ZAYED CENTRE
FOR RESEARCH
INTO RARE DISEASE
IN CHILDREN

Annual Report 2021

A GREAT ORMOND STREET HOSPITAL AND UCL PARTNERSHIP

CONTENTS

INTRODUCTION

Street view of Zayed Centre for Research

The Zayed Centre for Research into Rare Disease in Children at Great Ormond Street Hospital (GOSH) was built to bring together patients, researchers and clinicians and accelerate the research, diagnosis and treatment of children from around the world with rare and complex conditions. Opening shortly before the outbreak of COVID-19 in the UK, the Zayed Centre for Research's mission was stress-tested almost immediately. But the timing proved fortuitous as its specialist facilities meant it was quickly able to play an instrumental role in the world's first human challenge study of COVID-19 - work which would not otherwise have been possible at GOSH.

Implementation of alternative ways of working, close collaboration with specialist clinical colleagues and the staff vaccination programme all contributed to ensuring as much essential research as possible continued, with some teams able to capitalise on the unique interdisciplinary set up at the Zayed Centre for Research to pivot their research towards Sars-CoV-2 and virology in ways that they would not previously have considered.

Beyond the research dedicated to it, the pandemic had a significant effect on the delivery of all research programmes across GOSH and the UCL Great Ormond Street Institute of Child Health (UCL GOS ICH) in 2021. A combination of paused recruitment, staff redeployment/absence, delays to studies opening, lack of capacity within support departments as well as patient hesitancy meant a significant reduction in the level of research activity, a key focus for the Zayed Centre for Research.

However, researchers based at the Zayed Centre for Research continued to work with collaborators around the world to make significant headway in projects focused on diseases such as epilepsy, the previously fatal condition severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID) and leukaemia, among others.

In September, the Zayed Centre for Research welcomed its first VIP visitors since lockdown began, when the Crown Prince of Abu Dhabi, His Highness Sheikh Mohamed bin Zayed Al Nahyan,[1] toured the facility along with the Secretary of State for Health, Sajid Javid MP, and the Secretary of State for Education, Minister Nadhim Zahawi MP. November also marked two years since the Zayed Centre for Research first opened its doors, a poignant milestone and a moment to reflect on the challenges overcome and opportunities still ahead.

Despite the ongoing pandemic and the associated restrictions, the vision for the Zayed Centre for Research was borne out in 2021. It was at the heart of several major breakthroughs in research, world-firsts and has made steps as the UK's largest academic gene and cell therapy facility. This annual report details some of the landmark events that took place.

[1] His Highness Sheikh Mohamed bin Zayed was elected President of the United Arab Emirates on 14 May 2022

OUTPATIENT VISITS / CARE STATISTICS

OCTOBER 2019 – OCTOBER 2020

Visits by Specialty	Count
Cardiac Surgery	42
Cardiology	28702
Cardiothoracic Transplantation	927
Chem Pathology	6
Cleft	31
Clinical Genetics	824
Craniofacial	63
Cystic Fibrosis	1338
Dermatology	3666
Ear Nose and Throat	21
Extracorporeal membrane oxygenation (ECMO)	2
Endocrinology	205
Epilepsy	50
Fetal Cardiology	47
Gastroenterology	14
General Paediatrics	935
Haematology	1
Immunology	1201
Infectious Diseases	547
Metabolic Medicine	18
Nephrology	637
Neurology	44
Neuromuscular	68
Neurosurgery	269
Oncology	1
Orthopaedics	35
Pain Management	2
Plastic Surgery	54
Psychological Medicine	2
Pulmonary Hypertension	493
Respiratory Medicine	4161
Rheumatology	350
Specialist Neonatal and Paediatric Surgery (SNAPS)	1103
Spinal Surgery	10
Urology	75

In the first year of its opening there were 45,944 visits to Falcon outpatients and 16,678 unique patients. On average each patient had three appointments (a combination of in-person and virtual) during the year.

The top five specialties at the Zayed Centre for Research in 2019/2020 were:

1. **CARDIOLOGY** 62%
2. **RESPIRATORY MEDICINE** 9%
3. **DERMATOLOGY** 8%
4. **CYSTIC FIBROSIS** 3%
5. **IMMUNOLOGY** 3%

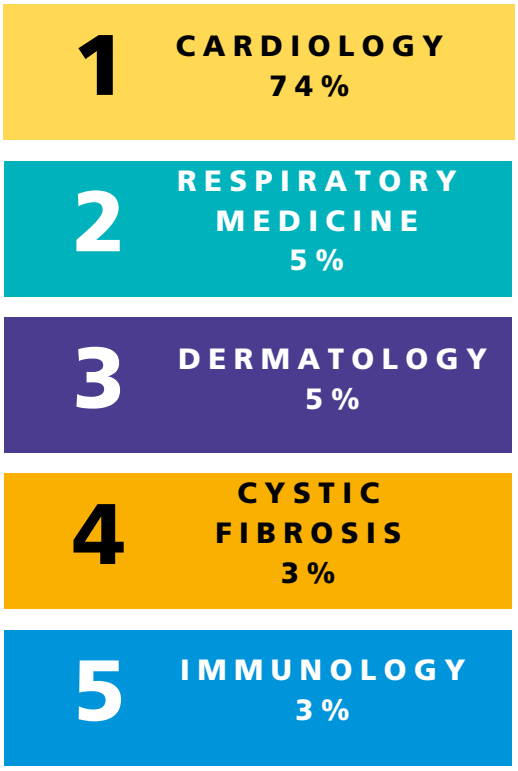
Although the majority of children visiting the Zayed Centre for Research when it first opened in 2019 were UK-based, it also welcomed a number of international patients.

Please see appendix for figures by country.

Visits by Specialty	Count
Audiological Medicine	2
Bone Marrow Transplant	3
Child and Adolescent Mental Health Service (CAMHS)	28
Cardiac Surgery	7
Cardiology	34533
Cardiothoracic Transplantation	1125
Cleft	6
Clinical Genetics	757
Craniofacial	29
Cystic Fibrosis	1191
Dermatology	2248
Ear Nose and Throat	41
Extracorporeal membrane oxygenation (ECMO)	7
Endocrinology	168
Epilepsy	18
Gastroenterology	8
General Paediatrics	1
Haematology	1
Immunology	1186
Infectious Diseases	380
Metabolic Medicine	5
Nephrology	10
Neurodisability	1
Neurology	137
Neuromuscular	176
Neurosurgery	162
Orthopaedics	25
Plastic Surgery	270
Psychological Medicine	70
Pulmonary Hypertension	627
Respiratory Medicine	2483
Rheumatology	138
Specialist Neonatal and Paediatric Surgery (SNAPS)	965
Urology	67

Despite the COVID-19 pandemic, between October 2020 and October 2021 there were 46,875 visits to Falcon outpatients and 15,806 unique patients, with each patient still attending (either in-person or virtually) an average of three appointments during the year.

The top five specialties remained unchanged from the previous year:



Despite the pandemic, very sick children from around the world still visited the Zayed Centre for Research, albeit in smaller numbers.

Please see appendix for figures by country.

FAMILY FEEDBACK

Falcon outpatients continued to meet its target of seeing up to 200 patients a day. Below is a selection of comments about the Zayed Centre for Research from families of patients. The comments were collated for NHS England throughout 2021.

"Gorgeous, kind staff - our son was very nervous and they made us feel so special. Super professional! Beautiful building!!"

"We owe GOSH everything & think the world of it. The care, expertise and everything in between make us very proud of our NHS. Thanks always and forever! P.S lovely new building. Reception staff great, very friendly and funny!"

"Lovely building, we were greeted straight away by a lovely, friendly member of staff. It is also very clean and organised and well sign posted. Thank you and stay safe."

"Falcon is fabulous. We can have all our tests in one place. It's airy, clean and well run."

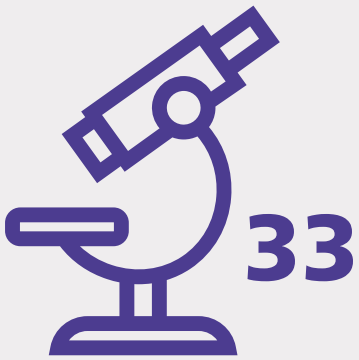
PATIENT STORY

GOSH patient April, age 7

April was rushed to GOSH when she was a baby where she was diagnosed with acute aortic stenosis, a congenital heart defect that meant her heart had to work much harder as the aortic valve in her heart did not work properly. She had several procedures at the hospital including major heart surgery when she was just a few months old. Now aged seven, April has started school and loves to go to the beach with her family. April continues to visit the Zayed Centre for Research as an outpatient while she continues to be monitored because she will need further valve replacements in the future.

RESEARCH

Research at the Zayed Centre for Research and across GOSH and UCL GOS ICH is underpinned by funding from the NIHR Great Ormond Street Hospital Biomedical Research Centre (NIHR GOSH BRC). The NIHR GOSH BRC is the only NIHR-supported BRC focusing entirely on paediatric research. The BRC provides cutting-edge facilities, world-leading expertise and access to over 200 rare disease patient populations. This allows GOSH staff and NHS, university and industry collaborators, to conduct pioneering translational research into childhood illnesses.



33

The current number of independent research groups led by Principal Investigators (PIs) located in the Zayed Centre for Research.

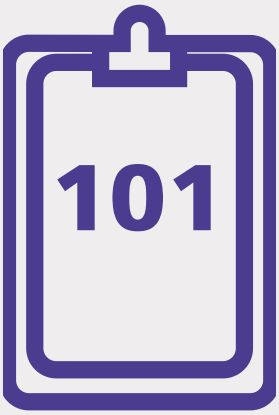
30

The number of new clinical research projects that have been led by Zayed Centre for Research PIs since it opened in October 2019. Objectives include drug development, medical devices and diagnostics. Six of these projects are clinical trials investigating new treatments, such as gene therapies.

One of these is a first in-human Phase 1 clinical trial testing the safety and effectiveness of a cell therapy (genetically engineered CAR-T cells) for B-cell acute lymphoblastic leukaemia (B-ALL), a difficult to treat blood cancer. This clinical trial is led by Professor Waseem Qasim (Professor of Cell and Gene Therapy, UCL GOS ICH).

Between April 2020 and April 2021 there were:

Number of active trials involving gene and cell therapies registered at GOSH, covering health categories including blood, cancer, neurological/neuromuscular, inflammation and immune system and metabolic and endocrine disorders. Seventeen patients were recruited for these trials in this time.



Number of clinical research publications featuring Zayed Centre for Research researchers, with 37 publications related to gene and cell therapies.

Number of gene and cell therapy products targeting cancers, immunodeficiencies and metabolic disorders manufactured at GOSH. These products were manufactured for use in clinical trials of rare conditions with limited treatment options and led by Zayed Centre for Research-based PIs including:

- A gene therapy for children with a rare, genetic disorder called Mucopolysaccharidosis type II (MPS II) led by Professor Adrian Thrasher (Professor of Paediatric Immunology and Wellcome Trust Senior Research Fellow, UCL GOS ICH).
- A gene therapy for X-linked Severe Combined Immunodeficiency (X-SCID), led by Professor Claire Booth (Mahboubian Professor of Gene Therapy, Consultant in Paediatric Immunology, UCL GOS ICH; Consultant in Paediatric Immunology, GOSH).
- Genetically engineered T cells for children with post-transplant lymphoproliferative disease (PTLD), a complication that can occur after a solid organ transplant, led by Professor Persis Amrolia (Professor of Transplantation Immunology, UCL GOS ICH; Consultant in Bone Marrow Transplant, GOSH).
- Genetically engineered CAR-T cells for complex blood cancers that have not responded to existing treatments, led by Professor Persis Amrolia.

LEVERAGED FUNDING

Between April 2020 and April 2021, the researchers at GOSH and UCL GOS ICH brought in additional income from from other UK-based and international charities, research councils and commercial organisations across the following research themes:

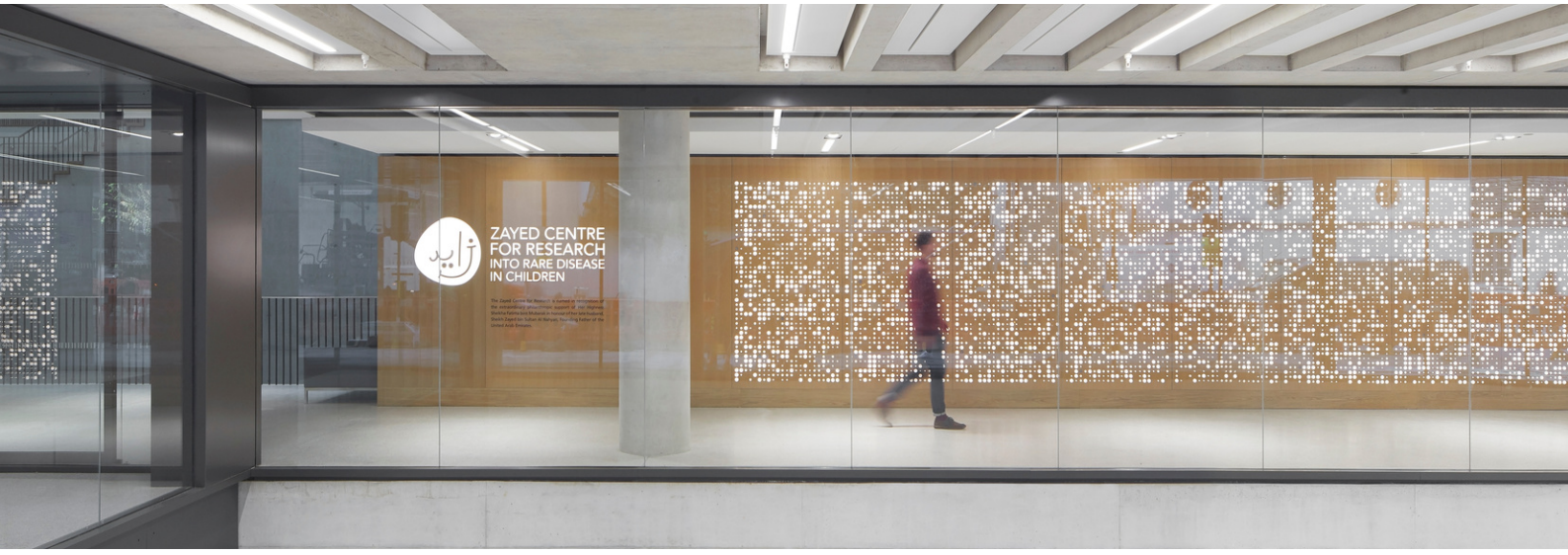
Advanced treatments for structural malformation and tissue damage	£9m
Gene, stem and cellular therapies	£13m
Genomics and systems medicine	£3m
Novel therapies for translation in childhood diseases	£37m

Examples of major grants awarded to teams based at the Zayed Centre for Research include:

- Doctor Karin Straathof (Principal Research Fellow, Honorary Consultant in Paediatric Oncology, UCL GOS ICH) received £1.4m from the J P Moulton Charitable Foundation for a clinical trial of genetically engineered T cells to treat a rare and fatal brain tumour, childhood diffuse midline glioma (DMG).

- Professor Waseem Qasim (Professor of Cell and Gene Therapy, UCL GOS ICH) received £821k from the Medical Research Council for a Phase 1 clinical trial testing the safety of a gene therapy (genetically engineered CAR-T cells) in treating B-cell acute lymphoblastic leukaemia (B-ALL), a difficult to treat blood cancer.

- Professor John Anderson (Professor of Experimental Paediatric Oncology, UCL GOS ICH) received £740k from Stand up to Cancer/CRUK for an innovative research programme looking at CAR-T cell therapy in neuroblastoma and medulloblastoma.



Zayed Centre for Research entrance walkway

2021 HIGHLIGHTS

February 2021 - Global collaboration announced to develop new treatments for paediatric diseases

Ahead of Rare Disease Day 2021, GOSH joined forces with three other leading children's research institutions on three continents to decipher paediatric illnesses, including rare diseases, and find better treatments. The hospital is working with Boston Children's Hospital, the Murdoch Children's Research Institute with The Royal Children's Hospital in Melbourne, and The Hospital for Sick Children (SickKids) in Toronto to evaluate genomic data, clinical data from patients, and scientific and medical expertise to accelerate the discovery and therapeutic development.

The partnership, known as the International Precision Child Health Partnership (IPCHiP), is the first major global collaboration around genomics and child health. IPCHiP's first project will involve epilepsy in infants, bringing together efforts already underway at the four hospitals.

Investigators at each site will enrol babies under age one with epilepsy, sequence their genomes, change treatment based on the findings when appropriate, and follow the children's development long-term. No patient will be identifiable from the data used, and no patient data will be shared across international borders.

The study will compare those who receive a genetic diagnosis with those who do not. Through this project, IPCHiP will establish systems to evaluate data responsibly across the different institutions.

Dr Amy McTague (Honorary Consultant Paediatric Neurologist and Research Fellow, UCL GOS ICH) who is based at the Zayed Centre for Research and is leading the epilepsy project, GeneSteps, in the UK said: "We know that for at least 50% of babies with epilepsy, there is a genetic cause. For some, having a specific genetic diagnosis can change treatment and we want to know if finding the genetic problem earlier improves epilepsy and development in the long-term."

The study will pioneer the use of rapid genome testing in epilepsy and will recruit 100 babies initially, with a larger study planned.

Zayed Centre for Research gene and cell therapy facility

April 2021 - Gene therapy offers a potential cure to children born without an immune system

In a study published in the New England Journal of Medicine, co-lead authors Professor Claire Booth (Mahboubian Professor of Gene Therapy, UCL GOS ICH; Consultant in Paediatric Immunology, GOSH) and Professor Donald Kohn (Professor of Paediatric Hematology/Oncology, Microbiology, Immunology & Molecular Genetics, Molecular & Medical Pharmacology, UCLA) reported the two to three year outcomes of 50 children who were treated in clinical trials with an experimental stem cell gene therapy for severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID) between 2012 and 2017.

The standard treatment for ADA-SCID involves once or twice weekly injections of the ADA enzyme until a matched bone marrow donor – usually a close family member – can be found. If a matched bone marrow donor is not available, patients require lifelong ADA injections along with preventative medicines. These treatments are expensive and therefore out of reach for patients in many countries. If approved, gene therapy would be a welcome new treatment option for ADA-SCID as it is a one-time procedure that has the potential to provide life-long results.

Two to three years after the treatment, all 50 children treated with the new gene therapy at GOSH, UCLA Mattel Children's Hospital and the National Institutes of Health (NIH) are alive and well. Of these, 48 are no longer showing symptoms of ADA-SCID, although they will have lifelong monitoring. In the two cases in which treatment wasn't successful, both children were able to return to current standard treatments, with one eventually receiving a bone marrow transplant. No serious side effects have so far been reported, with generally mild or moderate complications experienced from the necessary preparation for the gene therapy.

April 2021 - MicroRNA from stem cells could be used to treat babies while still in the womb

A team of researchers from GOSH, led by Professor Paolo de Coppi (Head of Stem Cells and Regenerative Medicine, UCL GOS ICH; Consultant Paediatric Surgeon, GOSH), and The Hospital for Sick Children (SickKids) in Toronto have used tiny liquid 'bubbles' of microRNAs from stem cells to regenerate under-developed lungs in rats still in the womb.

As babies develop in the womb, the growth of their lungs is a critical part of development, and any disruptions can lead to under-developed lungs, leading to disability or even stillbirth. Known as 'pulmonary hypoplasia', this condition usually occurs alongside other medical conditions or due to other malformations, like when the diaphragm fails to properly close during development. Infants born with the severest cases only have a survival rate of 60% and those who do survive face a lifetime of complications. Treatment options can involve surgery even before the baby is born but irreparable damage is often done to the lungs.

Now, scientists and doctors from two of the world's leading children's hospitals have come together to take advantage of the regenerative properties of stem cells isolated from amniotic fluid. These cells produce tiny liquid 'bubbles', called vesicles, containing microRNAs that boost the genes that support the developing lung. The team found that using microRNAs isolated from a donor's amniotic fluid stimulated lung growth, proper lung structure, and the creation of lung cells in the laboratory and in animal models of pulmonary hypoplasia.

Zayed Centre for Research laboratory

Zayed Centre for Research laboratory

May 2021 - New insight into when CAR-T is effective against childhood leukaemia

In CAR-T therapy, immune cells (T cells) are genetically engineered to contain a molecule called a chimeric antigen receptor (CAR) on their surface which can specifically recognise cancerous cells.

Dr Luca Biasco (Honorary Senior Research Associate, UCL GOS ICH) and Professor Persis Amrolia (Professor of Transplantation Immunology, UCL GOS ICH; Consultant in Bone Marrow Transplant, GOSH), together with their research teams, assessed the CAR-T cells of patients involved in the CARPALL Phase I Study, which used a new CAR molecule known as CAT-19 developed between UCL Cancer Institute and UCL GOS ICH, for treatment in children with acute lymphoblastic leukaemia.

The team compared CAR-T cells from patients who still had CAR-T cells detectable in the blood more than two years after their treatment, with individuals who had lost their CAR-T cells in the one to two months post treatment.

Using a technique called 'insertion site barcoding', researchers were able to study the fate of different types of CAR-T cells in patients after they were given. Using this barcoding technique, they were able to see 'stem cell memory T cells' play a central role both during the early anti-leukaemic response and in later immune surveillance, where the body recognises and destroys cancer cells. This suggests that this small sub-group of T cells are critical to the long-term success of the therapy.

Researchers say this work indicates that the teams caring for patients could measure the types of CAR-T cells present after someone has had their anti-leukaemia therapy, to gain an indication of whether they will be able to preserve their CAR-T cells into the future, avoiding relapse.

July 2021 – Gene therapy offers hope to children with rare and fatal brain diseases

While there are some conditions that we can now treat with gene therapy, others are still waiting while our teams work tirelessly to find a treatment or even a cure.

In 2009, Professor Manju Kurian (Professor of Neurogenetics, UCL GOS ICH) was a PhD student at GOSH when she discovered a rare condition called DTDS. Previously doctors thought it was a form of cerebral palsy but her work showed that it was caused by a single faulty gene. Children with DTDS are rarely able to learn to walk or speak. As they grow, they develop 'parkinsonism' - so called because of similarities to Parkinson's Disease. This includes slow movements, involuntary twisting postures of their arms and legs and whole-body stiffness.

There are currently no effective treatments or a cure and most children with DTDS sadly die before reaching adulthood, often from respiratory infections or other complications.

But in 2021, using a mix of laboratory tests and animal studies, Professor Kurian, who is now based at the Zayed Centre for Research and working closely with colleagues at the UCL GOS ICH, was able to cure mice with DTDS. She's also been able to use the cutting-edge facilities of the Zayed Centre for Research to grow human brain cells with DTDS – so called "brain in a dish" – and cure them of the condition. She will soon be applying for a clinical trial to offer hope of a treatment for DTDS and other degenerative brain disorders like it.

Professor Manju Kurian (Professor of Neurogenetics, UCL GOS ICH)

His Highness Sheikh Mohamed bin Zayed Al Nahyan visits the Zayed Centre for Research in September

September 2021 - Crown Prince of Abu Dhabi meets clinicians and researchers at the Zayed Centre for Research into Rare Disease in Children

GOSH hosted His Highness Sheikh Mohamed bin Zayed Al Nahyan,[1] Crown Prince of Abu Dhabi, the Secretary of State for Health Sajid Javid MP, and the Secretary of State for Education Minister Nadhim Zahawi MP at its Zayed Centre for Research into Rare Disease in Children, to tour the facility and learn more about the life-changing impact of its work.

Representatives from GOSH, GOSH Charity and UCL GOS ICH took the visiting group on a tour of the main laboratory in the Zayed Centre for Research, which has 140 dedicated research benches and is home to its genomics team. During the pandemic, their work has supported GOSH's response to COVID-19, including sequencing 15,500 samples from hospitals, the community and travellers returning to the UK to help scientists learn about the changing nature of the virus.

The delegation also saw the state-of-the-art specialist clean rooms - the largest single academic manufacturing unit for gene and cell therapies in the UK and one of the largest in the world – where products are manufactured for use in ground-breaking gene therapy trials. These facilities also enabled the manufacture of the COVID-19 virus to supply to the world's first human challenge trial earlier this year.

[1] His Highness Sheikh Mohamed bin Zayed was elected President of the United Arab Emirates on 14 May 2022

September 2021 - ViroCell Biologics and GOSH announce partnership to dislodge gene and cell therapy 'logjam'

ViroCell, an innovation-driven Contract Development and Manufacturing Organization (CDMO), is addressing the global viral vector supply demand imbalance that constrains the manufacture of novel cell and gene therapies. ViroCell focuses exclusively on the design and good manufacturing practice (GMP) manufacture of viral vectors and gene modified cells for clinical trials.

Viral vectors are harmless viruses that are used to 'trick' cells into accepting new genes. They are highly complex to make and their availability and effectiveness dictates whether a clinical trial of gene or cell therapy will work. ViroCell is focused where the viral vector design and GMP manufacturing bottleneck is most acute: the zone between pre-clinical concept and pivotal clinical trials. ViroCell is therefore filling the gap between 'small volume' academic core labs and 'large volume' CDMOs.

As part of the partnership with GOSH, ViroCell will more than double the UK's lentivirus vector manufacturing capacity for clinical trials in 2022 and secure the coveted position as the first UK CDMO to be able to deliver adeno-associated virus vectors to the cell and gene therapy markets.

The production of the vectors will take place in GOSH's Zayed Centre for Research into Rare Disease in Children. The ViroCell team's track record of manufacturing more than 100 viral vectors for clinical trials over the last 20 years coupled with the Zayed Centre for Research's state-of-the-art clean room suites, will enable ViroCell and GOSH to dislodge the logjam that currently prevents promising novel cell and gene therapies from entering clinical trials.

Zayed Centre for Research gene and cell therapy facility

November 2021 – GOSH celebrates second anniversary of Zayed Centre for Research into Rare Disease in Children

The Zayed Centre for Research turned two in November 2021. In addition to facilitating more than 105,000 patient visits to Falcon Outpatients since it opened in 2019, the Zayed Centre for Research has also been involved in several globally significant research developments, hosted some very important visitors, and is on track to become a central hub for vector manufacture following the announcement of a new partnership with ViroCell.

December 2021 - Lab-grown stomachs help to shed light on COVID-19 symptoms in children

Recent advances in lab-grown mini organs, also known as organoids, can provide scientists with invaluable tools to study how our organs function, both when they are healthy, and when they are impacted by disease. For the first time, an international team of scientists and doctors have used these advances to develop a lab-grown model of the human stomach. This can be used to study how infections in humans impact the gastrointestinal system. To do this, researchers isolate stem cells from patient stomach samples, and grow them under special conditions in the lab. This creates mini stomachs in a petri dish that can mimic the behaviour of a human stomach.

This development was pioneered by an international team, representing a collaboration between GOSH, UCL GOS ICH, and the Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Italy. It was led by Dr Giovanni Giuseppe Giobbe (Research Associate, UCL GOS ICH), Professor Nicola Elvassore (Lecturer in Paediatric Regenerative Medicine, UCL GOS ICH) and Professor Paolo de Coppi (Head of Stem Cells and Regenerative Medicine, UCL GOS ICH; Consultant Paediatric Surgeon, GOSH) with much of their work carried out in the Zayed Centre for Research.

The scientists were able to infect the mini stomachs from the outside by exposing the surface of the cells to SARS-CoV-2. From this they showed that SARS-CoV-2 could replicate within the stomach. Importantly, it replicated more noticeably in organoids that were grown from the child and late foetal cells, compared to adult and early foetal cells. The team now plan to continue their work with the mini stomachs aiming to study how the stomach develops from early in pregnancy through to adulthood. They also hope to look at the effects of other common gastrointestinal infections.

SPOTLIGHT ON: CANCER RESEARCH

T cells are specialised immune cells that patrol the body, seeking and clearing up cells that are infected, for example with a virus. But cancer cells can go unnoticed as they often look very similar to healthy cells. To use T cells as a cancer treatment, they are reprogrammed with a cancer 'detector' called chimeric antigen receptor (CAR). The CAR enables T cells to spot cancer cells and spring into action, directly destroying cancer cells and alerting other immune cells of the cancer threat.

While promising for some forms of childhood cancer, 'CAR-T therapy' can lead to life-threatening side effects and the cancer often returns as the treated T cells disappear from the body. Furthermore, obtaining children's cells and returning them requires harsh, invasive procedures that some children simply aren't well enough for.

Researchers based at the Zayed Centre for Research are tackling these issues head on. For example, in blood cancers like acute lymphoblastic leukaemia (ALL) Professor Persis Amrolia (Professor of Transplantation Immunology, UCL GOS ICH; Consultant in Bone Marrow Transplant, GOSH) and his team have developed a new CAR molecule that can bind more rapidly to the cancer cells and remove them, reducing side effects and improving cancer symptoms. They are investigating why CAR-T cells last longer for some patients, and not others (this is important because the loss of CAR-T cells means the treatment doesn't work), and how they can make CAR-T cells persist in the body. They have found that a special group of T cells are essential for destroying cancer cells. In parallel, Professor Waseem Qasim (Professor of Cell and Gene Therapy, UCL GOS ICH) and his team are leading research that uses 'off the shelf' CAR T-cells that work for anyone, so that children don't need to go through all the harsh measures to remove their cells.

A team led by Dr Karin Straathof (Principal Research Fellow, Honorary Consultant in Paediatric Oncology, UCL GOS ICH) is also working to tackle cancers with solid tumours, particularly neuroblastoma - a cancer that comes from the nervous system outside the brain. The team has developed a special CAR that instructs T cells to recognise a protein present only on the surface of neuroblastoma cancer cells. They've shown that this works, leaving healthy cells untouched, and now plan to start a clinical trial of CAR-T cell therapy for children with neuroblastoma who aren't responding to standard treatments.

Zayed Centre for Research street-level view over the laboratory

GENE AND CELL THERAPY FACILITY

The Zayed Centre for Research's gene and cell therapy facility consists of seven suites and is the UK's largest academic manufacturing facility for gene and cell therapies. It enables world-leading, first-in-man clinical trials, such as the first use of gene editing technologies in children; genetically engineered T cell therapy for childhood solid tumours; and virus-based gene therapy for disorders affecting the eye.

Over the last two years, two out of the seven manufacturing rooms in the gene and cell therapy facility have been used to manufacture SARS-CoV-2 for the UK Vaccine Taskforce in collaboration with industry partner, hVIVO.

Zayed Centre for Research gene and cell therapy facility

For method development it is crucial to obtain MHRA accreditation for the new facility. The NIHR GOSH Biomedical Research Centre (BRC) is working closely with the MHRA to achieve this. Similarly, the NIHR GOSH BRC has been working since 2017 to bring ex vivo CRISPR genome editing to good manufacturing practice level.

Several projects have started in 2022 which cover vector manufacture, biologics, gene and cell therapies and virus manufacture.

SPOTLIGHT ON: GENE THERAPY

July 2021 marked 20 years since the first patient, Rhys Evans from Wales, was treated with gene therapy at GOSH for X-SCID – he was the first patient to receive gene therapy in the UK. Since then, over 100 children have been treated with gene therapy at GOSH for dozens of different diseases. Many of these children would have been expected to die before their second birthday and gene therapy was transformational in allowing many of them to live normal lives and go to school. Back in 2001, the only treatment for patients like Rhys was a bone marrow transplant, an incredibly difficult procedure that requires a matched donor to be found, usually a sibling. Rhys became the first to receive this ground-breaking gene therapy and after a few weeks his immune system started to develop. He recently celebrated his 21st birthday.

GOSH patient Rhys, age 21

Stories like Rhys' would have not been possible without researchers and clinicians working in collaboration for the benefit of children with rare and complex diseases. Now, GOSH is a global centre of excellence for gene therapy and has treated more patients with the technology than anyone else in Europe – something that would not have been possible without the Zayed Centre for Research.

Gene therapy was pioneered at GOSH by Professor Bobby Gaspar (Professor of Paediatrics and Immunology, UCL GOS ICH) and Professor Adrian Thrasher (Professor in Paediatric Immunology and Wellcome Trust Senior Research Fellow, UCL GOS ICH) who is based at the Zayed Centre for Research. Much of this early research took place at the Wolfson Centre for Gene Therapy, supported by the Wolfson Foundation.

Most patients treated in clinical trials at GOSH with gene therapy have had different forms of severe combined immunodeficiency (SCID), a group of rare disorders caused by mutations in different genes involved in the development and function of infection-fighting immune cells. More recently, patients with a range of diseases from leukaemia to rare genetic conditions such as spinal muscular atrophy (SMA) and an inherited retinal disorder which causes children to lose their sight – Leber's congenital amaurosis (LCA) – have been treated in clinical trials.

Gene therapy research at the hospital is accelerating at a faster pace because of the Zayed Centre for Research. Rare disease researchers are now co-located with Falcon, the rare disease outpatients' clinic, so that they can learn from colleagues treating these conditions and 'reverse translate' these real outcomes to make changes to their own research that will benefit families. They have access to cutting-edge facilities and equipment specially designed for research of this nature and calibre, and they can easily spark new collaborations with other rare disease research colleagues and clinicians, pushing forward new ideas.

Professor Manju Kurian (Professor of Neurogenetics, UCL GOS ICH) conducts her research at the Zayed Centre for Research

Professor Claire Booth (Mahboubian Professor of Gene Therapy, UCL GOS ICH, Consultant in Paediatric Immunology, GOSH)

All of this has increased the rate at which gene therapies are being developed and tested for patient benefit. Among those leading the clinical trials are Professor Claire Booth (Mahboubian Professor of Gene Therapy, UCL GOS ICH; Consultant in Paediatric Immunology, GOSH) - who celebrated the successful results of a stem cell gene therapy clinical trial for ADA-SCID in May 2021 - and Professor Manju Kurian (Professor of Neurogenetics, UCL GOS ICH), who discovered the brain disorder dopamine transporter deficiency syndrome (DTDS) in 2009 and has subsequently helped develop a potential gene therapy cure for the disease. More detail on their work can be found in the highlights section of this report.

SUSTAINABILITY AND ENERGY EFFICIENCY

The Zayed Centre for Research comprises 13,000m^2 of space set over eight floors. The building has been designed with energy efficiency and sustainability in mind. To this end, several key design features ensure the building operates in an environmentally friendly way while maintaining efficiency:

- Photovoltaic systems (PV systems) are a renewable energy technology which transform the energy from the sun into electricity using photovoltaics. These photovoltaics, also known as solar panels, provide a reliable green energy solution. A PV system has been installed on the building, allowing generation of electricity through solar power.
- A gas-fired combined heat and power (CHP) unit has been installed to supplement grid-supplied electricity. CHP systems use gas to generate electricity on-site and use the heat generated to provide hot water for the site.
- A sophisticated electrical metering network has been installed to ensure power consumption can be monitored and tracked for efficiency.
- Heating systems, chilled water systems, gas systems and water systems are all monitored by meters to allow tracking of consumption and efficiency.
- The building is fitted with blinds that have been designed to minimise heat gains within internal spaces, consequently reducing the requirement for mechanical cooling.
- Heat recovery systems have been installed on air handler units to increase efficiency of space heating / cooling.

- Light-emitting diodes (LED) are semiconductor light sources that emit light when current flows through them. LED lighting has been installed throughout the building. A lighting control system has been installed to control lighting in all areas. High-performance movement detectors have also been installed in appropriate areas so that lights are automatically switched off in unoccupied areas. The control system also dims lights when full output is not required.

- A Building Energy Management System (BeMS) has been installed to reduce costs while improving staff comfort and working conditions. Programmed to operate in the hospital according to schedules, the system 'self-learns' and adapts the time the hospital switches heating on and off to match external weather conditions.

The indicators of operational performance are annual carbon dioxide emission per unit of area of the building caused by its consumption of energy, compared to a value that would be considered typical for this type of building. The operational rating is a numeric indicator of the amount of energy consumed during the occupation of the building over a period of 12 months, based on meter readings. The display energy certificate (DEC) for the performance of a building is labelled on an "A to G" scale in a similar way to many UK household appliances as this is a format easily recognisable to the public.

The Zayed Centre for Research building has been allowed to 'bed in' since its opening and is being operated in accordance with the original design. Operational performance is slightly above the benchmark with a rating of E, compared with typical performance of this type of building which is D. This is still in line with expectations for a new building in the initial operational period.

GOSH has employed a full-time dedicated Energy Manager who will be completing an audit of the Zayed Centre for Research over the first quarter of 2022/2023 including detailed analysis of the sub-metered data and a review of the controls' strategy in conjunction with the engineering team and building occupants.

A VERY SPECIAL THANK YOU

The Zayed Centre for Research into Rare Disease in Children was made possible thanks to a transformative £60 million gift from Her Highness Sheikha Fatima bint Mubarak, wife of the late Sheikh Zayed bin Sultan Al Nahyan, founding father of the United Arab Emirates, in 2014. We are also grateful to Research England, The Wolfson Foundation, John Connolly & Odile Griffith and the Mead Family Foundation whose generous support contributed to the creation of the Zayed Centre for Research. The Zayed Centre for Research is a partnership between Great Ormond Street Hospital, UCL and Great Ormond Street Hospital Children's Charity.

Artist Mark Titchner created an iconic piece of art for the Zayed Centre for Research.
Based on a Helen Keller quote, the interconnected design features interweaving pathways to represent the collaborative vision for the building.

APPENDIX

Acronyms

BRC	Biomedical Research Centre
GOSH	Great Ormond Street Hospital
NIHR	National Institute for Health and Care Research
PI	Principal Investigator
UCL GOS ICH	University College London Great Ormond Street Institute of Child Health

Falcon visits by country of residence:

Country of Residence October 2019 - October 2020	Count
Canada	1
Cyprus	1
England	16486
Falkland Islands	2
France	2
Germany	2
Gibraltar	2
Greece	1
Ireland	32
Jersey	3
Kuwait	2
Malta	14
Netherlands	1
New Zealand	1
Northern Ireland	15
Norway	1
Pakistan	1
Poland	1
Qatar	1
Scotland	21
Slovenia	1
Spain	2
UAE	1
USA	2
Wales	23
Other	59

Country of Residence October 2020 - October 2021	Count
Bulgaria	1
Cyprus	2
England	15696
Falkland Islands	1
France	1
Germany	2
Guernsey	1
Ireland	21
Jersey	4
Kuwait	1
Malta	7
New Zealand	1
Nigeria	1
Northern Ireland	10
Saudi Arabia	1
Scotland	18
UAE	2
Wales	23
Other	13

Great Ormond Street Hospital Children's Charity
40 Bernard Street
London WC1N 1LE

T: 020 3841 3083
E: izabella.siemicka@gosh.org