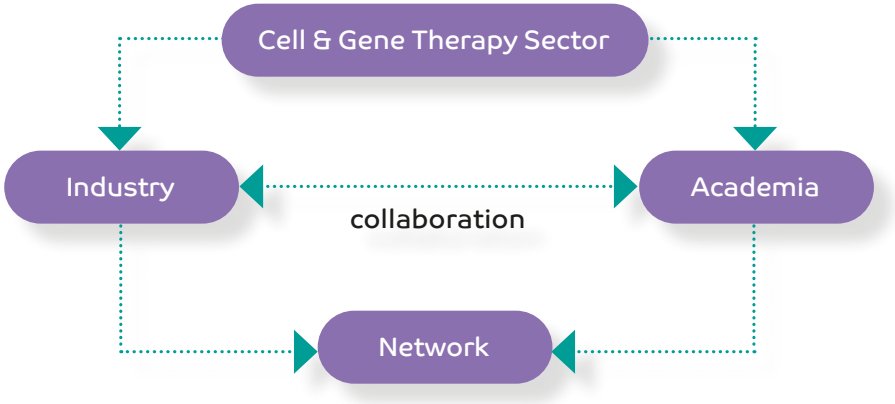


Figure 2: Illustration of the collaborative training environment

Regulation

The regulatory landscape of CGT is comparatively new and evolving in the field of medicines manufacturing. For example, temporary authorisation schemes were recently introduced for the approval of Covid-19 vaccines by international regulatory bodies. Prior to the emergency approval process for CGT, there were major hurdles and obstacles to approve gene-based therapies. The regulators worldwide were constantly updating their procedures, which was time consuming and costly for the developers.

Although many of the regulatory affairs professionals were upskilling in this area (usually from small molecule/biologics approvals), there was a clear need identified for specialised professionals dealing with gene therapy production. Major pharmaceutical companies may cope with this by upskilling their employees in that department, however, smaller biotechnology companies may have less capacity for upskilling their teams as they do not have the funding to run their own regulatory department. Fast-track approval and special dispensation for financial exemptions and exclusivity is also required to be able to deliver their product to the patient. The experts acknowledged that this may be problematic, and sustainable training courses in the form of continual professional training (CPD) for regulatory professionals should be available to counteract the demand for up-to-date understanding of the approval process. These types of courses should be linked with the regional regulatory authorities. The training courses should be managed and ran at educational institutions with help and assistance from industry.

Training courses and routes to upskilling in manufacturing and bioprocessing

Historically, industry has provided joint PhD opportunities in which the students spend a significant amount of time within the organisation, and they prefer this as it provides a source of talent into their company. In addition, some industry members have invested in an apprenticeship scheme, and although they value the scheme because it provides commitment by the apprentice and the organisation, it is not cheap to offer this type of training. Interestingly, industry experts were very open to the idea of providing focused workshops and training with some of the providers (academia and consultants). In general, participants from industry were highly supportive of online modular courses and blended learning approaches (to include a 2-3 day practical training element).

> *"Apprenticeship scheme is brilliant, although there is commitment, it's not cheap"*

Academic institutions can also deliver training in the CGT field, and this can be delivered at UG, PG, post-doctoral and professional levels to produce skilled personnel for the sector. The consultation identified that universities should consider providing additional courses and specific activities (e.g., within a specific discipline related to manufacturing and bioprocessing) in collaboration with industry, designed to offer the learners already working within a company the skills necessary to promote their learning and abilities within the sector. This may be in the form of continual professional development or a part-time, self-paced accredited programme.

Training is an important facet to maintain growth and innovation within the CGT sector. Most industry stakeholders provided adequate budgeting for training but stressed that the finances allocated to training should be used wisely, i.e., one course fits all, and training courses should benefit the majority of training courses to benefit the majority of their workforce. Training can be achieved via hands-on and/or modular courses to aid the workforce in their development path in the CGT area. In some cases, the biotech and pharma sector provide in-house upskilling training to their employees. In other cases, they may bring in consultants to train their employees. Nevertheless, industry stakeholders were keen to cooperate with academic and research institutes to develop specialised courses that are beneficial to the employers and employees alike.

> *"Online modular courses are more practical"*

Sustainability

In general, the results from the survey indicated that training courses should be developed in academic institutions, with the content agreed upon by a panel made up of academics and industry experts and based on the current and foreseeable training gaps. Once the courses have been identified and developed, they should benefit both internal (MSc and PhD students, post-doctoral staff) and external (industry delegates) learners.

This model should be sustained based on the income and developed by the academic and non-industry institutions with input from industry experts. This model should be sustained based on the income generated from delivery of these programmes to drive new opportunities and development. There may be areas of development that industry may contribute both financially and in-kind to the academic institutions and these must be explored too.

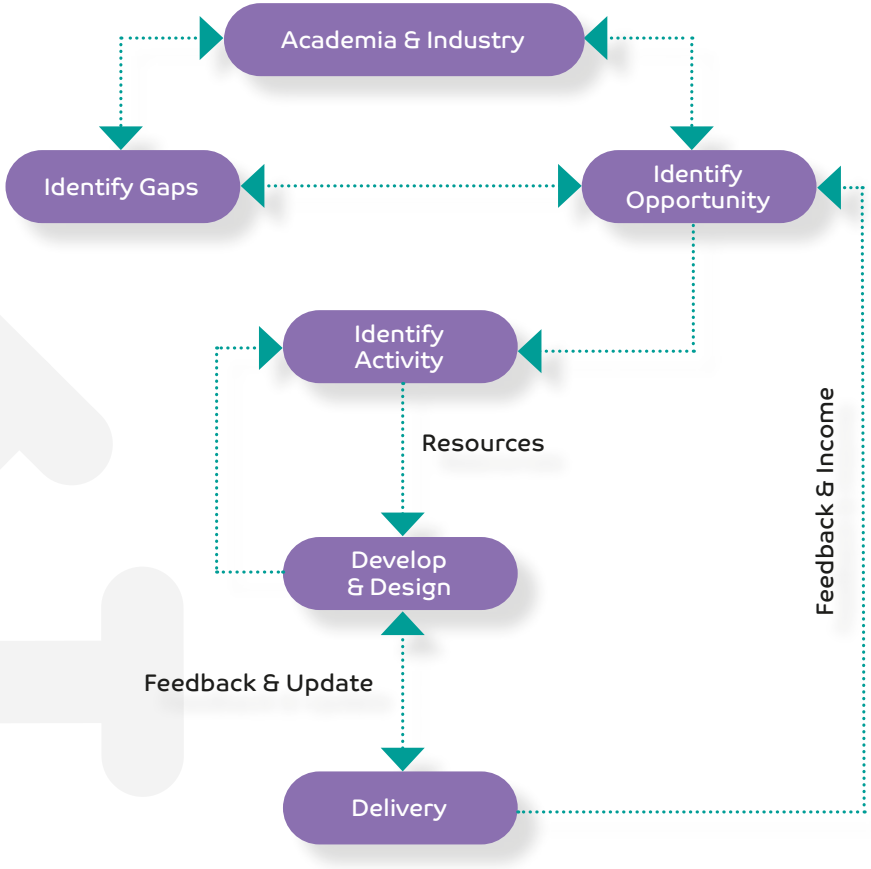


Figure 3: Designing and delivering training and activities

Training Courses and Programmes offered by the IHfGT

The Hubs offer a suite of training opportunities for individuals already in or interested in moving into the cell and gene therapy field (listed in Tables 1a and 1b). These include apprenticeships, online modules, practical placements, short courses, a new MSc in Advanced Cell and Gene Therapies (University of Sheffield), and a planned distance-learning MSc in Manufacture and Commercialisation of Advanced Therapies (UCL). In addition, the IHfGT (in collaboration with MRC and LifeArc) are developing new online courses to support the sector. These courses were designed based on the outcomes of the consultation conducted with experts in industry, academia and the wider CGT community to provide topics that may benefit the employees and the employers. Table 1b outlines courses that are in development as a result of the consultation.

In addition, the Hubs also offer training opportunities in the production of materials (including GMP grade) from their manufacturing facilities (Table 2). The Hubs provide high-level expertise, help, support and access in the production of GMP grade materials from early-stage research through to clinical development. Moreover, they can work flexibly to meet the needs and commitment of researchers for their funding applications.

Apprenticeships

Bristol

A key workforce development strategy being successfully utilised to address the demand for skills has been engagement in novel apprenticeship schemes. NHSBT was one of the original founding employers of the award-winning Advanced Therapies Apprenticeship Community (ATAC)[6]. The organisation employs apprentices from a range of Level 3 to Level 7 programmes, including Level 3 Science Manufacturing Technician, Level 5 Technician Scientist and Level 7 Senior Leader. Through a flexible, blended learning approach, apprentices develop a portfolio of evidence and complete an end point assessment to demonstrate acquisition of the required knowledge, skills and behaviours. In addition to bringing valuable new talent into the organisation[7], apprenticeships have facilitated the useful upskilling of existing members of staff at NHSBT.

NHSBT offer a Level 7 Regulatory Affairs Specialist apprenticeship programme[8]. Equivalent to Master's level competence, the Regulatory Affairs Specialist is responsible for developing and implementing strategies that allow an organisation to legally develop, manufacture, market and supply healthcare products. The learner will critically evaluate the evidence generated during the development and use of products. This is to ensure suitability to support obtaining and managing marketing authorisations, CE marks and approvals for clinical studies in line with legal requirements. The programme will enable the learner to take a leading role to ensure products comply with the regulatory requirements to receive an initial license for marketing. For this programme there is the option to undertake the Advanced Therapies route.

MSc Courses

Sheffield

The University of Sheffield has a track record in the application of cell and gene therapies for human disease. As part of the MSc in Advanced Cell and Gene Therapies, students learn about some of the successful clinical trials which have been undertaken in Sheffield, such as stem cell treatments of multiple sclerosis, gene replacement treatment for spinal muscular atrophy and antisense oligomers against SOD1-related amyotrophic lateral sclerosis. The course includes how clinical trial approval is obtained as well as some of the other innovative approaches that are in development and clinical trials, such as CAR T cell technology. Due to Sheffield's strengths in this area, a new short-course on Clinical Trial Design is being developed to provide additional support to stakeholders requiring more experienced personnel in this area.

The University of Sheffield MSc in Advanced Cell and Gene Therapies includes a module on Clinical Developments in Cell and Gene Therapies, which has sessions on the regulatory processes associated with the manufacture and use of cell and gene products. These sessions are provided by experts in the field, both from Sheffield and from industrial partners. In addition, sessions also discuss the necessary requirements of pre-clinical regulatory trials as well as ethical approval procedures, prior

[6] https://advancedtherapiesapprenticeships.co.uk/latest-news/casestudies/nhsbt
[7] https://advancedtherapiesapprenticeships.co.uk/latest-news/casestudies/lauren-howe-redefining-what-it-means-to-be-an-apprentice/
[8] https://advancedtherapiesapprenticeships.co.uk/latest-news/programmes/regulatory-affairs-specialist-for-advanced-therapies/

to securing clinical trial approvals. A new short-course to focus specifically on the regulatory aspects of the use of these products is currently being developed. In addition, a PG Cert in Advanced Cell and Gene Therapies, comprising of modules including Principles of Gene and Cell Therapy and Clinical Developments in Gene and Cell Therapy will become available, as well as each of these being available as standalone CPD modules.

Bristol

Furthermore, The University of West England (UWE Bristol) offers a Master's degree in conjunction with NHSBT in Applied Transfusion and Transplantation Sciences. The 30-credit level 7 module 'Management of Clinical Services' is available as a standalone course that covers regulatory frameworks, validation, risk reduction, leadership, management and accreditation. The module aims to develop critical evaluation with respect to service provision enhancement through the application of leadership and management theory and understanding of regulation and quality enhancement, with the aim of improving organisational value.

London

The Biochemical Engineering Department at UCL hosts an MSc course in Manufacture and Commercialisation of Stem Cells and Gene therapy. This one-year, full-time programme provides the latest advances in the rapidly growing sector of advanced therapies and regenerative medicine, as well as providing an in-depth industry perspective, research experience with internationally renowned research groups and key transferable skills to advance the student's career. The students are introduced to real-life case studies of novel therapeutic manufacture and the lectures are taught by academics and industry experts as guest speakers to provide industry-relevant scenarios. The approach to the teaching and learning focuses on lecture-based content, problem-based learning – where students work in small groups on real-life cases to solve open-ended problems and lab-based experience. The students will be expected to engage in critical discussion regarding the sector. The course also provides site visits and extensive laboratory training. On completion the course, the students will have developed key skills required of the translational pathway of gene therapies including topics in fundamental biology, viral/non-vector design, pre-clinical and clinical studies, GMP manufacturing, technology innovation, process analytical technologies, risk-based analysis (e.g. Quality by Design), quality assurance and control, clinical design, commercialisation and market authorisation.

In addition an MSc (via MBI®) Bioprocessing is also offered at the department at UCL which supports the working professionals to master bioprocess fundamentals, advance their bioprocessing skills and accelerate their career. This programme is comprised of a series of core and optional courses delivered in a modular format designed to fit around full-time work commitments. The programme is designed for students to have the flexibility to customise their curriculum. The taught modular degree provides the learner with the opportunity to study in an academic department recognised for its quality of research, innovative teaching techniques and strong connection with industry. The programme is taught by academics and sector leaders to advance and refocus their career.

Short Courses

During the consultation, experts indicated that they preferred 2-3 day training programmes (such as the UCL MBI suite of courses) or online modular self-paced courses that would not affect the organisation's day-to-day activities. Newer courses should be developed to account for the novel innovations taking place in the sector.

Bristol

Within NHSBT there is a well-embedded culture and practice of 'Lean' Continuous Improvement (CI). Our staff benefit from a dedicated CI support function who help to facilitate CI activity across NHSBT's diverse operational areas and also provide a range of CI training courses that are LCS (Lean Competency Systems) accredited by Cardiff University.

As part of our contribution to a coordinated, network-wide approach for a shared syllabus, we will offer bespoke learning sessions on Continuous Improvement which can be made available to the network and external participants. These sessions will be delivered remotely, to remove geographical barriers to participation and are available for 10 participants at a time.

Process improvement and reduction of process variability is critical in advanced therapies manufacturing. Adoption of Continuous Improvement

principles from other manufacturing industries to cell and gene therapy manufacturing sector allows to improve the process and reduce waste. NHSBT offers a foundation course on the Continuous Improvement fundamentals. This course is a Lean Competency System (LCS) accredited (LCS level 1a) and is an introduction to the 5 Lean Principles, Recognising waste and Elements of a 'Lean Cell'. Advanced Therapies manufacturing as a developing manufacturing discipline, adaptation of LCS to organisations will have several benefits such as linking the training with practical application, improving business performance along with a widely applicable standard to follow by the organisation.

In order to address the existing skills and training gap in the advanced therapies sector, a series of digital teaching sessions will introduce CI concepts and tools relevant to the Hubs' activities. This training will help to address challenges in advanced therapies manufacturing to reduce errors and improve manufacturing processes.

- **Human Factors**

  This module will focus on 12 most common precursors which influence people to make mistakes, and the countermeasures which could be used to reduce the possibility of errors occurring. This will consider factors such as operators, the equipment they use, the task they carry out and the environment in which they work.

  - **6S principles** – Another training module that emphasizes lean process improvement tool which promotes organising and managing a workplace that is well-kept, efficient, and safe. Utilising 6S can help to reduce waste and avoid many of the precursors to errors.
  - **Kanban inventory management** is a visual method for managing workflow. Kanban for inventory management uses visual cues to start the restocking process, this reduces waste, storage space and eliminates time consuming manual stock check procedures.
  - **Kamishibai** for audit readiness, a lean process improvement tool used for ongoing, regular mini audits. The goal of the mini audit is to check if expected standards are maintained and will help direct your team to recurring issues to be addressed.
  - **Error Logging** can show if processes are drifting towards failure. It will detect issues at an early stage and provide data for focused problem solving, preventing small issues becoming more serious quality incidents.
  - Reviewing error data for action and **Problem Solving** - This topic builds on error logging which helps in identifying root cause of problems and therefore and triggers problem solving based on the identification of the root cause of problems so that they can be eliminated.

Implementing a continuous improvement culture will enhance the manufacturing, QC and QA processes which in turn improves and streamlines the training processes and upskilling of staff.

MBI® Modular Short Courses

The Modular Training for the Bioprocess Industries (MBI) programme pioneered by UCL Biochemical Engineering is a series of intensive online, blended and/or face-to-face short courses designed for professionals in the bioprocessing industry. The MBI Programme has a long history of equipping the bioprocessing industry's workforce with up-to-date skills and knowledge of process options in order to rapidly develop validated, efficient and robust processes. It also provides invaluable insights on the latest technical and regulatory developments and achieves this via a flexible route that provides ongoing motivation, creativity and professional status for delegates. These courses are led by senior UCL Biochemical Engineering Faculty members and in collaboration with industrial experts. These short courses, such as Cell and Gene Therapy Bioprocessing, Antibody-targeted Therapy and Industrial Biotechnology amongst others, attract a diverse cohort of delegates ranging from life scientists and process engineers, who are keen to gain insights into the current trends in gene therapies, regulatory affairs and cutting-edge research. Each short course is UCL-accredited and can be taken individually or combined for a Master's level qualification.

Training for academic researchers

Bristol

One of the consultation's findings is the lack of practical experience in the CGT field. NHSBT provide training to their academic UK clients who seek process adaptation to GMP compliant methods that could help them to improve the manufacturing process and reduce development time when the process is transferred for manufacturing. This will be in selected aspects of the viral vector manufacturing process. With particular focus on AAV with an opportunity to better understand procedures within the requirements of GMP and regulatory compliance. This will enable early adoption of GMP principles into the R&D space.

As part of short training placements, participants will be introduced to various stages of a process with practical training as well as theoretical learning (which may include short introductory videos that can be accessed prior to placement). This will be supplemented by support from our quality assurance personnel to give insights into routine operational activity in our facilities.

This is an important activity to help retain staff within the IHfGT network by offering career development opportunities, as well as improving collaboration across the teams. For external users, offering academics the chance to gain experience in GMP and take that knowledge back to their research group will help to upskill the community and ensure a smoother transition from lab to clinical trial.

London

At the King's College London Gene Therapy Vector Facility, National Trainer support has been initiated to provide tailored support to the other Hubs to develop pharmaceutical quality systems and viral vector manufacturing protocols for AAV and LV products based on the expertise available at the London Hub. The support is dedicated to the researchers working within the Hubs network, by contacting the London Hub coordinator through a dedicated email address, to describe the issues encountered with protocol design or application.

Table 1a: Current IHfGT Training & Activities

Hubs	Programmes (FT, PT)	Short courses (F2F, online, blended)
London UCL Biochemical Engineering	MSc Cell & Gene Therapy Manufacture & Commercialisation (FT, 1-year)	Cell & Gene Therapy Bioprocessing & Manufacture (part of MBI suite of courses) (blended, 3 –day course)
London King's College London	KCL – GTVF (Training, seminars, visits, speaker events, formal discussions)	Viral vector production, purification & control GMP and Regulatory Compliance Regulatory, QA and QC matters GMP manufacturing (CPD)
Sheffield	MSc Advanced Cell and Gene Therapies (FT) (1-year F2F; MRC bursaries available to UK students)	
Bristol	Advanced Therapies Apprenticeship Master's degree research projects placement	MSc Module Management of Clinical Services, short course, 30 credit, Level 7 (in collaboration with UWE)

F2F – Face-to-Face
UWE – University of the West of England (Bristol)
FT - full time
PT - part time
GTVF - Gene Therapy Vector Facility

Table 1b: IHfGT Training Activities (under development)

Hubs	Programmes (FT, PT)	Short courses (F2F, online, blended)
London UCL – Biochemical Engineering	MSc Cell & Gene Therapy Manufacture & Commercialisation (PT, 2-year, online)	Gene Therapy, Stem Cells and Regenerative Medicine (short course, online)
Sheffield	PGCert Advanced Cell and Gene Therapies (FT)	**CPD modules:** • Principles of Gene Therapy (F2F) • Clinical Developments in Gene and Cell Therapeutics (F2F) • Beyond Cell and Gene Therapies (F2F) • Short Courses: • Clinical trial design (online) • Regulatory approval (online)
Bristol	Technical and practical based placements Inter-hubs staff exchange	**Continuous Improvement Foundation Course (LCS accredited LCS1a):** • Lean Competency Systems (LCS) • Human factors • 6S Principle • Kanban Inventory Management • Kamishibai for Audit Readiness • Error Logging & Reviewing Error Data for Action

Table 2: Manufacturing Activities

Hubs	Facility	Manufacturing/Production
London **KCL**	GTVF	GMP grade LV production GMP grade RV production GMP grade AAV production
Sheffield	GTIMC (operational in 2024)	
Bristol	NHSBT – Clinical Biotechnology Centre MHRA Licensed GMP Facility IMP Manufacture & Import License Dedicated QA & QC Testing Capability In-house QP for Batch Release Service	GMP grade Plasmids (up to 3g) GMP grade lentiviral vectors GMP grade AAV Viral vectors for pre-clinical studies

GTVF – Gene Therapy Vector Facility
GTIMC – Gene Therapy Innovation & Manufacturing Centre
NHSBT – NHS Blood & Transplant
QP – Qualified Person

Sustainability

It is essential that the courses and activities offered by the IHfGT (and more widely across the sector) are sustainable and up-to-date, and all Hub training courses will be reviewed and revised periodically to ensure they continue to address the current and foreseeable needs for the sector.

Bursaries and scholarships

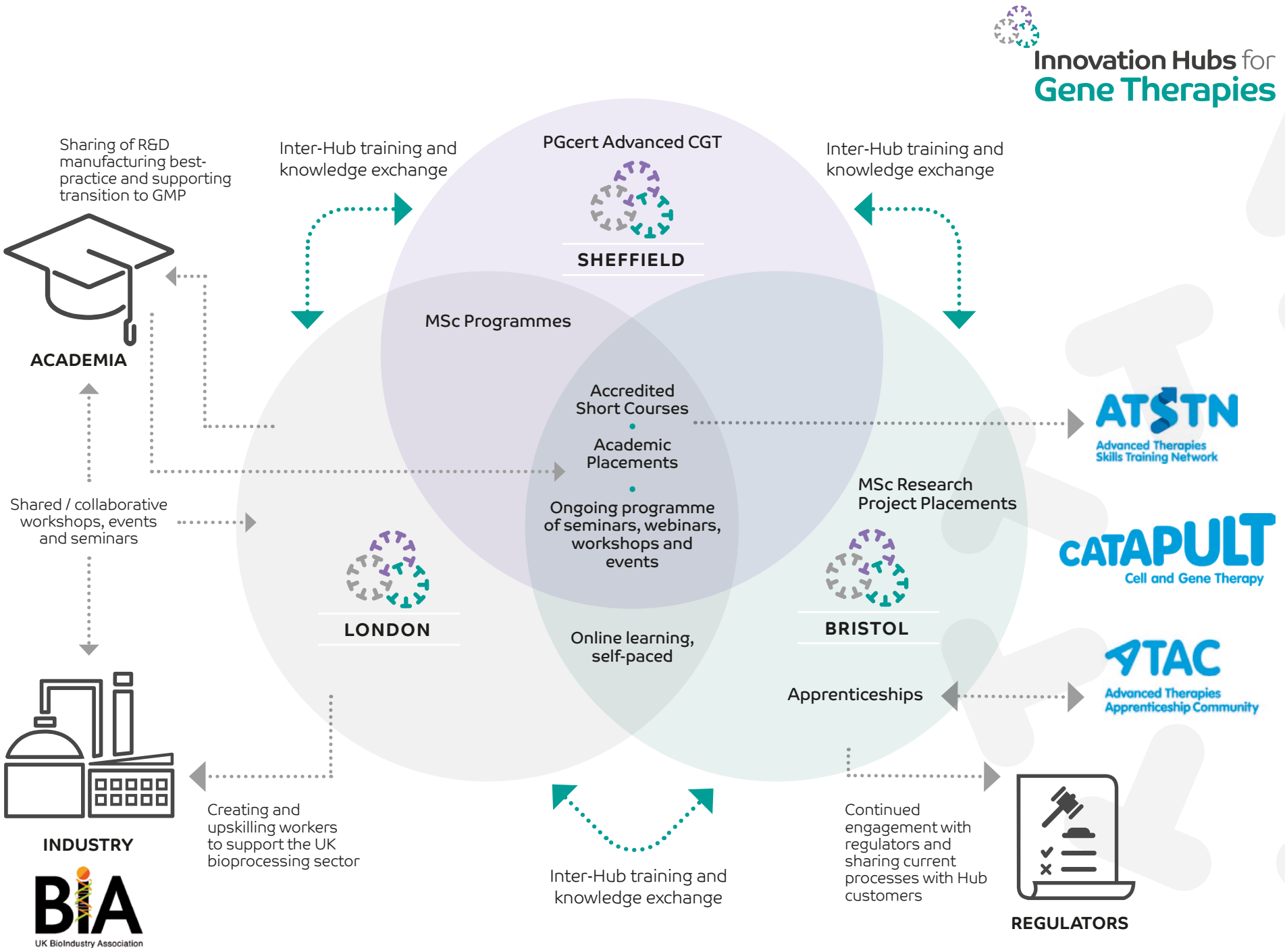
The Hubs are planning to fund scholarships for under-represented students in the long term through their collaborations with the private sector, i.e. biotech companies, equipment providers or pharma companies. As an example, the London Hub has already secured 2x industry-funded scholarships from Pall Biotech ($10,000 each) for disadvantaged students to attend the existing full-time MSc programme in cell and gene therapy. As a second source of scholarship-funding, the Sheffield Hub are engaging with the University's Campaigns and Alumni Relations (CAR) team, to explore the use of philanthropic donations for student bursaries.

Short courses

The Hubs will offer short, in-person training opportunities at-cost to staff from academic applicants and partners for whom the Hubs are manufacturing products for proof-of-concept studies and phase I clinical trials. There will be a surcharge for industrial partners who are looking to undertake the same training. These charges will ensure the Hubs can continue to offer these opportunities beyond the funding period.

Online, self-paced, and digital courses

Once established, the online courses offered by the three Hubs will continue to be updated, but the Hubs envisage their cost to be constant over time. As such, these courses will become part of the educational portfolio offered by the three institutions and will be curated by dedicated staff already in place. Like the other courses already running at the institutions, these will be offered for a fee that will guarantee the sustainability of the programmes (provided there is sufficient demand). The potential to continue provision of the courses established at the Hubs beyond the current programme of funding will be explored periodically based on the level of demand and feedback received.


Innovation Hubs for Gene Therapies
Sharing of R&D manufacturing best-practice and supporting transition to GMP
Inter-Hub training and knowledge exchange
PGcert Advanced CGT
SHEFFIELD
Inter-Hub training and knowledge exchange
ACADEMIA
MSc Programmes
Accredited Short Courses
Academic Placements
Ongoing programme of seminars, webinars, workshops and events
ATSTN Advanced Therapies Skills Training Network
MSc Research Project Placements
Shared / collaborative workshops, events and seminars
LONDON
BRISTOL
CATAPULT Cell and Gene Therapy
Online learning, self-paced
Apprenticeships
ATAC Advanced Therapies Apprenticeship Community
INDUSTRY
Creating and upskilling workers to support the UK bioprocessing sector
BIA UK BioIndustry Association
Inter-Hub training and knowledge exchange
Continued engagement with regulators and sharing current processes with Hub customers
REGULATORS

The Future

The CGT sector is becoming a major area in the field to revolutionise personalised medicine and treat rare diseases in the clinic. To leverage growing investment in this area, and ultimately for patient benefit, the infrastructure must be put in place. This infrastructure should augment the manufacturing capabilities, skills and training in tandem with the new innovations in the sector. Particular attention must also be given to promoting an inclusive workforce in the CGT space.

Historically, CGT treatments have focused on rare diseases (and ultra-rare diseases), A strong foundation today will launch the sector into the treatment of more conventional diseases with relatively large patient population, putting CGT at the centre of life-saving and life-changing therapies.

There is a critical level in the skills gap which may impact current and future investment in the area. Hence, a sustainable solution to the skills gaps in this sector is urgently required to enable the development of new and innovative CGTs. The sector must collaborate to attract, retain and enlarge the talent pool in the coming years. This may be achieved with the help of the CGT biotech and big pharma (and in collaboration with academic and research institutions), as well as other training providers (e.g., CGT Catapult, ATTC, ATSTN). Although the industry must come up with new strategies to counteract the skills shortage, it is also imperative that training providers communicate and enhance exposure to the courses already available and in development.

> *“Regular focused workshop between industry and academic delegates”*

The survey results indicated that there should be a continual interaction between academia, research institutes and industry. Partnerships should be developed and sustained through focused groups and workshops meeting periodically to examine and enhance the training activities available to best meet the needs of the sector. Additionally, in collaboration with other training providers, the Hubs should showcase their activities through exposure in conference workshops and participation with other UK (and European) providers. Moreover, there is an urgent need to provide access (not just visits) to the manufacturing sites – here, industry participation is key.

Aligning with our commitment to enhance the skills and knowledge of the advanced therapies workforce, a range of training and work placements in different formats will be provided by the Innovation Hubs. These training opportunities will be reviewed and enhanced based on the participation and future demand from the learners.

Acknowledgements

The Innovation Hubs would like to thank all those who participated in our consultation process and shared their valuable insight which has helped shape our training courses and programmes.

We would also like to thank our partners, particularly the Cell and Gene Therapy Catapult and BioIndustry Association Cell and Gene Therapy Advisory Committee, with whom we value our continued collaboration to address the skills gap in the UK advanced therapies sector.

Finally, thank you to all those that have engaged with our programmes to-date, and above all to the students and attendees who have participated in our courses and provided valuable feedback to ensure we continue to deliver the highest quality training for advanced therapies professionals.

Useful Resources

To find out more about the Hubs and the courses on offer, visit:

https://www.genetherapyhubs.uk/

https://www.ucl.ac.uk/biochemical-engineering/ucl-biochemical-engineering

https://www.sheffield.ac.uk/gtimc

https://www.kcl.ac.uk/lsm/research/innovation-hub-gene-therapy

https://www.nhsbt.nhs.uk/cellular-and-molecular-therapies/clinical-biotechnology-centre/

To find out more about the funders, visit:

https://www.lifearc.org/

https://www.ukri.org/councils/mrc/

https://www.ukri.org/councils/bbsrc/

There are several platforms that offer a range of free and paid-for training courses spanning the cell and gene therapy manufacturing and bioprocessing sector. A few are listed here.

Advanced Therapies Skills Training Network (ATSTN)

https://www.atskillstrainingnetwork.org.uk/

Launched in December 2020 and backed by £4.7 million in funding from the Department for Business, Energy & Industrial Strategy (BEIS) and Innovate (IUK), the ATSTN has been developed as a national initiative to drive growth across the advanced therapies and vaccine manufacturing industry, through offering access to training facilities and an online training platform which can address the UK's demand for skills.

Advanced Therapy Apprenticeship Community (ATAC)

https://advancedtherapiesapprenticeships.co.uk/

The scheme, overseen by the CGT Catapult, supports 137 apprentices in 36 companies.

Advanced Therapy Medicinal Products Training, NSF

https://www.nsf.org/training/series/advanced-therapy-medicinal-products-training?_locale=set

The Centre for Advanced Therapies Manufacturing Training

https://www.birmingham.ac.uk/research/centre-for-advanced-therapies-manufacturing-training/our-training.aspx

Hosted by the University of Birmingham, the centre provides training courses for those interested in ATMPs.

Biological and Advanced Therapies, King's College London

https://www.kcl.ac.uk/short-courses/biological-and-advanced-therapies-1

Advanced Therapy Treatment Centres

https://www.theattcnetwork.co.uk/case_studies/education-and-training-on-advanced-therapies-in-the-nhs

Cell and Gene Therapy Bioprocessing (MBI Training, Bioprocess Industries)

https://www.ucl.ac.uk/short-courses/search-courses/cell-and-gene-therapy-bioprocessing-mbi-training-bioprocess-industries ***(also need link to UCL portal)***

Annex 1 – Innovation Hub Services

Bristol Hub

Clinical Biotechnology Centre, NHS Blood and Transplant

NHS Blood and Transplant's Clinical Biotechnology Centre (CBC) has been a leader in the manufacturing of high-quality Investigational Medicinal Products and raw materials for clinical use for two decades. The Cellular and Molecular Therapies division has contributed towards the treatment of large numbers of patients, and NHSBT is committed to expanding its impact even further.

When it comes to GMP-grade plasmids and proteins, the NHSBT CBC is the top choice in the UK. An MHRA-licensed facility, the CBC is part of the Innovation Hubs for Gene Therapies manufacturing GMP grade lentiviral vectors and recombinant adeno-associated viral vectors at different scales to enable early-stage clinical studies.

CBC offers its platform technology for producing and purifying vectors and welcomes technology transfer for alternative methods based on clients' requirements. The CBC manufactures 10L and 40L vector batches using HEK293 suspension cells grown in stirred tank bioreactors. As an innovative ATMP manufacturer, CBC is flexible and adaptable to support other scales and cell culture formats and offers high-quality non-GMP vector manufacturing to support developers at pre-clinical stages to translate more therapies to clinical stages.

NHSBT has a highly skilled and experienced QA department and QP ensuring that all Investigational Medicinal Products produced meet the highest standards of safety and quality. This places NHSBT to be the established partner of choice for leading gene therapy groups across the UK and Europe. NHSBT is committed to excellence and ongoing skills development and poised to continue making a significant impact in the ATMP manufacturing industry for years to come.

Sheffield Hub

Gene Therapy Innovation and Manufacturing Centre (GTIMC), University of Sheffield

The Gene Therapy Innovation and Manufacturing Centre (GTIMC) will tackle the major challenges in gene therapy development for some of the most devastating rare diseases. Gene therapy is a promising treatment option for more than 7,000 rare diseases that currently have no cure. Gene therapies rely on engineered virus carriers as vehicles for the delivery of synthetic genes that correct disease-altered changes in multiple organs of the human body.

The GTIMC will enable new gene therapies to benefit patients more quickly. The state-of-the-art centre brings together academic institutions, NHS trusts, non-profit and industry partners across the north of England, Midlands and Wales enabling academic-led clinical trials of novel gene therapies.

The GTIMC will deliver essential translational support alongside extensive training and skills programmes to enable upskilling and address shortage of skills in Good Manufacturing Practice (GMP) manufacturing.

The centre will utilise highly efficient processes to manufacture clinical grade adeno-associated viruses (AAV) and provide all the necessary quality assurance for use in human trials at Advanced Therapies Treatment Centres and NHS trusts within the GTIMC and the national network.

London Hub

Gene Therapy Vector Facility, King's College London, in partnership with the Royal Free Hospital and University College London

The Kings College London Gene Therapy Vector Facility (GTVF) is a state-of-the-art facility established to support the scientific community in their delivery of the latest cutting-edge gene therapies into the clinic. With a legacy dating back to 2006, the GTVF is now one of the largest suppliers of GMP-grade viral vectors for clinical trials across Europe, offering Lentiviral vector, Retroviral vector and Adeno-associated viral vector (coming soon).

The GTVF is run by a large, professionalised team of ~50 people who have extensive experience in delivering end-to-end viral vector manufacture for both academic and commercial clients, with a focus on early stage clinical activity.

Lentiviral Vector (LV) and Retroviral Vector (RV)

The GTVF hosts four MHRA accredited, fully-equipped production cleanrooms for GMP vector production. With plans to open a further two cleanrooms in 2023, and more in 2024, the facility is purpose-built to handle a high volume of concurrent projects. The team currently makes use of a transient production/transfection system, using adherent cells with multi-layer cell factories. The GTVF has delivered >100 batches of LV and RV over its long history, and has extensive experience with supporting UK, European and US projects.

Adeno-Associated Viral Vector (AAV)

The GTVF is set to begin servicing clients with AAV vector in early 2024 with a large, dedicated team and state-of-the-art facilities. The team will initially make use of a well-characterised adherent cell line system, and with ongoing process development work will gradually move to adopt adherent/suspension bioreactor technology. There will be an initial focus on delivering the AAV9 serotype, though with wide-ranging expertise across a range of AAV serotypes, the team will expand into other serotypes over time.

End-to-End Service

The GTVF offers a client-driven end-to-end service, and is on hand to support with some or all of the following activities:

- **Project management**
- **Plasmid sourcing (as needed)**
- **Assay development**
- **Up-front pilot studies**
- **Small-scale pre-run testing**
- **Engineering test-runs**
- **Full-scale GMP manufacture**
- **QC testing and batch release**
- **Regulatory support**

Annex 2 – Skills Consultation Questions

The below set of questions were used as a guide to initiate discussions, but the interviews and discussions were unstructured. The interviewees were allowed to comment on specific topics relevant to their area of expertise and/or in general terms within the sector.

An introduction to the consultation process was provided to experts prior to the interview, which included information on the Innovation Hubs and their services.

Identifying Gaps

1. **Where would you identify the greatest need for your C&GT organisation (if relevant) and/or the wider sector with respect to training and skills development?**
2. **Rank your need for skills in those disciplines, as low/medium/high priority:**
    - R&D
    - Process Development
    - Manufacture and Production (including GMP)
    - Quality Management (QA)
    - Quality Control
    - Risk Management
    - Regulatory
    - Business Development
    - Clinical Trial Management
    - Process Economics / COGS
    - Health Economics and Market Access
    - Project Management
    - Other (please specify)
3. **What is your current approach to C&GT training new or existing employees?**
4. **Do you currently use any external skills or training programmes and activities for C&GT training?**
5. **Are there skills or training programmes that you believe are beneficial to your organisation and/or the C&GT sector?**
6. **Regarding the courses & programmes for training staff members, what is the preferred (remote/F2F), length, and level of training you would expect?**
7. **What is your approximate annual skills and training budget for C&GT operational roles?**
8. **How much time do you think is reasonable to allocate for skills and training development for your C&GT operational employees?**

Current Recruitment

9. **What roles are you primarily looking to fill within your organisation?**
10. **What skills would you consider essential when seeking candidates to work in operational roles within C&GT?**
11. **Where are you looking for skilled people and with what level of experience?**
12. **To what extent does EDI feature as part of your recruitment process to support skills and training activities now and potentially in the future?**

How can the Hubs help?

13. **What are your expectations of the Hubs with respect to C&GT skills and training?**
14. **Would additional training developed and provided by the Innovation Hubs be utilised by your organisation and/or by the wider sector?**
15. **If so, please specify your 3 key priority areas that you believe would benefit from additional skills/training development from the Hubs.**
16. **How do you think from your perspective the C&GT training should be organised and delivered?**

17. **What kind of training/skills programmes do you believe the Hubs should deliver?**

    - 1-year full-time MSc programmes
    - 2-year part-time distance-learning MSc programmes
    - Online modular courses
    - Practical, hands-on training
    - Weekend face-to-face courses
    - 3-4 day training courses
    - Other (please specify)

18. **How can the Innovation Hubs work with industry partners to support the Hubs' Skills Agenda?**

19. **What content or topics would be of particular interest if new courses were available?**

    - Fundamentals of Virology
    - Gene-modified Cellular Therapies
    - Viral Vector Production
    - GMP
    - Biosafety
    - Bioreactors and Manufacturing Platforms
    - Process and Product Analytics
    - Upstream and Downstream Processing
    - Quality by Design
    - Risk Assessment and CQAs
    - Control Strategy
    - Facility Design
    - Digitalisation
    - Other (please specify)

Future needs

20. **Currently we train and prepare people to be flexible in working with technologies that at present do not exist. From your perspective, which are the emerging technologies or areas in Advanced Therapies/C&GT, and what skills do you think will be required from trainees in 10 years' time?**

Innovation Hubs for
Gene Therapies

Email: viralvector@mrc.ukri.org
www.genetherapyhubs.uk