UCL INSTITUTE OF CHILD HEALTH

Great Ormond Street Hospital for Children NHS Trust

Research Review 2010

The child first and always

Zoe, age 17, suffers from hydrocephalus, also known as 'water on the brain'. Today she is in hospital to have some fluid drained and will hopefully only be in for a few days. She loves her cheeky monkey pyjama bottoms and doing her hair and make-up.

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Cover: Rosie is 10 months old and has been in hospital for nine of those months due to a gastro-intestinal problem. Her family are very used to hospital life now, and Rosie's older sister loves the playroom.

Hope is eight and suffers from a lot of allergies. She is here for an outpatient appointment on Kingfisher Ward so that her doctors can try to find out why she is always so tired.

Director's report

The UCL Institute of Child Health (ICH) is Europe's largest academic centre for research and education in children's health and disease. A highlight of 2010 was the establishment of several new research centres which significantly extend the Institute's paediatric research profile.

The Louis Dundas Centre for Children's Palliative Care became the first unit in the UK devoted to research and education in children's terminal illness. Myra Bluebond-Langner was appointed the first True Colours Chair in Palliative Care for Children and Young People, and she set about establishing a team to deliver high quality, collaborative studies to inform practice and policy in this important, but previously neglected area of paediatrics. In addition to the Dundas family and True Colours Trust, the new centre benefits from generous donations from the Charles Wolfson Charitable Trust, Marie Curie Cancer Care, and the Raisa Gorbachev Foundation.

The ICH's Nuffield Professor of Child Health, Professor Terence Stephenson, was awarded £4.6 million over five years by the Department of Health to establish a Policy Research Unit (PRU) for the Health of Children, Young People and Families. Senior colleagues who will lead work streams within the unit include Professor Ruth Gilbert, Professor Catherine Law, Dr Miranda Wolpert, Professor Helen Roberts and Professor Russell Viner. The PRU's aim is to provide evidence for policy and practice, so as to promote the health and wellbeing of children, young people and families.

Professor Faraneh Vargha-Khadem received pump-priming support from the Provost of UCL to develop a Centre for Developmental Cognitive Neuroscience (CDCN). The CDCN brings together cognitive neuroscience, neurology, neuro-imaging and neurophysiology as applied to children's brain studies, and also links with collaborators in mathematics, engineering and computer science. UCL is one of the UK's largest universities, with a myriad of departments, institutes and divisions, and it is crucial that we are able to collaborate with those who share interests and have complementary skills. The CDCN is an important step in this direction.

Members of the Institute continued to attract significant grant funding from external bodies, with new grants totalling more than £25 million during the year. Those leading successful bids in excess of £1 million were: Professor Andrew Taylor, Dr Silvia Schievano and Dr Tain-Yen Hsia for *Multi-scale modelling of single ventricle hearts for clinical decision support* (Fondation Leducq); Professor Russell Viner for *Improving the assessment and management of obesity in UK children and adolescents* (National Institute of Health Research [NIHR]); and Dr David Osrin for *Community resource centres to improve the health of women and children in Mumbai slums: a cluster randomized controlled trial of a complex intervention* (Wellcome Trust).

More than 300 new research papers were published during the year. Highlights include the identification of genetic factors regulating brain tumour types (Dr Tom Jacques and Professor Sebastian Brandner in *The EMBO Journal*), new methods for isolating photoreceptors allowing transplant to the diseased retina (Dr Jorn Lakowski and Professor Jane Sowden in *Human Molecular Genetics*), identification of a lymphocyte class with key function in autoimmune arthritis (Dr Kiran Nistala and Professor Lucy Wedderburn in *Proceedings of the National Academy of Sciences*) and identification of long-lasting lung disorders in children born extremely premature (Dr Sooky Lum and Professor Janet Stocks in the *American Journal of Respiratory and Critical Care Medicine*).

During the year, several staff received honours. Professor Anthony Costello was elected Fellow of the Academy of Medical Sciences for his achievements in research and education for global health; Professor Catherine Law was appointed to the NIHR College of Senior Investigators for achievements in child health policy

Zarrar (above) is 10 months old and he has come into hospital for an overnight stay. His body does not produce enough salt, and so his doctor wants to make sure that his medication is correct.

Patients from across the UK and beyond, stand to benefit from the UCL Institute of Child Health's work, revealing the nature of childhood disease, often via samples of tissue grown and investigated in the laboratory.

Director's report
continued

research; and Dr Margaret Mayston was named Australian Woman of the Year in the UK for her work on the physiotherapy of disabled children. We were delighted to hear of the knighthood for Hugh Stevenson in the Queen's Birthday Honours List. Hugh and his wife Catherine are long-standing benefactors of the Institute, and the Hugh and Catherine Stevenson Chair of Paediatric Oncology was conferred on Professor Kathy Pritchard-Jones during 2010.

A sad loss this year was the death of Professor Otto Wolff, former Dean of the ICH. A talented paediatrician and academic in metabolic medicine, Otto was a great supporter of the ICH right up to the months before his death at the age of 90. The Institute's main lecture series is named in his honour, and we greatly miss his attendance and participation (always with a penetrating question) at his eponymous lectures.

A number of Institute members gained academic promotion at UCL in 2010. Persis Amrolia became Professor of Transplantation Immunology for research in developing clinical protocols to harness the power of lymphocytes to fight both leukaemia progression and viral infection after bone marrow transplant and immunosuppression. These protocols are now widely used to treat seriously ill children for whom few alternative options exist.

Jugnoo Rahi became Professor of Ophthalmic Epidemiology for research which takes a life-course, epidemiological and genetic approach to visual impairment. As the first Director of the Ulverscroft Vision Research Group, Jugnoo has enabled interdisciplinary research in eye disease and initiated a new training programme to promote academic ophthalmology.

Lucy Wedderburn became Professor of Paediatric Rheumatology for research into the development of autoimmunity, with particular reference to juvenile arthritis and dermatomyositis. Lucy is leading work to identify biomarkers for predicting the course of autoimmune disease and for monitoring response to treatment.

Jonathan Wells became Professor of Anthropology and Paediatric Nutrition for research, combining detailed measurement of body composition and energetics, with the application of anthropological and evolutionary concepts to nutrition. His book, *Evolutionary Biology of Human Body Fatness,* is a seminal contribution in the modern epidemic of obesity.

Staff promoted to Reader were Dr John Anderson for research into immunotherapy as a treatment for malignancy, Dr Chris Clark for research into development of new methods for magnetic resonance imaging of the brain, Dr David Osrin for research involving randomised trials to improve newborn care in resource poor countries, and Dr Arturo Sala for research into the role of oncogenes in development and treatment of childhood tumours.

Professor Andrew Copp
Director
UCL Institute of Child Health

Eighteen-month-old Lily has been in hospital for four months and is a patient on one of our oncology wards. She has three more weeks of chemotherapy to go and then her mum is hoping that they can go home.

Chief Executive's report

Great Ormond Street Hospital (GOSH) is the UK's leading paediatric research institution. We put research at the heart of what we do because we want to find new and better ways to help the children we care for. And that means working closely with our partners.

This collaborative approach is central to our thinking, and in 2010, GOSH strengthened relationships with many other medical and academic institutions, both in the UK and worldwide. We have continued to work closely with our academic partner, the UCL Institute of Child Health (ICH), as well as colleagues within UCLPartners and those in the National Institute for Health Research framework, which includes the Medicines for Children Research Network and Central and East London Comprehensive Local Research Network.

Our Specialist Biomedical Research Centre (BRC) in Paediatrics, now in its fifth year, has made great progress in translating basic medical research into clinical benefits for children. One of last year's successes has been the BRC-supported ICH and GOSH collaboration, GOSgene, an initiative for the sequencing of DNA to pinpoint genetic mutations and aid in diagnosis, treatment and counselling for congenital disorders.

2010 was the first year of our five-year research strategy, and building these relationships is an important part of its implementation. To fully realise the strategy, we have also been investing in new technology, improving our infrastructure and, last but not least, investing in excellent researchers and their work. One staff member we have been delighted to welcome to our team has been Professor Kathy Pritchard-Jones, who joined our cancer unit in April 2010. An area of medical research that is especially relevant to GOSH is the application of treatments designed for adults to children; although they may be completely safe for a mature patient, careful investigation needs to be made into dose levels and side effects when they are given to developing children. This is particularly important in paediatric oncology, where chemotherapy and radiotherapy can have severe side effects, but too little intervention can run the risk of the cancer recurring. Professor Pritchard-Jones specialises in individualised treatments that can reduce these risks, and she discusses her pioneering work on page 15 of this Research Review.

Early in 2010, a team led by Professor Martin Elliott carried out a pioneering tracheal transplant on a young patient, Ciaran Finn-Lynch. This complex procedure was carried out in collaboration with staff from Careggi University Hospital, Florence, the University of Leipzig, the Italian National Transplant Centre and the Royal Free Hospital, and involved expertise in tracheal surgery, cardiac surgery and bone marrow stem cell transplant. In the year since then, the team has paid close attention to Ciaran's successful recovery, ensuring that the stem cells and blood supply have linked to his trachea properly. This observation is of particular importance following an innovative procedure such as this, but it also improves our understanding of the recuperation process for the benefit of future patients.

These are just a few examples from the approximately 800 active research projects being carried out and employed in Great Ormond Street Hospital and the ICH.

Dr Jane Collins
Chief Executive
Great Ormond Street Hospital
for Children NHS Trust

Some highlights of our research activity:

40 **research studies** were conducted in the Somers Clinical Research Facility, with more than

220 patients attending 932 research appointments.

More than 2,250 patients were included in studies adopted into the National Clinical Research Network Portfolio.

Over 223 **clinical trials** were set up;

33 **of which are commercially funded.**

551 patients were recruited to take part in research studies at **Great Ormond Street Hospital** through the Medicines for Children Research Network.

70 **research projects have been internally peer-reviewed through the Clinical Research Adoptions Committee;**

49 were approved.

By the end of 2010, we had

13 **active National Institute of Health Research-funded research projects and**

16 **active EU-funded research projects.**

Research and Development report

Together, Great Ormond Street Hospital (GOSH) and the UCL Institute of Child Health (ICH) form one of the world's leading children's health research centres.

As part of our mission to benefit children in the UK and worldwide, a five-year GOSH research strategy was launched in 2010, and concentrates our work in five key areas:

- Developing novel and improved diagnostics.
- Introducing innovative and leading-edge treatments and therapies through translational research.
- Performing high-quality clinical trials of medicines and therapeutics.
- Understanding and preventing the development and progression of childhood illnesses.
- Evaluating the impact and progression of disease and our interventions.

Our strategy is to build upon, and invest in, existing areas of strength, while also developing new areas of expertise where there is a clinical need. We will attract and support leading clinical academics and apply the latest technologies to our unique and diverse patient population in an effort to improve our understanding and treatment of childhood diseases. Over the next five years, we will realise our research strategy by investing in a number of areas including buildings, equipment and platform technologies, infrastructure for clinical trials, salary support for senior research leaders and investment in the training of future academic leaders in child health.

This strategy is essential for a cohesive approach to research across the Trust: to embed a research culture and thus integrate research with hospital operations, support clinical researchers, and align our aims with funders. By focusing on these aims, and making the most of our strengths and diverse patient population, we can continue to conduct research at the highest level to improve child health.

2010 also saw the establishment of a new Division of Research and Innovation within the Trust, bringing together the joint GOSH/ICH Research and Development Office, the Specialist Biomedical Research Centre in Paediatrics, the London and South-East England Medicines for Children Research Network (hosted within GOSH), and the Somers Clinical Research Facility. The Division of Research and Innovation has been organised to provide a better service for researchers and consists of a number of specialist teams: industrial liaison and clinical trial co-ordinators; a research governance team; costings and contracts staff; and the introduction of Clinical Research Facilitators. This arrangement will strengthen key areas within the Trust and facilitate a smoother research management process.

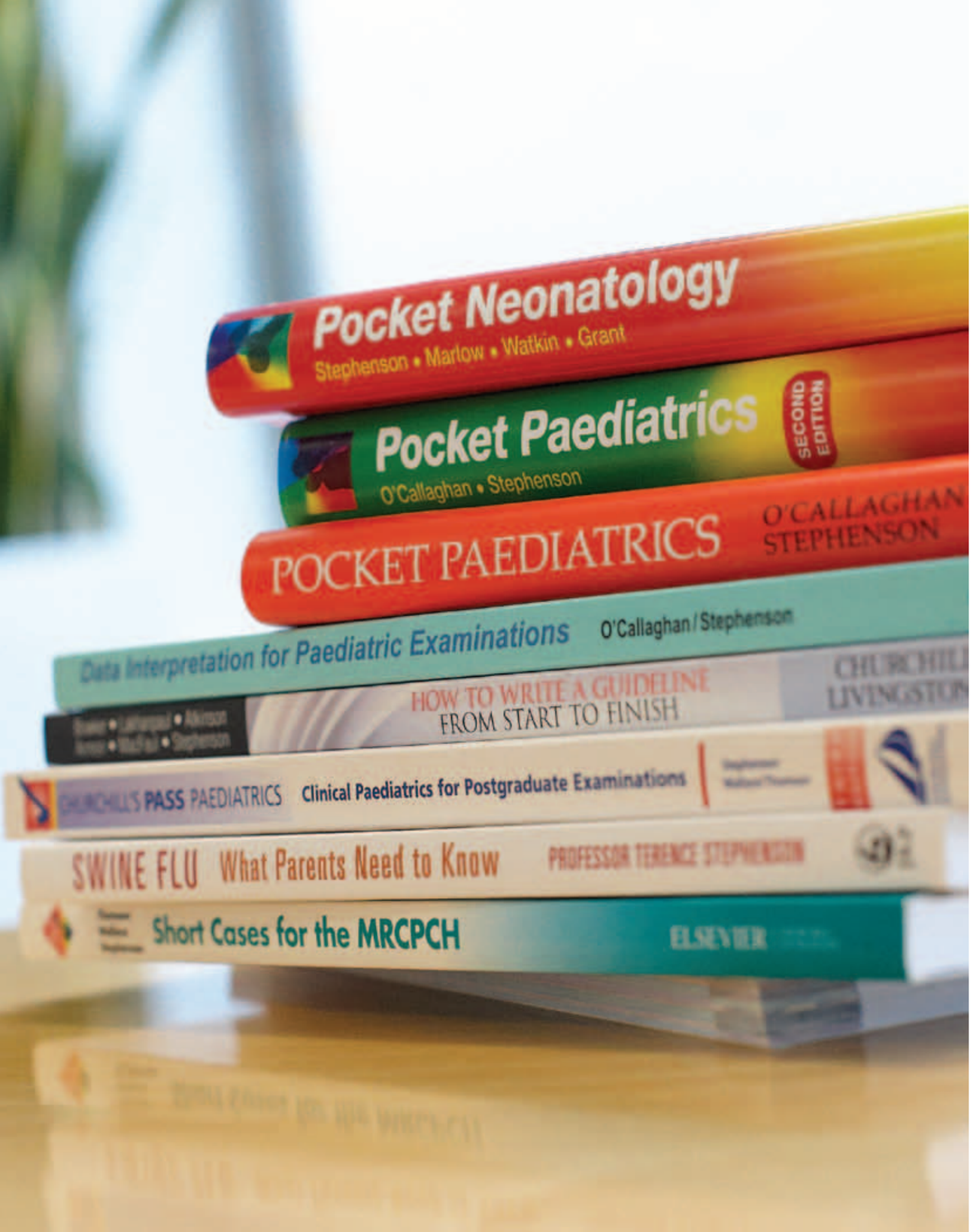
GOSH is committed to improving the health of children through research, and this extends beyond children attending the hospital. Through UCLPartners, one of the UK's first five Academic Health Science Partnerships, GOSH leads a child health programme aiming to benefit children at large and, through this and other strategic partnerships, we remain committed to improving the health of children worldwide.

Professor David Goldblatt
Director of Clinical Research and Development

Dr Lorna Gibson
Head of Research and Innovation

Research may be expensive, time-consuming and complicated, but we have to be the ones to push the field ahead. We owe it to our patients.

Ann, a PhD student, working in the UCL Institute of Child Health's rheumatology laboratories.



Research on children, for children

The last decade has seen great improvements in policy measures to promote paediatric research. Despite this, the majority of drugs used to treat children have never been licensed for paediatric use. Professor Terence Stephenson has led efforts to ensure paediatric medicine is founded on robust, evidence-based practice, and that governments listen to such evidence when forming health policy.

Professor Terence Stephenson
"I am the Nuffield Professor of Child Health at the UCL Institute of Child Health (ICH) and Great Ormond Street Hospital, and lead one of our eight research themes – General and Adolescent Paediatrics. I decided to be a paediatrician when I was a medical student and always wanted a clinical academic career as I love the combination of teaching students, researching diseases and treating patients.

"Although my initial research training was in laboratory science, I gradually became more interested in the challenges of research on children, for children. This has been a neglected field, partly because of the ethical problems sometimes involved. I have also become more involved in politics, advocating for children's needs at a national and international level as President of the Royal College of Paediatrics and Child Health.

"These two strands of my career have come together in my new post at the ICH as, with colleagues from inside and outside UCL, we have been awarded £4.6 million by the Department of Health to establish a new Policy Research Unit for the Health of Children, Young People and Families."

Helping to establish national paediatric health guidelines via a robust evidence base, Professor Stephenson has established a new Policy Research Unit for the Health of Children, Young People and Families.

"It's staggering to think how many answers there are to the question: 'What's the best way to treat this child?' – even when you're looking at a disease thought to have a fairly well-known cure," says Professor Stephenson, Nuffield Professor of Child Health at the UCL Institute of Child Health. "It just isn't the case that you simply take what's best for adults, or what has been tested in laboratory models, and extrapolate this to children. So many of the breakthroughs we've seen in paediatric healthcare couldn't have been done without specifically involving children."

This principle has been reflected throughout Professor Stephenson's career. His early studies revealed a huge diversity between different practitioners in both the types of antibiotics used to treat pneumonia, and their methods of delivery. More recently, this work has proven oral antibiotics to be as effective in treating pneumonia as those injected intravenously, with the former saving around £500 in treatment costs per patient.

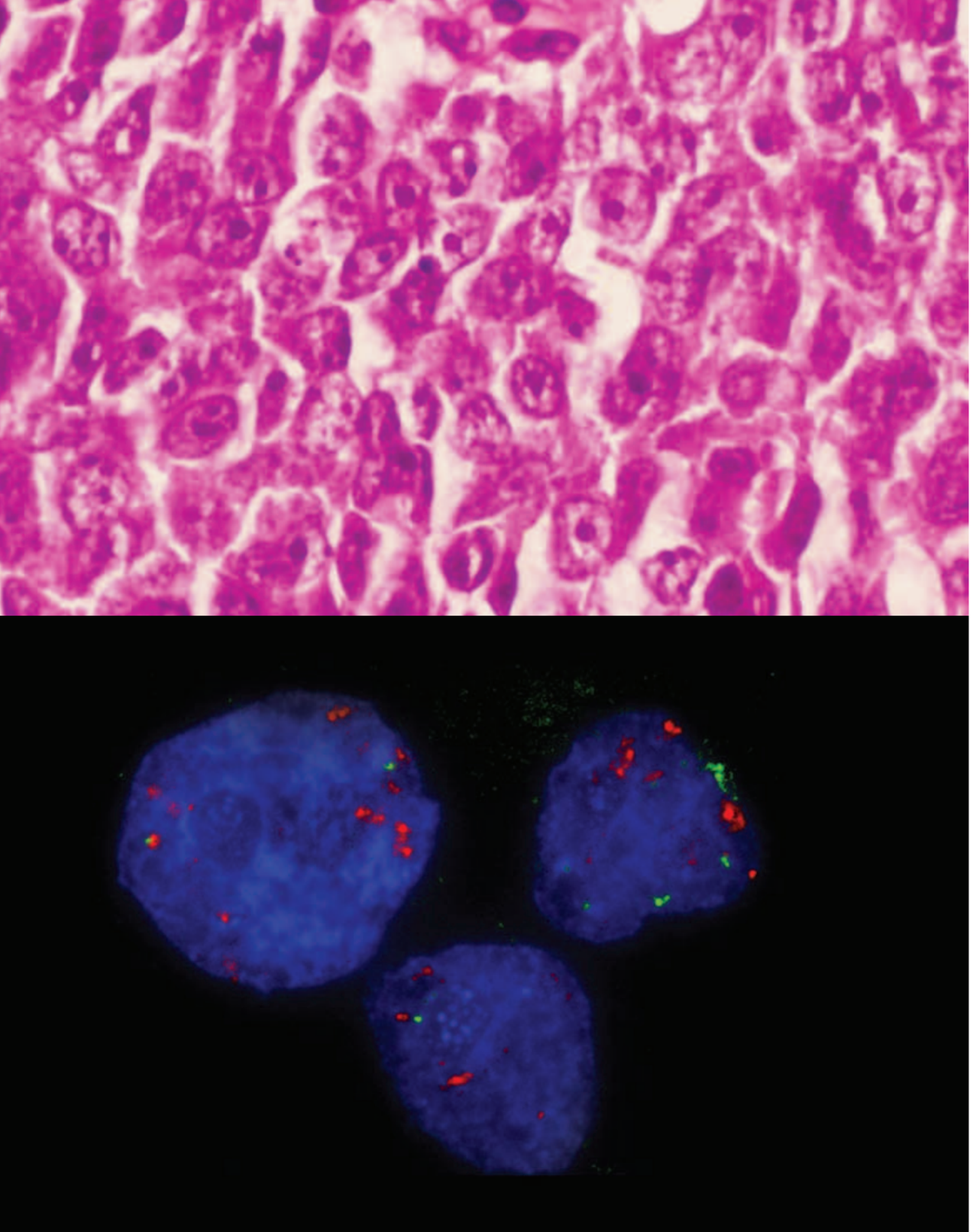
"The common criticism levied against involving children in this kind of research is that parents won't consent to taking part in the studies," says Professor Stephenson. "Our experience has been quite the opposite. Of the 400 families we approached for the pneumonia study, fewer than 40 declined. The results speak for themselves – not only was oral antibiotic treatment more cost-effective, but more importantly, it worked just as well as intravenous antibiotics. This means we can spare children the painful and frightening prospect of needle injections, and allow them to be treated at home – an enormous improvement for them and their families."

The establishment of supportive bodies, such as the Medicines for Children Research Network, has provided a much-improved framework for child-focused research studies in the UK. However, effectively bridging the gap between best practice, informative research and evidence-based policy remains a crucial issue. This challenge forms the focus of a major new collaboration being led by Professor Stephenson.

With the support of colleagues at UCL, the National Children's Bureau, the Anna Freud Centre and the Social Care Institute for Excellence, Professor Stephenson has set up a new Policy Research Unit for the Health of Children, Young People and Families, funded by the Department of Health.

"We were tasked by the government to address the key areas where modern healthcare is letting down today's children," says Professor Stephenson. "We'll be focusing on four main themes: health inequalities and health promotion, mental health in children under five years old, access to health services, and teenage issues such as smoking and obesity. In each of these areas, it's crucial we're able to deliver evidence that can genuinely change practice and improve children's health."

Professor Stephenson is aware that there won't be any quick fixes. Nevertheless, he is hopeful such evidence will encourage legislation in areas where obvious health gains are to be made. "This country has a free NHS, free schooling, and free contraception. Given this, it's remarkable we're facing an obesity epidemic and have the highest teenage pregnancy rates in Europe. We desperately need to engage the public and get them involved. I hope our research provides a much-needed nudge towards healthy preferences among legislators, the public, and a national media often preoccupied with scare stories and contrary health advice."



In search of targeted cancer therapies

Great Ormond Street Hospital has a long legacy of developing new and life-saving treatments for children with cancer. Though survival rates continue to improve, a pressing challenge remains to ensure children are not over-treated. Professor Kathy Pritchard-Jones' work is researching increasingly personalised treatments, to give children the best chance of a long-term cure without undue side effects.

Professor Kathy Pritchard-Jones

"When I gained my PhD almost 20 years ago, we were just beginning to scratch the surface of understanding the genetic changes which take place inside a cancer cell's DNA, and how these could predict a patient's response to treatment. We are now in the era of 'molecular medicine', which means that new anti-cancer therapies can be much more specific and with fewer side effects.

"However, we still need to do clinical research if children with cancer are to reap the full benefits of these new medicines. We have to ensure we offer new drugs, especially to children with the highest risk tumours, in a safe and controlled way.

"Having virtually every type of therapy required under one roof makes working here very special for staff, and far less stressful for patients and their families. One of the pleasures of my job is to be able to reassure most parents that we have treatments that can cure their child."

A section of tissue taken from a patient with Wilms' tumour (above) is shown to harbour cancer-causing mutations in the DNA within its cells (fluorescent red and green, below) when subjected to genetic testing.

Over the past 20 years, survival rates for children with cancer have climbed steadily. This is as much the result of clinical teams working closer together to consider a child's outcome, as it is of any breakthrough leading to new therapies. Improved scanning and microscopic imaging techniques have allowed clinicians to predict more accurately how tumours will respond to surgery or chemotherapy – crucial to determining the best treatment. However, by themselves, these techniques cannot provide confidence for clinicians to recommend that children should receive less chemotherapy, should their treatment be progressing well.

"Given the toxicity of many chemotherapy drugs, we have to get better at identifying who is likely to need prolonged or intensive treatment," says Kathy Pritchard-Jones, recently appointed as the Hugh and Catherine Stevenson Professor of Paediatric Oncology at the UCL Institute of Child Health (ICH). "Despite our best efforts, many children with cancer are consigned to months of potentially unnecessary drug therapies as a fail-safe in case their cancer comes back or does not respond. In an age of molecular medicine, I know we can do better."

Driving this work is a need to combat the often significant side effects experienced by children on chemotherapy drugs. Professor Pritchard-Jones' principal area of research is in Wilms' tumour, a relatively common cancer of the kidneys. Currently, treatments for the 50 per cent of these children who have a medium to high-risk Wilms' tumour, receive a drug called doxorubicin, known to carry a risk of causing damage to the heart later in life.

"The hospital has pioneered unique research into the long-term health of children with cancer," says Professor Pritchard-Jones. "Colleagues such as Dr Gill Levitt and her team have contributed hugely to our understanding of the late effects of chemotherapy, so we know the damage these drugs can cause. My challenge is to identify ways of determining which children might not need these drugs, and give them a more gentle treatment, without compromising their care."

Working with the advanced tissue-testing facilities at the hospital and the ICH, Professor Pritchard-Jones has recently completed a study to understand the biology underlying Wilms' tumour patients' responses to chemotherapy. The research indicates a further 50 per cent of children can beat their cancer without requiring doxorubicin. This translates to over 25 children a year who can avoid the risks of heart damage caused by this drug. In addition, the research has identified further biological pathways which could be targeted by new drugs to help the few children whose cancer simply does not respond to any current treatments.

Professor Pritchard-Jones is understandably keen to progress further with this research. "Techniques based around molecular medicine mean we're reaching a stage where our therapies can be targeted to patients' unique biological requirements," she says. "It means we can take a 'less-is-more' approach, sparing children risky and damaging treatment regimes, but be confident that we're going to stop the cancer from returning. This really is the future of cancer research, and I'm excited to be working collaboratively with specialists in the UK and around Europe to make a difference in this vital area."

Refusing to be beaten

Cilia – named after the Greek word for 'eyelash', but over a thousand times smaller – are tiny, rhythmically beating hairs found throughout the body. They move biological materials around and clean out the body's airways to prevent infection. There are also non-beating cilia, critical for cells to sense the world around them. Dr Hannah Mitchison's research aims to help the children whose cilia do not function properly, and for whom cures remain an elusive goal.

Dr Hannah Mitchison
"The fast-moving field of human disease genetics was an exciting place to be during my first postdoctoral research period as part of an international team effort that identified the gene responsible for Batten disease [CLN3]. This kick-started a new understanding of this family of at least 10 fatal neurodegenerative disorders. Gene identification has led to novel hypotheses about the causes of these diseases and allowed us to progress with genetic tests and clinical trials of new therapies.

"For the last decade, I have been increasingly involved in discovering the molecular basis of cilia-based disorders. Recently, I helped to found the Ciliopathy Alliance, which provides a collective voice for families, scientists and clinicians, to support and raise awareness of these diseases.

"I hope our molecular genetics approach, hugely boosted by our recent funding for whole exome analysis to identify further disease genes, will crack open what causes these ciliopathy disorders, just as it has for Batten disease and primary ciliary dyskinesia."

Understanding the function of cilia hairs – barely a thousandth of a millimetre (0.0002mm) wide and found either in solitude or in their hundreds on the surface of almost every cell in the human body – would be a challenge for any researcher. However, when these tiny hairs can beat in unison upwards of 20 times a second, come in a number of different forms and are built from over 600 proteins in a way which remains mysterious, the challenge becomes remarkable.

"Cilia are complex molecular nano-machines," says Dr Mitchison. "Until recently, we've not had many ways of modelling their function, no genetic tests available to diagnose children whose cilia do not work, and few treatments to offer those affected by these diseases."

The consequences of cilia functioning incorrectly – when the molecular hairs do not beat in sequence as they should, or do not send their normal communication signals – are far from trivial. The resultant diseases, known as ciliopathies, are responsible for a range of inherited birth defects, affecting embryonic growth and disrupting the development of organs ranging from the lungs and kidney to the eyes, the nervous system and the brain.

One form of ciliopathy, called primary ciliary dyskinesia (PCD), has been the focus of Dr Mitchison's collaborative work with GOSgene, the genetic identification programme run within UCLPartners. "PCD affects the cilia lining the respiratory tract," explains Dr Mitchison. "Because the tiny hair-like structures aren't beating properly, mucus and foreign particles aren't cleared from the lungs as they should be. This causes chronic recurrent infection and often permanent damage to these children's lungs. The problem to date is there hasn't been a consistent way of diagnosing PCD in order to begin early treatment."

Engaging with patients through support groups such as the Ciliopathy Alliance, and working with UCL Institute of Child Health colleagues such as Dr Steve Hart, Dr Mitchison has now contributed to international efforts that have identified 13 genetic mutations responsible for causing PCD. Several of these mutations are associated with the proteins which make up the cilia's hair-like projections – with any loss of function rendering inert the cilia's ability to beat. However, some of the mutations are linked to the cell's molecular transport system (the 'factory production line' by which proteins are assembled), revealing a hitherto unknown function for these genes.

"Our discoveries are beginning to shed light on these genuinely mysterious diseases," says Dr Mitchison. "We hope that further work will allow us to develop gene therapy – where healthy genes are inserted into the malfunctioning cells of the lungs – to provide a potential cure for children with PCD. We're only beginning to make the first steps towards this kind of therapy, but I'm hopeful that the more we learn about ciliopathies, the better chance we have of helping these children."

Joshua and Samuel's story
by their parents, Sarah and Michael
"When both our sons, Joshua now 13, and Samuel, 12, were born, they appeared to be healthy normal babies. This rapidly changed, and within 24 hours, both were admitted to the special care baby unit at our local hospital with respiratory distress and a chest infection. Both children improved spontaneously and were discharged for home care. Only two years later and after many further tests and investigations were the children diagnosed with primary ciliary dyskinesia, an autosomal recessive genetic condition. The tiny hairs or cilia don't work effectively, mainly in the lungs, ears and sinuses. The job of the cilia is to remove secretions – as they don't work, secretions sit and get infected.

"At this point, both boys were referred to a specialist paediatrician with an interest in respiratory medicine. He immediately commenced the correct treatment of targeted antibiotics, nebulisers and daily chest physiotherapy. Since their diagnosis, both Joshua and Samuel have met all their developmental milestones. This has not been without its ups and downs; both boys have a vascuport for intravenous antibiotics. They continue on multiple medications, antibiotics, nebuliser antihistamines, and reflux medications. A large part of their daily routine is made up of physiotherapy: 15–20 minutes twice a day when well, which increases when they are unwell.

"Sport is a very big thing in our house, and both boys enjoy football, swimming and cricket. They have many appointments at hospital and, despite this rare disease and the amount of treatment they have, both boys are bright, capable children, able to live as normal a life as possible."

Let the right sun in

For a health supplement readily available to purchase and 'good for your bones', we are some way from fully understanding the requirements and effects of vitamin D. Though labelled 'the sunshine vitamin' due to the way it is synthesised in our skin, its modes of action remain a relative mystery. Dr Elina Hyppönen's research is seeking to bring vitamin D out of the shadows and into the sphere of public health debates.

Dr Elina Hyppönen
"I became interested in epidemiology and public health, as to me it made more sense to focus on prevention where possible, than to strive to alter things once the damage had already been done.

"It was the findings from my PhD thesis which directed my subsequent research interests: I observed a strong dose-response association between infant vitamin D supplementation and the risk of type one diabetes in children. This was exciting as, until then, vitamin D had been considered as something that is mainly needed for bone health, and here we were showing evidence for possibly important influences on an autoimmune disease.

"The UCL Institute of Child Health has provided a very stimulating research environment, with further support provided by the Department of Health Public Health Career Scientist Award which I received in 2005. Currently, I lead a large international collaboration of studies with the aim of disentangling the causal from coincidental in the proposed health effects for vitamin D."

Further research into vitamin D may ultimately ensure at-risk groups, such as pregnant women, receive adequate dietary supplementation should this be required in countries where sunlight exposure is significantly reduced in winter months.

Vitamin D is not merely required for healthy bone growth – it maintains the correct levels of dissolved minerals, such as calcium and phosphorus, in our body, regulates certain types of cell growth, and affects our immune function. A lack of vitamin D is well-known to cause diseases such as rickets, where bones become soft and deformed. However, low vitamin D intakes are increasingly being associated with other diseases, with national vitamin D supplementation a controversial issue for legislation.

"Though certain oily fish contain dietary vitamin D, it is mainly produced in the skin following exposure to ultra-violet [UVB] rays from the sun," says Dr Elina Hyppönen, who has studied vitamin D-related disease since completing her PhD studies in Finland over 10 years ago. "There is strong variation in vitamin D status over the year, with a large proportion of individuals likely to have insufficient concentrations during winter and early spring."

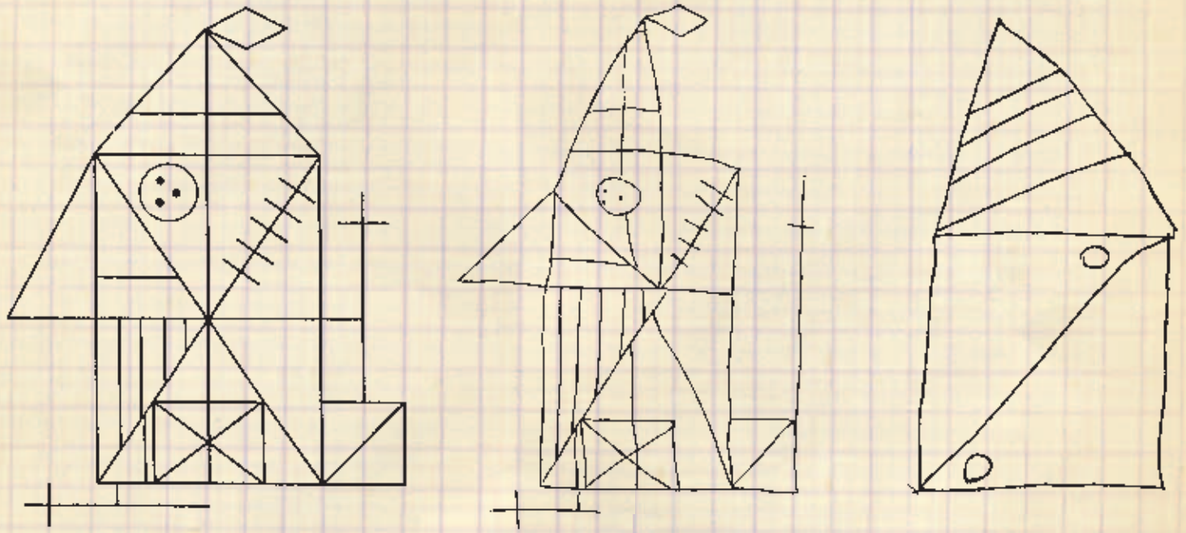
Dr Hyppönen currently works with large international collaborative studies, including the Sunlight Consortium. "We performed a genome-wide analysis of individuals' DNA to see whether there were any genes which pre-disposed to low vitamin D status," says Dr Hyppönen. "We found four genes associated with the risk of having lower vitamin D status, regardless of individuals' dietary intake, or exposure to sunlight."

Her initial research suggested an association between vitamin D supplementation and a reduced risk of type one diabetes. Since then, she and her colleagues have focused on cohort studies – where large population groups are studied from birth – to determine vitamin D's role in broader health issues such as obesity and cardiovascular health.

"We are now using these genes as proxy markers for low vitamin D levels, with an interest in looking to understand the wider effects of vitamin D deficiency. For example, we have recently carried out a study including over 45,000 individuals, to see whether the low levels of vitamin D seen in obesity were potentially a cause of the obesity, or resulted from it."

It transpired that low vitamin D levels were not linked to obesity, but that obesity leads to an increased risk of vitamin D deficiency and all the adverse health consequences related to it. This issue, of which environmental factors are causal or coincidental of childhood disease, remains an important challenge. "We have still not established the levels of vitamin D required to ensure healthy growth or best possible health," says Dr Hyppönen. "My work with the large collaborations brings together a critical mass of researchers and patients to ensure the questions we ask will provide practical answers to health issues relevant for adults and children alike."

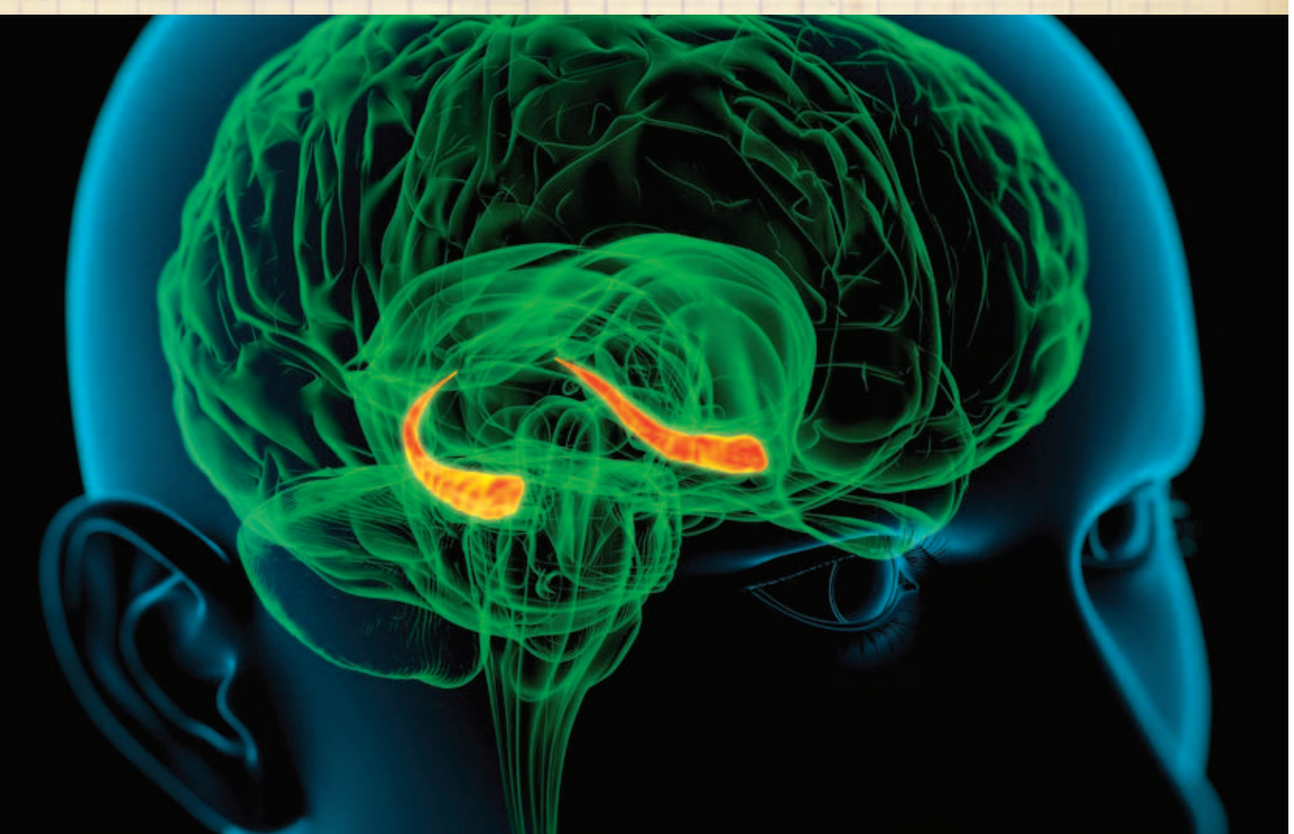
With 90 per cent of the general UK population considered to have sub-optimal levels of vitamin D for health in wintertime, and 15 per cent of these people at severe risk of developing vitamin D-related disease, it is crucial that interventions are targeted appropriately. "I suppose my aim is to keep children out of Great Ormond Street Hospital," says Dr Hyppönen. "I hope our work is able to formally associate vitamin D with some of the chronic diseases we suspect are linked to its deficiency, and thereby reduce the associated disease burden. However, diseases related to extreme vitamin D deficiency, such as rickets, should in this day and age be entirely preventable."



Original shape

Patient's copy

Recall after 40 minutes



Children with developmental amnesia can struggle to form memories, as shown by their ability to recall shapes over time (above). Research has shown that this is due to damage to the hippocampus (red and yellow, below), with affected children requiring specialist support.

Relearning how to learn

"What does it mean to be me?" is a question usually asked by philosophers rather than scientists. But if your brain is so damaged that it can't create long-lasting memories and a personal autobiography, making sense of your own identity becomes an enormous challenge. Professor Faraneh Vargha-Khadem is developing ways to support children with these severe and chronic forms of memory disorder, known as developmental amnesia.

Professor Faraneh Vargha-Khadem

"I arrived at the UCL Institute of Child Health in 1983 from the Montreal Children's Hospital McGill University, where I had been researching how the mind compensates for damage to just one side of the brain, and how this impacts on children's speech and language.

"Fascinated by the hallmark research of Margaret Kennard on the adaptability of the motor system, I hoped to explore how focal brain lesions affected children's higher cognitive function. A project grant from the Medical Research Council enabled me to establish a research group and, together with my colleagues, we started our first set of studies in the emerging field of developmental cognitive neuroscience.

"As a clinical neuroscientist, I have been fortunate to have access to unique patient groups, as well as the opportunity to establish interdisciplinary collaborations with imaging scientists and neurologists, enabling me to conduct translational research in a highly stimulating environment. I hope that our research will ultimately relieve patients of the burden brain injury can have on their lives."

Since the development of magnetic resonance imaging (MRI) techniques able to map the structure and activity of the brain in detail, there has been a revolution in the breadth and variety of questions we are able to answer about the human mind. Numerous aspects of language learning and memory have been modelled, with insights into what sets us apart from higher apes slowly, but steadily, evolving.

Nevertheless, the overwhelming majority of the mind's workings remain a mystery. Professor Vargha-Khadem, Head of the UCL Institute of Child Health's (ICH) Developmental Cognitive Neuroscience Unit, has dedicated her career to unlocking its secrets. Despite being a seemingly impossible challenge, there are pressing reasons for her to find ways in which her knowledge can benefit children who have suffered brain damage at an early age.

"Fifteen years ago, our team began to see children with no overt signs of brain damage, but an inability to bring to mind the memory of episodes and events of their lives," says Professor Vargha-Khadem. "Though these children can understand language and complete analytical tasks, they have major problems mapping their life experiences onto a timeline of past events. They struggle terribly to form a meaningful personal narrative. For example, they typically lose their belongings, get lost in unfamiliar surroundings, forget to deliver messages, and fail to remember their homework."

With Professors Mortimer Mishkin from the National Institute of Health in the US, and David Gadian from the ICH, Professor Vargha-Khadem traced the brain damage in these children to a seahorse-shaped structure within the temporal lobe, called the hippocampus. She noted that some children with this special form of brain damage had experienced a period of oxygen deprivation early in life, sometimes as neonates, and had gone on to develop severe memory problems later in childhood and adolescence.

"We're a long way from being able to repair the brain damage in these children," says Professor Vargha-Khadem. "However, our studies showed some children were more susceptible to the effects of oxygen deprivation than others. If we can find out why, then we might be able to prevent this damage from occurring in the first place."

The team now plans to follow up babies with heart defects or respiratory problems who undergo surgery, to better understand how their treatment affects brain development and subsequent learning. In parallel, Professor Vargha-Khadem and her team of collaborators are determined to develop educational tools and interventions to help children with hippocampal injury succeed in school and gain a degree of independence as adults.

"It's the children who bring the work of Great Ormond Street Hospital and the ICH together – they inspire us to gain a better understanding of their difficulties so we can devise methods of overcoming them, and help improve their quality of life", says Professor Vargha-Khadem. "It's so important for children to construct a rich tapestry of their life events and to learn from their past experiences. We hope that our research will eventually provide these children who have memory problems with the necessary tools to form an autobiography, and to capture their memories to share with others."

Ms Julie Lanigan
"An earlier career in catering inspired a love of food, leading me to study nutrition and dietetics. As I strove to provide a healthy diet for my own growing children, I was inspired to look deeper into the intriguing functions of the ingredients making up our meals.

"The culmination of my clinical and research interests is the development of Trim Tots, an intervention that aims to help families find the path to a healthier lifestyle."

Professor Atul Singhal
"I have always been fascinated by science, and nutrition in particular. From my early work at the Medical Research Council (MRC) Sickle Cell Unit in Kingston, Jamaica, it became clear that many of the clinical problems facing children were complicated by poor nutrition.

"Over the last 10 years at the MRC Childhood Nutrition Centre, we have developed and tested several interventions in children to reduce the long-term risk of obesity. The major challenge now is to see if these are just as effective in the real world and can be 'scaled-up' to prevent obesity in the wider community."

Healthy lifestyles

Reaching out to children and families with a programme to promote healthy living within their communities, Professor Atul Singhal and Ms Julie Lanigan are championing partnerships between nutritional researchers and local communities. Their Trim Tots programme stands to improve child health dramatically and reduce the long-term burden of childhood obesity.

Childhood obesity remains one of the UK's most urgent health issues. Despite efforts to raise awareness and implement clear policy, a quarter of children are overweight by the time they reach school age. The current burden on the NHS of obesity-related illnesses, including heart disease and diabetes, is estimated at £4.2 billion per year – forecast to double by 2050 if no action is taken.

Professor Atul Singhal and Ms Julie Lanigan have spent the last 10 years developing strategies to improve childhood nutrition and prevent obesity. "Our recent findings show a child's early nutritional intake and lifestyle are crucial in determining whether they go on to develop obesity-related illnesses," they report. "Between 70 and 90 per cent of overweight children have the early signs of obesity established by the time they go to school. Over one-fifth of these children will go on to become obese adults. It's so important for us to intervene early if we're going to improve the long-term health of these children."

Determined to ensure their work delivers real and sustainable improvements in child health, the team has developed unique models to promote healthy living. These include the MEND (Mind, Exercise, Nutrition... Do it!) healthy lifestyle programme, a community intervention to promote good health developed by Paul Sacher at the UCL Institute of Child Health.

Since its inception, the programme has been rolled out in over 400 centres worldwide, and benefited over 15,000 families. "MEND has shown us that with the right balance of nutritional advice, psychological support, education and community engagement, school children can undergo a clinically-measurable reduction in weight," says Professor Singhal.

With funding from the Medical Research Council, Sure Start and Great Ormond Street Hospital Children's Charity, Professor Singhal and his team are now rolling out a similar programme – Trim Tots – to target pre-school children.

"We've demonstrated the urgent need for younger children to receive this kind of support," says Ms Lanigan. "Our challenge now is to deliver the Trim Tots programme so local communities may benefit, as well as gather reliable scientific data to better understand some of the risk factors associated with obesity. It can be tricky when you consider some toddlers don't want to be weighed or prodded with callipers to find out their body fat content! But we've come up with fun ways for them and their families to get involved, as well as learning more about where food comes from and how to eat healthily."

Following a successful pilot, Trim Tots will soon be rolling out to centres across the UK. "We're lucky to have staff and families willing to work with us to improve children's long-term health and nutrition," says Professor Singhal. "Great Ormond Street Hospital's reputation has been crucial to gaining their trust and support. I genuinely don't think we could have got this initiative off to such a successful start anywhere else."

Lennon's story
by his mum, Clare
"I was willing to be involved in the Trim Tots project straight away. I was grateful for the opportunity to go somewhere once a week with my boys, Lennon, two, and new-born Ethan.

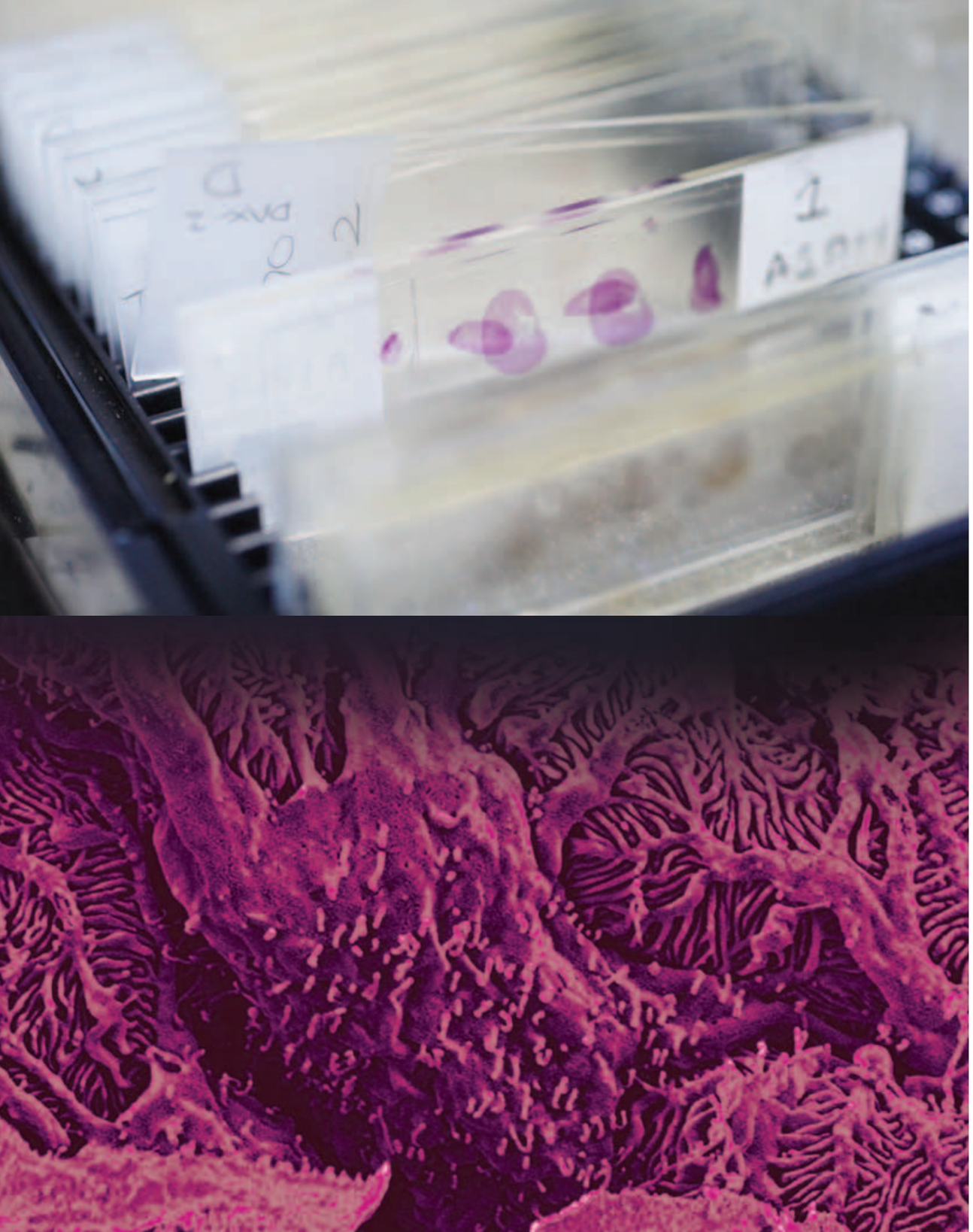
"There was free entertainment, fun games for the kids, and we learnt lots of new things. I particularly enjoyed the cookery lessons as I had always tried to make sure both boys had a balanced, healthy diet.

"The information from Trim Tots opened up a world of more home cooking. We were taught to make Lennon curious and interested in food, and to let him feel and touch the food. No sooner did Lennon help me prepare the dinner, than the following week he was eating broccoli like it was chocolate! I encouraged Lennon to spread his own sandwich filling and pour the pasta into the pan etc. I hadn't even thought of it before the Trim Tots team suggested it!

"I also looked at how we spend our time. Now if I turn the TV off and encourage the boys to sit at the table to do an activity, Lennon will say 'it's good we turn the TV off Mummy – we shouldn't watch too much!'

"The simple fact is, the lessons we learned, and the knowledge I have passed on to friends and family, has made a big difference to our lives. We remember our time at Trim Tots with fondness. We never felt pressured or ashamed due to a lack of knowledge or being provided with information we didn't previously have. We felt honoured.

"The Trim Tots programme and support for children and families at this vital age needs to be widespread. It should be available for all parents as they are the building blocks to nurturing a generation of health-conscious, educated young people."



Kidney cures from cancer drugs to citrus fruit

More than 40,000 people in the UK require long-term dialysis or transplantation due to failure of their kidneys, and around 1,000 of these are children. Great Ormond Street Hospital is the UK's largest centre for children with kidney problems. Dr David Long is a scientist, pioneering research to discover the mechanisms of kidney disease and develop new treatments.

Dr David Long

"My enthusiasm for kidney research started during my PhD, when I investigated normal kidney development and how this goes wrong in kidney disease. Professor Adrian Woolf and I discovered that proteins called angiopoietins play a key role in the initiation and progression of kidney disease, by controlling growth of kidney blood vessels. These studies led to the award of a Senior Fellowship from Kidney Research UK to build upon this finding with my own research team.

"The challenge for the future is to convert our basic laboratory findings into new treatments. The close ties between Great Ormond Street Hospital and the Nephro-Urology Unit at the UCL Institute of Child Health provide an ideal environment for this, and I am now studying angiopoietins in children with chronic kidney disease, in collaboration with Drs Rukshana Shroff and Lesley Rees. This is particularly important because there is currently no therapy that reliably corrects severe kidney problems; hence many patients need either life-long dialysis or transplantation. We hope to develop drugs to modify angiopoietins as treatments for both children and adults with renal disease."

From examining thin sections of kidney tissue (above) right through to probing the finest microscopic structures of the kidney's delicate filtering units (below), the research team are revealing new insights into preventing and treating childhood kidney disease.

Dr Long is committed to finding ways to help the one in 10 of the hospital's patients who require specialist input from its renal team. As Kidney Research UK Senior Research Fellow at the UCL Institute of Child Health's (ICH) Nephro-Urology Unit, he works closely with Dr Paul Winyard (Reader in Nephrology and Head of Unit) and consultants who treat children with kidney disease on a daily basis.

"With the provision of expert medical and supportive care, a majority of children treated by the renal team will grow healthily," explains Dr Long. "However, those who develop progressive kidney disease frequently go on to need dialysis – which seriously impacts on their quality of life. If their kidneys fail, then the children have to stay on dialysis until a donor kidney is found. For the majority, this means multiple and lengthy dialysis sessions in hospital each week, restrictions in their diet, and a significant impact on their schooling and social development."

Dr Long's research focuses on understanding the mechanisms causing childhood kidney disease, with the overarching aim of identifying ways to detect disease at an early stage, and prevent long-term kidney damage. Specifically, he and his team have been investigating the microscopic structures that filter the blood within the kidney, called the glomeruli. Their focus is to see which biological factors damage glomeruli and initiate kidney disease, so that they can work out how such factors might be blocked.

The team demonstrated that a group of proteins responsible for controlling blood vessel growth – angiopoietins – play a crucial part in the progression of kidney damage. "We saw that a disruption in the balance of these proteins was damaging the very fine structure of the blood vessels in the glomerulus," explains Dr Long. "What's exciting is that there are a number of drugs already available to control blood vessel growth, thanks to research in parallel fields such as cancer and heart disease. Applying this research to the kidney means we can begin to target new treatments for patients whose kidney disease is caused by damage to the glomerulus."

The multi-disciplinary nature of the clinical and research teams at the hospital and ICH means that Dr Long is able to explore several complementary research avenues at the same time. He and his team are working on further ways to prevent kidney damage by looking at the protective effects of naturally-occurring substances such as pectin, a type of sugar found in citrus and other fruits.

"We have exciting early data that pectin seems to reduce inflammation in the kidneys, lessening the effects of kidney damage," says Dr Long, "though we've got some work to do to fully understand the best doses and biological mechanisms involved. The result is another promising step towards therapies which might help children who currently have no cure for their disease."

The ICH team is also contributing to further clinical studies at the hospital, looking to identify the long-term risk factors for dialysis-related illness. It is hoped that the combined efforts in this and the studies previously mentioned will have a major impact on all children being treated for kidney disease in the hospital, throughout the UK and, ultimately, across the world.

Being able to examine individual patients' responses to treatments via the latest research is a crucial element of the rheumatology unit's work to advance the therapies they offer.

Personalising children's treatments for arthritis

Arthritis is a very real problem for as many as one in 1,000 children in the UK. Looking after these children is a complex issue. Professor Lucy Wedderburn's research aims to balance the dosage of drugs to reduce pain and swelling, while monitoring children closely to minimise the often debilitating side effects of current treatments for arthritis.

Professor Lucy Wedderburn

"In children, the immune system has to frequently fight off new infections, without also causing reactions against the body's own cells or tissues. During my clinical training I realised that not much is really known about how the immune system controls the balance between fighting infection yet staying 'tolerant' to our own body, and I have worked in this area ever since.

"My lab group focuses on what causes and drives arthritis and myositis, and in particular, the childhood immune system's role in remission, when it is achieved, and how we can predict children's response to treatment.

"Our future goal of 'personalised medicine', where each treatment plan will be based on an evidence-based set of factors [genes or other biological molecules] that we can measure, as well as family factors, will allow us to use the available treatments in a more targeted way. I hope this will lead to early remission in a far greater number of our patients."

Professor Wedderburn is aware of the extreme challenges children with arthritis face. "If the condition is not well controlled, then a typical day for a child with arthritis can start with them feeling pretty run down," she says. "The pain in their joints means just getting ready for school can be difficult. As the day progresses, they might experience aching flu-like symptoms throughout their body, due to the release of disease-signalling molecules called cytokines. This means by the end of the day they're fatigued, and that's before they have even taken their medication."

Currently the front-line treatment of choice is a drug called methotrexate. Its side effects can include sickness, loss of appetite, and liver damage. For some children, it has to be delivered by injection, which can cause both pain and distress. Though effective in combating the symptoms of arthritis in a majority of children, around a third of patients do not respond. Despite this, current treatment protocols require methotrexate to be prescribed before any second or third-choice drugs can be trialled.

"Taking a holistic view of a child's care has been crucial to the design of studies to improve the way we offer treatments for childhood arthritis," explains Professor Wedderburn. "With support from Sparks (Sport Aiding Medical Research for Kids), we initiated CHARMS (Childhood Arthritis Response to Medication Study) to evaluate how we might best ensure children receive a more personalised treatment for their condition, without prescribing unnecessary medication which we know may cause suffering, and may even be ineffective in some cases."

As Head of the UCL Institute of Child Health's Rheumatology Unit, Professor Wedderburn has recently contributed to work which has shown that in children whose arthritis responds well to methotrexate, the risk of any relapse is as likely following six months of treatment as it is after 12. The study also identified a protein which acts as a marker for those children more likely to relapse after stopping the methotrexate medication. The research provides evidence for a reduced dosage period – with a reduction in associated side effects – as well as confidence in identifying those children in whom it is safe to stop the drug.

However, the increasingly urgent challenge is to determine which children will not respond to front-line treatment. "We still see many patients each year whose disease does not respond to methotrexate," says Professor Wedderburn. "Less than 20 years ago, children with uncontrolled arthritis might have had to undergo several hip replacements before they reached the age of 25. Thanks to the development of new cytokine-blocking drugs, we now have to carry out less than a handful of hip replacements a year across all of our patients. But we're still some way from my ambition to ensure all these children grow up healthy and disease free."

Having applied new 'whole-genome' screening techniques to the unique patient group admitted to Great Ormond Street Hospital with arthritis, Professor Wedderburn and her team have begun to identify genetic markers which predict how well children will respond to methotrexate. Combining this predictive information with online tools to provide tailored advice to parents, the team hope to remain at the forefront of new developments to further personalise arthritis treatments. With support from Great Ormond Street Hospital Children's Charity, continuing success with this research will allow these children to enjoy an active childhood, secure in the knowledge that they will have the support they need to grow up healthy into their teenage and adult years.

It's the children who bring us together. They inspire us to gain a better understanding of their difficulties, often with astonishing results.

Maia, age nine, has been in hospital for five weeks and is awaiting a heart transplant. She loves having her mum and dad close by in the Italian Building, and often challenges them to a game of Scrabble.

Awards, honours and prizes 2010

Staff from the UCL Institute of Child Health (ICH) and Great Ormond Street Hospital received national and international recognition for their research achievements during 2010.

Professor Myra Bluebond-Langner was appointed True Colours Trust Chair in Palliative Care for Children and Young People, the first professor of paediatric palliative care in the UK.

Dr Luisa Boldrin was awarded the 2010 Dubowitz Prize for her paper, *Mature adult dystrophic mouse muscle environment does not impede efficient engrafted satellite cell regeneration and self-renewal.*

Dr Jennifer Brewin was awarded a PhD for her thesis, *Generation of EBV-specific cytotoxic T-cells that are resistant to calcineurin inhibitors for the treatment of post-transplant lymphoproliferative disease.*

Dr Mattia Calissano was awarded a PhD for his thesis, *Regulation of Brn-3b transcription factor by microRNAs: a possible paradigm for the regulation of essential genes.*

Dr Jonathan Cohen was judged the winner of the Oral Plenary Prize at the 2010 Medical Research Society meeting for clinician scientists in training. His winning topic was *Previous colonisation protects against pneumococcal pneumonia: learning from natural immunity.* He was also awarded a prestigious Pushpa Chopra bursary, designed to support the further research of outstanding individuals.

Dr Andrew Cook, with **Professor Lindsey Allan** and **Dr Ian Huggon,** won first prize in the 2010 British Medical Association Medical Book Awards, radiology section, for *Fetal echocardiography: a practical guide.*

Professor Andrew Copp was reappointed Director of the ICH, and was appointed to the board of the Bo Hjelt Foundation for Spina Bifida.

Professor Anthony Costello was elected a Fellow of the Academy of Medical Sciences.

Professor Carol Dezateux was awarded a CBE for services to science.

Professor Carol Dezateux, Ms Mona Khalid, Dr Rachel Knowles and **Ms Juliet Oerton's** research on rare diseases was featured in the Chief Medical Officer for England's annual report.

Dr Rachel Dobson was awarded a PhD for her thesis, *Tracking endogenous and grafted neural progenitor cells in normal and ischaemic brains using contrast agents and genetic labelling.*

Dr Caroline Fertleman was presented with an Outstanding Consultant Teacher Award at Local Level at the London Specialty School of Paediatrics' annual conference for the development of teaching at the Whittington Hospital.

Dr Rebecca Forth was awarded a PhD for her thesis, *Chemoreceptor renin-angiotensin system activity and the ventilatory response to acute hypoxia, hypercapnia and exertional hypoxia.*

Professor David Gadian was appointed Chairman of the British Chapter of the International Society for Magnetic Resonance in Medicine.

Dr Caroline Godfrey was awarded a PhD for her thesis, *Refining the genetics of muscular dystrophies with defective glycosylation of dystroglycan.*

Dr Nigel Hall was awarded a PhD for his thesis, *Necrotising enterocolitis: the inflammatory response and novel therapies.*

Professor Peter Hammond and colleagues' paper, *Face-brain asymmetry in autism spectrum disorders,* was selected as one of the 10 best papers presented on early childhood development in 2008 by the Canadian Centre of Excellence for Early Childhood Development in their annual Bulletin.

Dr Tom Jacques was invited to join the Biological Studies Group of the Children's Cancer and Leukaemia Group.

Dr Ritika Kapoor was awarded a PhD for her thesis, *Defining phenotype correlations in children with congenital hyperinsulinism.*

Dr Yukiko Kimura was awarded a PhD for her thesis, *Measurement of glutathione synthesis by isotope ratio mass spectrometry in systemic inflammation.*

Dr Panagiotis Kyrtatos was awarded an MB PhD for his thesis, *Cell targeting and imaging using magnetic nanoparticles.*

Professor David Latchman was awarded a CBE for services to higher education.

Professor Catherine Law was appointed to the National Institute for Health Research College of Senior Investigators.

Professor Linda Luxon, formerly Head of ICH's Audiological Medicine Unit, was awarded a CBE for services to medicine.

Dr Mark Lythgoe was awarded the 2010 Davies Medal by the Royal Photographic Society for a significant contribution in the digital field of imaging science.

Dr Chloe Macaulay was presented with an Outstanding Trainee Teaching Award at the London Specialty School of Paediatrics' annual conference.

Dr Juan Pedro Martinez-Barbera was awarded the Henning Andersen prize for the best research abstract submitted to the 49th European Society for Paediatric Endocrinology Annual Meeting, Prague 2010, for his paper, *Increased Wingless (Wnt) signaling in pituitary progenitor/stem cells gives rise to pituitary tumors in mice and humans.* He was also awarded the prize for the best research abstract at the 38th Meeting of the British Society for Paediatric Endocrinology and Diabetes, Manchester 2010.

Dr Margaret Mayston was named as Australian Woman of the Year in the UK, 2010.

Dr Odette Megnin was awarded a PhD for her thesis, *Electrophysiological correlates of audio-visual integration of spoken words in typical development and autism spectrum disorder.*

Dr Francesca Menghi was awarded a PhD for her thesis, *Genome-wide analysis of gene expression and alternative splicing in human medulloblastomas.*

Dr Halima Moncrieffe won an award at the Young Investigators Meeting of the 17th Paediatric Rheumatology European Society Congress, Valencia 2010, for her presentation, *A novel defect: CD39+ T cells are enriched in the inflamed joint but do not suppress.*

Dr David Mowatt was awarded an MD for his thesis, *An analysis of craniosynostotic osteoprogenitor cells and their potential for bone tissue engineering.*

Awards, honours and prizes 2010
continued

Dr Irina Papangeli was awarded a PhD for her thesis, *Analysis of pathways affected by loss of Tbx1 in mouse models of DiGeorge syndrome.*

Dr Nina Power was awarded a PhD for her thesis, *Postoperative behaviour changes and pain in children, two to 12 years, following inpatient and day-case surgery.*

Professor Kathy Pritchard-Jones was conferred the title of Hugh and Catherine Stevenson Professor of Paediatric Oncology.

Dr Robert Robinson was awarded an MD(Res) for his thesis, *An analysis of craniosynostotic osteoprogenitor cells and their potential for bone tissue engineering.*

Professor Peter Scambler was presented with the inaugural Angelo DiGeorge Medal at the 7th International 22q11.2 Deletion Conference, Coventry 2010.

Dr Sérgio de Sousa won the 2010 John M Opitz Young Investigator Award for his paper, *Nicolaides-Baraitser syndrome: delineation of the phenotype.*

Dr Philip Stanier was appointed a Trustee of the Middlesex Hospital and Medical School General Charitable Trust.

A team led by **Professor Terence Stephenson**, **Professor Ruth Gilbert, Professor Catherine Law, Dr Miranda Wolpert, Professor Helen Roberts** and **Professor Russell Viner** successfully bid to the National Institute for Health Research to establish a Department of Health Policy Research Unit for the Health of Children, Young People and Families.

Mr Hugh Stevenson, former Treasurer of the ICH and Chair of the Child Health Research Appeal Trust (CHRAT) Trustees Investment Committee, received a knighthood for services to the financial services industry.

Dr Michael Sury was awarded a PhD for his thesis, *Characterisation of awakening from anaesthesia in infants.*

Dr Sudhin Thayyil was awarded a PhD for his thesis, *Post-mortem MR imaging in foetuses, newborns and children.*

Dr Eliot Ward was awarded a PhD for his thesis, *Novel fusion protein-expressing lentiviral vectors ameliorate collagen induced arthritis.*

Dr Natalie Ward was awarded a PhD for her thesis, *Lentiviral vectors for treatment of haemophilia.*

Professor Lucy Wedderburn was elected to the Paediatric Rheumatology European Society (PReS) Council as their Scientific Programme Committee Chair during their 17th annual congress, Valencia 2010. She was also invited to sit on the Arthritis Research UK biomedical sciences panel.

Dr Paul Winyard was presented with an Outstanding Consultant Teacher Award at Regional Level at the London Specialty School of Paediatrics' Annual Conference for the promotion of novel pan-London programmes.

Dr Austen Worth was awarded a PhD for his thesis, *Analysis of the domain specific function of the Wiskott Aldrich Syndrome Protein, in vitro and in vivo.*

Grants and donations 2010
The UCL Institute of Child Health and Great Ormond Street Hospital Children's Charity continue to receive grants towards research from the following individuals and organisations:

A
Abbott Laboratories
Abbott Nutrition
The Academy of Medical Sciences
Actelion
Action Duchenne
Action Medical Research
Action on Hearing Loss (formerly the Royal National Institute for Deaf People)
Malcolm Hardy Addison
Age UK
The Anatomical Society
Angelina Our Star Appeal
Annabel McEnery Children's Cancer Fund
Antisoma
Arthritis Research UK (formerly Arthritis Research Campaign)
Association for International Cancer Research
Association Française contre les Myopathies
Association Monégasque contre les Myopathies
Asthma UK
AstraZeneca
Autism Speaks
AVI BioPharma

B
The Baily Thomas Charitable Fund
Barts and the London Charity
Batten Disease Family Association
Baxter
Bayer Schering Pharma
Mrs Heather Beckwith
Becta (formerly British Educational Communications and Technology Agency)
BIAL
Big Lottery Fund
Bill & Melinda Gates Foundation
BioMarin Pharmaceutical
Biotechnology and Biological Sciences Research Council
Bliss
Bone Cancer Research Trust
British Academy
British Academy of Childhood Disability
British Association for Paediatric Nephrology
British Council
British Heart Foundation
British Journal of Anaesthesia
British Lung Foundation
British Skin Foundation
British Society of Audiology
Bupa Foundation
Tiggy Butler

C
The C P Charitable Trust
Cambridge University Hospitals NHS Foundation Trust
Canadian Institutes of Health Research (formerly Medical Research Council of Canada)
Cancer Research UK
Canterbury Christ Church University
The CGD Research Trust
The Charles Wolfson Charitable Trust
CHDI
Child Growth Foundation
Child Health Research Appeal Trust
CHILDREN with CANCER UK (formerly CHILDREN with LEUKAEMIA)
Children's Brain Diseases Foundation (A Batten Disease Resource)
Children's Cancer and Leukaemia Group
Children's Hyperinsulinism Fund
Children's Liver Disease Foundation
The Children's Research Fund
The Children's Trust, Tadworth
Cincinnati Children's Hospital Medical Center
Ashton and Tilly Clanfield
CLEFT
CLIC Sargent
Colgate-Palmolive
CORDA (Coronary Artery Disease Research Association)
Mrs Janet Crawford
CREA
Cyberonics Europe
Cystic Fibrosis Trust
Cystinosis Foundation
Cystinosis Research Network

Grants and donations 2010
continued

D
James Datnow
DebRA (Dystrophic epidermolysis bullosa Research Association)
Department for Business, Innovation and Skills
Department for Children, Schools and Families
Department for International Development
Department of Health
Diabetes UK
Dimbleby Cancer Care
The Dromintee Trust
Duchenne Parent Project
Lord and Lady Dundas

E
Economic and Social Research Council
Eisai
Elimination of Leukaemia Fund
Emergency Nutrition Network
Engineering and Physical Sciences Research Council
Epilepsy Research UK
European Commission
European Respiratory Society
European Society for Immunodeficiencies
European Union

F
Fidelity International
Fight for Sight
Mr and Mrs Fitzpatrick
La Fondation Genevoise de Bienfaisance
Valeria Rossi di Montelera
Fondation Leducq
Food and Agriculture Organization of the United Nations
Mrs Thelma Fox

G
The Gavriel Meir Trust
Généthon
Genex Biosystems
Genzyme
Gilead
GlaxoSmithKline
GlaxoSmithKline Biologicals
The Gosling Foundation Limited
The Shauna Gosling Trust
Mrs Dorothy Graham
Great Ormond Street Hospital Children's Charity
Mr Hugh Greenwood
Grifols UK
The Guide Dogs for the Blind Association

H
Charles and Kaaren Hale
The Health Foundation
Health Protection Agency
Healthcare Infection Society (formerly Hospital Infection Society)
Heart Research UK
Hearts for Kids Trust Fund
Heinz
Hestia Foundation
Higher Education Funding Council for England
The Histiocytosis Research Trust
The Hospital for Sick Children (SickKids)
Human Early Learning Partnership

I
Ichthyosis Support Group
Imperial College Healthcare NHS Trust (formerly Hammersmith Hospital NHS Trust)
Institute of Education, University of London
International Association for the Study of Pain
Ipsen Limited
Isis Pharmaceuticals

J
J P Moulton Charitable Foundation
Janssen
Janssen Biotech, Inc. (formerly Centocor)
Jeans for Genes
The Jenner Institute
The Jennifer Trust for Spinal Muscular Atrophy
Johns Hopkins University
Joint Information Services Committee

K
The Kay Kendall Leukaemia Fund
Kidney Research UK
Kids Company
Kids Kidney Research (formerly The Kidney Research Aid Fund)
Kevin Kitching and Sinead O'Shea

L
Eugène and Stephanie Léouzon
Leukaemia and Lymphoma Research (formerly Leukaemia Research)
The Leverhulme Trust
The Bernard Lewis Family Charitable Trust
Lilly
Longview

M
Macula Vision Research Foundation
Macular Disease Society
Marie Curie Cancer Care
The Mary Kitzinger Trust
Masimo
Mason Medical Research Foundation
Harvey and Allison McGrath
Medical Research Council (MRC)
Medical Research Society
Medtronic
MEND
Meningitis Research Foundation
Meningitis Trust
Merck
The Mitchell Charitable Trust
MRC Clinical Trials Unit
MSS Research Foundation
Mundipharma
Muscular Dystrophy Association
Muscular Dystrophy Campaign
Myositis Support Group

N
National Institute for Health and Clinical Excellence
National Institute for Health Research (NIHR)
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke (National Institutes of Health)
National Institutes of Health
National Patient Safety Agency
National Specialised Commissioning Team, Department of Health
The Neuroblastoma Society
Newlife Foundation for Disabled Children (formerly Birth Defects Foundation/ BDF Newlife)
NHS Blood and Transplant
NIHR Biomedical Research Centre for Ophthalmology
NIHR Health Technology Assessment programme
North Bristol NHS Trust
North Thames Regional Cleft Lip and Palate Service
Novartis
Novo Nordisk
Nutricia

O
Ms Dorothy Oakley
Octapharma
Olivia Hodson Cancer Fund
The Georg und Emily von Opel Foundation
Organon Laboratories Ltd
Orphan Europe

P
Paediatric Rheumatology Discretionary Fund
PATH
The Pathological Society of Great Britain and Ireland
Pfizer
Philips
Philips AVENT
Physiotherapy Research Foundation
Nick and Miranda Pink
Primary Immunodeficiency Association
PTC Therapeutics

Q
Quintiles

R
Raisa Gorbachev Foundation
The Rank Prize Funds
Alexandra Raphael and family
Research Autism
Rho
RICC (Research into Childhood Cancer)
Roche Pharmaceuticals
Ronald McDonald House Charities
The Royal Academy of Engineering
The Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
The Royal College of Surgeons of England
Royal National Institute for the Blind
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S
Samantha Dickson Brain Tumour Trust
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Santhera Pharmaceuticals
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Shire HGT (Human Genetic Therapies)
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Summit
Sweets for Life Ltd
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T
Takeda Global Research and Development Centre
The Tavistock and Portman NHS Foundation Trust
Technology Strategy Board
Teenage Cancer Trust
Ms Florence Till
Tompkins Foundation
The Towergate Charitable Foundation
Trophos
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University College London
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University of London
The University of Manchester
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Wellbeing
Wellbeing of Women
WellChild
Wellcome Trust
Welton Foundation
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World Health Organization
Richard Wright

Y
Yorkhill Children's Foundation

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Nutritional and Surgical Sciences Theme

Theme Leader
Professor Alan Lucas MB BChir MA MD MRCP FRCPCH FMedSci

Nutrition Unit
Medical Research Council Clinical Research Professor and Head of Unit
Professor Alan Lucas MB BChir MA MD MRCP FRCPCH FMedSci
Professor of Biochemistry
Professor David Muller BSc PhD
Professor of Paediatric Nutrition
Professor Atul Singhal MB MRCP DCH MRCPCH BS MD
Professor of Anthropology and Paediatric Nutrition
Professor Jonathan Wells MA MPhil PhD
Honorary Professor of UCL
Professor Brian Wharton MD MBA DSc FRCP(L)(E)(G) FRCPCH DCH
Reader in Childhood Nutrition
Dr Mary Fewtrell MD BMBCh FRCPCH MRCP DCH MA
Honorary Senior Lecturer
Dr Margaret Lawson MSc PhD SRD

Surgery Unit
Nuffield Professor of Paediatric Surgery and Head of Unit
Professor Agostino Pierro MD FRCS(Eng) FRCS(Ed) FAAP
Honorary Reader
Dr Andreas Roposch MD MSc (Epidem) FRCS
Senior Lecturers
Dr Paolo de Coppi MD PhD
Dr Simon Eaton BSc PhD

Cancer Theme

Theme Leader (from April 2010)
Professor Kathy Pritchard-Jones BMBCh PhD FRCPCH FRCP

Molecular Haematology and Cancer Biology Unit
Wellcome Senior Research Fellow in Basic Biomedical Science, Reader in Molecular Neurobiology and Head of Unit
Dr Jonathan Ham BSc PhD
Hugh and Catherine Stevenson Chair of Paediatric Oncology (from April 2010)
Professor Kathy Pritchard-Jones BMBCh PhD FRCPCH FRCP
Professor of Paediatric and Developmental Pathology
Professor Neil Sabire BSc MBBS DM FRCPath
Emeritus Professor of Haematology and Oncology
Professor Judith Chessells MD FRCP FRCPath
Visiting Professors of Haematology and Oncology
Professor Paul Brickell BA MA PhD
Professor Ian Hann MD FRCP FRCPath
Reader in Paediatric Oncology
Dr John Anderson BA MB BS MRCP PhD
Reader in Cancer Biology
Dr Arturo Sala PhD
Senior Lecturer
Dr Mike Hubank BA PhD
Walport Lecturer in Paediatric Oncology
Dr Daniel Morgenstern MB BChir MA PhD MRCPCH
Lecturer
Dr Owen Williams BSc PhD

Cardiorespiratory Sciences Theme

Theme Leader
Professor John Deanfield MB BChir FRCP

Cardiac Unit
The British Heart Foundation Vandervell Professor of Congenital Heart Disease and Head of Unit
Professor John Deanfield MB BChir FRCP
Professor of Cardiothoracic Surgery
Professor Martin Elliott MD FRCS
Professor of Cardiology
Professor William McKenna BA MD DSc FRCP FESC FACC
Professor of Cardiovascular Imaging
Professor Andrew Taylor BA(Hons) MD MRCP(UK) FRCR
Reader in Inherited Cardiac Disease
Dr Perry Elliott MBBS MD MRCP
Senior Lecturers
Dr Andrew Cook PhD (British Heart Foundation Lecturer)
Dr Pier Lambiase BA PhD MRCP

Portex Unit of Paediatric Anaesthesia, Pain Research, Critical Care, Respiratory Medicine, Physiology and Physiotherapy
Professor of Respiratory Physiology and Head of Unit
Professor Janet Stocks PhD
Smiths Medical Professor of Anaesthesia and Critical Care
Professor Michael (Monty) Mythen FRCA
Emeritus Professor of Paediatric Anaesthesia
Professor David Hatch MBBS MRCS LRCP FRCA FRCPCH(Hons)
Honorary Reader in Paediatric Intensive Care
Dr Quen Mok MB BS MRCP MRCPI DCH
Honorary Reader in Respiratory Paediatrics
Dr Colin Wallis MBChB FCP(Paed) MD DCH FRCP
Senior Lecturers
Dr Mike Grocott BSc MBBS MD FRCA FRCP
Dr Eleanor Main BA PhD
Dr Mark Peters MB BCh MRCP
Dr Suellen Walker MBBS MM(PM) MSc FANZA FFPMANZCA
Honorary Senior Lecturers
Dr Paul Aurora BSc MBBS MRCP MSc (joint with Cardiac Unit)
Dr Robert Bingham MBBS FRCA
Dr Ann Black MBBS DRCOG FRCA
Dr Joe Brierley MBChB MRCP FRCPCH MA
Dr Mike Broadhead MBBS BSc MRCP FRCA (joint with Cardiac Unit)
Dr Philip Cunnington MBBS DA FRCA
Dr David de Beer BSc MBChB DCH FRCA
Dr Hilary Glaisyer MBBS MRCP FRCA
Dr Louise Harding MBBS FRCS
Dr Jane Herod BSc MBBS FRCA
Dr Richard Howard BSc MBChB FRCA
Dr Elizabeth Jackson BSc MBBS MRCP FRCA
Dr Ian James MBChB FRCA (joint with Cardiac Unit)
Dr Paula Lister MBBCh MPhil FRCPCH (joint with Infectious Diseases and Microbiology Unit)
Dr Adrian Lloyd-Thomas MBBS FRCA
Dr Su Mallory
Dr Richard Martin MBBS FRCA DCHyp FRSM MSBST
Dr Angus McEwan MBChB FRCA
Dr Reema Nandi MBBS FRCA, MD
Dr Kar-Binh Ong BA MBBS FRCA
Dr Andy Petros MBBS MSc FRCP FRCPCH
Dr Christine Pierce MD BSc BBS MRCP
Dr Steve Scuplak
Dr Sophie Skellett MA MB BChir MRCP FRCPCH
Dr Jonathan Smith MBBS BSc(Hons) FRCA
Dr Mark Thomas BSc MBBChir FRCA
Dr Isabeau Walker BSc MBBChir FRCA
Dr Glyn Williams MBBS FRCA MD
Dr Sally Wilmshurst MBChB(Hons) MRCP FRCA

Patient Care Research and Innovation Centre
Chair of Children's Nursing Research and Head of Unit
Professor Linda Franck PhD RN RGN RSCN FRCPCH FAAN
Senior Lecturer
Dr Faith Gibson MSc (Cancer Nursing) RSCN RGN CertEd RNT PhD
Honorary Senior Lecturer
Dr Debbie Sell SRSLT FRCSLT PhD

General and Adolescent Paediatrics Theme

Theme Leader
Professor Terence Stephenson DM FRCP FRCPCH

General and Adolescent Paediatrics Unit
Nuffield Professor of Child Health and Head of Unit
Professor Terence Stephenson DM FRCP FRCPCH
Professor of Paediatrics (until December 2010)
Professor Mark Gardiner MBBCh MD FRCPCH FMedSci
Professor of Paediatric Gastroenterology
Professor Alan Phillips PhD FRCPCH
Emeritus Professor of Child Health
Professor Brent Taylor PhD MBChB FRCP FRACP
Professor of Adolescent Health
Professor Russell Viner MBBD FRACP FRCPCH FRCP PhD
Senior Lecturers
Dr Eddie Chung MBChB MRCP
Dr Alastair Sutcliffe MD PhD MRCP FRCPCH PGdipCT
Dr Robert Senior BA MSc MBBS MPCPsych
Honorary Senior Lecturers
Dr Deborah Christie DClinPsych
Dr Haitham Elbashir MBBS FRCPCH DCH MD
Lecturer
Dr Sophie Khadr MBChB(Hons) MRCPCH DFSRH FSRH

Louis Dundas Centre for Children's Palliative Care
True Colours Trust Chair in Palliative Care for Children and Young People (from July 2010)
Professor Myra Bluebond-Langner PhD

Genes, Development and Disease Theme

Theme Leader
Professor Peter Scambler BSc MBChB FRCPath FMedSci

Clinical and Molecular Genetics Unit
Professor of Clinical and Molecular Genetics and Head of Unit
Professor Gudrun Moore BA PhD
Professor in Genetics and Fetal Medicine
Professor Lyn Chitty BSc PhD MBBS MRCOG
Professor of Paediatric Metabolic Disease and Hepatology
Professor Peter Clayton MD FRCP FRCPCH
Professors of Paediatric Endocrinology
Professor Mehul Dattani MD FRCP
Professor Peter Hindmarsh BSc MB MD BS FRCP
Professor of Clinical Chemistry
Professor Simon Heales BSc PhD CSci FRCPath
Emeritus Professor of Molecular Genetics
Professor Susan Malcolm PhD FRCPath
Emeritus Professor of Molecular Embryology
Professor Marilyn Monk BSc(Hons) MSc(Hons) PhD
Emeritus Professor of Paediatric Genetics
Professor Marcus Pembrey BSc MBBS MD FRCP FRCPCH FRCOG FMedSci
Emeritus Professor of Child Health and Growth
Professor Michael Preece MD MSc FRCP FRCPCH
Emeritus Professor of Biochemistry
Professor Bryan Winchester MA PhD

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Reader in Paediatric Endocrinology and Wellcome Trust Senior Research Fellow in Clinical Science
Dr John Achermann MA MD MRCP MRCPCH
Reader in Paediatric Endocrinology and Reader in Clinical and Molecular Genetics
Dr Maria Bitner-Glindzicz BSc MB BS PhD FRCP
Senior Lecturers
Dr Khalid Hussain MBChB MSc MRCP MRCPCH
Dr Shamima Rahman MA MRCP MRCPCH PhD
Honorary Senior Lecturers
Dr Caroline Brain MB MD FRCP FRCPCH
Dr Maureen Cleary MD MRCP MBChB
Dr Stephanie Grunewald MD
Dr Ashok Vellodi FRCP FRCPCH
Lecturer
Dr Kevin Mills PhD

Molecular Medicine Unit
Professor of Molecular Medicine and Head of Unit
Professor Peter Scambler BSc MBChB FRCPath FMedSci
Professor of Medical and Molecular Genetics and Wellcome Trust Senior Research Fellow
Professor Philip Beales BSc MD MRCP
Professor in Molecular Cardiology
Professor Paul Riley BSc PhD
Professor of Computational Biology
Professor Peter Hammond BA PhD
Honorary Professor
Professor George Fraser PhD DSc MA MB BChir MD FRCP FRCPC
Senior Lecturer
Dr Hannah Mitchison BSc PhD
Lecturer (until September 2010)
Dr Kate Everett BSc MPhil PhD PgDip

Medical Molecular Biology Unit
Professor of Human Genetics and Head of Unit
Professor David Latchman CBE MA PhD DSc FRCPath FRSA
Reader in Molecular and Cellular Biology
Dr Anastasis Stephanou BSc PhD
Senior Lecturer
Dr Ian Giles MBBS PhD MRCP
Honorary Senior Lecturer
Dr Richard Knight MD PhD
Lecturer
Dr Vishwanie Budhram-Mahadeo BSc MBBS PhD MRCP

Nephro-Urology Unit
Reader in Nephrology and Head of Unit
Dr Paul Winyard BM BCh MA PhD FRCPCH
Honorary Professors of Nephrology
Professor Robert Kleta MD PhD
Professor Adrian Woolf MA MD FRCPCH
Emeritus Professors of Paediatric Nephrology
Professor Martin Barratt CBE FRCP
Professor Michael Dillon FRCP FRCPCH
Reader in Paediatric Nephrology
Dr Lesley Rees MD FRCP FRCPCH
Honorary Readers in Paediatric Nephrology
Dr Richard Trompeter FRCP FRCPCH
Dr William van't Hoff BSc MD FRCP FRCPCH
Honorary Senior Lecturers (from December 2010)
Dr Detlef Böckenhauer MD PhD
Mr Francis Calder MB FRCS (joint with Guy's and St Thomas' NHS Foundation Trust)
Mr Abraham Cherian MBBS MS DNB FRCS FRCS(Paed Surg)
Mr Peter Cuckow FRCS (joint with North Middlesex University Hospital)
Mr Patrick Duffy MB FRCS
Mr Vass Hadjianastassiou DM FEBVS(Vasc Surg) FRCS(Gen Surg) BSc (joint with Guy's and St Thomas' NHS Foundation Trust)
Dr Daljit Hothi MBBS MRCPCH MD
Mr Geoff Koffman MBChB FRCS (joint with Guy's and St Thomas' NHS Foundation Trust)
Mr Nizam Mamode BSc MBChB MD FRCS(Gen) (joint with Guy's and St Thomas' NHS Foundation Trust)
Dr Stephen Marks MD MBChB MSc MRCP(UK) DCH FRCPCH
Mr Imran Mushtaq MD FRCS
Dr Rukshana Shroff MD MRCPCH PhD
Mr John Taylor MD FRCS (joint with Guy's and St Thomas' NHS Foundation Trust)
Dr Kjell Tullus MD PhD FRCPCH
Honorary Lecturers
Ms Eileen Brennan RGN RSCN ENB 147 DMS MSc
Mr Divyesh Desai MB MChir
Dr Sarah Ledermann MRCP

Infection and Immunity Theme

Theme Leader
Professor Christine Kinnon BSc PhD

Immunobiology Unit
Professor of Vaccinology and Immunology, Director of Clinical Research and Development, and Head of Unit
Professor David Goldblatt MBChB PhD FRCP FRCPCH
Professor of Immunology
Professor Robin Callard BSc MSc PhD DipMath BA(Maths) DSc
Professor of Experimental Immunology
Professor Tessa Crompton PhD
Professor of Paediatric Dermatology
Professor John Harper MD FRCP FRCPCH
Emeritus Professor of Molecular Immunology
Professor Malcolm Turner DSc(Med) PhD FRSC FRCPath
Lecturer
Dr Wei-Li Di MBBS PhD

Infectious Diseases and Microbiology Unit
Professor of Infectious Disease and Immunology and Head of Unit
Professor Nigel Klein BSc MBBS MRCP PhD FRCPCH
Honorary Professor
Professor Alan Phillips PhD FRCPCH
Senior Lecturers
Dr Mona Bajaj-Elliott BSc(Hons) PhD
Dr Paul Brogan BSc(Hons) MBChB(Hons) MRCPCH MSc PhD (joint with Rheumatology Unit)
Honorary Senior Lecturers
Professor Judy Breuer MBBS MD FRCPath
Dr Garth Dixon BSc MBChB PhD MRCP FRCPath
Professor Diana Gibb MBChB(Hons) MRCP MD MSc DipObs FRCPCH (joint with Centre for Paediatric Epidemiology and Biostatistics Unit)
Dr Susan Hall BSc PhD
Dr John Hartley BSc MBBS MSc DTM&H MRCP FRCPath
Dr Marian Malone MB BCh BAO FRCPath
Dr Karyn Moshal MBChB MRCP MRCPCH DTM&H
Dr Vas Novelli FRACP FRCP FRCPCH
Dr Delane Shingadia MBBS MPh MRCP FRCPCH
Dr James Soothill MD MBBS FRCPath
Dr Martin Weber MBChB MD(Res) DCH(SA) FRCPath
Lecturer
Dr Jonathan Cohen PhD

Molecular Immunology Unit
Professor of Molecular Immunology and Head of Unit
Professor Christine Kinnon BSc PhD
Professor of Human Molecular Genetics
Professor Robin Ali BSc PhD (joint with UCL Institute of Ophthalmology)
Professor of Transplantation Immunology
Professor Persis Amrolia BSc MBBS MRCP MRCPath PhD
Professor of Paediatrics and Immunology
Professor Bobby Gaspar BSc MB BS MRCP
Professor of Paediatric Immunology and Wellcome Trust Senior Fellow
Professor Adrian Thrasher MB BS PhD FRCP FRCPath FMedSci
Reader in Paediatric Immunology
Dr Graham Davies MA FRCP FRCPCH
Reader in Molecular Biology
Dr Kenth Gustafsson PhD
Reader in Molecular Genetics
Dr Steve Hart BSc MSc PhD
Reader in Stem Cell Transplantation
Dr Paul Veys MBBS FRCP FRCPath FRCPCH
Senior Lecturers
Dr Cathy Cale BSc MBChB PhD MRCP MRCPCH MRCPath
Dr Alison Jones MRCP PhD
Dr Waseem Qasim BMedSci MBBS MRCP MRCPCH PhD
Dr Penny Titman PhD
Lecturers
Dr Siobhan Burns MB BCh MRCPI PhD
Dr Paul Turner BMBCh BSc MRCPCH PhD
Dr Austen Worth PhD

Rheumatology Unit
Professor of Paediatric Rheumatology and Head of Unit
Dr Lucy Wedderburn BA PhD MBBS FRCP(UK) MRCPCH FRCP
Professor of Paediatric Rheumatology and Director of the Centre of Paediatric and Adolescent Rheumatology
Professor Patricia Woo CBE MB BS BSc PhD FRCP FRCPCH FMedSci
Senior Lecturer
Dr Paul Brogan BSc(Hons) MBChB(Hons) MRCPCH MSc PhD (joint with Infectious Diseases and Microbiology Unit)
Honorary Senior Lecturer
Dr Clarissa Pilkington BSc MBBS CCST MRCPCH
Lecturer
Dr Bin Gao MMed PhD

Neurosciences and Mental Health Theme

Theme Leader
Professor Francesco Muntoni MD FRCPCH FMedSci

Behavioural and Brain Sciences Unit
Professor of Behavioural Sciences and Head of Unit
Professor David Skuse MD FRCP FRCPsych FRCPCH
Professor of Developmental Psychopathology
Professor Peter Hobson MA MB BChir PhD CPsychol FRCPsych
Honorary Senior Lecturers
Rachel Bryant-Waugh MSc DPhil
Margaret DeJong MDCM, FRCPsych(Can) FRCPsych(UK)
Dr Jon Goldin MBBS BSc MBChB DCH MRCPsych
Dr Paramala Santosh MRCPsych MD DipNB(Psych)
Lecturer
Dr Jonathan Clayden MSc PhD

Developmental Biology Unit
Reader in Developmental Neurobiology and Head of Unit
Dr Patrizia Ferretti PhD
Reader in Developmental Biology
Dr Jane Sowden BA PhD
Reader in Craniofacial Developmental Biology and Genetics
Dr Philip Stanier BA PhD (joint with Neural Development Unit)
Honorary Senior Lecturers
Professor Agnès Bloch-Zupan BChD MBiolMedSc Specialist Certificate PhD
Dr Kanwal Nischal FRCOpth

Developmental Cognitive Neuroscience Unit
Professor of Developmental Cognitive Neuroscience and Head of Unit
Professor Faraneh Vargha-Khadem MA PhD

Senior academic staff 2010
continued

Visiting Professor
Professor Mortimer Mishkin MA PhD
Readers in Developmental Cognitive Neuroscience
Dr Torsten Baldeweg MD
Dr Michelle de Haan PhD
Honorary Senior Lecturers
Dr Luc Berthouze BSc Msc PhD
Dr Margaret Mayston BSc Msc PhD
Dr Peter Rankin BSc Msc DClinPsy
Lecturer
Dr Frederique Liegeois BSc MSc PhD
Honorary Lecturer
Dr Alexandra Hogan PhD

Dubowitz Neuromuscular Centre
Professor of Paediatric Neurology and Head of Unit
Professor Francesco Muntoni MD FRCPCH FMedSci
Honorary Professor
Professor Caroline Sewry PhD FRCPath
Reader in Cell Biology and Wellcome Trust University Award Holder
Dr Jenny Morgan PhD

Neural Development Unit
GlaxoWellcome Professor of Developmental Neurobiology, Head of Unit and Director of UCL Institute of Child Health
Professor Andrew Copp MBBS DPhil FRCPath FMedSci
Readers in Developmental Neurobiology
Dr Nick Greene BA PhD
Dr Andrew Stoker PhD
Reader in Neurobiology and Wellcome Trust University Award Holder
Dr Juan Pedro Martinez-Barbera BA PhD
Reader in Craniofacial Developmental Biology and Genetics
Dr Philip Stanier BA PhD (joint with Developmental Biology Unit)
Senior Lecturers
Dr Alan Burns BA PhD
Dr Thomas Jacques BA MA MB BChir PhD MRCP
Lecturer
Dr Erwin Pauws BSc PhD

Neural Plasticity Unit
Chair of Clinical Neurophysiology and Head of Unit
Professor Martin Koltzenburg MD FRCP
Walport Clinical Lecturer in Clinical Neurophysiology
Dr Kevin Shields MD PhD MRCP

Neurosciences Unit
Prince of Wales's Chair in Childhood Epilepsy and Head of Unit
Professor Helen Cross MB ChB PhD FRCP FRCPCH
Professor of Paediatric Neurosurgery
Professor Richard Hayward FRCS
Professor of Paediatric Neurology
Professor Fenella Kirkham MA MB BCh MRCP FRCP
Professor of Childhood Epilepsy
Professor Brian Neville FRCP FRCPCH (joint with National Centre for Young People with Epilepsy)
Professor of Paediatric Neuroscience and International Child Health
Professor Charles Newton MB ChB MD MRCP FRCPCH
Honorary Professor of Speech Pathology
Professor Sheena Reilly BAppSci PhD
Honorary Visiting Professor
Professor Christopher Gillberg
Reader in Paediatric Neuroscience
Dr Rod Scott MB ChB PhD MRCP MRCPCH
Senior Lecturer
Dr Vijeya Ganesan MB ChB MD MRCP MRCPCH
Honorary Senior Lecturers
Dr Sarah Aylett MBBS MRCP FRCPCH
Dr Stewart Boyd MD FRCPCH
Dr Lucinda Carr MD MBChB DCH FRCPCH
Dr Hilary Cass BSc FRCP FRCPCH MILT
Dr Naomi Dale BA MA PhD CPsychol(BPS)
Dr Carlos de Sousa MBBS BSc MD FRCP FRCPCH
Dr Catherine DeVile MA MBBS MD MRCP MPCPCH
Dr Christin Eltze MRCP MSc
Mr William Harkness FRCS
Dr Cheryl Hemingway MBChB BA(Hons) MMed FCP FRCPCH PhD
Dr Isabel Heyman BSc MBBS MRCPsych PhD
Dr Matthew Pitt MD FRCP
Dr Robert Robinson MA MBBS MRCP
Dr Alison Salt MSc DCH FRCAP FRCPCH
Jenefer Sargent MA MBBCh MRCP MSc
Dr Patricia Sonksen MD FRCP FRCPCH MBBS DObstRCOG
Mr Dominic Thompson MBBS BSc FRCS(SN)
Dr Sophie Varadkar BA MB BCh BAO DCH MSc MRCPI
Dr Steve White MA DPhil MB BChir MRCPsych FRCP

Ulverscroft Vision Research Group
Professor in Ophthalmic Epidemiology and Director of the Ulverscroft Vision Research Group
Professor Jugnoo Rahi MSc PhD FRCOphth
Honorary Professors
Professor Richard Abadi PhD
Professor Tony Moore FRCOphth
Honorary Reader
Miss Isabelle Russell-Eggitt MA FRCS FRCOphth
Senior Lecturer
Dr Jane Sowden BA PhD
Principal Research Fellow
Dr Richard Clement PhD BSc
Honorary Senior Lecturers
Dr Kanwal Nischal FRCOpth
Dr Dorothy Thompson BSc PhD MBCO
Honorary Lecturer
Dr Alki Liasis PhD CPSM

Imaging and Biophysics Unit
Reader in Imaging and Biophysics and Head of Unit
Dr Christopher Clark MSc PhD
Rank Professor of Biophysics and Chair of Biophysics
Professor David Gadian DPhil FMedSci
Professor of Medical Physics
Professor Andrew Todd-Pokropek PhD (joint with Department of Medical Physics and Bioengineering, UCL)
Honorary Professor of Medical Physics
Professor Isky Gordon FRCR FRCP FRCPCH
Senior Lecturer
Dr Mark Lythgoe PhD
Honorary Senior Lecturers
Dr David Atkinson PhD
Dr Lorenzo Biassoni MD MSc FEBNM
Dr Wui Khean Kling Chong MD MRCP FRCR
Professor Richard Iles PhD
Dr Keiran McHugh DCH FRCR FRCPI
Dr Dawn Saunders MB MD FRCR
Lecturers
Dr David Carmichael PhD
Dr Jonathan Clayden MSc PhD
Dr Patrick Hales PhD
Dr Martin King PhD
Dr Rodney Scott PhD MRCP

Population Health Sciences Theme

Theme Leader
Professor Carol Dezateux CBE MD MSc FRCP FRCPCH FFPHM FMedSci

Centre for International Health and Development
Professor of International Child Health and Head of Unit
Professor Anthony Costello MA MB BChir FRCP FRCPCH FMedSci
Professor in Global Health
Professor Therese Hesketh MFPHM MRCPCH PhD MPH DTM&H DCH
Emeritus Professor of International Child Health
Professor Andrew Tomkins MB BS FRCP FRCPCH FFPHM FMedSci
Emeritus Professor of Disability and International Development
Professor Sheila Wirz MEdFCST PhD
Emeritus Professor of International Child Health
Professor Sally McGregor MB BS MD DPH FRCP
Reader in Global Health
Dr Sarah Hawkes MB BS PhD
Reader and Wellcome Trust Senior Research Fellow
Dr David Osrin MB BCh MA MRCP MRCPCH DTM&H PhD
Honorary Senior Lecturers
Dr Richard Lansdown MA PhD DipPsych FBPsS Cpsychol
Dr Felicity Savage MS BM BCh FRCP
Lecturers
Dr Zelee Hill PhD
Dr Audrey Prost PhD
Dr Andrew Seal PhD
Dr Jolene Skordis-Worrall MCom PhD

Centre for Paediatric Epidemiology and Biostatistics Unit
Professor of Paediatric Epidemiology and Head of Unit
Professor Carol Dezateux CBE MD MSc FRCP FRCPCH FFPHM FMedSci
Professor of Medical Statistics
Professor Tim Cole BA BPhil MA PhD ScD HonFRCPCH FMedSci
Professor of Clinical Epidemiology
Professor Ruth Gilbert MSc MD MRCP
Professor of Public Health and Epidemiology
Professor Catherine Law OBE MD FRCP FRCPCH FFPH
Professors of Paediatric Epidemiology
Professor Marie-Louise Newell MSc PhD MFPHM
Professor Catherine Peckham CBE MD FFPHM FRCP FRCPCH FRCPath FRCOG FMedSci
Professor in Epidemiology and Public Health
Professor Christine Power BA MSc PhD MFPHM
Emeritus Professor and Principal Research Fellow
Professor Harvey Goldstein BSc PGrad Dip FBA PhD(hc)
Honorary Professors
Professor Diana Gibb MBChB(Hons) MRCP MD MSc Dip Obs FRCPCH (joint with Infectious Diseases and Microbiology Unit)
Professor Orly Manor BSc MSc PhD
Reader in Epidemiology and Public Health
Dr Elina Hyppönen MSc MPH PhD
Professor in Ophthalmic Epidemiology
Professor Jugnoo Rahi MSc PhD FRCOphth
Senior Lecturers
Dr Helen Bedford BSc MSc PhD FFPH FRCPCH
Dr Mario Cortina Borja BSc MSc PhD
Dr Xiayi Ke BSc MSc MSc PhD
Dr Patricia Tookey BA MSc PhD MFPHM
Dr Angie Wade BSc CStat MSc PhD ILTM
Honorary Senior Lecturers
Dr David Elliman FRCPCH MFPHM
Dr Elizabeth Miller BSc MB BS MFPH FRCPath
Dr Angus Nicoll CBE MSc FRCP FFPHM FRCPCH
Dr Sandy Oliver BA PhD
Lecturers
Dr Marco Geraci MSc PhD (from December 2010)
Dr Claire Thorne BA MSc PhD

Administration 2010

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Deputy Director, Education and Theme Leader, Infection and Immunity
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Director of Clinical Research and Development
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Director of the Clinical Research Adoptions Committee and Deputy Director, Clinical Research and Development
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Theme Leader, Cancer (from April 2010)
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Theme Leader, Cardiorespiratory Sciences
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Theme Leader, General and Adolescent Paediatrics
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Theme Leader, Neurosciences and Mental Health
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Theme Leader, Population Health Sciences
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Nuffield Professor of Paediatric Surgery
Professor Agostino Pierro MD FRCS (Eng) FRCS (Ed)
Director of the UCL Institute of Global Health
Professor Anthony Costello MA MB BChir FRCP FRCPCH FMedSci
Institute Manager, UCL Institute of Child Health
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Head of Research and Innovation
Dr Lorna Gibson PhD
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Secretary
Ms Justine Abbott BA(Hons) MBA MSc

Working with UCL Business PLC (UCLB)

UCLB is responsible for the management and exploitation of intellectual property (IP) arising from both the UCL Institute of Child Health (ICH) and Great Ormond Street Hospital (GOSH).

Through IP protection, proof of concept funding, leverage of translational grant funding and partnership with industry, our work with UCLB aims to maximise the positive social, health and economic benefits of ICH and GOSH discoveries. Some of the highlights from this review period are listed below.

- UCLB and the National Centre for Young People with Epilepsy signed a commercialisation agreement with Special Products Limited in preparation for the marketing of their buccal midazolam epilepsy treatment as a licensed medicine. This treatment was developed with Professor Brian Neville and Dr Rod Scott.
- UCLB evaluated eight new inventions arising from ICH and GOSH discoveries.
- UCLB filed two patents: the first on a marker that predicts response to anti-inflammatory therapies for arthritis (Professor Lucy Wedderburn) and the second on a maternal blood spot screening test for Down's syndrome (Professor Lyn Chitty and Dr Kevin Mills).

For additional information please contact
Dr Chris Williams, UCL Business PLC
T 020 7679 9000
E c.williams@uclb.com
www.uclb.com

UCLB Business

Four-year-old Vincent loves his fluffy dressing gown. He is a patient on Elephant Ward, part of our oncology unit, and has recently had a bone marrow transplant, so he is not allowed out of his room for a while. But his dad keeps him busy with games and DVDs.

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

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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.

Please visit www.ucl.ac.uk/ich/research-ich/research-and-development or www.gosh.nhs.uk for an online version of this review.

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

Bengali
অনুরোধ করলে নিম্নলিখিত ঠিকানায় থেকে এই লেখার অনুবাদ, বড় অক্ষর, ব্রেল বা অডিও বিবরণ পাওয়া যাবে।

English
Translations, large print, Braille or audio versions of this report are available upon request from the address above.

French
Traductions disponibles sur demande à l'adresse ci-dessus. Des versions en gros caractères, en braille ou audio sont également disponibles sur demande.

Polish
Tłumaczenia są do uzyskania na żądanie pod podanym powyżej adresem. Dokumenty w formacie dużym drukiem, brajlem lub audio są także do uzyskania na żądanie.

Punjabi
ਇਸ ਰਿਪੋਰਟ ਦੇ ਤਰਜਮੇ, ਅਤੇ ਇਹ ਰਿਪੋਰਟ ਵੱਡੇ ਅੱਖਰਾਂ ਜਾਂ ਬ੍ਰੇਲ ਵਿਚ, ਜਾਂ ਸੁਣਨ ਵਾਲੇ ਰੂਪ ਵਿਚ ਹੇਠ ਲਿਖੇ ਪਤੇ ਤੋਂ ਮੰਗ ਕੇ ਲਏ ਜਾ ਸਕਦੇ ਹਨ।

Somali
Turjubaan ayaa cinwaanka kor ku qoran laga heli karaa markii la soo codsado. Daabacad far waa-wayn, farta indhoolaha Braille ama hab la dhegaysto ayaa xittaa la heli karaa markii la soo codsado.

Tamil
பெரிய அச்சில், இந்த அறிக்கையின் மொழிபெயர்ப்புகள்,பெரய்லி அல்லது ஒலி பதிப்புகள் விண்ணப்பித்தால் கீழ்கண்ட விலாசத்தில் கிடைக்கும்

Turkish
Talep edilirse yukarıdaki adresten çevirileri tedarik edilebilir. Talep edilirse, iri harflerle, Braille (görme engelliler için) veya sesli şekilde de tedarik edilebilir.

Urdu
گزارش کرنے پر یہ رپورٹ ترجمے، بڑے حروف کی چھپائی، بریل یا آڈیو پر درج ذیل پتے سے حاصل کی جا سکتی ہے۔