FORUM

The Academy of Medical Sciences

Engineering the future through cell and gene therapies

Monday 7 July 2025

Summary of Academy of Medical Sciences' FORUM Sir Colin Dollery Lecture

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Introduction

Cell and gene therapies are an area of engineering biology – an interdisciplinary field that applies engineering principles to biology to build new biologically derived systems and products. The UK government has recognised there is a window of opportunity to harness engineering biology and its potential to solve some of the world's unmet medical needs.[1,2] Cell and gene therapies offer the potential to treat or even cure previously untreatable conditions. Supporting their development and delivery could bring transformative benefits to patients and bolster the UK as a centre for innovation.

Many health problems are caused by underlying genetic disorders, or a lack of healthy available cells to fight disease. Cell and gene therapies help restore or enhance the body's cellular and genetic functions to treat or even cure these conditions. Each cell and gene therapy is tailored to the condition it targets. These therapies target specific cells and/ or genetic material to offer customised treatment according to the biology of the patient:

- Cell therapies take healthy, functional cells either from the patient or donors, and reintroduce them into the body to replace or repair damaged systems and cells.
- Gene therapies modify the genetic material inside the cells of a patient to treat genetic conditions, as well as some cancers and infectious diseases.
- Cell and gene therapies can be combined, such as when cells are genetically modified outside of the body and reintroduced into the patient.

On 7 July, the Academy of Medical Sciences hosted the annual FORUM Sir Colin Dollery Lecture on 'Engineering the future through cell and gene therapies'. The event was chaired by the President of the Academy of Medical Sciences, **Professor Andrew Morris CBE FRSE PMedSci**. **Professor Adrian Thrasher FMedSci** delivered the lecture, which focused on the scientific progress and future of cell and gene therapies. His address was followed by an insightful panel that explored next steps to developing and delivering these therapies.

The panel included the following experts:

- **Professor Adrian Thrasher FMedSci**, Professor of Paediatric Immunology, University College London Great Ormond Street Institute of Child Health
- **Dr Jacqueline Barry**, Chief Clinical Officer, Cell and Gene Therapy Catapult
- **Chris Kessler**, parent of a child with a rare disease
- **Dr Anji Miller**, Senior Partner – Academic Engagement, Skills Lead for the Innovation Hubs for Gene Therapies and Programme Director - Translational Skills, LifeArc
- **Dr Andrew Wilfin**, Senior Country Medical Director, Vertex Pharmaceuticals

[1] House of Lords - Science and Technology Committee (2024), 1st Report of Session 2024-25, 14 January 2025. https://publications.parliament.uk/pa/ld5901/ldselect/ldsctech/55/55.pdf

[2] https://www.parliament.uk/business/lords/media-centre/house-of-lords-media-notices/2025/january-2025/dont-squander-the-scientific-opportunity-of-a-lifetime-uk-must-turbocharge-its-innovation-to-harness-engineering-biology-says-lords-report/

The science and future of cell and gene therapies

Over the past 30 years, cell and gene therapies have become cutting-edge technologies that can treat or even cure a range of conditions. In his lecture, Professor Adrian Thrasher spoke about his experience developing and using gene therapies to treat rare diseases. There is a large unmet medical need when it comes to rare diseases.

Collectively, 7% of the population have a rare disease, yet only 5% of rare diseases have licensed therapies. For many severe rare diseases, curative therapies are either imperfect or non-existent. **Gene therapy has become an incredibly effective and viable treatment for many rare diseases.**

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Professor Thrasher discussed the development of viral vectors to introduce genes into patients. Scientists can modify viruses to remove their ability to cause disease and replicate and design them to carry a therapeutic gene (for example, delivering a working copy of a particular gene if the patient's own version isn't functioning properly). These 'vectors' can then be used to target and 'infect' specific cells, transferring that gene into the cell. If a stem cell is infected, that stem cell will incorporate the therapeutic gene into its genome and its daughter cells will then also contain that gene. This means the body can be repopulated with the therapeutic gene.

In his lecture, Professor Thrasher mentioned several different types of viruses used as vectors to transport genetic material in the cell: oncoviruses[3] and lentiviruses,[4] which are retroviruses,[5] and Adeno-Associated Viruses (AAVs).[6]

The two vectors used primarily today are the lentiviral vector and the AAV vector. Much of Professor Thrasher's work has focused on understanding and developing treatments for primary immunodeficiency – inherited diseases that cause different problems in the immune system. Haematopoietic stem cells in the bone marrow are the foundation of the immune system. Gene therapies can be used to deliver therapeutic genes directly to haematopoietic stem cells, which then spread these genes throughout the immune system to treat the immunodeficiency.

[3] Oncoviruses, also known as gammaretroviruses, are a type of retrovirus that primarily infects dividing cells. They can cause cancer by infecting a cell with their own genetic material and altering its behaviour.
[4] Lentiviruses are a type of retrovirus that can cause persistent infections, with long periods between initial infection and the onset of symptoms. They can infect a wide range of cell types including non-dividing cells.
[5] Retroviruses are a type of enveloped virus that use RNA as their genomic material. They convert RNA into DNA within a host cell. These viruses are used in gene therapy because they can integrate genetic material into a cell's DNA. They are primarily used in ex vivo gene therapies (where cells are removed and modified outside the body, and then reintroduced.)
[6] Adeno-Associated Viruses (AAVs) are a small non-enveloped virus with a single-stranded DNA genome that can integrate into the host genome at a specific site. They are used for in vivo gene therapies (which are delivered directly into the body) and can target specific tissues and cells.

One of the most severe immunodeficiencies is severe combined immunodeficiency (SCID), a group of often fatal rare inherited disorders that severely weaken the immune system. In 2001, Professor Thrasher and his team designed a retroviral oncovirus vector that delivered therapeutic genes into the bone marrow cells of children with SCID. Over 20 years after the procedure, all ten patients are alive, because of the gene therapy alone. However, there were some complications as one developed leukaemia several years after the gene therapy was administered. This is because retroviruses integrate into the genome semi-randomly, which can cause unwanted effects such as cancer.

Gene therapy development for severe combined immunodeficiency (SCID)

1968: First successful bone marrow (hematopoietic stem cell) transplant for severe combined immunodeficiency (SCID)

1990: The first clinical trial for gene therapy treats a 4-year-old girl for SCID

2000s: First successful gene therapy treatments for SCID

2010: Newborn screening introduced for SCID

2010s to **2020s**: Gene therapies have shown remarkable efficacy and positive outcomes for SCID

Professor Thrasher and his team then explored using a lentiviral vector. Lentiviruses are more efficient at introducing genes into cells than oncoviruses and are less likely to trigger cancer. Professor Thrasher highlighted how using a lentiviral vector gene therapy to treat Adenosine Deaminase Deficiency (ADA) SCID has led to a 100% survival rate for patients receiving this treatment.

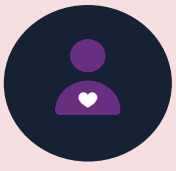
Gene therapies have had similar positive results for other diseases and could potentially treat adults as well as children. Professor Thrasher and his team developed a gene therapy to treat Wiskott-Aldrich Syndrome (WAS), a serious rare immunodeficiency disorder, using a lentiviral vector. After seeing positive results in children, Professor Thrasher then used the therapy to treat an adult patient with WAS, resulting in functional cell recovery and reduction in inflammation.

Professor Thrasher highlighted that gene therapy development could be more efficient if, once a vector technology has been approved by regulators, that platform technology could then be used for different diseases. For example, Professor Thrasher and his team designed a successful gene therapy to treat the autosomal recessive form of Chronic Granulomatous Disease (CGD), a rare genetic disorder. The development and delivery of this gene therapy took 40 years - but the same gene therapy platform has now been used to treat Leukocyte Adhesion Deficiency (LAD).

After discussing the progress made with gene therapies and his experience developing and translating these treatments, Professor Thrasher then introduced what the future may look like. He spoke about how *in vivo* gene therapies, via the Adeno Associated Virus (AAV) vector, are expanding

the reach of gene therapy to new conditions. *In vivo* gene therapy involves delivering genes directly into the body, rather than modifying cells outside the body (*ex-vivo*). Professor Thrasher used the AAV vector to introduce genes into the back of the eye for the first time, to treat Leber's congenital amaurosis (a group of genetic conditions that cause severe vision loss). There is now a licensed product to treat congenital amaurosis using an AAV vector.

Future applications for gene therapies



Gene therapies have been used to treat genetic conditions such as cystic fibrosis, haemophilia, Duchenne muscular dystrophy, and sickle cell anaemia, as well as cancers and viral infections.

Gene therapies could also soon be used as a potential treatment option for:

- Neurological diseases (such as Metachromatic Leukodystrophy, Alzheimer's, Parkinson's, Huntington's, Amyotrophic Lateral Sclerosis (ALS))
- Blood disorders (such as Beta-thalassemia)
- Metabolic conditions (such as Mucopolysaccharidosis (MPS3A), Phenylketonuria, Gaucher disease)
- Retinal diseases (such as Leber Congenital Amaurosis and Retinitis Pigmentosa)
- Diabetes type 1 and type 2
- Various cancers
- Cardiovascular diseases

Using viral vectors has enabled therapeutic genes to be added to the body, but there is now significant interest in gene editing. Gene editing holds great promise but requires careful monitoring for safety and toxicity. Instead of adding a new gene, gene editing aims to fix the faulty gene directly by using tools like CRISPR-Cas9, TALENs, and base editing. While gene editing is promising because of its precision, there are effects that we still do not understand – particularly as gene editing introduces changes to the genome which can be passed to future generations.

Key opportunities and next steps

Gene therapies have shown remarkable success in improving quality of life and even offering a one-time lifelong cure for patients.

The UK has played a particularly important role in the development and translation of cell and gene therapies. However, several challenges still hinder their progress and adoption.[7]

> In August of last year [2024], Charlie was born. At about seven weeks, my wife noticed that something wasn't quite right in terms of his development. We took him to our local A&E, and they told us that they strongly suspected a neuromuscular disorder [spinal muscular atrophy].
>
> There are roughly 30 babies in the UK that are born with [SMA] every year. There are now three approved treatments for SMA on the NHS, one of those being a gene therapy. The fact it's a one-time treatment is a huge thing from a parent's perspective. We were given a very clear understanding of the risks… the benefits outweighed the risks for us. And… cognitively, he's an entirely normal baby, which is incredible to my wife and I.
>
> The type of research that it takes to make one of these [gene therapies], I can't even fathom, but it's clearly decades and decades of research. And my wife and myself and my son are a complete testament to researchers and clinicians around the world that made this possible.
>
> **Chris Kessler, parent of a child who received a gene therapy**

[7] In 2019, the Academy of Medical Sciences' FORUM ran a workshop in partnership with the Cell and Gene Therapy Catapult on 'The future of gene therapies: next steps for the UK' which also identified key challenges and themes: https://acmedsci.ac.uk/file-download/70923664

During the event, an expert cross-sector panel discussed next steps to the development and delivery of cell and gene therapies, including:

Empowering patients and their families to make informed choices and access support

Cell and gene therapies can be complex, making it difficult for patients and their families to fully understand what is involved and give informed consent. Co-producing educational materials with patient groups, in multiple languages, would enable patients and their families to make informed treatment choices.

Information also needs to be tailored to individual circumstances, including honesty about long-term prognoses and possible complications. Peer-to-peer networks provide valuable opportunities to share experiences; however, there is also a need for patients and their families to have better access to holistic psychological support throughout the treatment journey.

Expanding early detection of conditions that can be treated with cell and gene therapies

Cell and gene therapies are often most effective when patients are treated early, before symptoms develop. Newborn screening is valuable for early treatment.

Although some conditions such as SCID are screened for, this could be more widespread – for example, for conditions such as Spinal Muscular Atrophy. Genome sequencing could also be used to enable screening for multiple conditions.

Exploring a collaborative approach to platform vector technologies

Collaborative approaches between sectors and organisations could enable the development of uniform vector platforms that could then be adapted to treat different conditions. This could also help reduce regulatory burden.

Implementing a data strategy to support cell and gene therapies

Current data infrastructure is fragmented with limited interoperability. This makes it difficult to collect long-term safety and efficacy data. The data from relevant patient registries could be more standardised and integrated. NHS data systems could also be improved for long-term tracking of outcomes and pharmacovigilance.

Overcoming skill shortages and training gaps in the workforce

There is a shortage of skilled professionals in the development of cell and gene therapies, and it can be difficult to access adequate training.

- Dedicated training programmes could support interdisciplinary working in the field and produce professionals that understand regulatory science, biomedical science and economics.
- Existing professionals could be upskilled so that they can drive forward the delivery of these therapies.

Developing streamlined regulatory approaches and simplifying approval processes.

Navigating regulatory frameworks can be a significant barrier for companies developing cell and gene therapies. The panel suggested the following solutions:

- Implement a regulatory framework that approves viral vector platforms, which can then be used to treat similar conditions without the need for re-approval.
- Overcome fragmentation across international regulatory bodies including the FDA and EMA.
- Streamline and simplify regulatory pathways and guidelines between relevant UK bodies, including around trial setup, the use of real-world data, and manufacturing requirements.

Exploring more innovative models to reimbursement and funding

Developing a gene therapy can cost billions, and they may not be profitable for the commercial sector. The high price of licensed therapies poses a challenge for healthcare systems, particularly for treating rare diseases with small patient populations.

- Existing reimbursement frameworks are not well-suited to accommodate the high costs of these one-time treatments. However, although the upfront cost can be extremely high, they may be cost-effective over a patient's lifetime. Reimbursement frameworks could weigh cost-benefit by assessing investment in a patient over their lifetime using new approaches to economic models: curing a disease at birth can eliminate decades of medical care, hospitalisations, and lost productivity.
- Increased funding is needed for academics to set up and run cell and gene therapy trials.

Setting up a national infrastructure for delivering cell and gene therapies[8]

- A national cell and gene therapy centre with the latest production facilities could position the UK as a prestigious leader in the field. This centre could also provide hands-on training opportunities.
- Access to treatment is uneven across the UK, and there are limited cell and gene therapy specialist centres. To address health inequalities, centres could be expanded throughout the UK, so patients have better equity of access and care.

[8] The Advanced Therapy Treatment Centre network is aiming to do this. The network addresses the unique and complex challenges of bringing pioneering advanced therapy medicinal products (ATMPs) to patients and currently focuses on accelerating ATMP clinical trials in the UK. https://www.theattcnetwork.co.uk/about

Conclusion

Cell and gene therapies are groundbreaking technologies with the potential to treat—and in some cases cure—a wide range of conditions, including those previously considered untreatable. Over the past three decades, significant progress in research has made these therapies increasingly effective and viable, particularly for rare diseases. Continued innovation, such as in *in vivo* gene therapies and gene editing, could further expand the scope of treatable conditions.

Despite their promise, the development and delivery of cell and gene therapies face several challenges. These therapies are complex to develop and manufacture, requiring a highly skilled workforce and sophisticated infrastructure. Gene therapy treatments for rare conditions often lack commercial viability due to high research and development costs. Regulatory and approval processes can be fragmented and slow. Healthcare systems require the necessary equipment, expertise, and funding to support adoption – the high upfront cost of these therapies can cause a significant barrier to reimbursement.

There is strong support for greater collaboration and coordination across sectors to address these challenges. Sharing knowledge and developing adaptable platform vector technologies could accelerate progress. Closer collaboration with regulators—both in the UK and internationally—could streamline trial approvals, real world data use, and manufacturing requirements. Innovative reimbursement models are needed to reflect the long-term value of one-time treatments. Establishing a national cell and gene therapy production centre could streamline development and manufacturing and provide hands-on training opportunities. Dedicated training programmes should focus on building the interdisciplinary skills required. A robust data strategy would support long-term monitoring of safety and effectiveness. Empowering patients and families with information and support throughout the treatment journey is essential, as is early screening to ensure timely and effective intervention.

The UK has played a pivotal role in the development and translation of cell and gene therapies and has an ambition to lead in this space. By working collaboratively to overcome current barriers, the UK could become a leader in the field and deliver life-changing treatments to patients with conditions once thought to be incurable.

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