UCL INSTITUTE OF CHILD HEALTH

Great Ormond Street Hospital for Children
NHS Foundation Trust

Research Review 2013/14

The child first and always

Contents

03 Director's report

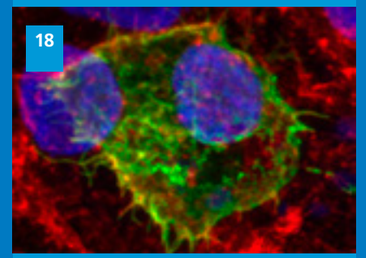
07 Chief Executive's report

08 Division of Research and Innovation report

13 **Personalising childhood cancer treatments**
Professor John Anderson

14 **New drug treatment for congenital hyperinsulinism**
Professor Khalid Hussain

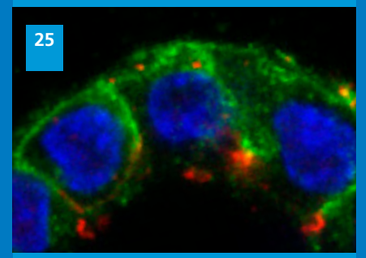
16 **A vision for treating childhood blindness**
Professor Jane Sowden



18 **Childhood parkinsonism**
Dr Manju Kurian

21 **Tackling respiratory disease**
Professor Chris O'Callaghan

22 **Early diagnosis for inherited deafness**
Professor Maria Bitner-Glindzicz



25 **Pioneering treatments for metabolic disorders**
Professor Paul Gissen

26 **Evidence-based medicine in the era of 'big data'**
Professor Ruth Gilbert

28 **The Somers Clinical Research Facility**

32 **Grants and donations**

36 **UCL Institute of Child Health's academic programmes**

38 **Administration**

Cover: Three-year-old Harry on Koala Ward.

Left: Baby Émilie is at the hospital to receive treatment for a hernia.

One-year-old Gabriela on Lion Ward.

Director's report

The UCL Institute of Child Health (ICH), with its partner Great Ormond Street Hospital (GOSH), is Europe's largest academic centre for research and teaching in children's health and disease. One of the highlights of the past year has been the launch, in March 2014, of the new ICH academic strategy.

The new academic strategy was developed over the past 18 months and informed by visits to other world-leading children's academic medical centres. This strategy is focused on five academic programmes:

- developmental biology and cancer
- developmental neurosciences
- genetics and genomic medicine
- infection, immunity, inflammation and physiological medicine
- population, policy and practice

There is one cross-cutting theme, around rare diseases, which links in very well with the planned development of the Centre for Research into Rare Disease in Children with the ICH, GOSH and Great Ormond Street Hospital Children's Charity. We now have all the building blocks in place to realise the benefits of the new programmes and are now working to ensure that the research and education, within the academic programmes at the ICH, interface seamlessly with clinical research and education at GOSH.

It has also been an exciting time for prestigious awards. At the ICH, we were awarded, in April 2014, Athena SWAN Silver status. This is an important recognition of the very good work at the ICH to address gender balance and the development of academic careers for both men and women, to ensure that gender does not adversely influence career prospects and trajectories. The Athena SWAN Self-Assessment team, led by Professor Shamima Rahman, worked tirelessly to achieve this award and to further embed good working practices. This is a very important step forward for the ICH, not least because it enables us to apply for future National Institute for Health Research (NIHR) Biomedical Research Centre awards and is likely to influence the views of other funders, who recognise that Athena SWAN Silver status is an important attribute in their assessment of institutions.

Our grant funding has increased sharply and for the last financial year was over £40 million, which is a tremendous success. We showed particular increases in NIHR funding. These funding awards have included numerous fellowship awards and I want to single out in particular the success we have had this year and last year, with the awards of NIHR Research Professorships. These awards are relatively new and each university or medical school can only nominate a maximum of two individuals. Only five are awarded nationally per annum and last year we were successful with Professor Persis Amrolia, who was awarded an NIHR Research Professorship in 2013 for his work in stem cell therapies and this year Professor Paolo De Coppi, who achieved an NIHR Research Professorship in 2014 for his work in regenerative medicine and oesophagus reconstruction. We were also successful in achieving a number of new NIHR Senior Investigators and it is notable that of the 16 new NIHR Senior Investigators awarded nationally, three were to staff at the ICH. These were Professors Phil Beales, Lyn Chitty and Neil Sebire. Warm congratulations to all of them.

Director's report

Continued

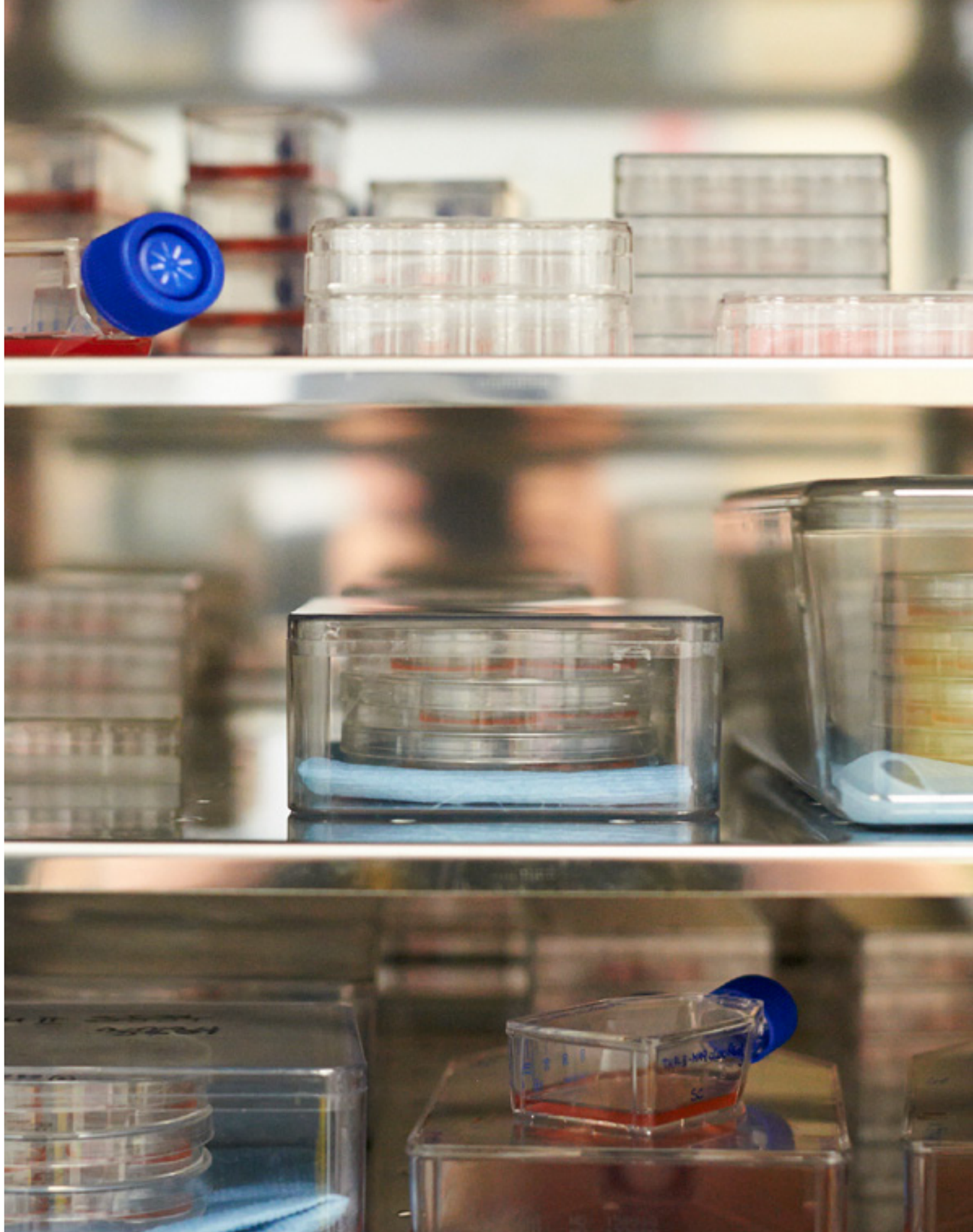
This has also been a record year for senior promotions at University College London (UCL). No fewer than nine members of staff were successful in being promoted to Professor. These nine are: Professors Torsten Baldeweg, Christopher Clark, Paolo De Coppi, Khalid Hussain, Mark Peters, Shamima Rahman, Philip Stanier, Alastair Sutcliffe and Angie Wade. Achievement of a UCL Professorship is very challenging and it is wonderful that so many of our staff have been successful in the latest UCL senior promotions round. A number of other members of staff were promoted to reader and senior lecturer.

I am pleased to say that recruitment has now started for Life Study. Life Study is the UK's latest and largest birth cohort study, funded by the Economic Social Research Council, Medical Research Council and UCL. It will recruit over 80,000 women with the intention of studying their infants from pregnancy, through childhood and into adult life. It is directed by Professor Carol Dezateux, who has been working with leading social, population, biomedical and clinical scientists from UCL and other UK universities, to develop and deliver this ambitious and scientifically innovative study. This is a huge undertaking and Carol and her team have worked extensively with partners in the NHS and UK statistical authorities to set up the infrastructure needed to run Life Study. Recruitment has now started at the first site at Barking, Havering and Redbridge University Hospitals NHS Trust. The whole ethos of this study is that it will provide information relevant to the improvement of the lives, health and wellbeing of children, both now and in the future.

UCLPartners, which was designated initially as an Academic Health Science Centre five years ago, applied for re-designation in autumn 2013. For this application, the proposal described six clinical academic programmes, of which one included child health. This application was successful, which was a great tribute to the strength and depth of clinical science across UCLPartners. Having child health as one of the six programmes is recognition of the importance of this work to the whole partnership and our challenge is now to work to align clinical care, research and education to maximise the benefits to the health and wellbeing of children and the adults they will become.

I hope that I have managed to convey some of the excitement and energy of the academic environment at the ICH. We have much to do, but we are building on great successes and the opportunities for the future are tremendous.

Professor Rosalind L Smyth *FMedSci*
Director
UCL Institute of Child Health



11-year-old Georgina on Squirrel Ward.

Chief Executive's report

Research is integral to Great Ormond Street Hospital (GOSH). By improving diagnoses and treatments and finding cures for some of the most complex and rare conditions, our work can benefit children in the UK and worldwide.

Research and innovation continue to be at the forefront of what we do. The quality of our research is evidenced not only by the positive results from a recent analysis of all the major paediatric centres worldwide, which was undertaken by Thomson Reuters (Evidence), but also by the impact our research has on delivering clinical care. In this year's review you will read just a few examples that highlight the importance of research to children, young people and their families.

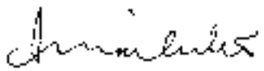
One of those examples is the work of Professor Khalid Hussain, Consultant Endocrinologist, whose scientific research in the laboratory has been translated into better treatments for children with low blood sugar levels. In addition, you can read about the impact that genetic discoveries are having on improving diagnoses for children and their families thanks to the work of Dr Manju Kurian, Consultant Neurologist, and Professor Maria Bitner-Glindzicz, Consultant Clinical Geneticist. Their research now paves the way for developing therapies for conditions for which no treatment currently exists. We hope that these and other features will provide you with an overview of the diversity of our research programme.

In many of these articles you will see the importance and strength of our partnership with the UCL Institute of Child Health (ICH). One of our priorities is to align ourselves further with the ICH's research programmes. The ICH launched its new academic strategy earlier this year, and with Professor Rosalind Smyth, Director of the ICH, we have established a joint working group to consider how we can align the research of our organisations to refresh and strengthen our approach to working together.

GOSH sees more children with rare diseases than any other hospital in Europe, and as such is uniquely placed to conduct research in this area. In last year's *Research Review* we talked about our plans with the ICH and Great Ormond Street Hospital Children's Charity to open the new Centre for Research into Rare Disease in Children. Thanks to a transformative donation from Her Highness Sheikha Fatima bint Mubarak, the hospital's ambition to build this centre is now possible. The development will also provide much-needed outpatient clinical space, completing the translational research pathway from pure research to practical patient involvement.

In keeping with our ambition to invest in rare disease research, GOSH hosted the launch of the first UK strategy for rare diseases. The hospital was chosen to host the announcement as it runs a large number of nationally commissioned services for rare diseases. At the launch, Health Minister Lord Howe outlined the UK's vision for research, support and training in the diagnosis and treatment of rare diseases.

In January 2015, we welcome our new Chief Executive, Dr Peter Steer, who joins us from Queensland, Australia where he has been the Chief Executive of Children's Health Queensland Hospital and Health Service. Peter shares our vision – to truly become a research hospital rather than a hospital that does research. Going forward we are looking to build on our excellent work to further embed research into the day-to-day working lives of our staff and the patients and families we treat.



Mr Julian Nettel
Interim Chief Executive
Great Ormond Street Hospital for Children NHS Foundation Trust

Division of Research and Innovation report

The Great Ormond Street Hospital (GOSH) Division of Research and Innovation continues to support world-leading efforts in advancing paediatric medicine at GOSH and the UCL Institute of Child Health (ICH).

Over the last year we have celebrated a number of successes, made possible through our National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) funding and infrastructure. The key objective of the BRC is to accelerate the discovery of the basis of childhood diseases, develop novel diagnostics, imaging modalities and new treatments, including stem cell and gene therapies. Our focus is on rare diseases, our core clinical and research resource, with the aim of delivering patient benefit nationally.

In October 2013 we were approached to participate in the Genomics England 100,000 pilot. The 100,000 Genomes Project has been established to deliver on the government's commitment to sequencing 100,000 genomes by the end of 2017. GOSH worked in partnership with two other UCL Partner Trusts, University College London Hospitals and Moorfields Eye Hospital. Between November 2013 and January 2014, GOSH collected over 650 samples, and as a partnership the UCL Partner NHS Trusts collected over 1,000 samples. We hope that our successful participation in the pilot will allow us to continue to play a key role as the national initiative develops. You can read more in this report about the successful role the Somers Clinical Research Facility played in this Genomics Pilot Study.

Improving research performance is a major priority for the Trust. Key NIHR performance metrics related to the time taken for a project to be initiated and the delivery of studies to time and target have been prioritised recently by the Trust. We have seen continued improvement in our performance against these key metrics. The metrics have been set to ensure that research studies are set up efficiently and with due consideration to feasibility and capacity. Improvement in performance as measured against these metrics is high on our agenda. As such we have established a local research fund to facilitate research and increase research capacity across the organisation.

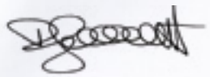
Two key appointments for the Research and Innovation Division were Dr Erin Walker and Dr Kate Oulton. Dr Walker is our patient and public involvement research lead, who has been appointed to advise and support researchers on how to effectively involve patients and the public in their research design. Dr Walker also supports our Young Persons Advisory Group. Dr Oulton is our nursing and allied health professional training lead. With Dr Oulton's direction, we aim to increase the number of nursing and allied health professionals who are engaged with and undertake their own research.

During 2013, Thomson Reuters (Evidence) were commissioned to undertake a bibliometric analysis of GOSH and ICH publications spanning 2008–2012. This analysis showed that, compared to the top paediatric research organisations in the world, GOSH and the ICH together ranked joint third on citation impact, fourth on the percentage of papers that were highly cited and fifth on the numbers of original research publications. In addition, the citation impact of our publications, which was twice the world average, was also above the average for UK medical research.

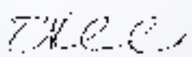
In 2012 the NIHR agreed to fund a GOSH UCL BRC for a second five-year term. As part of the BRC strategy, an external advisory board (EAB) was established to oversee the performance and strategy of the BRC. Consisting of international leaders in their fields and led by David Williams, Leland Fikes Professor of Pediatrics at Harvard Medical School and Chief of Pediatrics at Boston Children's Hospital, the EAB visited GOSH and UCL in May 2014.

The subsequent EAB report highlighted the excellent work being done at GOSH and the ICH in the field of rare diseases and contained useful suggestions on ways of improving and making an even higher impact.

We look forward to reporting further exciting developments next year.



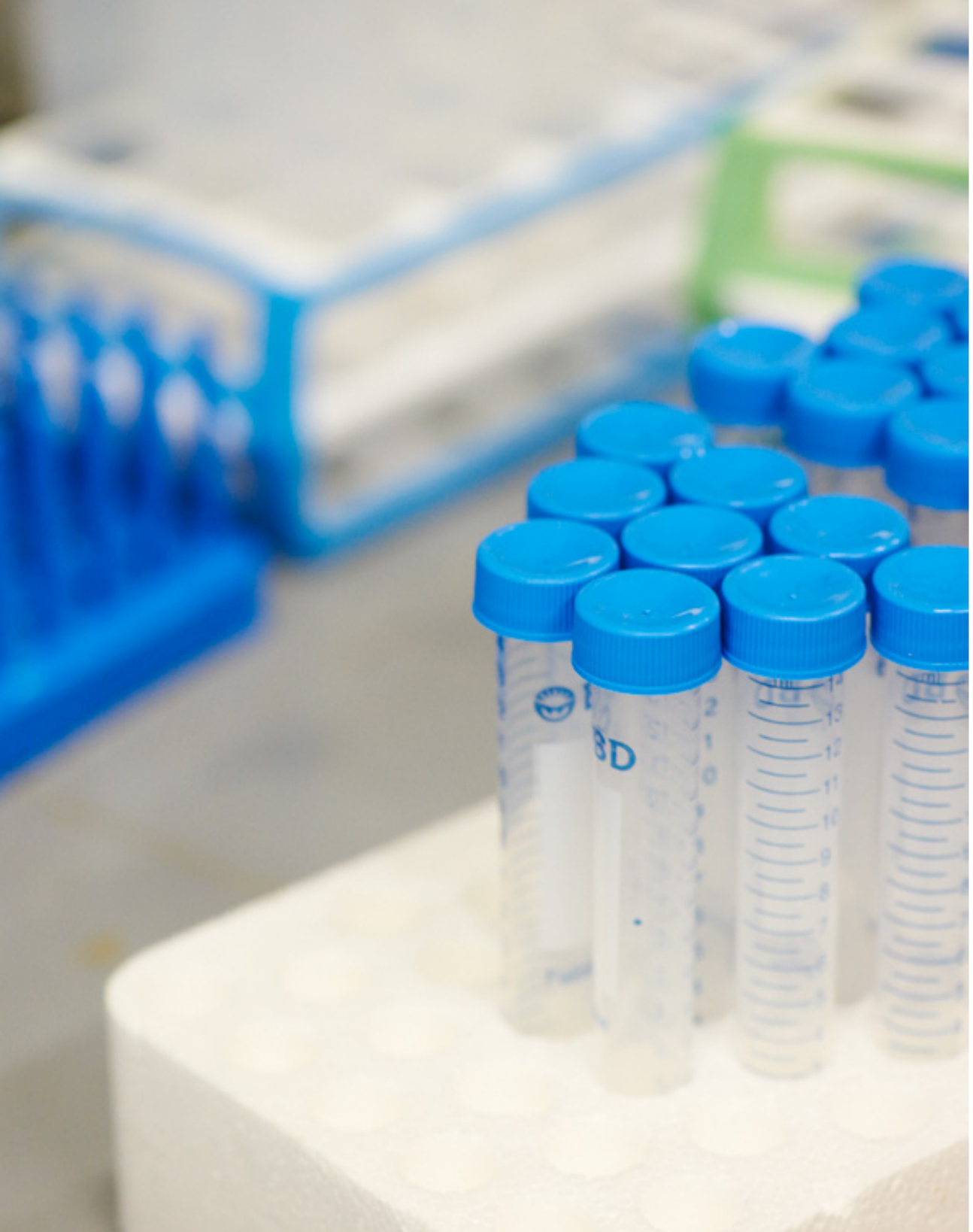
Professor David Goldblatt
Director of Clinical Research and Development



Ms Emma Pendleton
Deputy Director of Research and Innovation

“For many of the children and families that we see, we don’t have a treatment and we certainly don’t have a cure. The only thing that we really have to offer them is research.”

Professor Maria Bitner-Glindzicz



Professor John Anderson

"I studied biochemistry as a first degree before starting my medical degree. It was a particularly exciting time in the field of immunology, with the discovery in 1985–6 of how T cell diversity is generated. This was a solution to one of the great puzzles in biology. I recognised at that early stage of my career that understanding the immune system could be pivotal to tackling cancer.

"Paediatrics was always my favourite discipline in medical school and so it was a natural development for me to end up studying T cells and childhood cancer. I am indebted to Cancer Research UK, the Department of Health through the Higher Education Funding Council for England and Great Ormond Street Hospital Children's Charity for supporting me through four consecutive fellowships since 1995 when I started my PhD, and most recently with a Research Leadership Award from Great Ormond Street Hospital Children's Charity. I am extremely proud to have worked at GOSH and the ICH since 1998. Patients and colleagues are my daily inspiration."

Personalising childhood cancer treatments

Over 30 children every week are diagnosed with cancer in the UK. Current cancer treatments generally involve a one-size-fits-all approach, meaning some children may not respond to treatment, whereas other patients are over treated. Professor John Anderson is using advances in scientific research to develop treatments tailored to a child's specific cancer.

"Survival rates for certain types of cancers have vastly improved over the last 20 years," says John Anderson, Great Ormond Street Hospital Children's Charity Professor of Experimental Paediatric Oncology at the UCL Institute of Child Health (ICH) and a Consultant Oncologist at Great Ormond Street Hospital (GOSH). "Yet, for some groups of children, such as those with rare childhood cancers, not all treatments lead to cures, while for others, lengthy treatments result in long-term and unpleasant side effects. Radical new approaches are urgently needed to develop new and gentler cancer treatments."

The key focus of Professor Anderson's research is to harness the power of the body's immune system to attack the cancer. In cancer, the balance between the growth of the tumour and the immune system's ability to reject the cancer lies in favour of the tumour's growth. Tipping this balance in favour of the immune system is how immunotherapy works.

"Because of the immune system's extraordinary power, its ability to remember what it has attacked and its exquisite precision, immunotherapy has the potential to achieve complete, long-lasting remissions and cancer cures, with few side effects," says Professor Anderson, whose research is currently supported by Great Ormond Street Hospital Children's Charity, the Wellcome Trust and Children with Cancer UK. "Cancer immunotherapy has already had some early success in the treatment of leukaemia. Our research builds on this idea in childhood cancers urgently requiring new treatments, such as neuroblastoma and high grade glioma."

Professor Anderson and his group are focusing on using immune cells – specifically T cells – to recognise and kill cancer cells. In one approach, they are using novel genetic engineering techniques to redirect T cells to recognise tumour cells. This work is particularly focused on neuroblastoma, one of the most aggressive childhood cancers.

"Neuroblastoma cells express a protein called GD2 on their surface," explains Professor Anderson. "We want to engineer T cells taken from a patient's body to specifically express proteins that can recognise GD2 and then kill neuroblastoma cells. As GD2 is not expressed on any other cells, this type of treatment could attack the cancer without damaging healthy cells, resulting in fewer side effects for children." The team are poised to launch an early phase clinical trial, funded by Cancer Research UK, to test the safety and effectiveness of this new treatment for neuroblastoma.

In another approach he is investigating a rarer subset of T cells called gamma delta T lymphocytes as alternate killer cells for childhood cancer immunotherapy. The group have recently developed techniques for expanding these cells from blood in the laboratory to sufficient numbers for injection back into the patient. "We are testing whether these expanded cells are better than normal T cells in migrating into tumours, killing cancer cells and surviving in the body," says Professor Anderson.

The work of Professor Anderson and his team is pivotal in trying to create more effective treatments for childhood cancers. He adds: "Approaches to children's cancer have changed radically over the last 15 years. We hope our new targeted treatments will bring about improvements in cancer care using gentler treatments."

David's story
by his mum Kristina

"When David was born the doctors immediately knew something wasn't right. He didn't cry, he was very floppy and looked blue. After being rushed to a specialist baby care unit at our local hospital, doctors discovered David's blood sugar levels were extremely low. We had heard of conditions with high blood sugar levels, like diabetes, but we had never heard of anyone with low blood sugar.

"Ten days after David was born he was transferred to GOSH. At the time we felt so many different emotions. While we knew his condition was serious enough to be transferred to a specialist children's hospital, we also knew it was one of the best children's hospitals in the world.

At a difficult time it was reassuring to know David was going to receive the best possible care.

"After a few tests the doctors told us that David had congenital hyperinsulinism, but none of the drugs stabilised David's sugar levels. It was then Professor Khalid Hussain discussed the option of having his whole pancreas removed, but he also offered an alternative – a drug called sirolimus. We were nervous at the time but knew this was a better option.

"Once David was given the drug, it was amazing. Within a few weeks he was much better and we were able to bring him home. He is now reaching all the milestones a healthy baby would, like walking, running and talking and every day we can see him getting better.

"The Hyperinsulinism team at GOSH have been extremely helpful. They have always answered our questions about David's condition and his treatment. We will always be eternally grateful to GOSH for everything they have done for us."

Professor Khalid Hussain
"After completing my medical degree at Glasgow University I initially trained as a GP. It was during my GP training that I developed a passion for paediatrics and neonatology. I went to Australia and trained at the Monash Medical Centre to become a fully qualified neonatologist.

"I was always interested in glucose physiology from my junior doctor days of measuring blood sugar in newborns. When I returned from Australia I applied for a research job at the ICH/GOSH to work on hypoglycaemia under the mentorship of Professor Sir Albert Aynsley-Green. It was here that my passion for understanding the molecular mechanisms of childhood hypoglycaemia, especially congenital hyperinsulinism, was ignited and I began my research career. Our research has transformed the GOSH congenital hyperinsulinism centre into one of the major centres in the world looking after these complex patients.

"What fascinates me most about translational research is that I can make a difference to the lives of the children that I care for in the hospital. Translational research allows you to take the clinical problem into the laboratory and understand the patho-physiology of the disease process and then ultimately translate that to patient benefit. It is this sort of research that continues to motivate and drive me to achieve better treatments for children with congenital hyperinsulinism."

New drug treatment for congenital hyperinsulinism

Congenital hyperinsulinism is a condition where the pancreas makes too much of the hormone insulin, causing low blood glucose levels. Professor Khalid Hussain has managed to save four patients at Great Ormond Street Hospital (GOSH) from having their pancreases removed thanks to the discovery of a new drug treatment.

"Your body's ability to control blood glucose levels through insulin production is absolutely vital for you to function normally. Too much glucose (hyperglycaemia) or too little glucose (hypoglycaemia) in your blood can be detrimental," explains Khalid Hussain, Professor of Paediatric Metabolic Endocrinology at the UCL Institute of Child Health (ICH) and Honorary Consultant in Paediatric Endocrinology at GOSH.

GOSH is recognised as a national and international referral centre for children with severe forms of hypoglycaemia due to too much insulin production (congenital hyperinsulinism). The congenital hyperinsulinism centre at GOSH, led by Professor Hussain, is designated by NHS England as one of two centres of excellence in the UK for the diagnosis and treatment of the condition.

"As a national referral centre we see children with the most severe forms of congenital hyperinsulinism, where children do not respond to conventional medical therapy. The only available treatment involves eliminating the source of insulin, through either a complete or partial removal of the pancreas," says Professor Hussain.

His research has completely transformed how doctors make this decision. Working with collaborators in Finland, Professor Hussain's research team have shown that an imaging technique, known as an 18F-DOPA-PET/CT scan, can show more precisely which parts of the pancreas are producing excessive insulin. If a small part of the pancreas is identified then only partial surgical removal is required, preventing hypoglycaemia.

"The 18F-DOPA-PET/CT scan allows surgeons to better identify the 'hotspots' in the pancreas. It has radically changed the way these infants are now managed. This is a significant improvement on previous invasive, technically demanding and non-specific techniques used to make this diagnosis. We are now refining this approach as newer and better imaging technologies become available," says Professor Hussain.

On the other hand, if the entire pancreas is affected then the whole organ needs to be surgically removed. Professor Hussain stresses though, this is not a cure. "Removing the entire pancreas causes the opposite effect. Children then go on to develop diabetes and require regular insulin injections. They also require enzyme replacement therapy to supply the enzymes responsible for digestion. Our clinical research has focused on developing a better treatment option for these children."

In a landmark study led by Professor Hussain and published in 2014, researchers pinpointed the molecular pathway most likely to be responsible for the overproduction of insulin in children where the whole pancreas was affected. They then searched for an existing drug capable of blocking this pathway, and identified the drug sirolimus, which has been used to treat renal transplant patients.

Four GOSH patients who had not responded to conventional medication and whose only remaining option was to have their whole pancreas removed, were offered sirolimus as an alternative treatment. All four patients responded well to sirolimus treatment and were discharged home safely without the need to remove their pancreas.

"One year on, all the patients are doing well, with stable blood glucose levels and no significant side effects. Identifying the key pathways involved in this disease has helped us to find the most suitable treatment for these patients. We hope that in the long-term, the treatment will lessen the severity of the condition, enabling children to be moved onto more standard medication. This new discovery could change the way children with congenital hyperinsulinism are managed in the future," says Professor Hussain whose research is supported by the Wellcome Trust, the Medical Research Council, Diabetes UK and The Children's Hyperinsulinism Fund.

A vision for treating childhood blindness

More than a million children will spend the rest of their lives with irreversible blindness. Sight loss affects all aspects of a child's daily life and is critical to their development and progress. Professor Jane Sowden's research is at the forefront of international efforts to develop new cures for childhood blindness and improve knowledge of the causes of eye conditions.

Professor Jane Sowden

"My research career began with my final year project at the University of Oxford, where I first explored the genetic processes that regulate early development. This led to my PhD and postdoctoral research in genetics and gene regulation, inspired by the work of embryologists studying mammalian development, by discoveries of the role of genes in the formation of the body, and inherited human diseases.

"Receiving an MRC Career Development Award provided me with the exciting opportunity to combine these areas of interest, to begin my own research investigating eye development and its genetic regulation in health and disease, first at the UCL Institute of Ophthalmology, and then at the ICH since 1998.

"During this time I have been fortunate to work with some inspirational collaborators and talented young researchers on revealing how the eye develops from the early stages of embryogenesis and how these processes are disrupted by gene mutations that lead to visual defects and disease. Knowledge of the cause of disease and discoveries in the field of stem cell biology have led us to pursue innovative research trying to regenerate and repair diseased tissue in the eye.

"I'm motivated by the limited treatment options for children born with eye disease, and the challenge of developing new cell and gene-based therapies to prevent blindness."

Thirty per cent of all cases of childhood blindness or partial sight are caused by diseases affecting the photoreceptors – specialised light-sensitive cells that line the retina at the back of the eye. "We know from research over the past two decades that many cases are caused by gene mutations that are inherited, but we do not yet have treatments for these conditions," says Jane Sowden, Great Ormond Street Hospital Children's Charity Professor of Developmental Biology and Genetics at the UCL Institute of Child Health (ICH).

Over the last decade, and working collaboratively with Professor Robin Ali at the UCL Institute of Ophthalmology, Professor Sowden's research team have been developing cell-based therapies to reverse childhood blindness. "The idea that sight could be restored by transplanting new photoreceptor cells to replace those lost through disease is one of the most exciting scientific challenges in regenerative medicine," explains Professor Sowden.

In 2012, the joint UCL team published a landmark study that showed they could partially restore the sight of mice that had been born with a form of blindness. This remarkable result was achieved by transplanting immature photoreceptor cells into their retina. The cells then matured and formed the vital connections needed to transmit visual information to other cells in the retina, and onwards to the brain.

"To develop this as a treatment for retinal disease we are working to harness the power of stem cells to grow human photoreceptor cells for transplantation," says Professor Sowden. In a second important study published in 2013, the UCL team became the first in the world to successfully transplant photoreceptor cells grown 'in a dish' from mouse stem cells. "This demonstrates that stem cells can provide unlimited quantities of photoreceptors for transplantation," says Professor Sowden.

She thinks both studies are important milestones on the road to developing treatments for human blindness. "There are a number of challenges we need to overcome before we can translate this research into patient benefit. But based on the similarities between the mouse and the human retina, these studies show exciting promise for new treatments for currently untreatable eye conditions."

In parallel, her team have been expanding knowledge of the genetic causes of childhood eye defects. This year the team discovered a new gene, which causes coloboma, a condition in which a baby's eyes do not develop normally during pregnancy. "Children who are blind or partially sighted can have other disabilities, and the majority of families do not receive a genetic diagnosis. By improving genetic diagnosis for these conditions we can support precise management and early treatment, and provide information to the family about the cause of their condition," says Professor Sowden.

Working collaboratively with the GOSH Regional Genetics Laboratories, the team have translated their research on an inherited form of childhood glaucoma to set up the UK's first nationally-available genetic diagnostic test for this condition. "We are working on providing other new tests that screen for mutations in multiple genes to improve diagnosis for these rare eye conditions," says Professor Sowden, whose research is supported by the Medical Research Council, Fight for Sight, The Rosetrees Trust, The Micro and Anophthalmic Children's Society (MACS), The Special Trustees of Moorfields Eye Hospital and the National Institute for Health Research Biomedical Research Centre at GOSH and UCL.

"Through increasing our understanding of the genes involved in these conditions and our progress towards developing new therapies, I hope that in the future we are able to offer new treatments to restore and preserve the sight of children with untreatable blindness," she adds.

Childhood parkinsonism

Infantile parkinsonism-dystonia (IPD) is a newly identified condition in which children experience movement difficulties similar to Parkinson's disease. Dr Manju Kurian discovered the cause of IPD and is now pressing ahead to develop the first effective treatment for children with this life-limiting condition.

Dr Manju Kurian

"After completing medical school at the University of Cambridge I began specialising in paediatric neurology – caring for children with diseases that affect the brain and nervous system. What struck a chord with me early on was the limited relief modern medicine provided these children, despite advances in many other areas of medicine. Recognising this was because of a lack of understanding of the causes of disease I embarked on a PhD at the University of Birmingham.

"During my PhD, I visited a number of families who had children with infantile parkinsonism, and I was particularly struck by the enormous difficulties that these brave children and their amazing families face every day, just trying to undertake essential tasks for daily living.

"Finding the disease-causing gene for IPD has been a major breakthrough, and I have been awarded a number of national prizes in recognition of this research. In addition, it has led to a number of important international collaborations with groups in the USA and Italy with whom we work closely on the research. I feel very motivated to try and better understand this devastating disease, in order to develop new treatments. It is precisely for this reason that I was immensely proud to join GOSH and the ICH in 2011 so that I could combine clinical and academic work to focus on the specialist management of these children while researching novel treatments. Finding therapies for this disorder will remain a high priority for my research."

"IPD is a life-limiting neurological condition. Within months of being born children experience uncontrollable movements and by childhood they go on to develop Parkinsonism, becoming rigid and finding it difficult to initiate movement," explains Dr Kurian, a Wellcome Trust Intermediate Clinical Fellow at the UCL Institute of Child Health (ICH) and a Consultant in Paediatric Neurology at Great Ormond Street Hospital (GOSH).

Driven by the lack of answers and treatment options that were offered to children and their parents, Dr Kurian began researching the molecular cause of IPD. In 2011, through detailed genetic analysis of two unrelated families, she made a key breakthrough. Her research showed that IPD was caused by a mutation in a gene that codes for the dopamine transporter – SLC6A3. This faulty gene severely affects the transport of the neurotransmitter dopamine – an important chemical found in the brain known to be depleted in Parkinson's disease.

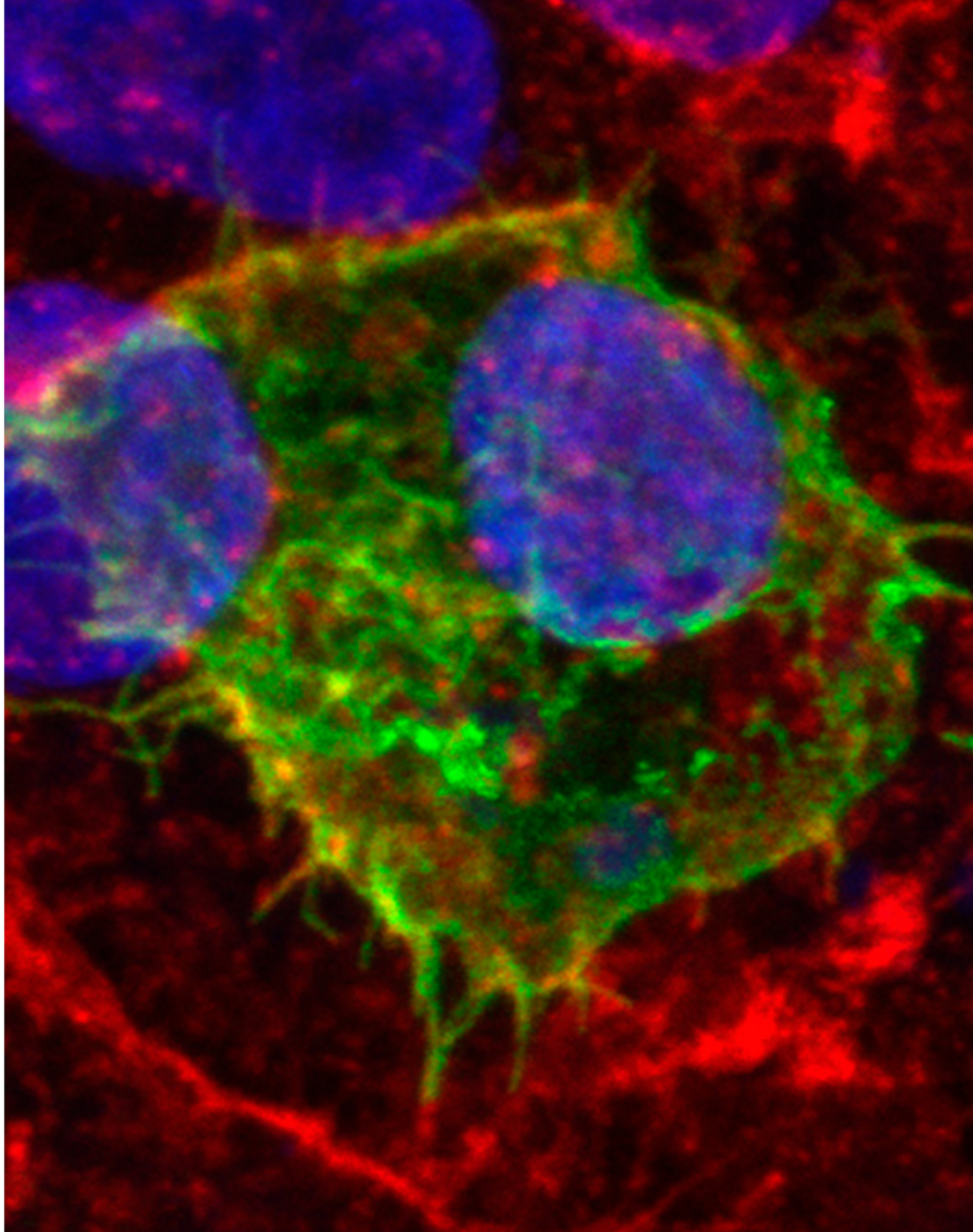
Dr Kurian emphasises the impact this finding had on the children and families under her care. "Many children with IPD had previously been misdiagnosed with cerebral palsy because of the similarities in movement difficulties. They had been tried on a combination of drugs, sometimes for years, to control their symptoms, but with little effect. Parents would say 'I used to think we had done something wrong' when actually this is a genetic condition."

Through Dr Kurian's work, GOSH is now recognised as a leading international centre for the diagnosis and clinical management of IPD, receiving referrals from the UK as well as internationally from countries including Germany, USA, Israel and Pakistan. Since her ground-breaking discovery, over 25 children and young adults in the UK and across the world have received a correct diagnosis. She expects more cases will be identified as the condition remains under diagnosed because of its similarities with cerebral palsy.

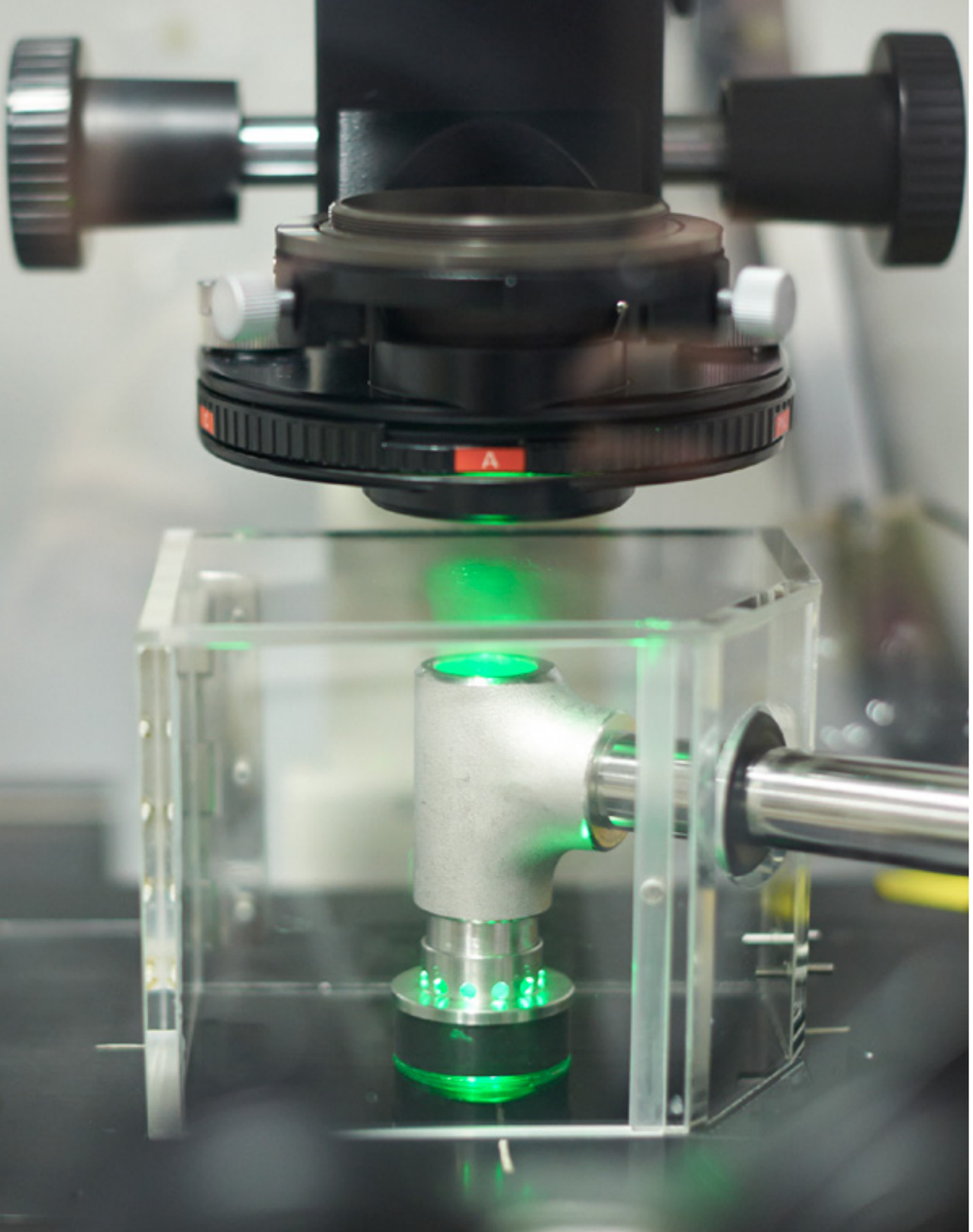
Her clinical work has also resulted in a greater awareness of which existing drugs lead to improvements. "We are now better placed to manage the movement difficulties these children experience. Some drugs allow children a little more voluntary movement and we are working to share treatment plans with neurologists around the world." Yet this is just the first step. "None of these treatments are life-saving and in my opinion we should be aiming for better."

Dr Kurian and her team are now embarking on their next programme of research, to develop the first effective treatment for IPD. She is building on GOSH and the ICH's strengths in landmark gene discoveries. Combining this with its international expertise in gene therapy, one of the early approaches being adopted is to replace the faulty gene. She acknowledges the support she has received from Great Ormond Street Hospital Children's Charity, the Wellcome Trust, the Medical Research Council, Action Medical Research and the AADC Research Trust, which has allowed her to capitalise on the early momentum she has built.

What is remarkable is that IPD is just one of a number of neurological conditions Dr Kurian is currently tackling. Her research extends to childhood epilepsies and other neurodegenerative conditions, all of which have had some early successes. Yet, the long-term goal for each condition remains the same: "To improve both the child's day-to-day life and their chances for the future," she adds.



High powered microscopy to look at different parts of the cell using fluorescent dyes.



Tackling respiratory disease

Respiratory disease is one of the biggest threats to children's health worldwide and there is a huge need for research to address this. As Head of Respiratory, Critical Care and Anaesthesia at the UCL Institute of Child Health (ICH), Professor Chris O'Callaghan's work is contributing to a greater understanding of lung disease and the development of novel strategies to tackle these conditions.

Professor Chris O'Callaghan

"Being let loose in a laboratory during my undergraduate training made me realise how little is really known once 'you scratch the surface' and this is still the case in so many areas.

"A doctorate of medicine on aerosol drug delivery, at the University of Nottingham with Professor Tony Milner, gave me an excellent research introduction to physiology and aerosol physics. It also gave me the opportunity to work with Professor Peter Mansfield who was awarded the Nobel Prize for developing MRI scanning.

"Training in respiratory medicine in the UK was in its infancy so I moved to work with Professor Peter Phelan's team at the Royal Children's Hospital in Melbourne. I was able to continue my research in respiratory cilia and to develop novel models to study the motile cilia that line the ventricular cavities of the brain leading to a PhD on brain cilia. The ciliary models have provided an excellent foundation to our work on the effects of inflammation and bacterial and viral infection in respiratory disease and meningitis."

"Education has also been a major interest with a focus on the huge potential to improve health outcomes internationally by developing context specific, video intense multimedia training."

"My move to the ICH and Great Ormond Street Hospital has put me in one of the best environments to take my interests in respiratory research and multimedia education forward."

Millions and millions of microscopic hair-like projections called cilia lining our airways, beat over a million times a day to clean our airways and protect our lungs from damage and infection. Unknown to most, cilia also line the fluid filled ventricles of the brain, each beating over three million times a day.

By establishing techniques to investigate respiratory and brain cilia, Professor Chris O'Callaghan's research has had a major impact on the diagnostic testing of children with inherited defects in their cilia, primary ciliary dyskinesia (PCD).

Professor O'Callaghan explains how his early research led directly to his team developing methods that are now used worldwide to diagnose PCD. "While looking at cilia in the airways, we also developed an interest in the cilia that line the fluid filled ventricles in the brain. It became clear that the frequency of brain cilia beating, which is around 40 beats per second, could not be recorded using conventional methods. We had to develop novel high-speed video imaging methods to analyse their function in detail. Using this system we were then able to redefine how respiratory cilia function and recognised how it could very accurately detect the abnormalities of cilia in children with PCD."

This research formed the cornerstone of his successful bid to the National Commissioning Group (NGC) that now funds the UK national diagnostic service for patients with PCD. "The presentation of children with PCD is very different from other lung conditions such as cystic fibrosis. By diagnosing as early as possible we aim to prevent the very severe lung damage children with PCD develop," says Professor O'Callaghan. The increasing numbers of children diagnosed has led to the establishment of a further NCG for managing the treatment of children with PCD. Professor O'Callaghan's team have trained many centres around the world, including ones in China and Australia, in the diagnostic techniques he established.

At the same time, Professor O'Callaghan also recognises some of the more immediate challenges faced in respiratory infection research, such as the rise in antibiotic resistance and why patients in intensive care are more prone to life-threatening hospital-acquired infections. "We have discovered that high levels of stress hormones can make one of the bacteria that may cause life-threatening pneumonia on intensive care much more dangerous and resistant to antibiotics," he says.

Professor O'Callaghan is also researching alternative therapies to antibiotics. "There is great concern about the increasing resistance of bacteria to antibiotics. With some exceptional scientists we are exploring the use of viruses called bacteriophages, which attach themselves to bacteria and kill them. Unlike antibiotics – which kill all bacteria, including the ones in our bodies that help us – bacteriophages are very specific, just killing the bacteria we want to kill." This work is supported by SPARKS and Great Ormond Street Hospital Children's Charity, with the aim that at some stage in the future they may be trialled in children on intensive care and with cystic fibrosis.

He adds: "Understanding the mechanisms of respiratory disease is essential to help us target future treatment strategies. This will be achieved, as has our previous research, working with an excellent team of researchers and collaborators, locally, nationally and internationally."

Early diagnosis for inherited deafness

Making an early and accurate diagnosis can have a profound impact on the care of a child. Using the latest gene screening technologies, Professor Maria Bitner-Glindzicz has developed the UK's first dedicated genetic test for children with a deafblindess condition, Usher syndrome.

Professor Maria Bitner-Glindzicz

"My career in science and medicine started very close to home at University College London. As a medical student, I enjoyed every single specialty I studied, from psychiatry to surgery.

"After graduation I began to think about clinical genetics as a potential career, as it combined academic medicine, science, adult medicine and paediatrics. I sought career advice from Marcus Pembrey, Professor of Clinical Genetics at the ICH and Sue Malcolm, Professor of Molecular Genetics at the ICH. They encouraged me to apply for a Medical Research Council Clinical Training Fellowship to fund a PhD.

"I was able to study a very rare form of deafness, which Marcus and Sue had been researching. Together with our collaborator we identified the first gene-causing isolated deafness in humans.

"My research training in the field of deafness really opened my eyes to what remained to be done for deaf children and their families. I took up post-doctoral studies during an MRC Clinician Scientist Fellowship and haven't looked back since then.

"Of all the forms of childhood deafness that I see, Usher syndrome is about the most severe and isolating. It can totally cut people off from society. I have met adults with Usher syndrome who have not had the benefits of modern treatments such as cochlear implantation. Although they are brave and resilient, I really hope that we will be able to develop treatments and cures for Usher syndrome for the children we are diagnosing today."

"Management of childhood deafness has improved vastly over the last decade through initiatives such as Newborn Hearing Screening. However, the genetic cause of deafness is only identified in 20 per cent of children we see. For a significant number of children we are unable to provide a definitive diagnosis as we simply have not had the genetic tests," says Maria Bitner-Glindzicz, Great Ormond Street Hospital Children's Charity Professor of Clinical Molecular Genetics at the UCL Institute of Child Health and Honorary Consultant in Clinical Genetics at Great Ormond Street Hospital (GOSH).

One of the challenges in developing genetic tests for childhood deafness has been the number and size of genes involved. This has made genetic diagnosis technically difficult and also time-consuming. However, with the advent of newer, faster and cheaper genetic technologies, researchers are poised to improve and expand tests offered to patients with deafness.

Her research into Usher syndrome exemplifies the importance of making an early and accurate diagnosis. Usher syndrome is a disorder that causes the loss of two vital senses: hearing at birth and vision later on in childhood. Until recently no laboratory in the UK was offering a genetic test specifically for Usher syndrome.

Taking advantage of the latest gene-screening technologies and working with the North East Thames Regional Genetics Service at GOSH, Professor Bitner-Glindzicz has developed a single genetic test for Usher syndrome; the first test of its kind in the UK. A diagnosis which previously took years, requiring tests to be performed abroad, can now be done within three months. The test has also been approved as a national diagnostic service to benefit all children in the UK.

Professor Bitner-Glindzciz highlights the profound impact this new test has had on the children and families in her care. "Although the confirmation of Usher syndrome is a difficult diagnosis to give, we can now offer families the early support required to help manage their child's hearing and vision. At the same time we have used the test to rule out Usher syndrome in children with deafness like Khadeeja [see case study opposite], as it incorporates a number of genes causing inherited deafness alone, without other medical problems. We can also offer parents genetic counselling to inform them of the exact likelihood of passing any disease-causing genes to any children they may have in the future."

Moving forward, she wants to harness the power of this genetic information to better predict the long-term outcomes for these children. "One of the things we have long struggled with in Usher syndrome is connecting the genotype [genetic mutation] to phenotype [the physical changes caused by that fault]. The question I hear most often in my clinic is 'what does the future hold for my child?' Working with the largest national cohort of people with Usher syndrome, we are attempting to answer exactly those questions," says Professor Bitner-Glindzciz, whose research is supported by Action on Hearing Loss, Jeans for Genes, SPARKS and UCL Grand Challenges.

Success in this field can be bitter sweet as the nature of these conditions means there is still little that can be done by way of treatment. Yet Professor Bitner-Glindzciz recognises the hope research offers to children and families at GOSH. "For many children that we see, particularly in clinical genetics at GOSH, we do not have a treatment and we certainly do not have a cure. The only thing that we really have to offer many of the families that we see is research. It's this research that gives them hope for their children's future."

Khadeeja's story
by her dad Jahangir

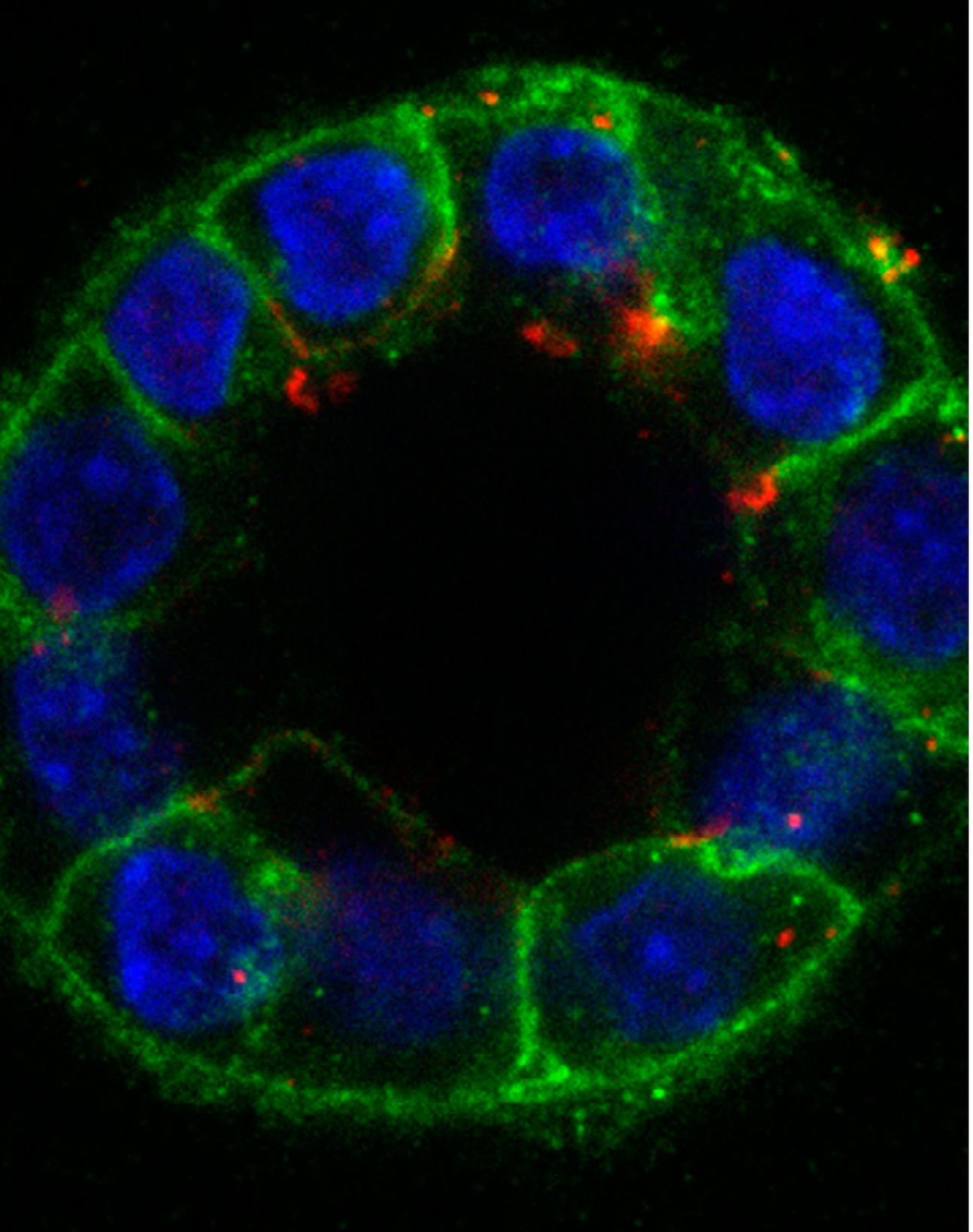
"When Khadeeja was born, everything seemed fine, but when she was six months old we noticed she would only respond to us if she could see us. She subsequently failed a hearing test and at the age of one Khadeeja was diagnosed with deafness. The news came as a tremendous shock to the family.

"At the time we were referred to Great Ormond Street Hospital as we really wanted more information about why Khadeeja was deaf and what the cause was. We were seen by Professor Maria Bitner-Glindzicz, who was able to tell us Khadeeja's deafness was hereditary but not the exact cause.

"Professor Bitner-Glindzicz encouraged us to keep in touch with her, as genetic testing was improving all the time. As the years passed by I would occasionally ask her for more information. Just over a year ago I received a phone call from her telling us her group had developed a genetic test that could be offered to Khadeeja.

"Her work into developing this test has had an enormous impact on our family. We now know the exact cause of Khadeeja's deafness. This information will help Khadeeja to make plans and decisions later on in life and there is no doubt the test will benefit others. I have huge admiration for Professor Bitner-Glindzicz's work. Throughout the years she never forgot our daughter and family despite first seeing us many years ago.

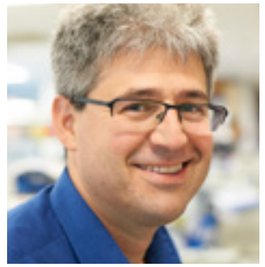
"We have had a number of setbacks over the years and having a child who is deaf has presented different challenges. Yet, Khadeeja has grown up to be like most teenage girls. When she was young I never thought she would listen to music like she does today. Our hope for her future is bright. We are encouraged by the progress she has made in school and I no longer worry as I used to when she was a baby."



Cell model of ARC syndrome using mouse kidney cells to better understand what effect mutations have on cell structure.

Pioneering treatments for metabolic disorders

Great Ormond Street Hospital (GOSH) has been at the forefront of research into metabolic disorders since the late 1800s, when Sir Archibald Garrod first described a group of such conditions. Professor Paul Gissen's research builds on this long legacy as he aims to translate his gene discovery work into new treatments for children.



Professor Paul Gissen

"As a medical student at the University of Glasgow I spent a number of summers working in the laboratory, including six weeks in the team of Nobel Laureate Professor Sydney Brenner at the University of Cambridge. I was fascinated by the genetic research they were undertaking and this ignited my interest in this field.

"I first became exposed to metabolic disorders while I was undertaking my paediatric training at Royal Manchester Children's Hospital, Sheffield Children's Hospital and Birmingham Children's Hospital. Here I saw firsthand the close link between genetics and metabolic medicine. I spent my formative research years at the University of Birmingham where I completed my PhD. I was able to identify several novel disease-causing genes responsible for inherited paediatric metabolic disorders.

"As a doctor you realise there are hundreds of different diseases that have no treatment. As a clinician scientist I am inspired by the opportunity to discover something that nobody has discovered before and to use this new knowledge to improve the lives of the children under my care. One of the things that makes GOSH and the ICH special is the 'can do' attitude. This, combined with the excellent expertise of doctors and scientists in such a concentrated area, makes it an exciting place to work."

"Literally thousands of chemical reactions are occurring in each of the cells in our bodies every minute of the day, says Professor Gissen, a Wellcome Trust Senior Clinical Fellow at the UCL Institute of Child Health (ICH) and Honorary Consultant in Paediatric Metabolic Disease at GOSH. "These metabolic pathways are, for most of us, very finely tuned and enable us to function in a normal way. Unfortunately, in children with metabolic diseases a mutation in a gene can lead to a failure of critical chemical reactions."

Although metabolic disorders are the overall theme running through Professor Gissen's research, his main focus has been on a rare childhood disorder that affects multiple organs and cells. Known as arthrogryposis renal dysfunction cholestasis (ARC) syndrome, this life-limiting condition affects different parts of the body such as the liver, kidney and bones. His team discovered mutations in two genes, VPS33B and VIPAR, as being the cause of ARC syndrome.

"There is an urgent need to develop treatments for ARC syndrome. Through discovering which genes are mutated, we now have the information needed to begin developing the first effective treatment," says Professor Gissen, whose research is supported by the Wellcome Trust, Children's Liver Disease Foundation, European Research Council and the National Institute for Health Research Biomedical Research Centre at GOSH and UCL.

One approach being adopted is to replace the faulty gene through gene therapy. While life expectancy for most children is limited to less than one year, the team has recently identified a group of patients with a milder form of the syndrome who survive at least until school age. This finding has given hope to Professor Gissen about the effectiveness of gene therapy as a potential treatment, as even a small increase in the therapeutic proteins produced through gene therapy could drastically improve the quality of life and life expectancy of these children. As the main centre in the world for research into ARC, his work has the potential to significantly impact the lives of children and families with this condition in the UK and worldwide.

At the other end of the spectrum, Professor Gissen's work aims to close the knowledge gap on how these mutated genes give rise to ARC syndrome. He explains: "Your cells are made up of thousands of different proteins, each located to a precise area of a cell. This exact distribution is essential for each protein to function correctly. VPS33B and VIPAR are involved in moving proteins to different parts of the cell, like a cargo transport system. Using a mixture of microscopy and cellular techniques, our aim is to work out precisely what effect these mutations have on the cell."

More recently, Professor Gissen has been involved in a number of clinical trials for metabolic disorders. "Over the last 20 years the field of metabolic disorders has seen the successful development of a number of new treatments," he says. "At GOSH we have one of the largest patient populations with these conditions. We are working with pharmaceutical companies on clinical trials to offer the latest therapies to children where treatment options are limited. By being involved in clinical trials it offers an insight into a different type of research. Having identified the disease-causing genes for ARC syndrome, I hope we can bring our research full circle and develop the first effective treatment."

Professor Ruth Gilbert

"After I qualified from medical school at the University of Sheffield I began my training as a junior doctor. I had a nagging concern about how whether what we were doing was right – what was the evidence? This feeling never really went away during my clinical training, so epidemiology was an obvious choice and I had always been interested in public health or community health as it was known back then. In 1987 I was presented with an amazing opportunity to carry out some epidemiological research when I was invited to work on the Avon cot death study.

"Working with paediatricians in Bristol and Bath, we set out to study the contribution of infections to cot death. As part of that study we asked parents a separate question about their baby's sleeping position. The answer to this question proved to be a major risk factor –sleeping on the front was associated with a four to five fold increase risk of cot death. It was this study that led to the highly successful national campaign in 1991 – Back to Sleep. This simple piece of advice, to place young babies on their backs when they are going to sleep, reduced the rate of cot deaths in the UK by more than two-thirds.

"I then joined the ICH as a Wellcome Trust Training Fellow in Clinical Epidemiology. The quality and expertise of researchers within ICH, the success of UCL in supporting 'big data' initiatives, and the local interactions I have with clinicians for studies like the CATCH trial, make this the best place in Europe for the type of work I'm doing. Ultimately, my research is driven by making sure we do the right things in healthcare."

Evidence-based medicine in the era of 'big data'

Evidence-based medicine is about making use of the best available scientific information to answer questions in clinical practice. It is now one of the central pillars of modern healthcare. Over the last 25 years, Professor Ruth Gilbert's research has informed decisions on issues such as which sleeping position is safest for newborns to national policy on prenatal and neonatal screening.

"The increasing availability of data from healthcare, education, social care and other sectors, known as administrative data, offers fantastic opportunities for evidence-based medicine," says Ruth Gilbert, Professor of Clinical Epidemiology at the UCL Institute of Child Health (ICH) and Honorary Consultant Epidemiologist at Great Ormond Street Hospital. "As part of the era of 'big data' we can analyse this information to measure rare and long-term health outcomes across the whole country at relatively low cost. This offers opportunities to generate new evidence and to measure the implementation of evidence into practice."

One example of the added value of administrative data is the CATCH (CAThether Infections in CHildren) trial; a trial involving 14 of the largest paediatric intensive care units in England. Led by Professor Gilbert, the study compares central venous catheters – tubes used to deliver medicines directly into veins – in children receiving intensive care. "We wanted to determine whether coating the catheter tubing with antibiotics or heparin reduces infection," says Professor Gilbert.

One innovation in the trial has been linking data from participants to electronic health records to capture long-term outcomes from the trial. Professor Gilbert explains: "Hospitals routinely collect a variety of information for health record keeping purposes. This information is a valuable and rich source for health research but it rarely contains all the different types of information required for research. One way to address this is to link different sets of information together to create more comprehensive datasets for analysis."

Professor Gilbert's team have also linked administrative data from national infection surveillance and all paediatric intensive care units across the country to help place the results from the trial into the wider context of the NHS. "If evidence from the trial is to be implemented into practice, we need to work out the cost of a change in catheter type for all patients in intensive care, not just those taking part in the trial," says Professor Gilbert.

Moving forward, Professor Gilbert has a leading role in two 'big data' initiatives, both involving networks across the UK. She leads the maternal and child health theme for The Farr Institute of Health Informatics Research, London, which focuses on administrative healthcare and primary care data. She is also Deputy Director for the Administrative Data Research Centre (ADRC) England – a consortium of six institutions in England, which aims to widen use of administrative data across government departments and other agencies.

"By harnessing the power of large datasets for research we hope to improve understanding of children's lives and to build a stronger evidence base for policy and service development in the UK," says Professor Gilbert. For example, linkage between data from the healthcare sector and the education and social care sectors would help to understand children's wider needs beyond health, such as special education or social care provision, and educational achievement. Studies that link data across sectors are starting to appear. Professor Gilbert's research within the ADRC England aims to address some of the challenges relating to confidentiality, security and data quality, so that linked administrative data can be used more widely for research.

Somers Clinical Research Facility

Positioned in the heart of Great Ormond Street Hospital (GOSH), the Somers Clinical Research Facility (CRF) provides child friendly facilities for children and young people voluntarily taking part in clinical research and expert support for studies into childhood diseases. Since its opening in 2008, over 1,700 patients have been involved in clinical studies at the Somers Clinical Research Facility.

"Clinical research is the way to improve care, diagnosis and treatments and is a core part of the work at GOSH," explains Dr William van't Hoff, Head of the CRF[1] and a Consultant Paediatric Nephrologist at GOSH. "Yet, it is very difficult to conduct research on busy clinical wards. It requires facilities with dedicated space and time, and specifically trained staff. The CRF supports patient centred clinical research and facilitates the translation of leading edge research into real benefits for patients at GOSH and beyond."

The CRF provides a critical link between the UCL Institute of Child Health's science base and the diverse patient population and clinical expertise at GOSH. The team is made up of specialist paediatric research nurses, data co-ordinators, a trial pharmacist, a play specialist and an administration team, reflecting the multidisciplinary nature of clinical research. It houses an outdoor and indoor play area, seven purpose built clinical investigation rooms, a sample preparation laboratory and a drug preparation room.

"Drug companies trialling new treatments for children need to work with experienced children's hospitals and facilities. Dedicated facilities combined with experienced staff trained in paediatric research allow us to support clinical research to the high standard required," says Lorraine Hodsdon, Head of Nursing for Clinical Research.

Earlier this year, the CRF was involved in a nationwide genomics pilot study. It enrolled patients with rare inherited diseases to have their entire genome sequenced. Working collaboratively with University College London Hospital and Moorfields Eye Hospital, it acted as the central co-ordination site for the three institutes. This successful partnership resulted in over 60 per cent of the national total being recruited through the three sites, 50 per cent more than expected.

Recognising the nature of clinical research, the CRF aims to provide support to children and families through the lifetime of a trial. "Children can sometimes be here for the whole day. We offer a range of activities, from arts and crafts to games to make their stay, and their family's stay, as enjoyable as possible," says Eleanor Rolle-Marshall, CRF Operations Manager.

For many patients who come to the hospital, participating in research as part of their clinical treatment is their only option. The team ensures an excellent standard of care by guaranteeing the availability of dedicated beds for those participating in clinical trials. It also works closely with the rest of the hospital to co-ordinate patient visits in order to provide a seamless transition between their appointment and participation in research.

While supporting clinical research is a core focus of the facility, engaging with young patients is also a high priority. The Young Persons Advisory Group (YPAG), supported by the National Institute for Health Research Clinical Research Network, meets regularly at the CRF to share their views and opinions on research. This group comprises children and young people who have taken part in clinical research. In addition, the CRF has supported ground-breaking events with the YPAG, such as Generation R, which was held at the Science Museum and raised national awareness about the importance of children's research and encouraged participation.

"Children take part in clinical trials by giving up their free time. Sometimes this may not benefit them within their lifetime but could be beneficial to future children and that is an incredibly generous thing to do. The most inspiring thing about working at the CRF is seeing children helping other children," says Dr van't Hoff.

[1] The CRF is supported by JN and Dame Phyllis Somers and the National Institute for Health Research Biomedical Centre for GOSH and UCL

Joe's story

"My first memory of GOSH was travelling up in the taxi from Sittingbourne where we live. I was only six at the time, but remember my mum crying when I was diagnosed with idiopathic juvenile arthritis. I thought arthritis was just something that old people get. At the time I couldn't walk, play football or go to school. The bit that upset me the most was missing out on seeing my friends and doing the things that other boys my age were doing.

"I was put on steroids and methotrexate, but there were some bad side effects. For example, I used to get out of breath easily playing football. It was during a trip to the hospital that I was made aware of a new clinical trial, a drug called canakinumab, which was still at the testing stage. It was a bit daunting at first but the alternative involved having an injection every day, so I was eager to try this new option!

"I started the new trial of canakinumab at the Somers CRF at the hospital. I visit once a month for my injection as well as having other tests done. Even though we're there for most of the day, the time passes quite quickly; they have play specialists to entertain us and TVs to stop us getting bored. Everyone is so nice to me there. Once, the staff surprised me with a birthday cake and singing. I was so embarrassed I didn't even look up from my drawing, but it was a lovely thing for them to do.

"The difference the drug has made to my life is amazing. Beforehand I could barely walk, now I hardly notice I've got arthritis. I now play for Doddington Village who won the league last year, which was great. The doctors and nurses at GOSH have made such a difference. Without doctors and scientists working hard to develop these new drugs and treatments, my life would be very different to how it is now."

“What fascinates me most about translational research is that I can make a difference to the lives of the children that I care for in the hospital.”

Professor Khalid Hussain

Grants and donations

Great Ormond Street Hospital and the UCL institute for Child Health continue to receive grants and donations towards research from the following individuals and organisations:

A

The AADC Research Trust
Abbott Laboratories Ltd
AbbVie Inc
The Academy of Medical Sciences
Actelion Pharmaceuticals Ltd
Action Medical Research
Action on Hearing Loss
AFM Téléthon
Agilent Technologies UK Ltd
Alexion Pharmaceuticals Inc
Ali's Dream
The Alternative Hair Charitable Foundation
AMAG Pharmaceuticals Inc
Amgen Inc
Anatomical Society
ApoPharma Inc
Arle Capital Partners Limited
Arthritis and Rheumatism Council for Research
Arthritis Research UK
Association for International Cancer Research
Association of Cardiothoracic Anaesthetists
Association of Paediatric Anaesthetists of Great Britain and Ireland
Astellas Pharma Europe Ltd
Astellas Pharma Inc
Asthma UK
AstraZeneca
Augustea Group
AusAID
Autism Research Centre
Autistica

B

Barnet Council
Barnet Primary Care Trust
Barnsley Hospital
Barts and the London Charity
Baxter Innovations GmbH
Baxter International Inc
Bayer Healthcare Pharmaceuticals
Chris Beazley, Tom Clementi and Hugh Cocke
Behçet's Syndrome Society
BGC Partners
Big Lottery Fund
Biogen Idec Hemophilia
BioMarin Pharmaceutical Inc
Biotechnology and Biological Sciences Research Council
Biovomed
Birmingham City University
bluebird bio Inc
Sofia and Gennadiy Bogolyubov
Graeme Boy and Richard Lester
The Brain Tumour Charity
Breast Cancer Campaign
Brighton and Sussex Medical School
Bristol-Myers Squibb Company
British Academy
British Council
The British Dietetic Association
British Heart Foundation
British Journal of Anaesthesia
British Kidney Patient Association
British Neuropathological Society
British Oculoplastic Surgery Society
British Skin Foundation
British Society for Paediatric Endocrinology and Diabetes
British Society of Audiology
British Society of Paediatric Gastroenterology, Hepatology and Nutrition
The Bubble Foundation UK
Bupa Cromwell Hospital
Bupa Foundation
The Burdett Trust for Nursing
Butterfield Trust
The Butterfly AVM Charity

C

The Sophie Cameron Trust
Canadian Institutes of Health Research
The Cancer Fund
Cancer Research UK
Candlelighters
Canterbury Christ Church University
Caring Matters Now
Castang Foundation
The Isla Cecil Brighter Future Fund
Cellectis
Central & East London Local Clinical Research Network
Cerebra
Charité - Universitätsmedizin Berlin
CHDI Foundation
Child Growth Foundation
Child Health Research Appeal Trust
Children with Cancer UK
Children's Arthritis Trust
Children's Cancer and Leukaemia Group
Children's Hyperinsulinism Fund
Children's Liver Disease Foundation
The Children's Research Fund
Chinese Academy of Medical Sciences
Chiron
The Chronic Granulomatous Disorder Society
Cincinnati Children's Hospital Medical Center
City Bridge Trust (grant held by The DIPEx Charity)
CLEFT
Clinical Endocrinology Trust
Clinique
CORE
CR Marine&Aviation
CryoLife Inc
Cure CMD
The Lauren Currie Twilight Foundation
Cystic Fibrosis Trust

D

Roald Dahl Foundation
Danone Baby Nutrition (Nutricia Ltd)
Dr Genevieve and Mr Peter Davies
DEBRA (Dystrophic Epidermolysis Bullosa Research Association)
Department for International Development
Department of Health
Development Studies Association
Diabetes Research and Wellness Foundation
Diabetes UK
Duchenne Parent Project
Lord and Lady Dundas
The Houghton Dunn Charitable Trust
The Dunhill Medical Trust

E

Economic & Social Research Council
Eisai Ltd
Eli Lilly and Company
Elimination of Leukaemia Fund
Emergency Nutrition Network
Engineering and Physical Sciences Research Council
Epilepsy Action Research
Epilepsy Research UK
European Commission
European Medicines Agency
European Research Council
European Society for Immunodeficiencies
European Society for Paediatric Endocrinology
European Society for Paediatric Gastroenterology, Hepatology and Nutrition
European Society of Hypertension
The Evelyn Trust

F

Face Value Appeal
Fight for Sight
The Nancie Finnie Charitable Trust
Merrill, Amelia and Tatiana Fitzgibbons
Mr & Mrs Fitzpatrick
Fondation Genevoise de bienfaisance Valeria Rossi di Montelera
Fondation Leducq
Fondazione Citta della Speranza
Fondazione Eugenio Litta
Fondazione Livio Patrizi
Food Standards Agency
Gwyneth Forrester Trust
Friends of Landau-Kleffner Syndrome
Fundação para a Ciência e a Tecnologia (Portuguese Foundation for Science and Technology)

G

Bill & Melinda Gates Foundation
Généthon
Genetic Alliance UK
Genome Canada
Genzyme
Gilead Sciences Inc
GlaxoSmithKline
Global Alliance for Chronic Diseases
GlycoVaxyn AG
GN ReSound
Legacy of Bettine Goldberg
Raisa Gorbachev Foundation
The Gosling Foundation
The Shauna Gosling Trust
Great Ormond Street Hospital Children's Charity
The Guide Dogs for the Blind Association
Guy's and St Thomas' Charity

H

Paul Hamlyn Foundation
Hammersmith Hospital
The Sue Harris Trust
Cathal Hayes Research Foundation
The Healing Foundation
The Health Foundation
Heart Research UK
The Hestia Foundation
Higher Education Funding Council for England
The Histiocytosis Research Trust
Bo Hjelt Spina Bifida Foundation
The Olivia Hodson Cancer Fund
Horst-Bickel Award
House of Fraser

I

ICAP plc
Ichthyosis Support Group
ImmunoBiology Ltd
Imperial College Healthcare Charity
Imperial College Trust
Innovative Medicines Initiative
Inspiration Biopharmaceuticals
Institute of Education, University of London
International Fund for research on Congenital Adrenal Hyperplasia
International Serious Adverse Event Consortium
International Society for Heart and Lung Transplantation

Continued

The Ipsen Fund

Ipsen Ltd

J

Janssen Biotech Inc

Stanley Thomas Johnson Foundation

K

Kidney Research UK

Kids Kidney Research

King's College Hospital NHS Foundation Trust

King's College London

Conor Kitching and family

L

Dorothy & Spiro Latsis Benevolent Trust

Leukaemia & Lymphoma Research

The friends and family of Mark Levinson

The Anna Lewis Brighter Future Fund

The Lily Foundation

Natalie and Ian Livingstone

Mark and Janine Long

The Love Hearts Appeal

Legacy of Oliver Lovell

The Lullaby Trust

Lupus UK

M

Macula Vision Research Foundation

The Mahboubian Family Trust

Marks and Spencer plc

Juan Reig Mascarell

Scott and Suling Mead

Mason Medical Research Foundation

Medical Research Council

The family and friends of Geeta Mehta

Meningitis Research Foundation

Merck & Co., Inc

Merck Serono Ltd

Merck Sharp & Dohme

Micro and Anophthalmic Children's Society

Milena Carvajal – Prokartagener Foundation

Miltenyi Biotec GmbH

The Laurence Misener Charitable Trust

Mitsubishi Tanabe Pharma Europe Ltd

Morgan Stanley

J P Moulton Charitable Foundation

MRC Institute of Hearing Research

MRC Medical Research Foundation

Multiple Sclerosis Society

Muscular Dystrophy Association

Muscular Dystrophy Campaign

Myasthenia Gravis Association

Myositis UK

N

National Eye Research Centre

National Health and Medical Research Council

National Institute for Health Research

National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care for South Yorkshire

National Institute for Public Health and the Environment

National Institute of Academic Anaesthesia

National Institute of Allergy and Infectious Diseases

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

National Institutes of Health

National Patient Safety Agency

NBIA Disorders Association

Netherlands Organisation for Scientific Research

The Neuroblastoma Society

Newcastle University

Newlife Foundation for Disabled Children

Nierstichting (Dutch Kidney Foundation)

NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London

NIHR Maudsley Biomedical Research Centre and Dementia Unit

NIHR Moorfields Biomedical Research Centre

Norton-Freeman Charitable Trust

Novartis

Novo Nordisk

Nuffield Foundation

O

Octapharma AG

Legacy of John Oldham

Orphan Europe

Orthopaedic Research UK

OSCAR Campaign

Otsuka Pharmaceutical Co., Ltd

Oxford Biomedical Research Centre

OxThera AB

P

Paediatric European Network for Treatment of AIDS

Paediatric Rheumatology Discretionary Fund

Legacy of Muriel Payne

Phil and Yvonne Parry

PATH

Pathological Society of Great Britain and Ireland

Pediatric Brain Tumour Foundation

PerkinElmer Inc

Pfizer Ltd

Phillips Avent

Primary immunodeficiency Association

Legacy of Pamela Pitt

Promethera Biosciences

Prosensa Therapeutics BV

Protalix Biotherapeutics

PTC Therapeutics

Public Health England

Public Health Laboratory Service

Public Health Research Consortium

R

Alexandra Raphael and family

Raptor Pharmaceutical Corp

Raynaud's and Scleroderma Association

The Research Council of Norway

Research Into Childhood Cancer

The Reuben Foundation

Roche

Rosetrees Trust

Royal Academy of Engineering

The Royal College of Ophthalmologists

Royal College of Paediatrics and Child Health

The Royal College of Psychiatrists

The Royal College of Radiologists

The Royal College of Surgeons of England

Royal Free London NHS Foundation Trust

Royal Holloway, University of London

Royal National Institute of Blind People

Royal National Orthopaedic Hospital NHS Trust

The Royal Society

Legacy of Gillian Rumsby

Legacy of Esther Ryan

S

Sandoz International GmbH

Sanofi Aventis

Sanofi Pasteur

Saudi Arabian Cultural Mission

Save the Children UK

Science without Frontiers

Scleroderma Society

Sense

Sheffield Hospitals Charity

Shire plc

Siemens Medical Solutions

Sir Halley Stewart Trust

The SMA Trust (Spinal Muscular Atrophy)

The Lee Smith Foundation

Sparkle Children's Charity

Sparks

The Special Trustees of Moorfields Eye Hospital

Family and friends of Wilber Squires

St George's, University of London

Stillbirth and Neonatal Death Society

The Stoneygate Trust

Sucampo AG

Summit Corporation plc

Swiss Anorexia Nervosa Foundation

Swiss National Science Foundation

Synageva BioPharma

T

Takeda Global Research & Development Centre Ltd

Technology Strategy Board

The Baily Thomas Charitable Fund

The Sir Jules Thorn Charitable Trust

Towergate Charitable Foundation

Trophos

Pierre Elliott Trudeau Foundation

The Tuberous Sclerosis Association

U

UBS Optimus Foundation

UCL BioResource

UCL Hospitals Biomedical Research Centre

UCL Institute for Global Health

UCL School of Life and Medical Sciences

UK Children's Neurological Research Campaign

UK Dermatology Clinical Trials Network

UK National Screening Committee

UK Stem Cell Foundation

The Ulverscroft Foundation

UNICEF

Uniserve (Holdings) Ltd

United Arab Emirates University

United Nations High Commissioner for Refugees

University College London

University College London Business

University Hospital Southampton NHS Foundation Trust

University of Bristol

University of East London

University of Florence

University of Liverpool, MRC Centre for Drug Safety Science

The University of Manchester

University of Milan

University of Oxford

University of Tartu

V

The 3VB Charitable Trust

Vasculitis Foundation

Vasculitis UK

Victorian Neurotrauma Initiative

Vitaflo International Ltd

W

Legacy of Winifred Ward

The Waterloo Foundation

Wellbeing of Women

WellChild

Wellcome Trust

The Welton Foundation

Westminster Medical School

Whittington Hospital NHS Trust

Wiskott-Aldrich Foundation

The Lord Leonard and Lady Estelle Wolfson Foundation

World Health Organization

Y

Yorkhill Children's Charity

Young Epilepsy

Z

ZonMw

UCL Institute of Child Health's academic programmes

Developmental biology and cancer

Head of Programme
Professor Andrew Copp

Deputy Head
Dr Jonathan Ham

The aim of the programme is to study the key processes necessary for normal development and tissue homeostasis that are altered in childhood diseases. The sections are:

Cancer – to understand the molecular basis of childhood cancers and to develop more effective therapies for children with cancer, by combining basic research in cell and molecular biology with translational cancer research and clinical trials.

Developmental biology of birth defects – to use techniques of genetics and developmental biology to improve our understanding of, and develop novel treatments and preventive strategies for, clinically important birth defects.

Stem cells and regenerative medicine – to promote and expand translational stem cell research and harness the great potential of regenerative medicine for childhood disease.

Developmental neuroscience

Head of Programme
Professor Francesco Muntoni

Deputy Head
Professor Helen Cross

The primary focus of the developmental neuroscience programme is to minimise the impact of disorders affecting the developing central and peripheral nervous system. The sections are:

Clinical neuroscience – to minimise the clinical impact of neurological disease by improving diagnosis, studying disease mechanisms and evaluating novel therapeutic strategies.

Molecular neurosciences – the molecular neurosciences programme focuses on understanding the genetic and molecular causes of neuromuscular diseases, with the ultimate aim of translating this knowledge into treatment of patients.

Cognitive neuroscience and neuropsychiatry – our main goal is to identify the brain networks underlying cognitive, motor, emotional and mental health status in children and adolescents with neurodevelopmental disorders or brain injury/disease.

Neuroimaging and neural networks – research involves the development and application of advanced neuroimaging techniques for improved understanding of disease in childhood, including improvements in diagnosis and prediction of outcome.

Genetics and genomic medicine

Head of Programme
Professor Phil Beales

Deputy Head
Professor Maria Bitner-Glindzicz

The aim of the programme is to use genetics, imaging and biological indicators to understand predisposition to disease and what constitutes health during childhood and throughout the life course. The sections include:

Centre for translational omics – to create, integrate and maintain data and informatics platforms to support genomic, proteomic and other 'omic research and its healthcare applications.

Genetics and epigenetics in health and disease – this section focuses on disease gene discovery, the architecture of the genome, inheritance patterns and the regulation of gene expression.

Experimental and personalised medicine – this section aims to blend together, for the first time, experimental medicine with precision medicine approaches to deliver better, more targeted therapies to patients to ensure optimal responses.

Infection, Immunity, Inflammation and Physiological Medicine

Head of Programme
Professor Adrian Thrasher

Deputy Head
Professor Lucy Wedderburn

The aim is to deliver world class interdisciplinary research for children with infectious, immunological and inflammatory disease, children with life threatening respiratory disease, children in pain and critically ill children on intensive care.

Immunobiology – our mission is to undertake research into the cellular, molecular, genetic and clinical aspects of paediatric immunology and thereby establish an international reputation in the general field of immunobiology.

Infection, inflammation and rheumatology – the aim is to encourage world-class research into understanding the mechanisms and treatment of inflammatory, immunological and infectious diseases.

Molecular and cellular immunology – the section researches the molecular basis of primary immunodeficiency disorders, and other related haematopoietic disorders and is developing improved forms of treatment.

Respiratory, critical care and anaesthesia – the multi-disciplinary research teams investigate the causes, consequences and treatments of cardio-respiratory diseases in childhood.

Population, Policy and Practice

Head of Programme
Professor Catherine Law

Deputy Head
Professor Russell Viner

Our aim is to promote the health of children and young people and the adults they will become.

Clinical epidemiology, nutrition and biostatistics – providing evidence through developing methods for analysing and linking data to improve healthcare policies, services and clinical practice for children and young people, improving surveillance and screening to better understand the longer-term effects of some conditions and infections in order to improve child health policies, and conducting research on the impact of nutrition on the health and development of infants and children to develop both clinical and public health practice and professional training.

Child and adolescent mental health, palliative care and paediatrics – bringing a robust generalist perspective to research, teaching and training in child and adolescent health for the wider UCL community, serving children and young people with life-limiting conditions and life-threatening illnesses in the UK and across the world. This is done through palliative care research to inform practice and training, exploring social cognition, and aetiology, epidemiology and prevention in child and adolescent mental health, particularly social communication disorders and eating disorders.

Life course epidemiology and biostatistics – examining how biological, behavioural and psychosocial processes operate across an individual's life course or across generations. This will be used to influence the development of disease risk and explore what influences how we grow and develop from the womb into adulthood. Using innovative statistical methods, and influencing policy and practice to reduce health inequalities, the aim is to improve the health and wellbeing of the population overall. Our life course research uses cohort studies such as the 1958 Birth Cohort, the Millennium Cohort Study and Life Study.

Administration

The Planning and Executive Committee of the UCL Institute of Child Health

From 1 March 2014

Director
Professor Rosalind Smyth

Deputy Director (Education)
Professor Christine Kinnon

Deputy Director (Research)
Professor Gudrun Moore

Director (NHS engagement)
Professor David Goldblatt

Head of Developmental Biology and Cancer Programme
Professor Andrew Copp

Head of Developmental Neurosciences Programme
Professor Francesco Muntoni

Head of Infection, Immunity, Inflammation and Physiological Medicine Programme
Professor Adrian Thrasher

Head of Population, Policy and Practice Programme
Professor Catherine Law

Head of Genetics and Genomic Medicine Programme
Professor Philip Beales

Rare Diseases (cross-cutting theme)
Professor Bobby Gaspar

Interim Chief Executive of Great Ormond Street Hospital for Children NHS Foundation Trust
Mr Julian Nettel

Institute Manager
Ms Wendy Knowles

The Board of Great Ormond Street Hospital for Children NHS Foundation Trust

Chairman of the Trust Board and Members' Council
Baroness Tessa Blackstone

TRUST BOARD EXECUTIVE DIRECTORS

Chief Executive
Mr Jan Filochowski (until 31 December 2013)

Interim Chief Executive
Mr Julian Nettel (from 1 January 2014)

Co-Medical Director
Dr Barbara Buckley (until 31 December 2013)
Dr Catherine Cale (from 1 January 2014)
Professor Martin Elliott

Interim Chief Operating Officer
Mr Robert Burns (until 30 June 2013)

Chief Operating Officer
Ms Rachel Williams (from 1 July 2013)

Director of Human Resources and Organisational Development
Mr Ali Mohammed

Chief Nurse and Director of Education
Mrs Elizabeth Morgan

Chief Finance Officer
Mrs Claire Newton

NON-EXECUTIVE DIRECTORS

Ms Yvonne Brown
Mr David Lomas
Ms Mary MacLeod
Mr John Ripley
Professor Rosalind Smyth
Mr Charles Tilley

Special Trustees for Great Ormond Street Hospital Children's Charity

Chairman of Special Trustees
Mr Alan Hodson

Trustees
Ms Gabrielle Abbott
Ms Susan Burns
Dr Diana Dunstan OBE
Mr Hugo Llewelyn
Sir Mark Potter (until 31 March 2014)
Mr Christopher Spratling

Associate Trustees
Mr Simon Brewer
Mr Simon Stormer
Mr Michael Weston
Dr Edward Wozniak

Right: Five-year-old Lita on Peter Pan Ward

UCL Institute of Child Health

30 Guilford Street
London WC1N 1EH
020 7242 9789
www.ucl.ac.uk/ich

Great Ormond Street Hospital for Children NHS Foundation Trust

Great Ormond Street
London WC1N 3JH
020 7405 9200
www.gosh.nhs.uk

Design Manager
Great Ormond Street Hospital
Fourth floor
40 Bernard Street
London WC1N 1LE
E design.work@gosh.org

Thank you to everyone who was interviewed for, or gave permission for their picture to be used in this review, as well as the many members of the UCL Institute of Child Health and Great Ormond Street Hospital staff who helped during its production.

For an online version of this review please visit www.gosh.nhs.uk/research-and-innovation