University of Southampton

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ADVANCING LIFE SCIENCES

INSTITUTE FOR LIFE SCIENCES

SPOTLIGHT ON
The IfLS leadership team

NEWS AND FEATURES
Developing the next generation of interdisciplinary researchers

PUBLICATIONS
A sample of research outputs

FOUNDING MEMBER OF THE RUSSELL GROUP

WELCOME

Front cover and page 29: Human patient-derived liver ductal cell organoid (cell membranes outlined and nuclei counterstained in green).

Image credit: Joshua Green Jenkinson and Dr Nicole Prior

It is a great pleasure to write this introduction for the 2024 Annual Report for the Institute of Life Science (IfLS). The importance of interdisciplinary research relevant to healthcare and the wider life sciences continues to strengthen.

The IfLS represents a strategic investment by the University of Southampton to ensure that we remain at the forefront of this critical and exciting area of research. In our 2022 strategy we identified "Engineering better Health" as a strategic theme for the University, and the Institute is vital to the delivery of this, bringing together researchers and expertise in biology, medicine, computer science, mathematics as well as engineering and the physical sciences.

We have also supported this by recently initiating a strategic hiring campaign under the same theme. The IfLS is core to the delivery of this ambition. This builds on its past track record of initiating and fostering successful internal and external partnerships in diverse fields including imaging, dementia, ageing and musculoskeletal health.

I hope that you enjoy learning about the latest progress in the projects and programmes coordinated by the IfLS and look forward to its continuing success.

Professor Mark Spearing
Vice-President (Research and Enterprise)
University of Southampton

The Institute for Life Sciences is one of the University's four strategic interdisciplinary research institutes with a remit to bring together expertise from across the University to tackle society's challenges in life sciences.

We have an established reputation for working collaboratively, taking disruptive approaches through interdisciplinary team science and building networks with interdisciplinary collaborations at the heart of the Life Sciences community. We do this by supporting researchers from a range of disciplines to work together to broaden scientific opportunities and address key issues in health, society, and enterprise, aligned with the University's triple helix strategy.

This year's Annual Report highlights the breadth and expertise in interdisciplinary life sciences at Southampton and focuses on collaborative engagement towards real-world impact. This is an era of rapid advances across scientific disciplines, where advances in computation find ways of making an impact in life sciences research.

The IfLS continues to support researchers harnessing new technologies and developing new methodologies and insights into interdisciplinary life sciences and their benefits to society, economy and technology. I hope you enjoy reading about the case studies highlighted in this report.

Professor Max Crispin
Director of the Institute for Life Sciences
University of Southampton

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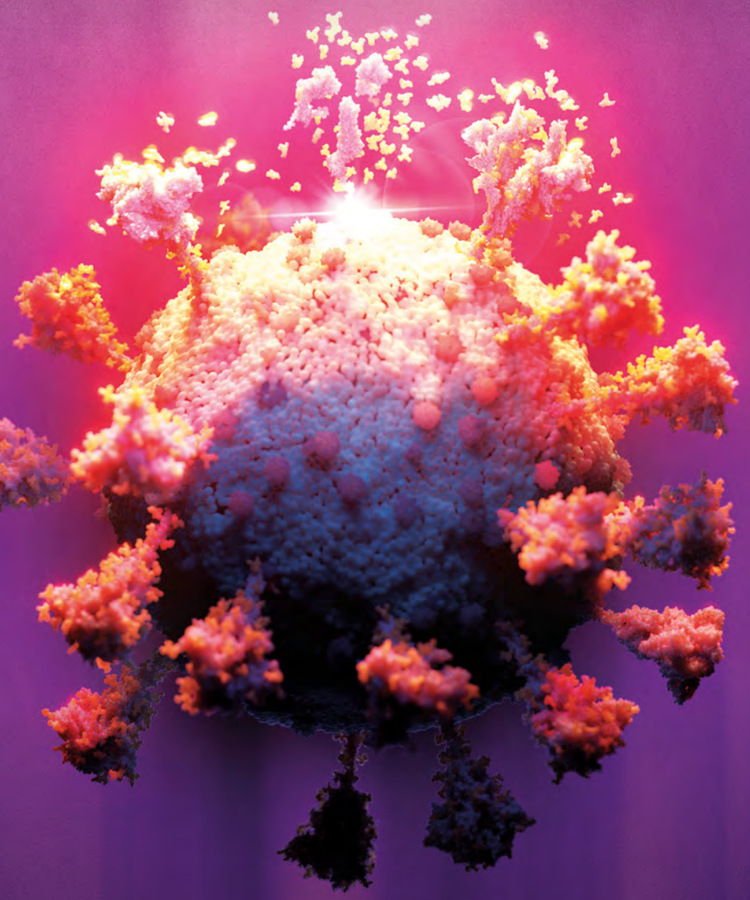
Find out more:
www.southampton.ac.uk/life-sciences

SPOTLIGHT ON THE LEADERSHIP TEAM



The Institute for Life Sciences (IfLS) leadership team has recently been refreshed with the appointment of a new Director Professor Max Crispin, and Professor Mary Barker as the second Deputy Director, alongside Professor Hywel Morgan. Here we talk to them about their backgrounds, what they bring to the IfLS and what the future holds.

Find out more:
www.southampton.ac.uk/life-sciences

PROFESSOR MAX CRISPIN DIRECTOR OF THE IFLS

Max Crispin, Professor of Glycobiology, was appointed as Director of the IfLS just over a year ago.

He said: "Southampton has a culture of interaction and is good at interdisciplinarity. When I moved here in 2017, one of my research programmes, supported by Against Breast Cancer, was in cancer therapies. Coming here really helped catalyse that research through collaboration with preclinical expertise in the Centre for Cancer Immunology. My team has since developed wider collaborations with colleagues in Medicine, Chemistry and Biological Sciences.

"When the IfLS Directorship arose, I was at a stage where I wanted to give something back to the University, to demonstrate the importance of interdisciplinarity. I had seen the value of these interactions in my own research and was well-placed to champion this way of working.

"This first year as Director has been hard work but magnificent. My priorities have been to review our strategic themes, expand activity in areas where we haven't previously engaged strongly, such as arts, humanities and social sciences, identify ways in which we can add value to the experience of interdisciplinary PhD students, and to celebrate the success of our members."

Left: Mechanisms of SARS-CoV-2 Inactivation using UVC laser radiation, Devitt G et al. (2024) *ACS Photonics* 11 (1), 42-52
Image created by Nexu Science Communication

REFLECTING CURRENT AND FUTURE CHALLENGES

"Right now, there are huge opportunities to develop interdisciplinary life sciences but none of us know exactly what the future holds," said Max. "So, we need to be flexible and ready to seize and respond to opportunities when they emerge."

The IfLS has refreshed its strategic research themes to reflect changes in the scientific landscape. Themes are identified where the University has excellence, capacity to grow through interdisciplinary collaboration, one or more enthusiastic leaders, and a strong alignment with societal need, routes to funding and potential for impact. A notable example of previous success is the National Biofilms Innovation Centre, which began life as the Biofilms and Microbial Communities theme, and has subsequently evolved into an internationally prominent programme of research, translation and innovation.

"One area where we aim to diversify our engagement is adolescent health. There is an urgent need to focus on the challenges faced by young people, particularly following the pandemic; our new Deputy Director, Professor Mary Barker, is leading this theme, and working productively with other Institutes."

Another area of focus is the application of data science within life sciences challenges. Max said, "The advancement of computer science, artificial intelligence and machine learning have the potential to transform the future of life sciences. We have access to many data sets that can help inform our research, but one individual academic or discipline doesn't have all the skills required to exploit this information. We need to bring together experts across disciplines to harness the possibilities of these large and complex data. Southampton's interdisciplinary culture means that researchers are very well-placed to innovate, which we can achieve by being flexible, ambitious and bold in establishing new collaborations."

Southampton has the capacity, skills and culture to contribute to the many grand challenges facing society. The IfLS welcomes proposals for new strategic themes from its members.

ADDING VALUE THROUGH FUNDING AND SUPPORT

The IfLS has supported almost 100 interdisciplinary PhD students since 2011. Each postgraduate researcher has two or more supervisors from different disciplines and works on a project that requires the integration of skills from more than one field. Working at the interface between disciplines can be inherently uncomfortable and challenging, but yields great benefits over time.

This year the Institute organised an insightful full day workshop for interdisciplinary researchers from across the University, to develop skills in communicating across discipline boundaries.

Max said, "It was a pleasure to meet our next generation of researchers and I hope the workshop sowed the seeds of future friendships and research collaborations."

Researchers have also benefited from exploring early ideas for translation and enterprise in the company of a panel of experienced business mentors, including Royal Society Entrepreneur in Residence, Dr Kam Pooni. The IfLS has hosted a Royal Society Entrepreneur since the scheme started in 2017 and hopes to welcome a new entrepreneur in 2025.

CELEBRATING SUCCESS

"Our definitions of success are not just about the University, but also the wider economy and health of the region. The Institute is keen to celebrate the achievements of our community and share case study highlights through the IfLS LinkedIn group," said Max.

Find out more:
www.southampton.ac.uk/life-sciences

PROFESSOR HYWEL MORGAN
DEPUTY DIRECTOR OF THE IFLS

Deputy Director Professor Hywel Morgan, Professor of Bioelectronics, has been involved in the IfLS strategic direction from its inception. He was among the driving forces who demonstrated the impact that an interdisciplinary institute could create at the University.

Hywel moved to Southampton in 2003 to work at the interface of engineering, medicine and life sciences. He said: "At the time there was very significant activity going on at the University to try and drive interdisciplinary research across a number of areas. Several University Strategic Research Groups (USRGs) had been established that connected researchers from different disciplines who wanted to work together.

"I was collaborating with colleagues in Medicine and Biological Sciences and we all wanted to develop a more formal institute for life sciences that built on the success of the USRGs.

"We recognised there was a huge opportunity to bring people together from different disciplines."

The IfLS was established in 2011 with Professor Peter JS Smith as founding Director. As one of the deputy directors, Hywel helped Peter deliver the strategy and expand interdisciplinary life science activities across the University.

Hywel said: "It has really established itself as a catalyst to add value to the faculties in terms of life sciences research and enterprise. Over the years, it has enabled lots of new research activities and impact.

"But at the heart of the IfLS are the members and that is reflected in the collaborative nature of the Institute."

Over the last year the refreshed IfLS leadership team has reflected on the Institute's strategic direction.

Hywel said: "We need to be thinking about how we generate impact, and not just economic impact. We also need to focus on enabling opportunities to translate our research into the clinic and the marketplace."

Hywel has co-founded two spinout companies since he joined Southampton, and also received an MBE for his role in developing the PeRSo respirator hood during the COVID-19 pandemic.

He said: "The delivery of research is vitally important, but translating it into the marketplace or clinic is equally important. Our link with the NIHR Southampton Biomedical Research Centre is crucial as they use unique tools, facilities and world-changing expertise to take new discoveries, treatments and technologies into the clinic.

"We need to ensure that our academics are enabled to take their excellent research and translate it into impact for the benefit of patients, society and the economy. This is not just about creating spinout companies but also about how they can influence local government and public leaders.

"Interdisciplinarity is important at Southampton. Many new discoveries have been made by people who are interacting and learning from other disciplines. They are forging a path where they have taken ideas from one discipline and used them to understand another discipline. This has spawned a lot of new ideas and new research.

"In Engineering, we have developed tools that have enabled many of the discoveries that we now see in Medicine and Biological Sciences. The tools have been invented by people working at the interface of interdisciplinary science.

"The IfLS has had a great influence on the many academics at Southampton who are working at that interface. We are proud to have established an environment in which these interdisciplinary groups can be supported and flourish."

Right: Image credit Professor Hywel Morgan

"The IfLS has contributed significantly to regional investment and regional networks, but there's also a growing awareness of how the life sciences research that is carried out at Southampton can be translated into benefits for social and economic good."

PROFESSOR MARY BARKER
DEPUTY DIRECTOR OF THE IFLS

New Deputy Director Professor Mary Barker has a background and training as a psychologist and has been at Southampton for the last 30 years where she has worked as a member of the Medical Research Council Life Course Epidemiology Centre, Medicine at Southampton, and now has a split post with Health Sciences and Environmental and Life Sciences at Southampton.

Mary became IfLS Deputy Director a year ago and is also IfLS Theme Lead for Adolescent Health.

She first became involved with the IfLS six years ago following a conversation with founding IfLS Director Professor Peter JS Smith about the significance of her research in adolescent health. As a result of this a new IfLS theme was created.

Mary said: "Adolescent health is a naturally interdisciplinary topic. My work involves public health and social sciences, but we also collaborate with arts, humanities, engineering and electronics and computer science.

"Adolescence is fundamentally a period of biological growth, so it has deep roots in biology, nutrition and health, but also in psychology and sociology. With young people now forming 25 per cent of the global population, there has been a growing investment in young people's health and in our understanding of the significance of young people's health for the future of the UK and the world.

"As Deputy Director of the IfLS, I see my role as reaching out to parts of the University such as arts and humanities and social sciences. These are areas where the IfLS hasn't traditionally had a lot of members and we want to expand that membership and engage with those groups.

"Human behaviour is complicated and if we want our scientific research to have maximum impact on human health, we need to understand how people work and interact, and what motivates and engages them. We can't pursue life sciences research without taking into account the important impact of our social and cultural lives."

Mary is committed to strengthening the IfLS' engagement with the other University interdisciplinary research institutes – the Sustainability and Resilience Institute, the Southampton Marine and Maritime Institute and the Web Science Institute – as well as broadening its civic engagement.

She said: "The Institute's wider remit includes facilitating the growth of the University's civic engagement and social good.

"For a long time, the IfLS has contributed significantly to regional investment and regional networks, but there's also a growing awareness of how the life sciences research that is carried out at Southampton can be translated into benefits for social and economic good.

"Our research in adolescent health, combined with that emerging from the IfLS theme of Global Health are areas where we can implement this process of translation.

"We can build on the strong relationship we have with the public health teams in Southampton and across the region to support communities that we know have the greatest need."

Find out more about the Institute for Life Sciences:
www.southampton.ac.uk/life-sciences

www.linkedin.com/groups/8554247/

OUR THEMES

The IfLS has recently refreshed its strategic research themes to reflect the changes in the scientific landscape. These themes represent Southampton strengths and growth potential in interdisciplinary life sciences research and the aim is to build these collaborative communities towards grant success and impact.

If you are interested in contributing to these interdisciplinary challenges please contact IfLSAdmin@soton.ac.uk

Image credit: Professor Hywel Morgan

Find out more:
www.southampton.ac.uk/life-sciences

ADOLESCENT HEALTH

"The excitement and creativity we generate by bringing together colleagues from across the University is a huge benefit to our research to promote health and wellbeing with and for young people. Game designers, geographers, biologists, clinicians, anthropologists and psychologists, amongst many others, all contribute to life science research with young people."
Professor Mary Barker
IfLS Theme Lead for Adolescent Health

The IfLS Adolescent Health theme focuses on the physical and mental health and wellbeing of adolescents to ensure healthy futures for young people and future generations.

Nearly a quarter of the world's population is adolescents and as a 'relatively healthy' group, their needs have been neglected in the past.

But adolescence is a specific phase of the life course when profound physiological, social and psychological development takes place, and this can determine their health and wellbeing trajectories for rest of their life. It is common knowledge that we are currently experiencing a huge increase in young people seeking help for mental health problems.

In order to create healthier populations, we need to better understand and meet the needs of these young people. IfLS researchers are working with young people to create healthier, more hopeful futures through a variety of initiatives including public health interventions to improve diets and increase their physical activity, engaging with health care decision-makers and providers, and supporting sick young people to manage their conditions as well as they can.

BROAD INTEREST OMICS (BIOMICS)

"We are at a very exciting time in interdisciplinary life science research. The potential for novel discovery using omics technologies combined with the computer science methodologies is immense."
Professor Sarah Ennis
IfLS Theme Lead for BiOmics

Advances in technology have generated unprecedented amounts of data that can be exploited to understand human disease and inform its clinical management.

Researchers in the IfLS BiOmics theme are interrogating and interpreting the data to further our understanding of disease by providing insight into the complex interplay of molecules within organisms.

Working closely with NHS partners, they are using omic technologies to evaluate DNA (genomics), RNA (transcriptomics) and proteins (proteomics).

Using mathematical modelling, machine learning and other algorithms to extract information and patterns from large data sets, researchers are studying the unique processes that take place within cells that can lead to disease or poor health outcomes in humans and help track changes in the environment.

These results are then being used to answer clinical questions in areas such as cancer and autoimmune and respiratory diseases. They are translating their findings into novel techniques for clinicians to treat their patients, make predictions about prognosis and drug responsiveness.

INTERDISCIPLINARY MUSCULOSKELETAL HEALTH:

MYAGE

Our activity in interdisciplinary musculoskeletal health combines two networks MyAge and FortisNet.

"Ageing is clearly a pressing societal problem. MyAge and the UK Ageing Networks are powerful tools to help unite the national intellectual capability, bring the problem into sharp focus and enable the UK to generate solutions."
Professor Peter J S Smith
MyAge Director

MyAge: *Muscle resilience across the life course: from cells to society* is one of 11 UK Ageing Networks funded for three years by UK Research and Innovation. Led by the IfLS, together with colleagues from Birmingham, Nottingham and Imperial, this collaborative network has worked to address muscle loss in later life by promoting interdisciplinary collaboration in the UK and with international partners.

Professor Carolyn Greig, from Birmingham, said: "The UKRI government funding body has set us a challenge to transform ageing research in the UK. Ageing is a 'wicked' problem which is best addressed through a collective effort – bringing different disciplines together – such as biology and social science. We're also working alongside stakeholders within industry, policy and public contributors to help find ways to improve the health of older people, as well as reaching out and connecting with experts internationally."

A major output is the MyAge Roadmap setting priorities for future muscle ageing research.

http://dx.doi.org/10.5258/SOTON/P1128

FORTISNET

"Our musculoskeletal health has great impact upon our general health, ability to work and to be socially engaged, especially as we age. FortisNet aims to nurture collaborations and to translate musculoskeletal health research in order to make a real difference to patients' lives."
Dr Claire Clarkin, Dr Nicholas Fuggle and Professor Alex Dickinson
IfLS Theme Leads for FortisNet

The global population is living longer bringing about a number of challenges, especially in musculoskeletal health.

FortisNet is an interdisciplinary research network of clinical, academic and industrial partners that aims to develop products and services to transform musculoskeletal health across the life course.

Launched by the University in 2016, FortisNet has fostered collaborations with other UK universities, health care providers, patients and industry to develop new technologies, interventions and practices that will have a positive effect on people's lives.

It brings together experts in regenerative medicine, physiology, engineering, orthopaedics, prosthetics and orthotics, rehabilitation and assistive technologies, epidemiology and clinical trial design and much more.

Its current aims are:

- to improve lives by developing treatments and medical devices
- to address gender, ethno-cultural and other inequalities
- to work responsibly with stakeholders and data for co-production, in the treatment and prevention of musculoskeletal disease.

Find out more:
www.southampton.ac.uk/life-sciences

FUTURE DIAGNOSTICS

"The Future Diagnostics theme aims to build capability that can rapidly drive innovation from discovery to delivery. The research will exceed beyond a narrow definition of diagnostic tests used by healthcare professionals to aid diagnosis, to include measurements and monitoring for screening, surveillance, treatment optimisation and wellbeing."
Dr Al Edwards
IfLS Theme Lead for Future Diagnostics

Innovation in diagnosis, prognosis, monitoring, precision medicine and analytics is central to tackling many health grand challenges and has been identified as a major priority area for the UK by policy makers and expert stakeholders.

Future diagnostics can benefit many areas of healthcare. Testing innovation can reduce the harm and cost of viral and bacterial infections, help prevent and manage cardiovascular disease, and is vital to advance cancer treatment by identifying which patients will benefit from the latest therapies. Artificial intelligence (AI) and data science will benefit from more frequent and accurate measurements that can help clinicians detect disease, differentiate between similar conditions, select the most suitable treatments and monitor responses to treatment.

The IfLS Future Diagnostics theme encompasses Southampton research excellence across the full lifecycle from fundamental science driving discovery through to real-world evaluation of new products.

It aims to bring together strengths in diagnostics-related research, support researchers at all levels, secure external investment, connect end-users with researchers to drive diagnostic innovation.

GLOBAL HEALTH

"Global health transcends borders and offers opportunities to advance health equity and drive transformative change, ensuring that communities irrespective of location can thrive."
Professor Shane Norris
IfLS Theme Lead for Global Health

Today's global health landscape is characterised by both significant achievements and pressing challenges.

Non-communicable diseases like heart disease, diabetes, and cancer are now the leading causes of death, driven by ageing populations, urbanisation, and lifestyle changes putting a strain on health systems, particularly in low- and middle-income countries.

Infectious diseases such as tuberculosis, malaria, and HIV/AIDS persist as major public health threats, especially in regions with limited access to prevention and treatment.

Mental health is gaining recognition as a critical global health issue, yet services remain underfunded and inadequately integrated into healthcare systems, particularly in lower-income areas.

Climate change also poses an escalating threat, exacerbating the spread of vector-borne diseases, food insecurity, and displacement.

Despite advancements in medical research and technology, access to these innovations remains uneven, with significant gaps between high- and low-income countries.

To address these interconnected challenges, a holistic and multi-sectoral approach is needed.

The IfLS Global Health theme supports researchers from across the University in having a greater global health impact in two critical areas:

- addressing non-communicable disease risk factors (particularly mental health) of young people in Africa working with the IfLS Adolescent Health theme;
- managing multiple chronic conditions as more and more adults often have several morbidities.

INTERDISCIPLINARY DEMENTIA AND AGEING CENTRE (IDEAC)

"The brain is enclosed in the skull and inaccessible, so we need to use tools that are advanced, multiple and from different disciplines such as mathematics, physics and engineering. IDeAC is leading the way internationally in uncovering the causes of the disease, identifying ways of preventing it and developing exciting new avenues for treating dementias."
Professor Roxana Carare and Professor Chris Kipps (UHS)
IfLS Theme Leads for IDeAC

IDeAC is a network bringing together experts from the University of Southampton and University Hospital Southampton to increase the understanding of dementia and brain ageing and how to treat and care for people with these conditions.

These experts include basic scientists, clinicians, health and social care delivery researchers, epidemiologists, imagers, mathematicians, and computing and data scientists. They focus on four themes within the field of dementia research and care:

- basic and translational science
- diagnosis and prognosis
- clinical trials and therapeutics
- dementia care and prevention

Their work also includes exploring the influence of early-life factors in the development of dementia and cognitive impairment and ways that these risk factors may be reduced to prevent dementia development.

SOUTHAMPTON IMAGING: LIGHT FOR LIFE

"New technology advancements lead to new insights and the most exciting advances are at the interface of disciplines. Biophotonics and imaging truly builds on these pillars of interdisciplinary research philosophy and hopes to enable new discoveries and novel applications across life sciences including health and environment."
Professor Sumeet Mahajan
IfLS Theme Lead for Light for Life

Imaging has become an essential part of scientific research, from biomedical sciences to engineering to optoelectronics and has led to fundamental developments in life sciences.

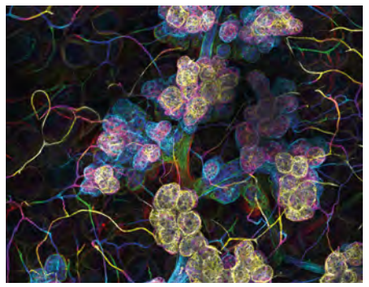
Scientists in the IfLS Light for Life theme are developing and using ground-breaking imaging techniques to solve some of society's biggest challenges in areas including dementia, musculoskeletal health and cancer, infectious diseases, respiratory medicine, environmental health and climate change.

They are using imaging across scales, from molecules to humans, to create novel tools and technologies to advance life science research and enable the provision of state-of-the-art facilities.

These imaging techniques can provide a diversity of information from the nano to the macroscale allowing our researchers to push the boundaries in areas such as disease diagnostics and risk prediction, reproductive health, cancer immunology, biofilms and anti-microbial resistance, regenerative medicine, drug discovery, plant and marine biology.

Members are collaborating with scientists across the University, as well as with medical physicists and clinicians at University Hospital Southampton and with industry and national and international partners.

STEM CELLS AND ORGANOIDS



"Research using stem cells and organoids is an exponentially growing field globally, enabling experiments in human-based systems that were previously infeasible. The establishment of this new IfLS theme reflects the expansion of this field here in Southampton exemplified by the strategic recruitment in this area and drive towards precise bioscience."
Dr Nicole Prior and Dr Salah Elias
IfLS Theme Leads for Stem Cells and Organoids

Research on stem cells and organoids (3D cell models of organs) has expanded greatly over past decades, drawing together developmental biology, regenerative medicine, disease models and computational modelling.

This IfLS theme brings together expertise and people from Biological Sciences, Medicine and STEM. Their aim is to gain new insights into basic biology and translational medicine, with a vision of enhancing our understanding of the underpinning of human health and disease.

They will be actively forming a collaborative network to produce new grant proposals and highlight externally the work in this field being done across the University.

IfLS researchers have established new collaborations in stem cells and organoids research, towards patient-derived tissue research; created new opportunities to enhance human stem cell and organoids research focusing on access to patient tissue; developed the Stem Cell and Organoids theme conference that focused on the importance of early career researchers; and supported Southampton's Southern Stem Cell and Regeneration Network (SSCRNet) that highlights and connects colleagues with high profile external researchers.

QUANTITATIVE BIOLOGY

"Our ability to turn observations into predictions is at the core of quantitative biology. By leveraging mathematical, statistical, and computational techniques, we can transcend what we observe, enabling us to anticipate behaviours and patterns that have yet to be discovered."
Dr Owen Rackham
IfLS Theme Lead for Quantitative Biology

As the resolution and scale of observing biological systems increase, biological sciences are rapidly evolving into a data science. This transformation brings new challenges, fosters novel collaborations, and reshapes our approach to life sciences research.

Scientists within the IfLS Quantitative Biology theme are at the forefront of integrating data-driven insights with theoretical models to uncover hidden patterns and predict the behaviour of biological processes across scales, from molecules to entire ecosystems. These models are not only enhancing our understanding of the natural world but also equipping us to intervene and manipulate these systems in predictable ways.

Achieving success in quantitative biology is inherently interdisciplinary. The IfLS theme unites physicists, chemists, mathematicians, clinicians, computer scientists, and more, blending their expertise to bridge the gap between theoretical predictions and experimental data. This synergy is crucial for tackling some of biology's most pressing challenges, from unravelling the complexities of cellular behaviour to forecasting ecological changes and advancing personalised medicine.

Above left: Stem cells and mouse mammary gland development
Image credit: Dr Salah Elias

Join our community
Please get in touch if you are interested in finding out more or have research interests that fits within any of the IfLS themes.

Contact us on
IfLSAdmin@soton.ac.uk

GROWING STRENGTH IN DATA ANALYSIS – AT THE HEART OF LIFE SCIENCES

The IfLS is supporting growth in research using data analysis, mathematical models and computational simulations to understand biological systems and relationships.

Dr Owen Rackham with PhD students Disha Mehta and Morien Nicholas

Find out more:
www.southampton.ac.uk/life-sciences

SOUTHAMPTON WORLD EXPERT COMBINING AI AND COMPUTATIONAL BIOLOGY

Computational biology has triggered an explosive growth in our understanding of stem cells and our ability to use them for disease modelling, regenerative medicine and drug discovery. Potential applications include immunotherapy and degenerative disease.

IfLS member Dr Owen Rackham is an international expert in the application of machine learning in cell reprogramming and disease-gene association. He leads an interdisciplinary team working on combining artificial intelligence (AI) with high-throughput biology to identify key regulators that can control cell fate to find novel routes for cell conversion or targeted therapies.

Owen, who is an Associate Professor of Systems Biology, believes that as well as opening up new therapies, the field has the potential to change the process of scientific discovery from 'guided trial and error at the bench' to a new kind of 'biological engineering'.

INSPIRED BY A NOBEL PRIZE WINNER

Owen's interdisciplinary work was inspired by Shinya Yamanaka and his Nobel prize-winning discovery. Our bodies are comprised of at least 400 different cell types that all begin life as embryonic stem cells. These stem cells are pluripotent, meaning they have the potential to develop into any cell type (except the amniotic sac and placenta). Shinya discovered that if you introduce just four regulatory genes to any of these different cells, they revert to their pluripotent state.

The discovery suggested that any cell type could be converted into another cell type, opening up a wide range of therapeutic possibilities.

As part of his PhD, Owen streamlined this process by creating an algorithm to predict what genes would need to be used in a cell type, depending on what properties you wanted it to have. Partnering with a clinical collaborator at Monash University, in Australia, the algorithm was validated, published and spun out into a company – Mogrify, that is turning the technology into cell and gene therapies, addressing needs in ophthalmology, otology, metabolic and other areas of degenerative disease.

Owen's research allows the techniques to be applied to a wide range of fields. He said: "The computational infrastructure that I need for working on cancer is not very different to the computational infrastructure needed to work on ageing. "The privilege of being on the computational side is the opportunity to work on a problem with people with different expertise and understandings, and being exposed to new problems and new ways of thinking."

IMPACT ON HEALTHCARE RESEARCH

Owen's work is being implemented across a range of healthcare research including:

Combatting cancer – Owen is working with Sean Lim, Professor of Haematology and Translational Immunology, in Medicine, to develop new immunotherapeutic approaches to blood cancer. When cancer occurs, the body's immune system tries to attack it using T cells. But eventually these T cells become exhausted and can no longer attack the tumour in the same way. Owen's technologies are being used to convert the exhausted T cells back into non-exhausted T cells, enabling the patient's immune system to continue to attack the tumour. This research is supported by PhD student Dishha Mehta whose work is accelerating the depth of the collaboration.

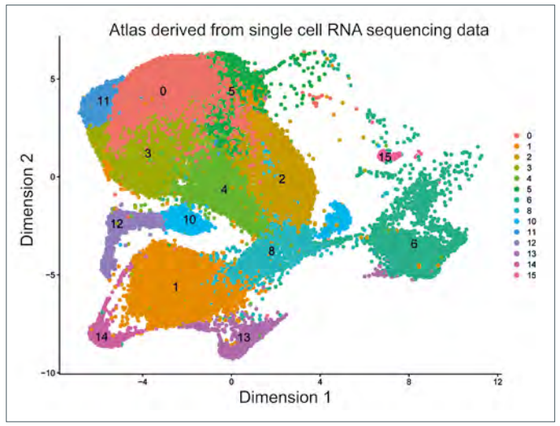
Reversing ageing – Owen is working with IfLS colleague Dr Nicole Prior, a Lecturer in Stem Cell Biology, to combine his computational techniques with her ground-breaking work on organoids. Organoids are laboratory models of organs grown from stem cells that give scientists an opportunity to view how organs form. This research generated from IfLS networking events and provides new insights on human development and disease, and a way to see how drugs interact with them. Together Owen and Nicole are trying to understand the underlying molecular mechanisms that cause changes in how our organs function as we get older. Owen said: "By making a micro-organ from a young donor, and one from an old donor, we can use my methods to work out how to make the old micro-organ look more like the young micro-organ, and provide a model for identifying and evaluating drugs that can reverse the effects of ageing."

Understanding early human development – Owen is working with colleagues in Biological Sciences and Medicine on an IfLS-funded study combining the use of organoids and AI to study early development to understand infertility and early developmental disorders. Building these organoids could provide the solution to enabling large-scale screening for effective drug treatments that can then be used to train a generative AI model to make predictions about how to treat patients. Owen said: "One of the powerful things about the generative approach is that it gives us the possibility to work on parts of biology that may otherwise be difficult to do."

THE FUTURE

Owen is now extending his research to try and develop an entirely novel cell type. A Biotechnology and Biological Sciences Research Council (BBSRC) Pioneer award is enabling him to use AI to extend the universe of cell types, and IfLS PhD student Morien Nicholas is supporting the research.

He said: "The longer-term vision is that we try to make new cell types that are as useful as they possibly can be for treating a disease."



An atlas of different cell types sampled from from the immune system of multiple individuals. This atlas is constructed as a large and representative baseline with which to compare patients' cells, to better understand the effects that a tumour can have on our immune system and to predict how to reverse them.

FUNDING BOOST FOR SOUTHAMPTON STRUCTURAL BIOLOGY

IfLS member Professor Ivo Tews is leading a £2m Biotechnology and Biological Sciences Research Council (BBSRC) grant that is boosting structural biology at Southampton and across the UK.

Biomolecules such as proteins and DNA are vitally involved in immunity and diseases and it is important to study their atomic structure to understand how they work.

ADVANCES IN STRUCTURAL BIOLOGY

Artificial intelligence (AI) is providing exciting new possibilities to predict the three-dimensional structure of biomolecules and is driving rapid progress in the field.

Insights from studying the 3D structures of these molecules are transforming our understanding of living systems and our ability to use that understanding to promote health and use in biotechnology.

But capturing molecular function requires more than a snapshot. Crucially scientists need to see the biomolecules move but this is a challenge.

The rapidly evolving field of experimental structure determination has recently been boosted with the BBSRC grant that was developed and coordinated by Ivo, as Chair of the Collaborative Computational Project No. 4 (CCP4), a UK-led international collaboration that aims to develop, test, distribute and promote software for macromolecular crystallography. Macromolecules in biological and medical sciences include proteins such as antibodies and enzymes. To study their structure in atomic resolution, they can be analysed by a technique called macromolecular crystallography.

The network includes partners from the Diamond Light Source, the Research Complex at Harwell, the MRC Laboratory of Molecular Biology Cambridge, and the Universities of Liverpool, Newcastle and York.

PUSHING BOUNDARIES

The project will push boundaries in the computational analysis of experimental data and create molecular movies that allow researchers to observe molecules in action.

At Southampton, protein structure determination and X-ray crystallography are well embedded techniques. Significant IfLS support included instrumentation for crystal imaging that has enabled Ivo to permeate interdisciplinary research programmes across the University with structural biology techniques.

His expertise, together with the University's macromolecular crystallisation facility, will be instrumental in Southampton's part of the project that is addressing the current challenges in the computational aspect of macromolecular crystallography.

It aims to improve structure analysis from both X-ray diffraction and electron diffraction to extend the utility of macromolecular crystallography.

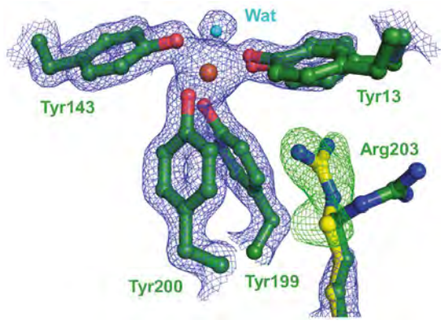
Ivo said: "We propose to harness the power of deep learning approaches into the process of structure determination and validation for proteins, carbohydrates, DNA and RNA, as well as complexes containing one or more of these molecule-types. With a multi-technique, multi-data and multi model approach, we aim to deliver a dynamic description of the macromolecules that is closer to life, and therefore more descriptive of their function."

HAVING AN IMPACT ON NOVEL APPROACHES TO CANCER

One of Ivo's flagship projects is a collaboration with colleagues in Medicine to discover new information about how our immune systems could help to improve cancer treatment. Working with immunologists, chemists and computer experts across the University, as well as Diamond Light Source and the University of Hamburg, the team found that the body's antibodies could identify and fight cancer cells more effectively with specific modifications to fire them up.

They believe the findings could pave the way to improve antibody drugs that target cancer as well as auto-immune diseases.

Professor Max Crispin, IfLS Director, said: "Structural biology is the epitome of interdisciplinary research, and the range of applications is extraordinary. The new techniques being pioneered will secure an exciting future for structural biology in the UK and beyond."



The work by Ivo Tews allows visualising dynamic processes in proteins. Shown here is a change in conformation, allowing a marine bacterium to bind different states of iron (distinguished by charge). This is important for survival in the seas.

"These interdisciplinary, dynamic approaches have given us new information about how to engineer antibodies to deliver stronger immune responses."

Professor Mark Cragg
Centre for Cancer Immunology


Professor Mahesan Niranjan

USING MACHINE LEARNING TO UNDERSTAND COMPLEX DISEASE

"It is not just about providing a data analysis service but putting the effort into really understanding what the biological or medical question is. This properly integrated working is both challenging and rewarding." said Professor of Electronics and Computer Science Mahesan Niranjan (Niranjan).

Numerous IfLS networking opportunities, studentships and seed funding over the last decade have enabled Niranjan to develop a significant interdisciplinary research portfolio at the interface of computing and biology.

Niranjan's research focuses on the use of machine learning (ML) to help understand complex diseases and over the years he has collaborated with a range of colleagues on a variety of research projects. He not only builds models of accurate predictions, but also focuses on quantifying the related uncertainty.

He said: "What you learn about the data you are studying from the difference between systematic and random errors can be very informative.

"Through small scale seed funding, PhD studentships, conferences and meetings and informal introductions, the IfLS has created an environment in which interdisciplinary research in life sciences is facilitated. This benefits the wider life sciences research community."

INITIAL IFLS SUPPORT

One of Niranjan's first projects came about through an IfLS introduction, and involved PhD students, Yawwani Gunawardana, and Ashley Heinsen, co-supervised with former colleague Dr Topher Woelk.

He said: "One of the problems we studied was about gene expression and how it is regulated at different levels – the transcriptome and proteome. The former is easy to measure, but most biological action is at the level of proteins. We tried to establish how ML models could be built to explain one level of measurements from the other. By modelling at the interface, and analysing errors made by the models, we could identify which proteins are regulated systematically differently from others."

A DECADE OF RESEARCH

Over the last decade Niranjan's research has benefited from the many networking opportunities and studentships that the IfLS offers. He has collaborated on a variety of different projects, such as fracture risk, COVID-19, and tuberculosis (TB).

Fracture risk – Niranjan and Dr Nicholas Fuggle, from Medicine, were awarded IfLS pump-priming funding to combine ML and imaging techniques to develop computer technologies to help diagnose people with osteoporosis and reduce their risk of fracture.

COVID-19 – the IfLS facilitated a joint project between Niranjan and Professors Tom Wilkinson and Diana Baralle in Medicine that analysed which treatments would be most beneficial to COVID-19 patients.

Protein biomarkers in tuberculosis (TB) – the IfLS catalysed the collaboration between Niranjan, Professor Paul Elkington and Dr Hanna Schiff, from Medicine, to identify protein biomarkers that can distinguish active pulmonary TB cases from healthy individuals and patients with other respiratory infections.

Find out more:
www.southampton.ac.uk/life-sciences

IFLS STUDENTSHIPS

Niranjan says IfLS studentships have been crucial to this interdisciplinary research. He said: "PhD students are central to a scholarship. Academics' time is drawn in so many directions, whereas a PhD student can focus on systematically carrying out the required research over three and a half years, and often draw us into territory we have not been before.

Niranjan is currently jointly supervising IfLS PhD student Alex Thomas, together with Professor Benjamin Macarthur, in Mathematics, and Dr Julian Legg, from the University Hospital Southampton, on his research to understand sleep apnoea in paediatrics.

Niranjan said: "Adults can attend a sleep lab where instruments take measurements while they sleep to understand what is going on. But with small children you can't do that, so we are using ML to try and infer the underlying the cause of their issues by working with simple measurements such as measuring the oxygen saturation in their blood and their blood pressure."

CURRENT RESEARCH

In his latest research, Niranjan is working with NIHR Clinical Lecturer in Interventional Radiology Dr Ganesh Vigneswaran looking at the success of a procedure to treat prostate problems – prostate artery embolization (PAE) that blocks an artery supplying blood to the prostate so that the prostate is stopped from growing.

He said: "We are creating a model that will assess routinely collected patient data to predict whether PAE is likely to be appropriate and successful for a particular patient. This tool could offer a time critical opportunity for clinical decision-making and patient counselling in urology and interventional radiology clinics."

EMBEDDING INTERDISCIPLINARITY IN EDUCATION

Niranjan believes that interdisciplinary training and education is essential to making real progress in these exciting areas. He said: "It is often not just a question of researchers from different disciplines teaming up, they also need to develop an appreciation of the scientific questions, the experimental limitations and the modelling assumptions.

"Southampton offers an excellent interdisciplinary environment to collaborate in research across discipline boundaries, which is beneficial to researchers across the University. But with respect to education there are structural challenges that need to be overcome."

SHEDDING LIGHT ON BRAIN ACTIVITY

IfLS researchers are exploring a variety of technologies including stem cells, organoids and the metabolic environment to shed light on a range of neurodegenerative diseases.

UNDERSTANDING THE TRIGGERS FOR NEUROLOGICAL DISEASES

Seed funding from the IfLS has enabled Southampton researchers to explore why certain proteins 'misfold' in the brain leading to a range of neurodegenerative diseases including Alzheimer's and Huntington's.

In many neurodegenerative diseases there are accumulations of normal proteins that are found in all human brains. But for reasons that are unclear these proteins start to misfold and become sticky, depositing inside nerve cells and causing different diseases.

The research has been led by Amritpal Mudher, a Professor of Neuroscience and Phil Williamson, a Professor in Biochemistry and Molecular Biophysics. Amrit said: "These are normal proteins so there is something in the environment of the cell that prompts this protein to change its shape, become sticky and deposit. This process can't be reversed and the deposit starts to become toxic.

"We are not clear why this happens although we do have some clues from the age and genetic background of individuals. For example, Alzheimer's disease does not affect young people, which suggests that there is something about the younger brain that makes it more resilient, or that there is something in the older brain that makes it more vulnerable.

"Additionally, we know that individuals who inherit some genes are more likely to get the disease. Until we find out what triggers this change, we can't really stop that process occurring."

To understand why this misfolding occurs, scientists need to watch the proteins misfold and deposit in as close an environment to the brain environment as possible.

Amrit said: "By using genetic tools from the brains of fruit flies we can express disease-related human proteins that will deposit over time and then we can look at the cellular environment to see how it changes when the protein misfolds.

"This will allow us to identify factors that help the protein misfold and then we can target these factors therapeutically to prevent this process.

"The IfLS seed funding really helped us to achieve this.

"The research was able to pick up the way that certain proteins folded and deposited in the braincell. It also enabled us to test a specific diet to incorporate a non-perturbing tag into the proteins as they were being synthesised to more easily visualise them as they were misfolding.

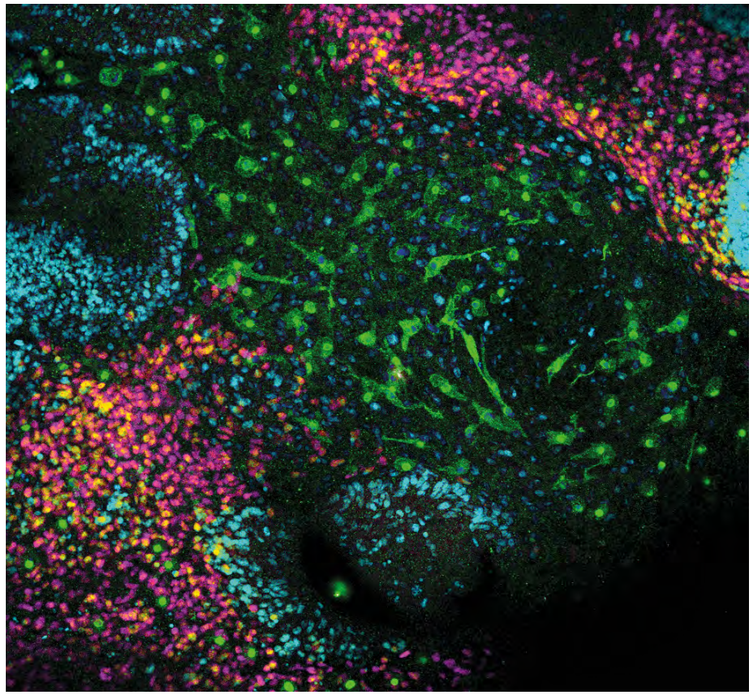
Amrit said: "These outcomes could have multiple effects for patients and medical care beyond one particular disease. By understanding the cellular environment that promotes different proteins to misfold, we can work out what triggers this process in different diseases and can start to look at ways to intervene and stop these triggers."

The team was awarded a Leverhulme grant to continue investigating how the cellular environment influences protein folding and aims to apply to the Alzheimer's Society to investigate how changes in the brain metabolome influence the onset and progression of Alzheimer's disease.

IfLS pilot grants have enabled the researchers to work together to get to this point. Amrit said: "The IfLS support provided the opportunity for me to work with other disciplines to understand what triggered these changes."

Right: A mature day 41 cerebral organoid showing the successful integration of microglia (green) and distinct brain regions

Below left: Professor Phil Williamson and Professor Amritpal Mudher



CREATING BRAIN ORGANOIDS TO UNDERSTAND ALZHEIMER'S

IfLS scientists are creating laboratory-grown brain tissue known as organoids to be able to decipher the role of inflammation in Alzheimer's disease.

Professor of Neuroimmunology Diego Gomez-Nicola, Lecturer of Stem Cell Biology Dr Nicole Prior and Postdoctoral Researcher Andrew O'Connor have been awarded Higher Education Innovation Funds (HEIF) from the IfLS to grow brain organoids from induced plutipotent stem cells (iPSCs) that have the potential to develop into almost any cell type.

These organoids can then be used to understand how cells work in the brain or how specific molecules could be important for disease relevant functions.

Diego's research interests are in inflammation in the brain, while Nicole's research is in creating organoids predominantly from the liver. Together they have been able to create these brain organoids that include microglia – the main immune cell in the brain.

They have been partnering with Alzheimer's Research UK's Oxford Drug Discovery Institute (DDI), with whom Diego has collaborated with for a number of years and who have an interest in inflammation in the brain in the context of dementia.

Diego said: "By creating these brain organoids, we will be able to generate further collaborations and grant applications, including those with the Oxford DDI."

The IfLS seed funding enabled Diego and Nicole to work together for the first time and allowed Nicole's team to move into a new area of research. She said: "Previously we have developed organoid systems from stem cells you would find in the body but in this research we have started with pluripotent stem cells which is new for us. It has given us an opportunity to break into a new research space."

Diego said: "We are creating a complex system that contains all the cells that reside in the human brain and is connected and interacting in a meaningful way. This will enable us to understand how cells communicate with each other in health and in disease. This understanding can be used to test potential drugs or whether a particular mechanism is important for a disease."

Nicole added: "These brain organoids allow us to know exactly where the drug is going and what mechanisms it is altering. The same sample can be observed over a number of days.

Diego said: "This project is part of the growing interest and expertise in Southampton around advanced cellular models. One of the IfLS strategic themes focuses on Stem Cells and Organoids and the IfLS has invested in developing collaborative activity. By creating these capabilities, we can try and develop even more complex organoids and organoid-based models."

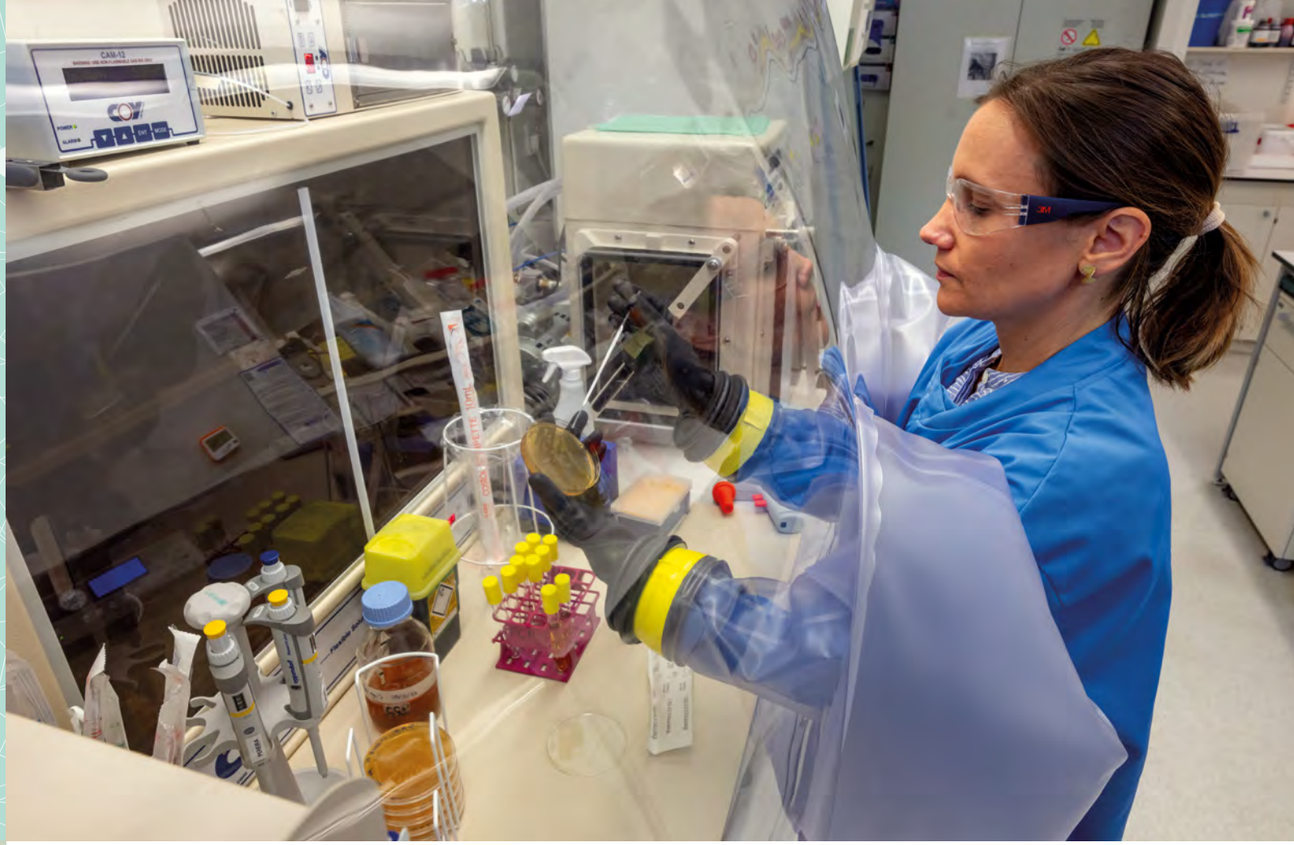
> "This project is part of the growing interest and expertise in Southampton around advanced cellular models."
>
> **Diego Gomez-Nicola**
> Professor of Neuroimmunology

Nicole added: "This pump priming funding enabled us to produce the initial data that will be transformative in bringing human brain organoids to Southampton. Having this in-house expertise will unlock a multitude of possibilities for neuroscientists in the University."

The IfLS funding has also supported early career researcher Andrew to move into a new area of. He said: "Brain organoids is an area that I was interested in, so this project has been a great opportunity for me to work on and improve my skillset."

USING INNOVATIVE TECHNOLOGIES TO IMPROVE HEALTHCARE

Novel technologies are being used by IfLS researchers to repair bone fractures with bubbles and understand how pharmaceutical drugs interact in the gut.



CAN BUBBLES BE USED TO HELP REPAIR BONES?

Tiny bubbles could lead to a new way of treating bone fractures, thanks to Southampton research supported by the IfLS.

The project, led by Nick Evans, a Professor of Bioengineering, is exploring how these bubbles can be used to transport drugs to the site of a broken bone that has failed to heal on its own.

Bone fractures are a significant public health problem – costing the UK around £2 billion each year – and with one in three people breaking a bone in their lifetime.

Most will get better on their own – but every fracture carries the risk of failing to heal properly. This complication, known as a non-union, occurs in between five percent and 10 percent of cases, and can cause severe pain and disability and often lead to surgery.

The economic cost of bone fractures is expected to increase as the number of older people in the UK grows, meaning there is an urgent need for new non-invasive and cost-effective treatments.

Nick worked with colleagues from the University of Oxford on the study that recruited patients from University Hospital Southampton (UHS). Eight patients with broken bones in their upper arms had microbubbles injected into their bloodstream. These microbubbles are routinely used in ultrasound imaging.

The results show that these small bubbles can be successfully carried to the site of a fracture where a pulse from an ultrasound device is then used to pop the bubbles open, releasing a drug at the target location.

Nick said: “Our early results are extremely promising. We have shown that microbubbles get to bone fractures and might be used to deliver drugs to the right place at the right time. The method could offer a less invasive alternative to surgery for non-union fractures in the future.

“IfLS funding has helped us understand in the lab how these microbubbles interact with human bone cells and has forged a new interdisciplinary collaboration between us and colleagues working on cutting edge imaging techniques.”

Simon Tilley, a Consultant Orthopaedic Surgeon at UHS who was involved in the study, said:

“The concept of using microbubbles to aid bone fracture healing is huge. Non-union fractures are devastating for individuals and represent an enormous cost to society. Reducing the amount of time it takes to heal these fractures would have major benefits for patients and hospitals alike.”

The team is now looking at how many microbubbles reach the fracture site and if this amount changes depending how long the bone has been broken. They are also testing new microbubble formulations to see what other drugs they could carry.

IMPROVING HEALTH AND WELLBEING USING MOLECULAR IMAGING

Innovative molecular imaging by IfLS researchers is shedding light on the interaction of pharmaceutical drugs with the gut microbiome and the repercussions this has on health and wellbeing.

These new insights can be used to develop microbiome-targeted interventions to reduce adverse drug reactions and improve drug efficacy.

The human gastrointestinal tract is inhabited by trillions of microbes, single-celled organisms that play a vital role in health and wellbeing by shaping and modulating our immune systems. There can be up to 1,000 different species of microbe in each person’s gut.

Pharmaceutical drugs can affect these microbes resulting in a number of issues, including reducing the amount of drug absorbed into the intestine, decreasing or increasing the effectiveness of the drug, and causing drug side effects. They can also inhibit the growth of gut microbes.

Dr Fatima Pereira, from Biological Sciences, together with Dr Sam Thompson and Professor Sumeet Mahajan, from Chemistry, have developed a new approach to monitor these drug-microbiome interactions non-invasively and in situ to identify which of the 1,000 different types of microbes are affected.

The team is using an innovative combination of click-chemistry, spectroscopy and cell sorting.

Firstly, the drug is synthesised to create a ‘molecular spy’ to help detect which microbes are directly interacting with the drug. The microbes are then examined using spectroscopy to ensure the drug is interacting and working. Then a dye is added (click-chemistry) that lights up the drug inside the cells.

Fatima said: “This allows us to separate the microbes that are interacting with the drug from the microbes that are not. This rapid high-throughput approach can be used to screen many healthy individuals and patients for microbiome-drug interactions and could be extended to a range of therapeutic drugs.

“The identification of key microbes interacting with pharmaceuticals will enable the development of precision microbiome-based interventions to improve drug efficacy and reduce adverse effects.”

Fatima credits the IfLS for supporting the research. She said: “This is a truly interdisciplinary project that was funded and brought together by the IfLS. Our results are very exciting and will hopefully result in better patient outcomes by enhancing the effectiveness of current treatments.”

Opposite page: IfLS PhD student Sam Sloan measuring microbubble oscillations

Top: Fatima Pereira manipulating gut microbiome samples in an anaerobic chamber

Left: Former IfLS PhD student Dr Rose Bannister with Dr Sam Thompson

UNDERSTANDING LIVING SYSTEMS

First-ever 3D image of a complete giraffe placenta, enabling groundbreaking mathematical modeling of whole organ function and advancing our understanding of life sciences and evolutionary biology

IfLS researchers are exploring the full range of living systems. Here we share how researchers are investigating the development and role of the placenta, and how reef corals are helping regenerate bones.

Find out more:
www.southampton.ac.uk/life-sciences

Left: The interdisciplinary team of Dr Anandita Umapathy, Dr Davis Laundon and Professor Rohan Lewis examine 3D placental images to uncover new insights into placental efficiency and reproductive success across species

INVESTIGATING PLACENTAL EFFICIENCY

Southampton interdisciplinary research into the development and role of the placenta has recently been awarded two Biotechnology and Biological Sciences Research Council (BBSRC) grants worth over £1m. The research team credits historical and ongoing support from the IfLS with helping to achieve this success.

The two projects focus on the functioning of, and evolution of, the placenta. One is exploring the efficiency of the placenta in delivering food to the fetus, while the other is looking at how the placenta protects the fetus from medicines and other harmful substances, such as diesel nanoparticles.

The research involves a collaboration between Professor Rohan Lewis, from Medicine, Dr Bram Sengers, from Bioengineering, and Dr Neil Gostling, from Biological Sciences. Postdoctoral researcher Dr Davis Laundon is research co-investigator on the first project and Dr Anandita Umapathy, from Medicine, and IfLS-funded PhD student Lois Brewer are involved in the second.

Rohan said: "We have supervised a number of IfLS-funded PhD students, we are all members of the IfLS and we have had IfLS support in developing collaborative interdisciplinary research for more than a decade.

EXPLORING THE EFFICIENCY OF THE PLACENTA

The first project is looking at the placenta's efficiency in transferring food from the maternal blood to the fetus and in cleaning the fetal blood.

Rohan said: "If you look at a heart or a liver in different mammals, they are all pretty similar, but placentas are wildly different. By understanding why they are different, we can understand what is fundamentally important for successful reproduction, particularly in humans. This could give us new insights into pregnancy diseases and their potential treatment.

"This project is studying placentas that contain finger-like projections called villi. These placental villi evolved independently, in humans (primates) and in cows and sheep (hoofed animals). In humans, placental villi are in direct contact with maternal blood, but in cows and sheep, these villi are embedded in maternal tissue and have no contact with maternal blood, which means nutrients have to travel further to reach the baby.

"Using new 3D imaging approaches from our colleagues in the Biomedical Imaging Unit and the μ-VIS X-ray Imaging Centre, we are studying placental structure across multiple scales to try and understand how biology has developed in different ways to be efficient, which could inform novel solutions to engineering problems.

"We are also working with the Rosalind Franklin Institute to develop machine learning and AI approaches to help us analyse and segment the huge amount of data we are getting."

Neil said: "My research has focused on evolution in the earliest 'animals', mammals, birds and dinosaurs; and recently, thanks to the IfLS, the Dodo. This research involved working with μVIS. By scanning the braincase of a spinosaur we were able to produce an endocast (a model of the skull, the brain and associated soft tissue) and deduce its sensory capabilities, and by scanning a Dodo skeleton we will be able to analyse the gait of this iconic bird. It has been fascinating to apply these skills to the placenta and all its diversity."

Bram added: "Applying mathematical models to placental structures will allow us to explore how different structures affect the function of the placenta in a way that the images alone cannot."

IDENTIFYING CHEMICALS THAT CROSS THE PLACENTA

The second project is trying to understand the types of chemicals that cross the placenta most effectively.

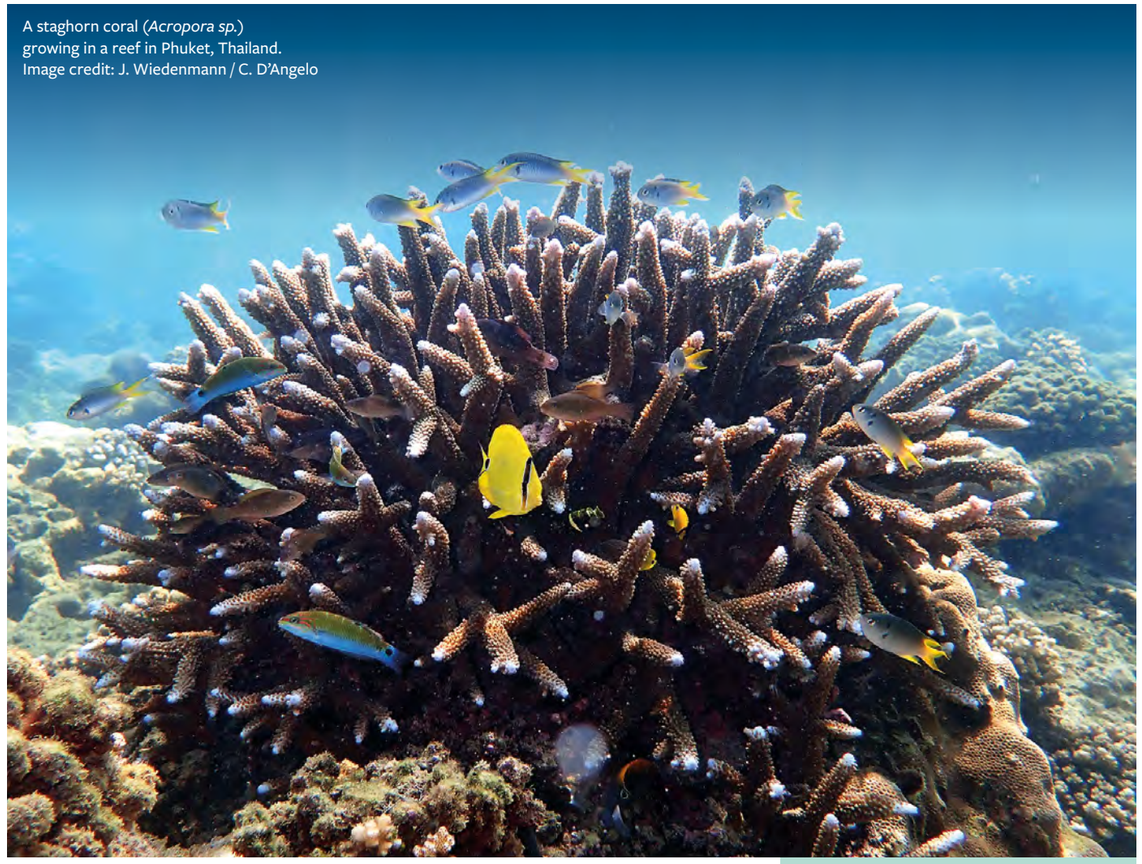
New microscopes have enabled the discovery of tiny (nanoscale) structures in the placenta. These tiny holes – called trans-syncytial nanopores – can be 2,000 times thinner than a human hair but are big enough for many medicines and environmental toxins to pass through.

"This discovery changes the way we think about the placental barrier, from a solid wall between the mother and the fetus to something more like a fine sieve," said Rohan.

"Once we have a better understanding of the nanopores, future studies will be able to assess their impact on fetal health."

Bram added: "By modelling the placental transfer of drugs, we were able to show that many substances were diffusing across the placenta which led us to discover the nanopores. The current project will develop computer models to help predict how novel drugs and toxins cross the placenta.

"Using the knowledge this project will generate, scientists could design medicines more likely to travel through the nanopores and reach the fetus. Lois' IfLS-funded PhD project is an example of this, where we are modelling how antibodies such as IgG transfer across the placenta. These are important for the baby's immunity but could also deliver antibody-based drugs to the fetus or protect the fetus from antibody-based drugs that the mother needs."



A staghorn coral (*Acropora sp.*) growing in a reef in Phuket, Thailand.
Image credit: J. Wiedenmann / C. D'Angelo

REGENERATING BONES WITH REEF CORALS

Southampton interdisciplinary research between Ocean and Earth Sciences (OES) and Medicine is exploring the use of reef corals in bone regeneration.

Led by Professor Jörg Wiedenmann, from the Coral Reef Laboratory in OES, the IfLS-funded project is investigating how the physical properties of reef coral skeletons can be manipulated to produce the best specimens for use in bone regeneration.

Jörg, Associate Professor Cecilia D-Angelo, Dr Loreto Mardones-Velozo, Raphaela Gracie and George Clarke, from OES, collaborated with Professor Jon Dawson, Dr Janos Kanczler, Dr Roxanna Ramnarine Sanchez and Aya Ben Issa, from Human Development and Health, in Medicine.

Jörg said: "We found that the growth of hard corals is strongly influenced by the levels of nutrients in the water and the density and microstructure of the coral skeleton changes as we manipulate the water's nutrient levels.

"This enables us to customise the make-up of the coral skeletons for applications in medical research."

THE MEDICAL CHALLENGE

Sometimes parts of bones need to be replaced due to accidents, diseases or surgery. If a gap is over a certain size, then the bone won't regenerate naturally.

This gap needs to be bridged and ideally a material needs to be used that will subsequently allow the regeneration of the natural bone material.

"We are proud of the totally sustainable environment that we have created at Southampton. We can grow corals in-house, so we don't need to take them from the field where they are a threatened species."

Professor Jörg Wiedenmann

Associate Professor Cecilia D'Angelo in the Coral Reef Laboratory preparing corals for experiments

Find out more:
www.southampton.ac.uk/life-sciences

"This has been a fascinating interdisciplinary exploration into the exciting potential of corals as new, sustainable graft materials for bone repair and regeneration."

Professor Jon Dawson
Professorial Fellow of Regenerative Medicine

"Coral skeletons are well suited for this purpose as they have a porous structure like natural bone, they are very hard yet still have a degree of flexibility," said Jörg. Currently, research relies mostly on coral material in the form in which it grows in the natural environment.

Jörg added: "Bone cells need to be able to migrate into the pores of the replacement material and we can now deliberately manipulate the size and shape of these pores to find the ideal structure."

The interdisciplinary team used the IfLS seed funding to see if they could improve the acceptance of the coral skeleton by bone cells in the regeneration process.

Roxanna added: "We were excited to see that there are indeed pronounced differences in the speed of growth and survival of human bone marrow cells on coral skeletons that were grown in different nutrient environments."

Jörg said: "At Southampton, we are in a unique position where we have researchers working on corals and researchers working on bone regeneration. This provided a great opportunity to drive this research forward."

RESEARCH IMPACT

There are two key findings of the research. Firstly, the confirmation that the coral skeleton can be manipulated to make it more advantageous to bone regeneration applications.

Secondly, that aquarium-grown coral skeletons can be used as potential bone regeneration material.

Jörg said: "We are proud of the totally sustainable environment that we have created at Southampton. We can grow corals in-house, so we don't need to take them from the field where they are a threatened species. The capacity to simulate different nutrient environments for long term experiments sets us apart from other coral reef research groups across the globe."

IFLS SUPPORT AND FUTURE RESEARCH

Jörg says the seed funding has been a great facilitator in getting this project going.

He added: "It has also enabled early career researchers, PhD students and technicians to be involved to carry out the essential investigations."

The team is now planning to apply for an Engineering and Physical Sciences Research Council (EPSRC) grant for future research.

The experimental aquarium facility of the Coral Reef Laboratory at Southampton's Waterfront Campus

USING DATA TO DRIVE DEVELOPMENTS IN PATIENT CARE

With the explosion in the generation of data, IfLS researchers are using various data technologies to drive forward patient care.

Professor Christine Currie, Dr Carlos Lamas Fernandez, Dr Alexandra Hogan and Dr Edilson Arruda

USING AI TO ASSIST OESOPHAGEAL CANCER TREATMENT

Artificial intelligence (AI) and machine learning could help multidisciplinary teams (MDTs) become more efficient in deciding the best treatment for patients with oesophageal cancer.

The project is a collaboration between NIHR Clinical Lecturer in Interventional Radiology Dr Ganesh Vigneswaran, Professor of Gastrointestinal Surgery Tim Underwood, Professor of AI Gopal Ramchurn, and Associate Professor in Translational Epigenomics Dr Zoë Walters.

Surgical Registrar (Wessex) Doctoral Candidate in Cancer Sciences Navamayooran Thavanesan (Nav), who is jointly funded by the IfLS and University Hospital Southampton, is playing an instrumental role in the research.

Oesophageal cancer is complex, with treatment options often depending on a myriad of factors. Every week MDTs meet to decide on the best course of treatment for cancer patients and these MDTs are becoming massively overloaded with cases.

Ganesh said: "MDT meetings can last four hours and it's important to ensure consistent decisions for equitable care. Using basic ML algorithms, we modelled team decision-making and predicted treatment outcomes for patients based on their individual circumstances.

"In today's era of data-driven healthcare, the benefits of machine learning are only beginning to be utilised. However, with the growing power of machine learning, and AI as a whole, there has rightly been a parallel concern about responsibility and transparency. In critical decisions like cancer treatments, it's vital to interrogate the model to understand how the AI model is making predictions."

Nav has been central in collecting, curating and modelling data on which the final models have been developed.

Ganesh said: "Nav has been integral to this research. He started off not knowing any ML and has really taken the bull by the horns. He has collected and coded all the data from about 1,000 Southampton oesophageal cancer patients from the last 10 to 12 years."

Nav added: "This project has been an amazing experience, made possible for me through the IfLS studentship programme. As a clinician having come into this sphere with no prior background in coding or statistical modelling, the challenge has been significant but incredibly rewarding.

"The guidance and support of my supervisors has been key and I have greatly enjoyed being part of research that has potential to translate to the bedside. It has the potential to effect a paradigm shift in the cancer MDT space."

Later this year the AI model will be deployed in the background (shadow mode) for the upper gastrointestinal MDTs in Southampton. This will enable the AI decisions to be compared to the decisions made by the MDTs and see whether they align.

PhD Student Nav Thavanesan is researching AI applications in cancer care at Southampton's Innovation for Translation Research Group

Ganesh said: "It will be exciting to see how effectively our AI tool will work running in the background. This will enable us to identify any problems and build trust in the tool with clinicians and patients.

"We are also testing our models on an external dataset from Oxford University Hospitals and the early results show that it is performing well across different regions, demonstrating its potential for use across the NHS.

"We have been approached by clinicians from different specialities who are interested in deploying a similar approach to other cancers and MDTs."

IMPROVING THE FLOW OF PATIENTS THROUGH HOSPITAL

A new partnership between Salisbury NHS Foundation Trust (SFT) and the University to improve the flow of surgical patients through the hospital has been created with funding from the IfLS.

Led by Christine Currie, Professor of Operational Research at Southampton, and Dr Alexandra Hogan, Consultant Anaesthetist at SFT and Professor (adjunct), in Health Systems and Workforce, in Health Sciences, Southampton, the project is an exciting programme of collaborative research exploring how operational research can drive improvements in peri-operative management.

The NHS Trust serves approximately 270,000 people, many with complex surgical needs. Similarly to the experience of many NHS Trusts post-pandemic, SFT has faced significant challenges with rising waiting lists, limited resources, increasing demand and workforce fatigue. SFT contacted the University to see if they could work together to help bring new perspectives to the issues involved.

Peri-operative flow (the time from a patient being booked for surgery until they have had the operation and are discharged back to primary care) involves multiple stages and there is potential for considerable variability between individuals' experiences.

The Salisbury Operational Research Track – Improving Together (SORT-IT) programme was established and brought together academics from across the University with representatives from SFT's nursing, medical, managerial and administrative staff.

The team was awarded Higher Education Innovation Funds (HEIF) by the IfLS to carry out a scoping project to develop the understanding and gather the information to identify potential future research and bids for further funding.

Christine said: "Many hospitals have a problem with operations being cancelled very close to, or on the day of the operation. This can happen for a variety of reasons including their fitness for surgery having changed since their pre-assessment, theatres over-running or recovery rooms being full. At this late notice it is difficult to find patients to take their place and it can also be frustrating for the patient whose surgery has been cancelled.

"We have been working with the team at SFT to find out what existing data we can access, what processes they already have there and what the key issues and bottlenecks are.

"We have gathered information across the whole peri-operative period, so that we can really understand the flow that the patients go through.

"The team has used computer simulation and statistical analysis to provide some preliminary results that help to understand the behaviour of the system. This is the first step in what we hope will be a lot more collaborative projects between us and SFT."

> "The development of the SORT-IT programme has helped us to look for new ways to understand what can often appear to be insurmountable problems."
>
> **Dr Alexandra Hogan**
> Salisbury NHS Foundation Trust

Alexandra added: "The development of the SORT-IT programme has helped us to look for new ways to understand what can often appear to be insurmountable problems. We are discovering just how important it is to ensure that every part of the complex peri-operative pathway, no matter how small or brief (from how operating lists are constructed, to who enters timing data in theatre, to the time it takes to return a patient to the ward), is examined in great detail to identify where we can improve.

"Working alongside University colleagues allows us to bring academic rigour to this work, ensuring that the methodology we apply is of a high standard. In a sense we are learning together about how to adapt and thrive in a currently challenging environment where there is very high service demand, and to ensure excellent patient care. SFT is excited to see where SORT-IT takes us next".

MAKING A POSITIVE DIFFERENCE IN THE COMMUNITY

The IfLS is committed to ensuring its interdisciplinary research helps the wider community by establishing links with partners and industry.

INTERDISCIPLINARY RESEARCH TO PREVENT PRESSURE ULCERS IN VULNERABLE POPULATIONS

Early Career Researcher Dr Silvia Caggiari has been leading an IfLS-funded project exploring the potential of using artificial intelligence (AI) to improve the function of a dynamic seating system to automatically detect postural changes whilst sitting, promote postural support and reduce the risk of damage to skin and soft tissue of vulnerable individuals.

Silvia, a Senior Research Fellow in the Skin Sensing Research Group (SSRG), has been working with Professor Peter Worsley, from SSRG, Dr Ying Ye, from the Institute of Sound and Vibration Research, and Aergo Health company, an enterprise based in London.

Immobility represents one of the main risk factors for pressure ulcer (PU) development, with regular repositioning representing a preventative strategy. PUs typically affect individuals with a restricted ability to move and impaired sensation.

They often require a large range of equipment including specialist seating devices to provide postural support and alignment for their pelvis, trunk and head. However, the majority of the available systems offer a static support with generic cushions that are unable to adapt user positions or allow movements, limiting the possibility of actively self-managing their own posture. This can contribute to more time spent in the same position that can lead to development of PUs.

Aergo Health developed a dynamic seating system that incorporates a closed loop of six pressure sensitive air cells for posture correction and pressure relief. The company was founded by Sheana Yu who has lived with scoliosis (curvature of the spine) and was passionate about innovating smart solutions for managing posture.

Silvia and the team have investigated biomechanics, physiological and dynamic characteristics including vibration and noise to evaluate the performance of the Aergo device.

Silvia said: “During my PhD, I developed an AI algorithm to detect posture and mobility while lying and sitting. The algorithm uses pressure data to identify how often people move and what postures they adopt.

“Working with Aergo Health has provided a fantastic opportunity to evaluate how powerful the algorithm is and how the chair responds to movements.

“It can tell when a person has been in the same position for a prolonged period of time and adjust it so that they are in a different position.”

Pete added: “The Skin Health Research Group has a long history of working with bed and chair manufacturer industry on developing smart interfaces to help them optimise their devices.

“This project has been a great opportunity to establish a long-standing collaboration between mine and Ying’s research groups and work together towards scientific and technical innovations in seating for pressure ulcer prevention. We have also been able to establish an affiliation with commercial healthcare partner Aergo Health and open up opportunities to support further research and knowledge exchange activities.”

The new technology could be translated to a variety of clinical situations and settings and will target a wide range of vulnerable patients to be able to self-manage their posture and mobility.

Silvia has already presented her research at a number of conferences, was part of the European Pressure Ulcer Advisory Panel Group to contribute to clinical guidelines for pressure ulcer prevention, and has been awarded an Engineering and Physical Sciences Research Council (EPSRC) Business and Commercialisation Fellowship.

EVALUATING THE ROLE OF COBOTS IN HEALTH AND SOCIAL CARE

Health scientists at Southampton have been collaborating with Hampshire County Council (HCC) to evaluate the deployment of collaborative, exoskeleton robots (or ‘cobots’) across health and social care settings.

Health and social care workers routinely engage in physically demanding tasks such as bending, squatting, lifting patients, and prolonged standing. Despite existing guidelines and training for safe moving and handling, the incidence rate of musculoskeletal disorders (MSDs) remains high in care workers, indicating a pressing need for additional ergonomic solutions like cobots.

Cobots support people who do a lot of moving and handling activity in their work by assisting the user’s movement and promoting movement.

The Council introduced these cobots across some of their health and social care settings to assist care workers’ movements when they are carrying out activities such as transferring service users from a wheelchair to a bed. The exoskeleton protects the upper body by distributing the weight from the back to their legs to other body parts. Southampton student Shilpy Bhat is carrying out a PhD exploring this, complemented by Southampton research led by IfLS member Dr James Gavin, a Lecturer in Musculoskeletal Health.

During two staff engagement events at the council’s headquarters in Winchester, the collaborative team showcased the cobot deployment to HCC staff, discussing the benefits and uses of the new technology. Participants explored potential barriers to using exoskeletons in care settings.

James said: “The aim of the research was to deliver evidence-based guidance for implementing exoskeletons in care environments, potentially benefiting similar settings considering technological adoption. Whilst this project delivers knowledge exchange, Shilpy’s PhD research is driving the evidence-base in adopting cobots in real-life health and social care settings. The findings may also inform broader efforts to address the physical challenges faced by caregivers and assess the feasibility and sustainability of cobot technology in health and social care.”

Shilpy added: “My research is to provide a holistic understanding and insight into the factors influencing the implementation and sustainability of cobots in adult social care.”

James added: “The IfLS support has been absolutely invaluable in enabling this research and in developing guidance and recommendations on the implementation of future technologies (beyond cobots) in health and social care settings. It has also allowed me to link this back into my role as a lecturer by allowing me to involve my undergraduate students in the research.

“It is a great example of the University’s triple helix of encompassing knowledge exchange, research and education.”

> “This project is a great example of the University’s triple helix of encompassing knowledge exchange, research and education.”
>
> **Dr James Gavin**
> Lecturer in Musculoskeletal Health

Top: Dr James Gavin and Olivia Richards working with Catherine Knighton of Hampshire County Council on the implementation of cobot (collaborative robot) technology for health and social care

Opposite page: Image credit: Smart air cushion from Aergo Health

DEVELOPING THE NEXT GENERATION OF INTERDISCIPLINARY RESEARCHERS

The IfLS has co-funded PhD studentships since 2011.

IMPACTING HEALTH BY ANALYSING THE PARTICLES OF AIR POLLUTION

Liam Edgeway

IfLS PhD student Liam Edgeway is working with IfLS members Professor Matt Loxham, Professor Mark Jones, Professor Gavin Foster and Professor Andy Milton to explore the toxicology of shipping-related air pollution.

Liam said: "I am specifically looking at a component of air pollution called particulate matter (PM). These are particles in the air that we all breathe on a daily basis.

"Particulate matter is associated with more than seven million deaths annually worldwide, according to the World Health Organization. An estimated 400,000 of these premature deaths are associated with PM emitted from shipping, therefore, we need to better understand how PM exerts its damaging effects.

"The composition of PM varies depending on its source (cars, planes, ships) and these invariably have different components that require in-depth analysis to understand which components cause negative health impacts and how they do this. In particular, I am interested in the effects of metals associated with PM.

"Particulate matter is often classified based on size – the smallest of these particles, known as ultrafine PM, are around 1,000 times smaller than the width of a human hair. There is no known 'safe level' of exposure for ultrafine PM, and the concentration of these particles in our air is currently unregulated.

"The health effects of air pollution are a global problem and we need to improve the air not only for us but for generations to come. We are researching the effects of the different components of PM so that we can provide a more well-rounded understanding of their effect on biological systems, which will also inform future regulations and policy.

"As an IfLS PhD student I am part of a community where I can engage with people from different fields and understand the new and unique research that is being carried out."

"Liam's research is allowing us to gain new insight into how source-specific components of particulate matter might affect the cells of our lungs, and so how air pollution might damage health. Through working on developing new interdisciplinary methodological insights, he is also adding logistically and intellectually to the work of other researchers in the group, so the value of his studentship is greater than a single project."

Professor Matt Loxham
Supervisor of IfLS PhD student
Liam Edgeway

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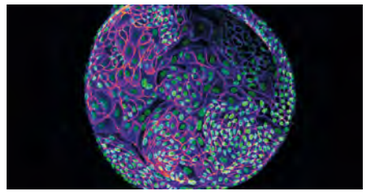
UNDERSTANDING THE CELL FATE OF LIVERS



IfLS PhD student Joshua Green Jenkinson's research uses liver organoids (cell-based models) to understand how cellular metabolism is rewired during cell fate changes and drives liver development and regeneration.

Joshua, who is supervised by Southampton stem cell and organoid expert Dr Nicole Prior and Professor of Biomolecular Medicine Dr Jonathan Swann, said: "The liver is an organ with a wide range of functions from detoxification to the storage of sugars and the production of proteins. It is also notable as the only internal organ in the adult human body capable of regenerating.

"To model liver development and regeneration in the lab we use liver organoids that allow us to model cell fate changes in a controlled environment without confounding signals from the rest of the body.

"We have developed methods using nuclear magnetic resonance (NMR), a technology that is similar to magnetic resonance imaging (MRI), that allows us to measure the metabolites (small molecules in metabolic pathways) and monitor them during liver cell fate changes.

"The research has shown that liver organoids can be cultured in sufficient quantities for analysis and that regenerating and developing liver organoids have a distinct metabolomic profile."

Joshua's PhD is jointly funded by the IfLS and the Gerald Kerkut Charitable Trust. Professor Gerald Kerkut enjoyed a long and distinguished career in the areas of physiology and biochemistry at the University of Southampton.

Joshua is working with colleagues in Chemistry and Medicine and says that this interdisciplinarity has been an indispensable factor in enabling his research.

CREATING 'MINI LIVERS' TO AID DRUG DEVELOPMENT

IfLS PhD student Amanda Gilbert's research focuses on the development of cell models containing the different zones.

Creating an in vitro model containing this zonation could potentially provide opportunities for the development of new treatments for liver disease, generate material for transplantation and improve the toxicity screening of potential drugs.

Amanda's PhD supervisors are Dr Nicole Prior, Lecturer of Stem Cell Biology, and Dr Jonathan West, whose research focuses on the development of high throughput microfluidic approaches for cell and molecular handling.

Amanda said: "The liver is a really complex organ that carries out a lot of functions that are often quite contrasting in nature such as the breakdown of glucose and the synthesis of glucose. In order for these opposing functions to be carried out effectively, they are separated into three different zones.

"Many of the models that are currently used don't take into account this spatial separation. What I am trying to do is alter the nutrients that the liver organoids are exposed to, to create a model that has the functionality of all of the zones. This would provide an improved understanding and give us a better insight into what happens in all the zones and how they interact with one another.

"If we can create this model, it could potentially be used in the drug development industry to screen drugs more accurately and identify if there are any issues at an earlier stage.

"There's a lot of people with liver disease and being able to apply my research to quite a prevalent cause of ill health would be very rewarding.

"Being part-funded by the IfLS has been an incredible opportunity for me. I have presented at an IfLS poster session where I connected with Dr Bram Sengers, from Bioengineering. Together we have developed a computational model of my cultures to predict how nutrient availability changes in different conditions, allowing us to refine the experimental conditions being tested in our cultures."

Dr Nicole Prior, Amanda Gilbert and Joshua Green Jenkinson

IFLS PUBLICATIONS 2023 – 2024

A sample of publications from our interdisciplinary postgraduate students and early career researchers

Institute for Life Science (IfLS) PhD students work on novel interdisciplinary research projects with support from a supervisory team across the project disciplines. This supportive interdisciplinary environment, shaped by the IfLS and host faculties, creates a unique training and development experience for the next generation of leaders.

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