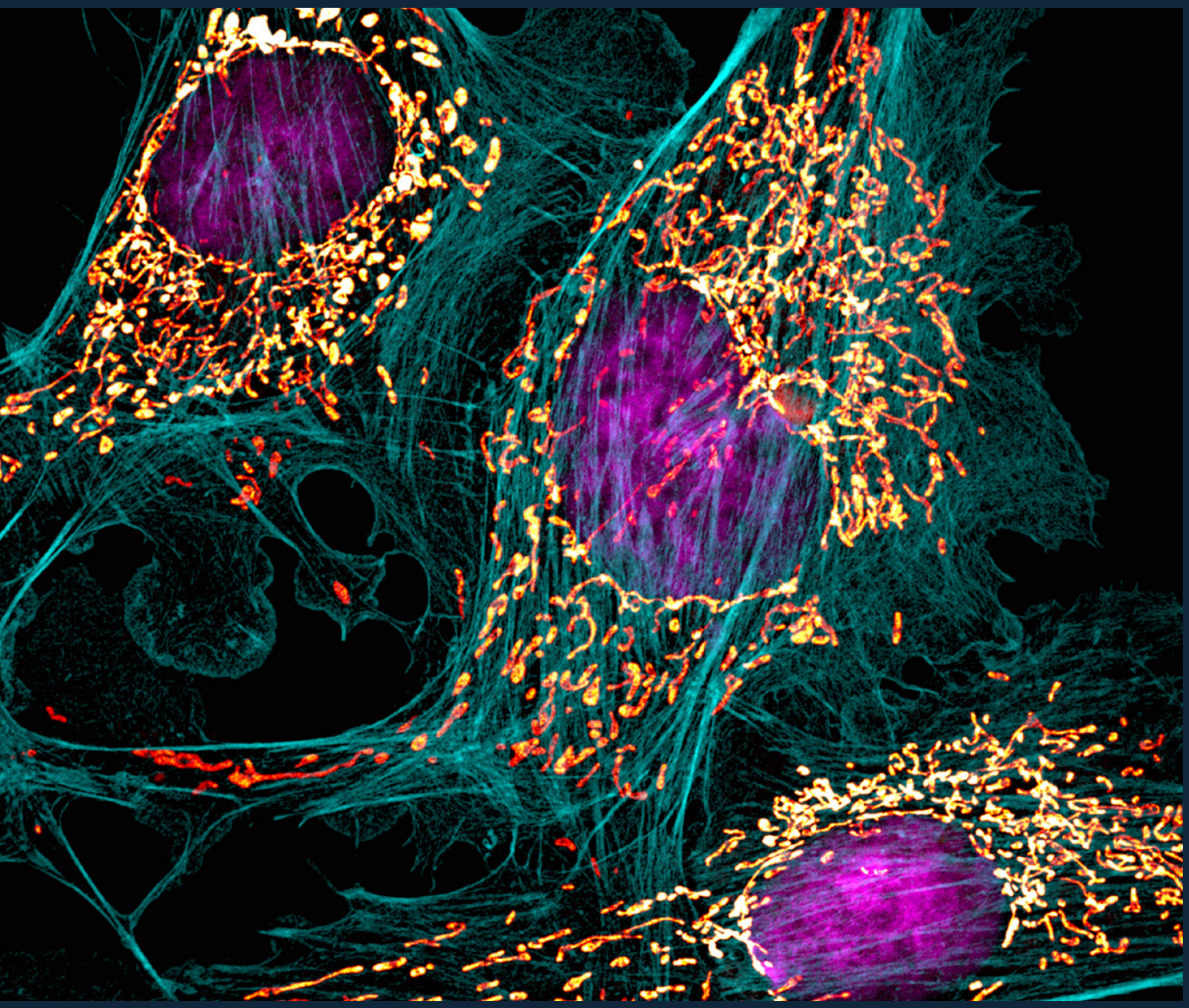
University of Nottingham
Biodiscovery Institute



We are shaping the future of health and biotechnology

We are the Biodiscovery Institute

nottingham.ac.uk/go/biodiscovery-institute

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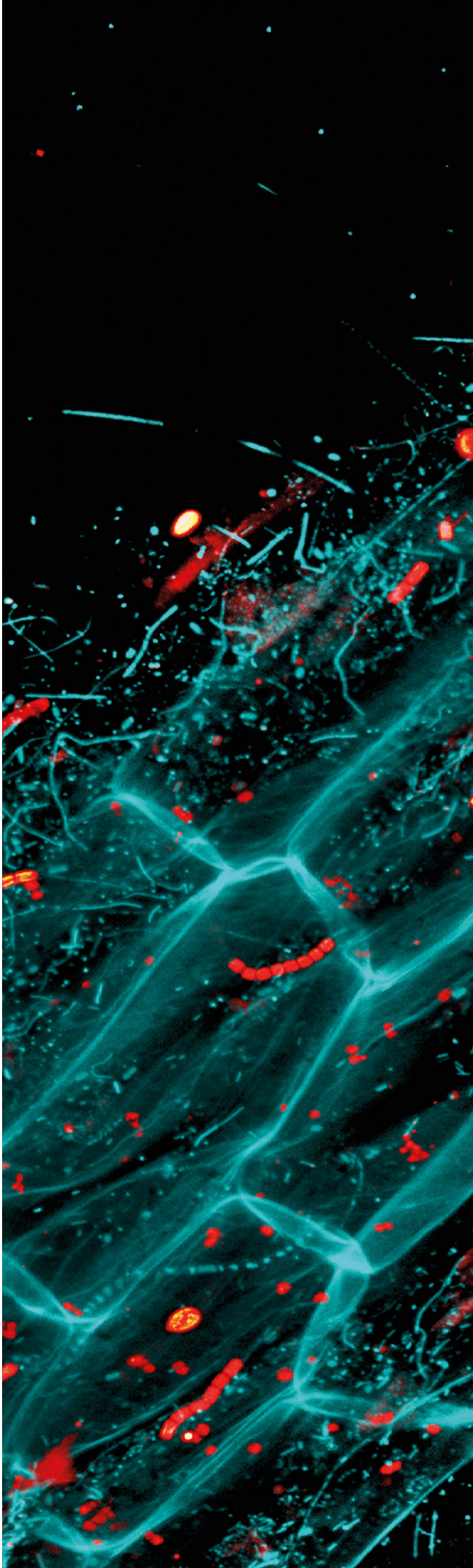
Acknowledgements

This second version of the brochure has been prepared with input from many people in the Biodiscovery Institute (BDI).

I would specifically like to thank Tessa Payne, the Research Theme leads and other members of the BDI InTraNet Committee and Isabel Bleach for their help in bringing everything together.

Neil R. Thomas
Deputy Director of the Biodiscovery Institute
July 2023



Foreword

By Chris Denning, Director of the Biodiscovery Institute

Welcome to the Biodiscovery Institute (BDI), a £100 million world-leading hub of interdisciplinary research excellence that is shaping the future of health and biotechnology.

Our mission is simple in notion, yet complex in nature: Through chemical and biological discovery and engineering we diagnose, treat, and cure disease, and provide security for quality of life.

The BDI houses 850 academics, researchers, clinicians, support staff, students and visitors united to use, or support, scientific endeavour to deliver change for better human, animal and planet health. We foster an innovative environment that has leveraged £300 million funding since 2014 across six research themes. These tackle global challenges by bringing together interdisciplinary diversity from across the university to enable collaboration with academia, industry and government, which occurs locally, nationally and internationally.

Our recent successes underscore this ethos. The £23.4 million renewed National Biofilms Innovation Centre combines expertise from academia (Nottingham, Edinburgh, Liverpool, Southampton) with 200 industrial partners. Translational activity continues via Nottingham's £23.3 million Biomedical Research Centre. This includes respiratory diseases, where activity in BDI has increased, including securing an £8.3 million interdisciplinary award from Wellcome Trust to unpick the molecular genetics of impaired lung function. A £5.1 million EPSRC award supports design of bio-instructive materials for translation-ready medical devices, while a £8.8 million Medical Research Council Doctoral Training Partnership (Nottingham, Birmingham, Leicester) will create advanced interdisciplinary models of disease.

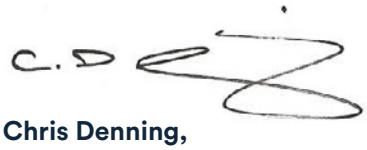
Activity is underpinned in various ways. BDI has established an Additive Biofabrication Laboratory to use three-dimensional (3D) printing to create structures that direct the behaviour of biological systems. With growth of artificial intelligence, coding and bioinformatics to underpin our research, the Advanced Data Analysis Centre / Digital Research Service has relocated to BDI. We have refreshed the existing equipment base, purchased state-of-the-art imaging and analysis platforms, and showcased clinical translation of technologies, detailed later in the brochure.

Our ethos fosters initiatives that are adopted university-wide. The Nottingham Healthcare Innovation Platform is one example, working with nurses and physicians to identify and solve areas of clinical need. Our Covid-19 Asymptomatic Testing Service developed and ran > 150,000 non-invasive saliva tests to keep the university populace safe. Project Period, supplying free sanitary products at point of need, is now across seven campuses, having started in BDI.

A shared passion in scientific discovery, translation and communication enables these successes. But nurturing a vibrant and inclusive research culture is essential to ensure everyone is valued, has a voice, and can maximise their potential, regardless of gender, race, religion, or mental and physical health. Our approach is, and must remain, one of ground-up freethinking by our research community, who then take ownership of their ideas. We promote autonomy, proficiency, and purpose, and are working to embed these values within our culture.

The BDI 2023-2028 strategy is focused on research, facilities and culture, with emphasis on biotechnology and biomedical translation. I hope you find inspiration in this snapshot of the BDI and our six research themes:

- Defeating Cancer
- Demystifying Biomolecular Complexity
- Engineering Biology
- Pioneering Therapeutics
- Regenerating and Modelling Tissues
- Taming Microbes



Chris Denning,
Director of the Biodiscovery Institute

Brief history of the Biodiscovery Institute

The Biodiscovery Institute has evolved from the Centre for Biomolecular Sciences (CBS), which was a pioneering purpose-built multidisciplinary research facility created by the University of Nottingham to synergise biomolecular research between faculties. The first phase, CBS1, opened in 2003, and was occupied by ~150 researchers focused on medicinal chemistry, microbiology, chemical and structural biology. CBS1 was expanded with building CBS2 in 2008 which broadened the range of research to include regenerative medicine, tissue engineering and synthetic biology and more than doubled the number of researchers to 350. A further building expansion to add multiple research groups from both the City Hospital and Queen's Medical Centre in the areas of cancer, digestive and respiratory research was completed in 2019 as CBS-E. This complete building complex now forms the Biodiscovery Institute with unrivalled mammalian tissue culture and parallel liquid handling facilities together with intensive research activity in fundamental biology, engineering biology, pre-clinical and clinical research being conducted by over 850 researchers.

850

Researchers

Our research themes:

We are globally respected leaders across six key research themes.

- Defeating Cancer
- Demystifying Biomolecular Complexity
- Engineering Biology
- Pioneering Therapeutics
- Regenerating and Modelling Tissues
- Taming Microbes

Research theme one: **Defeating Cancer**

We advance the prevention, diagnoses and treatment of cancer. We bring together biologists, oncologists, pathologists and surgeons with the aim of detecting the disease early and stopping it from spreading. We pioneer research and treatments and train a new generation of cancer researchers to tackle the disease. We have developed innovative immunotherapies for cancer that stimulate the body's immune system.

Cancer research is being undertaken by many researchers across a diverse range of disciplines within the Biodiscovery Institute (BDI). Three key units within the BDI that are focused on defeating cancer are the University of Nottingham Centre for Cancer Sciences (CCS), the Nottingham Breast Cancer Research Centre (NBCRC), and the Children's Brain Tumour Research Centre (CBTRC).

The CCS comprises academics working in a variety of different cancer settings and brings together scientists and clinicians with diverse experience in biological and translational areas of oncology and stem cell biology. CCS researchers within the BDI have expertise in cell and molecular biology, endothelial biology, immunology, the tumour microenvironment, clinical cancer medicine and therapeutic cell biology. The CCS researchers are also involved in educating the next generation of cancer researchers through teaching on the first tailor-made undergraduate Cancer Sciences programme in the UK.

NBCRC was established in 2018 and builds on the international reputation for its breast cancer research with many seminal discoveries now used globally in the diagnosis and treatment of breast cancer. The centre allows inclusive cohesion of a large multi-disciplinary team of breast cancer researchers and clinicians. Research at NBCRC is focussed on three key areas: Detect it early, Stop the spread, and Treat it right. Current research continues to improve our understanding of breast cancer, delivering novel diagnostics and therapies, as well as increasing awareness of the disease.

The CBTRC was established in 1997 and includes both university and NHS researchers. The aim of the centre is to improve the understanding, treatment and outcomes of children / young adults who develop brain tumours. We're dedicated to helping children who are diagnosed with brain tumours, both now and in the future.

Research highlights

A significant donation has enabled the establishment of the £4 million Nottingham Ovarian Cancer Research Centre (Srinivasan).

More than £1 million received for research to develop new treatments for advanced prostate cancer and to train the next generation of prostate cancer researchers (Mongan).

£6 million of £23 million grant awarded by Innovate UK to Nottingham (Rakha, Co-I) for Scaling Up England's Digital Pathology, Imaging and AI Centres of Excellence. Includes a 30% contribution from industry.

NC3Rs 2022-2026. Human stem cell models of de novo tumorigenesis to replace the use of animals for the study of cancer initiation. £120,000 (Allegrucci-PI, Merry and Grabowska-CoIs).

Industrial research collaboration: Bristol Myers Squib beLAB1407 grant of £520,000 (Srinivasan).

Gordian Pharma & Oncodesign (Dijon, France) - consultancy based on establishment of neurosurgical resection models in rodents to facilitate localised brain tumour drug delivery using a proprietary pharmaceutical compound (Rahman, Smith).

As part of university's Global Engagement Strategy for Indonesia, research theme members attended meetings with Indonesian university leaders and government officials, enabling discussions on future research collaborations.

Theme Leads: Cinzia Allegrucci, Sheela Jayaraman and Ruman Rahman

Example publications from the theme

Hurvitz SA. et al. Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial. Lancet, 2023, 401:105-117. **doi: 10.1016/S0140-6736(22)02420-5.**

Danenberg E, Bardwell H, Zanotelli VRT, Provenzano E, Chin SF, Rueda OM, Green A, Rakha E, Aparicio S, Ellis IO, Bodenmiller B, Caldas C, Ali HR. Breast tumor microenvironment structures are associated with genomic features and clinical outcome. Nat Genet., 2022, 54:660-669. **doi: 10.1038/s41588-022-01041-y.**

Alblihy A, Shoqafi A, Toss MS, Algethami M, Harris AE, Jeyapalan JN, Abdel-Fatah T, Servante J, Chan SYT, Green A, Mongan NP, Rakha EA, Madhusudan S. Untangling the clinicopathological significance of MRE11-RAD50-NBS1 complex in sporadic breast cancers. NPJ Breast Cancer, 2021, 7:143. **doi: 10.1038/s41523-021-00350-5.**

Aiyappa-Maudsley R, Storr SJ, Rakha EA, Green AR, Ellis IO, Martin SG. 2022. CYP2S1 and CYP2W1 expression is associated with patient survival in breast cancer. J Pathol Clin Res., 2022, 8(6):550-556. **doi: 10.1002/cjp2.291.**

Nicholson R, Menezes AC, Azevedo A, Leckenby A, Davies S, Seedhouse C, Gilkes A, Knapper S, Tonks A, Darley RL. Protein Kinase C Epsilon Overexpression Is Associated With Poor Patient Outcomes in AML and Promotes Daunorubicin Resistance Through p-Glycoprotein-Mediated Drug Efflux. Front. Oncol., 2022, 12:840046. **doi: 10.3389/fonc.2022.840046.**

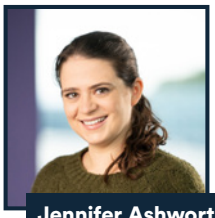
Egbuniwe IU, Harris RJ, Nakamura M, Nestle FO, Akbar AN, Karagiannis SN, Lacy KE. B lymphocytes accumulate and proliferate in human skin at sites of cutaneous antigen challenge. Journal of Investigative Dermatology, 2022, 142:726-731. **doi: 10.1016/j.jid.2021.06.038.**

Yao A, Storr SJ, Inman M, Barwell L, Moody CJ, Martin SG. Cytotoxic and Radiosensitising Effects of a Novel Thioredoxin Reductase Inhibitor in Brain Cancers. Mol Neurobiol., 2022, 59:3546-3563. **doi: 10.1007/s12035-022-02808-4.**

Akhil J. et al. Wireless Electrical-Molecular Quantum Signalling for Cancer Cell Induced Death. bioRxiv 2023.03.02.529075; **doi: doi.org/10.1101/2023.03.02.529075**

To view the updated list of publications visit **nottingham.ac.uk/research/research-areas/biodiscovery-institute**

Spotlight on early career researchers:
Training the next generation of research leaders



Jennifer Ashworth

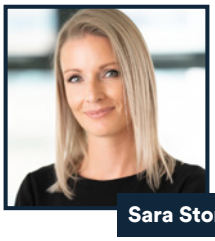
Jennifer Ashworth is an Anne McLaren fellow, working cross-school between the School of Veterinary Medicine & Science and the School of Medicine. With a background in materials science, her main research interest is developing tissue-mimetic biomaterials for 3D cell culture, for application to cancer research and the study of fibrotic diseases. **nottingham.ac.uk/vet/people/jennifer.ashworth**

Isiome Egbuniwe

Isiome Egbuniwe is an NIHR-funded academic clinical lecturer in histopathology. She is currently working as part of the Nottingham Cholangiocarcinoma Research Consortium; her overarching research goal is the identification of new therapeutic and prognostic targets in this cancer. **uk.linkedin.com/in/isioma-egbuniwe-ebueku-mbbs-phd-25861a32**

Tim Ritzmann

Tim Ritzmann is an NIHR-funded academic clinical lecturer in paediatric neuro-oncology. His current research is focused on paediatric ependymoma, which is the second most common brain tumour of childhood. He was awarded the UK's Children's Cancer and Leukaemia Group Young Investigator Award in 2022 for collaborative work with a team in Denver, Colorado on the ependymoma immune environment. **researchgate.net/profile/Tim-Ritzmann**



Sara Storr

Sara Storr is Assistant Professor in Cancer Sciences following completion of a Nottingham Research Fellowship in May 2022. Her current research is focussed on investigating the role of DARPP-32 in cancer, understanding how loss of expression contributed to changed cancer cell behaviour; and understanding DARPP-32 in the setting of addiction to drugs of abuse. **nottingham.ac.uk/medicine/people/sarah.storr**

Research theme two: **Demystifying Biomolecular Complexity**

Here we answer the core question: why is something working, and why is it having a beneficial impact? We use our state-of-the-art methodologies to understand why biomolecular structures behave the way they do. Our theme is diverse and involves multi-disciplinary approaches to tackle the most important fundamental questions which can be translated to new understanding and ultimately impact including benefit. From our analysis of blood-clotting disorders to looking at the intricacies of high-value spider web silk production, our leading-edge insight into biomolecular complexity provides important learnings.

The understanding of biological processes at a molecular level and the design, generation and evaluation of compounds that probe and report on these processes or interfere with their occurrence requires a multidisciplinary approach involving biochemistry, chemistry, pharmacology, molecular and structural biology. Our research into structural biology aims to understand biological processes and applied research in the areas of target identification. We do this by determining protein structures and studying the structure / function of complexes formed with drugs and natural ligands using protein crystallography, cryo-electron microscopy and associated techniques.

We research into the genetics, pharmacogenetics, and molecular pathophysiology basis of respiratory diseases, in particular asthma and Chronic Obstructive Pulmonary Disorder (COPD), that often lead to tissue remodelling resulting in fibrosis. Genetics and genomics holds great promise to identify new genes and pathways that may be therapeutic opportunities for common respiratory diseases including getting the right drug to the right patient.

With respect to our gastrointestinal focussed research, our focus is on the human bacterial pathogen *Helicobacter pylori*. We aim to understand how bacterial virulence factors interact with host cells to provoke a more severe inflammatory response.

Our research is fundamental and spans multiple areas of human translation including; neurdegeneration, cancer, antibiotic resistance, respiratory disease and regenerative medicine.

Research highlights

The Nottingham National Institute for Health and Care Research (NIHR) Biomedical Research Centre (BRC) focusses on identifying and taking rapid advantage of new developments in the basic sciences and translating these into clinical practice. We do this by driving innovation in experimental science and translate research into breakthrough treatments, new technologies and advanced medicines. The Nottingham NIHR BRC has recently been funded for another five years.

New research published in **Nature Genetics** has identified over 1,000 genetic signals related to lung function and implicated genes and pathways that may be therapeutic opportunities to treat diseases like asthma and Chronic Obstructive Lung disease (COPD). The Wellcome Trust have recently awarded the researchers from Nottingham, Leicester and Cambridge Universities £8.8 million to translate these findings to clinical benefit.

https://www.nottingham.ac.uk/news/nottingham-researchers-share-in-8.8-million-award-for-lung-research

A new research initiative explores a novel molecular toolkit for cell type specific adenosine receptor pharmacology funded by the Medical Research Council: Exploiting a novel molecular toolkit to explore cell type specific adenosine receptor pharmacology and regulation at endogenous levels of expression. £2 million 2022-2027. PI Steve Hill. Co-Is: Chris Denning, Jeanette Woolard, Barrie Kellam, Stephen Briddon, Laura Kilpatrick, Sam Cooper.

Theme Leads: Ingrid Dreveny and Ian Sayers

Selected recent publications

Roper, S.J., Linke, F., Scotting, P.J., Coyle,B. 3D spheroid models of paediatric SHH medulloblastoma mimic tumour biology, drug response and metastatic dissemination. Sci Rep., 2021, 11:4259. **doi: 10.1038/s41598-021-83809-6.**

James V, Nizamudeen ZA, Lea D, Dottorini T, Holmes TL, Johnson BB, Arkill KP, Denning C, Smith JGW. Transcriptomic Analysis of Cardiomyocyte Extracellular Vesicles in Hypertrophic Cardiomyopathy Reveals Differential snoRNA Cargo. Stem Cells Dev,. 2021, 30:1215-1227. **doi: 10.1089/scd.2021.0202.**

Kaneko, K., Zaitoun, A. M., Letley, D. P., Rhead, J. L., Torres, J., Spendlove, I., Atherton, J.C., Robinson, K. The active form of Helicobacter pylori vacuolating cytotoxin induces decay-accelerating factor CD55 in association with intestinal metaplasia in the human gastric mucosa. J.Pathol., 2022, 258:199-209. **doi: 10.1002/path.5990.**

Ketelaar ME et al. Phenotypic and functional translation of IL33 genetics in asthma. J Allergy Clin Immunol., 2021, 147:144-157. **doi: 10.1016/j.jaci.2020.04.051.**

Soukarieh F, Mashabi A, Richardson W, Oton EV, Romero M, Roberston SN, Grossman S, Sou T, Liu R, Halliday N, Kukavica-Ibrulj I, Levesque RC, Bergstrom CAS, Kellam B, Emsley J, Heeb S, Williams P, Stocks MJ, Cámara M. Design and Evaluation of New Quinazolin-4(3H)-one Derived PqsR Antagonists as Quorum Sensing Quenchers in Pseudomonas aeruginosa. ACS Infect Dis., 2021, 7:2666-2685. **doi: 10.1021/acsinfecdis.1c00175**.

Sanchez-Bailon MP, Choi SY, Dufficy ER, Sharma K, McNee GS, Gunnell E, Chiang K, Sahay D, Maslen S, Stewart GS, Skehel JM, Dreveny I, Davies CC. Arginine methylation and ubiquitylation crosstalk controls DNA end-resection and homologous recombination repair. Nat Commun., 2021, 12:6313. **doi: 10.1038/s41467-021-26413-6.**

Comez D, Glenn J, Anbuhl SM, Hikers R, Smit MJ, Hill SJ, Kilpatrick LE. Fluorescently tagged nanobodies and NanoBRET to study ligand-binding and agonist-induced conformational changes of full-length EGFR expressed in living cells. Front. Immunol., 2022, 13. **doi: 10.3389/fimmu.2022.1006718**

Brennan A, Layfield R, Long J, Williams HEL, Oldham NJ, Scott D, Searle MS. An ALS-associated variant of the autophagy receptor SQSTM1/p62 reprograms binding selectivity toward the autophagy-related hATG8 proteins. J Biol Chem., 2022, 298:101514. **doi: 10.1016/j.jbc.2021.101514.**

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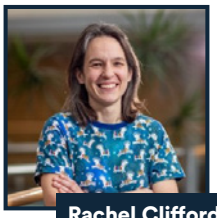

Rachel Clifford

Rachel Clifford started her Anne McLaren Fellowship in June 2020. Rachel's research focuses on understanding epigenetic mechanisms of gene expression in relation to lung disease and responses to inhaled exposures. She is also interested in using epigenetic marks as biomarkers of disease, cell type and age. **nottingham.ac.uk/medicine/people/r.clifford**

Kavita Raniga

Kavita Raniga is an industrial CASE PhD student working in collaboration with GlaxoSmithKline on developing complex models for enhanced predictive drug-induced cardiotoxicity screening using hPSC-derived cardiac cells. Alongside her research Kavita leads on Project Period, aiming to reduce the stigma of menstruation and menopause in the workplace and alleviate period poverty. **researchgate.net/profile/Kavita-Raniga**

Research theme three: **Engineering Biology**

We engineer microbes to make useful products from greenhouse gases, waste products and low-cost feedstocks. Our work has the potential to make clean, sustainable and affordable products including transport fuels, useful chemicals, animal feed, vaccines and pharmaceuticals, and in turn reduce societal reliance on fossil fuels. Our ambition is to develop the technologies required to implement a more sustainable bioeconomy.

Industrial biotechnology research in the Biodiscovery Institute includes the BBSRC/EPSRC Synthetic Biology Research Centre (SBRC) and the Nottingham Engineering Biology Labs (NEBL).

The BBSRC/EPSRC SBRC is a world-leading centre for Clostridium research and microbial gas-fermentation. It has a multidisciplinary critical mass of researchers funded by research councils and industry who use a wide range of microbes capable of recycling carbon into the chemicals and fuels modern society needs in a sustainable manner, or for therapeutic biotechnology including vaccine development, phage therapy and preventing spore germination in the microbiota. Synthetic biology approaches using metabolic engineering, proprietary genome engineering tools and systems approaches are being used to optimise each chassis for the conversion of waste gases and biomass into industrially useful fuels and chemicals, or for therapeutic applications.

Nottingham Engineering Biology Labs (NEBL) use a range of genetic and biological techniques to engineer microbes with new useful properties. We develop powerful synthetic biology technologies including massively parallel genetic design and construction, and design or edit DNA from individual DNA bases ('letters') all the way up to rewriting whole genomes. We apply these technologies to engineering microbes and their metabolism for applications in biomanufacturing, biocatalysis, sustainability, and health; often using diverse organisms best suited to each challenge, including *Clostridium, E. coli*, yeast and cyanobacteria.

Research highlights

The Synthetic Biology Research Centre (SBRC) led by Nigel Minton secured a £1.5 million Engineering Biology 'Research, Community and Capacity Development' Award with the goal of eliminating CO_2 production from fermentation processes.

BDI academics have recently been awarded two 'themes' (clusters of four PhD related studentships) via the EPSRC CDT in Sustainable Chemistry:

1. Bioelectrochemical Applications for Sustainable Technologies (BeAST): Katalin Kovacs.

2. Sustainable biocatalytic solutions for key chemical transformations: Ellis O'Neill, Ben Blount, John Heap.

Theme Leads: John Heap and Klaus Winzer

Example publications from the theme

Sellés Vidal L, Murray JW, Heap JT. Versatile selective evolutionary pressure using synthetic defect in universal metabolism. Nat Commun., 2021, 12:6859. **doi: 10.1038/s41467-021-27266-9.**

Aldholmi M, Ahmad R, Carretero-Molina D, Pérez-Victoria I, Martín J, Reyes F, Genilloud O, Gourbeyre L, Gefflaut T, Carlsson H, Maklakov A, O'Neill E, Field RA, Wilkinson B, O'Connell M, Ganesan A. Euglenatides, Potent Antiproliferative Cyclic Peptides Isolated from the Freshwater Photosynthetic Microalga Euglena gracilis. Angew Chem Int Ed Engl., 2022, 61:e202203175. **doi: 10.1002/anie.202203175.**

Salinas A, McGregor C, Irorere V, Arenas-López C, Bommareddy R, Winzer K, Minton NP, Kovacs K. Metabolic engineering of Cupriavidus necator H16 for heterotrophic and autotrophic production of 3-hydroxypropionic acid. Metab Eng., 2022, 74:178-190. **doi: 10.1016/j.ymben.2022.10.014.**

Humphreys J, Debebe BJ, Diggle SP, Winzer, K. Clostridium beijerinckii strain degeneration is driven by the loss of Spo0A activity. Front. Microbiol., 2023, 13:1075609. **doi: 10.3389/fmicb.2022.1075609.**

Rumah BL, Stead CE, Claxton Stevens BH, Minton NP, Zhang Y. In vivo genome editing in type I and II methanotrophs using a CRISPR-Cas9 system. ACS. Synth. Biol., 2023, 12:544-554. **doi: 10.1021/acssynbio.2c00554.**

Whittle MJ, Bilverstone TW, van Esveld RJ, Lücke AC, Lister MM, Kuehne SA, Minton NP. A novel bacteriophage with broad host range against Clostridioides difficile ribotype 078 supports SlpA as the likely phage receptor. Microbiol Spectr., 2022, 10:e0229521. **doi: 10.1128/spectrum.02295-21.**

Blount, B. A. et al. Synthetic yeast chromosome XI design enables extrachromosomal circular DNA formation on demand. bioRxiv 2022.07.15.500197. **doi:10.1101/2022.07.15.500197.**

Foulquier C, Rivière A, Heulot M, Dos Reis S, Perdu C, Girbal L, Pinault M, Dusséaux S, Yoo M, Soucaille P, Meynial-Salles I. Molecular characterization of the missing electron pathways for butanol synthesis in Clostridium acetobutylicum. Nat Commun., 2022, 13:4691. **doi: 10.1038/s41467-022-32269-1.**

Passmore IJ, Faulds-Pain A, Abouelhadid S, Harrison MA, Hall CL, Hitchen P, Dell A, Heap JT, Wren BW. A combinatorial DNA assembly approach to biosynthesis of N-linked glycans in E. coli. Glycobiology, 2023, 33:138–149 **doi:10.1093/glycob/cwac082.**

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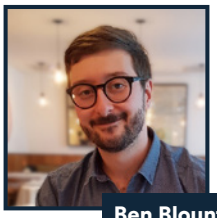
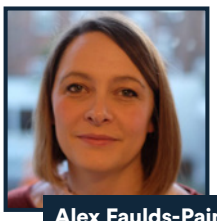


Ben Blount

Ben Blount is a Nottingham Research Fellow in the School of Life Sciences, using Engineering Biology and Synthetic Genomics to uncover fundamental insights and develop strains for biotechnology applications. **nottingham.ac.uk/life-sciences/people/benjamin.blount**



Alex Faulds-Pain

Alex Faulds-Pain is a Senior Research Fellow in the School of Life Sciences, using Engineering Biology for biomanufacturing including in combination with Glycotechnology to develop new vaccine candidates. **nottingham.ac.uk/life-sciences/people/alexandra.faulds-pain1**

Chris Humphreys

Chris Humphreys is a Senior Research Fellow in the School of Life Sciences, specialising in developing Clostridial genetic tools and engineered acetogens for industrial biotechnology. **nottingham.ac.uk/life-sciences/people/c.humphreys**

Ellis O'Neill

Ellis O'Neill is an Assistant Professor in the School of Chemistry, having previously been a Nottingham Research Fellow. He is working at the chemistry / biology interface on algal biotechnology and compounds useful as food supplements, materials and antibiotics. **nottingham.ac.uk/chemistry/people/ellis.o'neill**

Research theme four: **Pioneering Therapeutics**

We harness the wide breadth of cross-cutting science to harmonise and support key research activities aligned to modern-day therapeutics discovery and development. Projects include identifying new approaches for the prevention and treatment of infectious disease, cardiovascular disease, respiratory disease and cancer angiogenesis, as well as immunotherapy cancer treatments and eye drops that reverse degeneration of sight.

We are involved in all aspects of pre-clinical therapeutic discovery including that of small molecule drugs, biopharmaceutics and vaccines. More broadly we have expertise in biomarker identification, medicine chemistry and high-throughput screening, DMPK, pre-clinical models and advanced drug delivery.

Our researchers focus on a number of therapeutic challenges including the identification of new selective ligands for G-protein coupled receptors using fluorescence; improving the targeting and efficacy of brain and breast cancer drugs using protein nanocages; addressing the developing issue of antimicrobial resistance through the identification of new antibiotics for future use in both human and animal health; combining structural biology, in silico methods and organic synthesis to generate compounds that are active against respiratory diseases including idiopathic pulmonary fibrosis and tuberculosis.

Researchers are undertaking pioneering research aimed at understanding biological processes, and applied research in the areas of target identification, bioassay development and drug discovery. Biological chemistry research involves the use of analytical, computational and synthetic chemistry methods, together with those in molecular and structural biology to investigate, disrupt and harness a wide range of biological systems from single peptides and proteins through to bacteria, plants and higher animals.

Research highlights

The excellent research performed within Pioneering Therapeutics is the result of the highly collaborative nature of the theme both with scientists and clinicians from within the Biodiscovery Institute and university and also from industry and other research institutes.

Key areas of research continue to include the development of computational tools, fluorescent ligands and complementary structural studies to aid drug discovery. Recent grant success allows work to continue in identifying new chemical biology approaches to study P2Y2 receptors in health and disease and enables the exploration of specific G-protein.

Further work within the theme focuses on identifying novel antimicrobial agents. Vaccine development is one such avenue and funding has been secured to use novel synthetic biology approaches to develop a glycan / glycoconjugate platform to generate vaccines as well as to develop a practical outer membrane vesicle vaccine platform directed against *Clostridioides difficile*. Other ongoing funded work includes the translational study of an antimicrobial agent (LY256) which also targets *Clostridioides difficile*.

An additional area of recent grant success is in respiratory medicine therapeutics. Modelling lung conditions using multidisciplinary approaches allows the delineation of disease mechanisms and identification of novel drug targets and biomarkers and may highlight drug repurposing opportunities.

Theme Leads: Weng Chan and Claire Seedhouse

Example publications from the theme

Murray, E.J., Dubern, J.-F., Chan, W.C., Chhabra, S.R. and Williams, P. A Pseudomonas aeruginosa PQS quorum-sensing system inhibitor with anti-staphylococcal activity sensitizes polymicrobial biofilms to tobramycin. Cell Chemical Biology, 2022, 29:1187-1199. **doi: 10.1016/j.chembiol.2022.02.007**

Tarantini, F.S., Brunati, M., Tarvella, A., Carrano, L., Parenti, F., Hong, K.W., Williams, P., Chan, K.G., Heeb, S, Chan, W.C. Actinomadura graeca sp. nov.: a novel producer of the macrocyclic antibiotic zelkovamycin. PLoS ONE, 2021, 16: e0260413. **doi: 10.1371/journal.pone.0260413**

Al-Beltagi S, Preda CA, Goulding LV, James J, Pu J, Skinner P, Jiang Z, Wang BL, Yang J, Banyard AC, Mellits KH, Gershkovich P, Hayes CJ, Nguyen-Van-Tam J, Brown IH, Liu J, Chang KC. Thapsigargin Is a Broad-Spectrum Inhibitor of Major Human Respiratory Viruses: Coronavirus, Respiratory Syncytial Virus and Influenza A Virus. Viruses, 2021, 13:234. **doi: 10.3390/v13020234.**

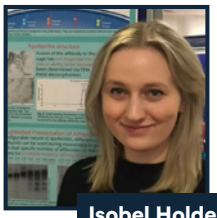
Karyal C, Palazi P, Hughes J, Griffiths RC, Persaud RR, Tighe PJ, Mitchell NJ, Griffin R. Mimicking Native Display of CD0873 on Liposomes Augments Its Potency as an Oral Vaccine against Clostridioides difficile. Vaccines (Basel), 2021, 9:1453. **doi: 10.3390/vaccines9121453.**

Baldi BG, Radzikowska E, Cottin V, Dilling DF, Ataya A, Carvalho CRR, Harari S, Koslow M, Grutters JC, Inoue Y, Gupta N, Johnson SR. COVID-19 in Lymphangioleiomyomatosis: An International Study of Outcomes and Impact of Mechanistic Target of Rapamycin Inhibition. Chest, 2022, 161:1589-1593. **doi: 10.1016/j.chest.2021.12.640.**

Chetty S, Armstrong T, Sharma Kharkwal S, Drewe WC, De Matteis CI, Evangelopoulos D, Bhakta S, Thomas NR. New InhA Inhibitors Based on Expanded Triclosan and Di-Triclosan Analogues to Develop a New Treatment for Tuberculosis. Pharmaceuticals (Basel), 2021, 14:361. **doi: 10.3390/ph14040361.**

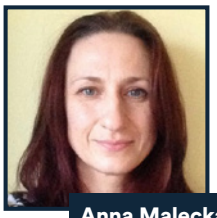
Ramis J, Middlewick R, Pappalardo F, Cairns JT, Stewart ID, John AE, Naveed SU, Krishnan R, Miller S, Shaw DE, Brightling CE, Buttery L, Rose F, Jenkins G, Johnson SR, Tatler AL. Lysyl oxidase like 2 is increased in asthma and contributes to asthmatic airway remodelling. Eur Respir J., 2022, 7;60:2004361. **doi: 10.1183/13993003.04361-2020.**

Spotlight on early career researchers:
Training the next generation of research leaders



Isobel Holden

Isobel Holden completed an EPSRC CDT PhD in advanced therapeutics and nanomedicines in the BDI and currently holds an EPSRC Doctoral Prize Fellowship to create targeted magnetoferritins for selective, potent treatment alongside enhanced MRI imaging of breast cancer. **nottingham.ac.uk/pharmacy/people/isobel.holden**



Anna Malecka

Anna Malecka first came to the University of Nottingham in 2010 as an MSc student in Cancer Immunology and Biotechnology and continued her career at UoN through PhD and later working as a Research Fellow. In April 2022 Anna was appointed Assistant Professor in Immunology at the School of Veterinary Medicine and Science. Her research focuses on deciphering the crosstalk between immune cells and their environment and its role in the development of cancer and infections in humans and animals with the aim of finding new therapeutic targets. **nottingham.ac.uk/vet/people/anna.malecka1**

Research theme five: **Regenerating and Modelling Tissues**

Regenerating and Modelling Tissues aims to develop new approaches to help repair or replace diseased and damaged tissue of the human body. To achieve this, we combine approaches from different fields of research, from biomaterials engineering, nanotechnology, and stem cell technology. We conduct basic and applied research programmes to understand the cellular and molecular processes underlying an array of human diseases and to control these processes for therapeutic benefit.

We create new materials that can respond to stimuli and are compatible with biological systems, and that can self-assemble into microscopic structures and which possess functional biointerfaces that influence cell behaviour. We develop new methods to control stem cell phenotype and to direct their differentiation into defined phenotypes. Using these biomaterials and cells, we can create *in vitro* models of normal and diseased tissue to aid our understanding of the disease process and the development of novel therapeutics. In addition, these cells and biomaterials hold potential for clinical translation to restore tissue function which has been lost through damage or disease.

Here are few of the key techniques used to address these important biological questions: bioelectronics for modulating and sensing bioelectricity, advanced stem cell-derived technology and gene editing to model human diseases in a dish for fundamental research and drug discovery, non-viral delivery systems of DNA, mRNA and proteins to control tissue regeneration, and precision assembly of complex cellular 3D microenvironments with optical tweezers and bioprinting.

Research highlights

Our international research work has been boosted by a five-year £1.4 million grant from the AO Foundation for a project entitled 'Instructive bone regenerating hydrogel for translational bone repair'. This Is a collaborative award for this research theme (Matta) with the University of Zurich and Sun Yat-sen University.

Funding success have included awards from:

BBSRC/NC3Rs: £250,000 (Hannan);

BHF: £301,000 (Denning);

MRC: £2 million (Co-Is Briddon, Cooper, Denning, Kellam, Kilpatrick, Woolard); MRC IAA award (Rawson).

We have developed our commercial engagement through a four-year collaboration with Estee Lauder Companies (Matta), Astra Zeneca research funding of £1.2 million for Gordon Moran (PI) and Nick Hannan (Co-I), and MRC-AIM ICASE studentship with GlaxoSmithKline and AstraZeneca.

Theme Leads: Mattea Finelli and Nick Hannan

Example publications from the theme

Rimland, C. A., Tilson, S. G., Morell, C. M., Tomaz, R. A., Lu, W. Y., Adams, S. E., Georgakopoulos, N., Otaizo-Carrasquero, F., Myers, T. G., Ferdinand, J. R., Gieseck, R. L., 3rd, Sampaziotis, F., Tysoe, O. C., Ross, A., Kraiczy, J. M., Wesley, B., Muraro, D., Zilbauer, M., Oniscu, G. C., Hannan, N. R. F., Forbes, S. J., Saeb-Parsy, K., Wynn, T. A. & Vallier, L. Regional Differences in Human Biliary Tissues and Corresponding In Vitro-Derived Organoids. Hepatology, 2021, 73:247-267. **doi: 10.1002/hep.31252.**

Knaust AE, Cuello F, Saleem U, Loos M, Mosqueira D, Laufer S, Schweizer M, van der Kraak P, Flenner F, Ulmer BM, Braren I, Yin X, Theofilatos K, Klampe B, Schulze T, Pinto Y, Vink A, Harding S, Mayr M, Denning C, Eschenhagen T, Hansen A. Reversal of mitochondria-associated membrane microdomain dysfunction in human cardiomyocytes with phospholamban p.Arg14del mutation by Ca2+ scavenging. EMBO J., **3:e13074**

Nasir A, Thorpe J, Burroughs L, Meurs J, Pijuan-Galito S, Irvine DJ, Alexander MR, Denning C. Discovery of a Novel Polymer for Xeno-free, Long-term Culture of Human Pluripotent Stem Cell Expansion. Adv. Healthc. Mater., 2021, **doi: 10.1002/adhm.202001448.**

Akhil Jain, Gustavo F Trindade, Jacqueline M Hicks, Jordan C Potts, Ruman Rahman, Richard JM Hague, David B Amabilino, Lluïsa Pérez-García, Frankie J Rawson. Modulating the biological function of protein by tailoring the adsorption orientation on nanoparticles. Journal of Colloid and Interface Science, 2021, 587:150-161. **doi: 10.1016/j.jcis.2020.12.025.**

Wu Y, Yang J, van, A, Berardo A, Corridori I, Feng J, Xu J, Titirici M.-M, Rodriguez-Cabello J. C, Pugno N M, Sun J, Wang W, Tuttle T, Mata A. Disinfector-Assisted Low Temperature Reduced Graphene Oxide-Protein Surgical Dressing for the Postoperative Photothermal Treatment of Melanoma. Adv. Funct. Mater., 2022, 32:2205802. **doi.org/10.1002/adfm.202205802.**

Yang B, Lledos M, Akhtar R, Ciccone G, Jiang L, Russo E, Rajput S, Jin C, Angelereou MGF, Arnold T, Rawle J, Vassalli M, Marlow M, Adams DJ, Zelzer M. Surface-controlled spatially heterogeneous physical properties of a supramolecular gel with homogeneous chemical composition. Chem Sci., 2021, 12:14260-14269. **doi: 10.1039/d1sc04671c.**

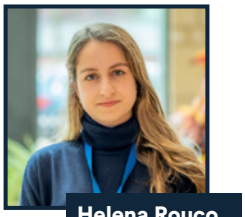
Spotlight on early career researchers:
Training the next generation of research leaders

Akhil Jain

Akhil Jain is a research fellow in Dr Frankie Rawson's group. Akhil's research focuses on developing new bioelectronics-based approaches to modulate cell function by using bioelectronics, nanotechnology, material & surface chemistry, bioelectronics, and cell biology. In future, he wants to apply this research to develop quantum converting nanomaterials for sensing, diagnostics, and therapeutics. **nottingham.ac.uk/pharmacy/people/akhil.jain**

Aishah Nasir

Aishah Nasir is a research fellow working across multidisciplinary fields to develop biomaterial model systems of children's brain tumours, stem cells and cardiomyocytes to improve pre-clinical testing or develop novel medical devices. Her research aims to identify animal-free surfaces to support clinical grade human pluripotent stem cell (hPSC) generation and development of heart-in-a-dish platforms for cardiac disease modelling. **nottingham.ac.uk/medicine/about/divisions-and-units/cancer-and-stem-cells/people/aishah.nasir**



Helena Rouco

Helena Rouco is a Margarita Salas postdoctoral fellow in Professor Alvaro Mata's group. Her current research aims are to develop 3D in vitro platforms for cell culture via multicomponent self-assembly, as well as on the manufacturing of microfluidic devices by combining molecular self-assembly and 3D printing. **researchgate.net/profile/Helena-Rouco**

Research theme six: **Taming Microbes**

Some microbes make us sick, others are important to our health. Biofilms, communities of microbes that attach to each other and surfaces, are central to our most important global challenges – from antimicrobial resistance and food safety to water security. Our bug-resistant polymers applied to urinary catheters and development of vaccines against pathogenic bacteria are making a difference to people's lives.

Understanding microbe evolution and sociology and their relevance to antimicrobial resistance is the key focus for our research. As a group of molecular microbiologists, we apply multidisciplinary approaches to design novel antimicrobials, and understand bacterial communities with the aim to prevent, detect, manage and engineer biofilms.

Our research interests specifically focus on the ways in which bacteria control virulence through cell-cell communication (quorum sensing) and targeting these mechanisms as an antimicrobial strategy though the inhibition of bacterial quorum sensing signalling mechanisms, novel target discovery and the development of new approaches to treat biofilm-mediated infections.

In addition, we investigate bacterial protein secretion, the interrelationship between quorum sensing and metabolism and its impact on microniches within biofilms on surfaces and in 3D skin infection models. We research environmental sensing and gene regulation in bacteria, notably by non-coding RNAs and post-transcriptional regulatory mechanisms and we are working to uncover the molecular genetic mechanisms underpinning how plague (black death) spreads through the environment and its animal hosts. Moreover, we investigate the mechanisms of action of biofilm resistant biomaterials for preventing medical device associated infections.

Research highlights

Funding for follow-on phase of National Biofilms Centre received from BBSRC/IUK (Camara PI, Hardie Co-I: £7.5 million).

Research Funding totalling £8 million form UKRI: EPSRC (to design bio-instructive materials for translation ready medical devices: Alexander PI, Paul Williams Co-I), NERC (to understand soil survival and re-emergence: the continued threat of plague: Atkinson), BBSRC 21ALERT (for the nanoscale characterisation of biological and bioinspired materials using Integrated Fluidic Force - High-Resolution Confocal Microscopy: Yakob PI, Paul Williams, Camara, Hardie Co-Is).

Funding from industry totalling £200,000 from Haleon (a UK health-tech company: Paul Williams) and Unilever (Kim Hardie) to characterize oral biofilm inhibition.

Steve Atkinson has contributed to a Channel 5 documentary, 'The Black Death'.

Theme Leads: Kim Hardie and Stephan Heeb

Example publications from the theme

He Y, Abdi M, Trindade GF, Begines B, Dubern JF, Prina E, Hook AL, Choong GYH, Ledesma J, Tuck CJ, Rose FRAJ, Hague RJM, Roberts CJ, De Focatiis DSA, Ashcroft IA, Williams P, Irvine DJ, Alexander MR, Wildman RD. Exploiting Generative Design for 3D Printing of Bacterial Biofilm Resistant Composite Devices. Adv Sci., 2021, 8:e2100249. **doi: 10.1002/advs.202100249.**

Ng Y-K, Grasso M, Wright V, Garcia V, Williams P, Atkinson S. The Quorum Sensing System of Yersinia enterocolitica 8081 Regulates Swimming Motility, Host Cell Attachment, and Virulence Plasmid Maintenance. Genes, 2018, 9:307-321. **doi.org/10.3390/genes9060307**

Dubern JF, Romero M, Mai-Prochnow A, Messina M, Trampari E, Gijzel HN, Chan KG, Carabelli AM, Barraud N, Lazenby J, Chen Y, Robertson S, Malone JG, Williams P, Heeb S, Cámara M. ToxR is a c-di-GMP binding protein that modulates surface-associated behaviour in *Pseudomonas aeruginosa*. NPJ Biofilms Microbiomes, 2022, 8:64. **doi: 10.1038/s41522-022-00325-9.**

Soh EY, Smith F, Gimenez MR, Yang L, Vejborg RM, Fletcher M, Halliday N, Bleves S, Heeb S, Cámara M, Givskov M, Hardie KR, Tolker-Nielsen T, Ize B, Williams P. 2021; Disruption of the *Pseudomonas aeruginosa* Tat system perturbs PQS-dependent quorum sensing and biofilm maturation through lack of the Rieske cytochrome bc1 sub-unit. PLoS Pathog., 2021, 17:e1009425. **doi: 10.1371/journal.ppat.1009425.**

Fenn, S., Dubern, JF., Cigana, C., De Simone, M, Lazenby, J., Juhas, M., Schwager, S., Bianconi, I., Döring, G., Elmsley, J., ,Eberl, L., Williams, P., Bragonzi, A., Cámara, M. NirA is an alternative nitrite reductase from *Pseudomonas aeruginosa* with potential as an antivirulence target. mBio., 2021, 12:e00207-21. **doi: 10.1128/mBio.00207-21.**

Dubern, J-F, Hook, AL, Carabelli, A, Change, C-Y, Lewis-Lloyd, CA, Luckett, JC, Burroughs, L, Dundas, AA, Humes, DJ, Irvine, DJ, Alexander, MR and Williams, P. Discovery of a polymer resistant to bacterial biofilm, swarming and encrustation. Sci Adv., 2023, 9:eadd7474. **doi: 10.1126/sciadv.add7474.**

To view the updated list of publications visit **nottingham.ac.uk/research/research-areas/biodiscovery-institute**

Spotlight on early career researchers:
Training the next generation of research leaders

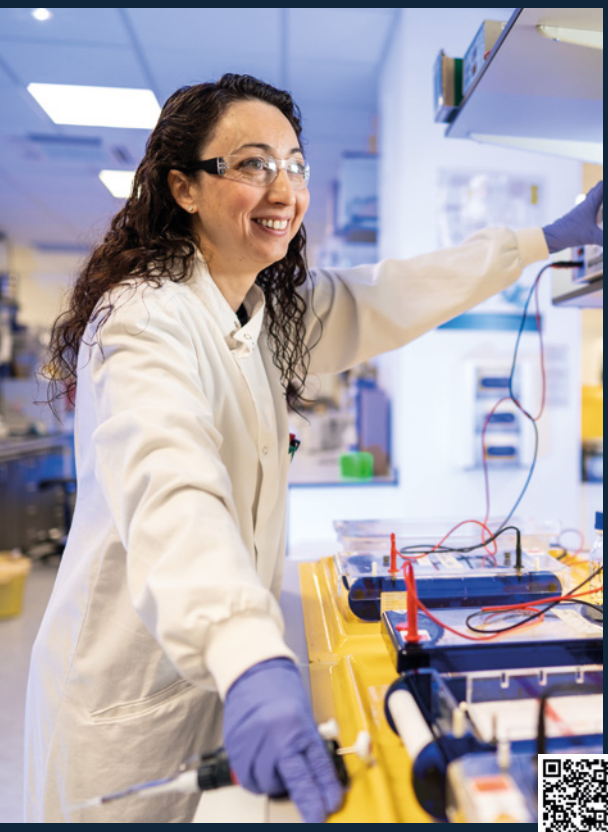
Sam Fenn

Sam Fenn received his PhD as part of the Wellcome Trust Antimicrobials and Antimicrobial Resistance DTP programme here at the University of Nottingham in 2022. His research focused on characterising novel therapeutic targets in the problematic multi-drug resistant pathogen *Pseudomonas aeruginosa*. He continued his fascination of the heterogeneous nature of the infection microenvironment and the role of diminishing oxygen availability in disease establishment and progression as a Fellow with National Biofilms Innovation Centre with Professor Miguel Cámara. Sam has secured a five year role as a Research Fellow at University College Cork, Ireland in the APC Microbiome Centre where he will be researching similar themes in the Gram positive pathogen *Staphylococcus aureus* and *Streptococcus pneumoniae*.' **nottingham.ac.uk/Life-Sciences/people/samuel.fenn2**

Shaun Robertson

Shaun Robertson moved to Nottingham in 2018 as an Innovation Research Fellow with the National Biofilms Innovation Centre (NBIC). His research focused on understanding polymicrobial biofilm interactions, through developing a simplified model to allow manipulation of these communities under relevant environmental conditions. Through NBIC Shaun has had extensive industrial engagement on successful proof of principle projects. His keen interest in commercialisation of research supported by NBIC training programmes underpinned the successful award of an Innovate UK iCURe fellowship. Shaun is currently taking the lead on the development of a rapid diagnostic for *Pseudomonas aeruginosa* in people with Cystic Fibrosis. He is developing a business plan and securing funding to launch a spinout company in 2024 while continuing research to identify markers for other microbial pathogens. **nottingham.ac.uk/life-sciences/people/shaun.robertson1**

Large scale facilities



The Biodiscovery Institute includes a £100 million suite of buildings housing over 700 researchers, clinicians and support staff.

Our exceptional facilities include mammalian cell culture suites with capacity that exceeds almost any academic facility in the world, with over 120 class two microbiological safety cabinets. This is supported by major strengths in molecular and cell analysis, particularly around imaging and super-resolution microscopy.

Our super resolution microscope facility comprises of a Zeiss 780 confocal microscope combined with an Elyra PS1 Super resolution system with full environmental control. With HTA licensed laboratories, we hold a significant number of tissue samples including the world's largest tissue microarray for breast cancer.

Three robotics suites in the institute span stem cell culture and differentiation, to recombinant protein production in yeast, through to plating of our bespoke 83,000 compound library, which represents a diversity of chemical structures. A recent funding award has enabled us to purchase a Zeiss Cell discoverer 7 automated high throughput environmentally controlled microscope that will include a robotics plate loading system in the future. The Synthetic Biology Research Centre (SBRC) fermentation unit is designed to facilitate industrial and academic research towards the development of new fermentation technologies and products. Additional large-scale fermenters allow novel re-engineered bacterial strains to convert greenhouse gas, through carbon capture, into protein for animal feed, tackling climate change. These suites can be repurposed, as shown by the stem cell robot being deployed to provide high throughput asymptomatic testing for Covid-19 across the university and NHS during 2020 and 2021.

Capabilities in cell, tissue and material engineering and bioprinting in 2D and 3D require next level analytical platforms. These span the length-scales of macro- (cell behaviours, physical attributes) to micro- and nano-scale. The latter includes protein crystallisation and highfield (800 and 600 MHz) NMR optimised for challenging systems (proteins / RNA / lipids etc). Our systems have capabilities such as high sensitivity cryogenically cooled probes, solid-state magic angle spinning (Ultrafast spinning up to 65 KHz), reaction monitoring, metabolomics and automation for screening.

Outreach and public engagement

Detailed information on each investigator can be found here:

Our scientists and communicators work together to take our research to the public with informative and educational activities that are fun and interactive.

We support local charities, and are involved in local, national and international initiatives through direct and social media outlets to promote the BDI and the University of Nottingham (UoN). We aim to make science education more accessible and interactive to all, and work with local schools to encourage young people to consider a career in science.

Art helps us dissolve boundaries between art and science. The Nottingham Breast Cancer Research Centre worked with the Breast Cancer Art project to create an exhibition of individual stories of lives affected by breast cancer. BDI works with Nottingham CityArts on the HeART project; funded by the UoN and the charity Ignite this brings together local community groups to create science-inspired artworks which will be showcased at a range of Nottingham exhibitions. Further funding will allow this pilot study to be expanded across several other disciplines and link into university-wide mental health and wellbeing initiatives. **city-arts.org.uk/project/heart/**

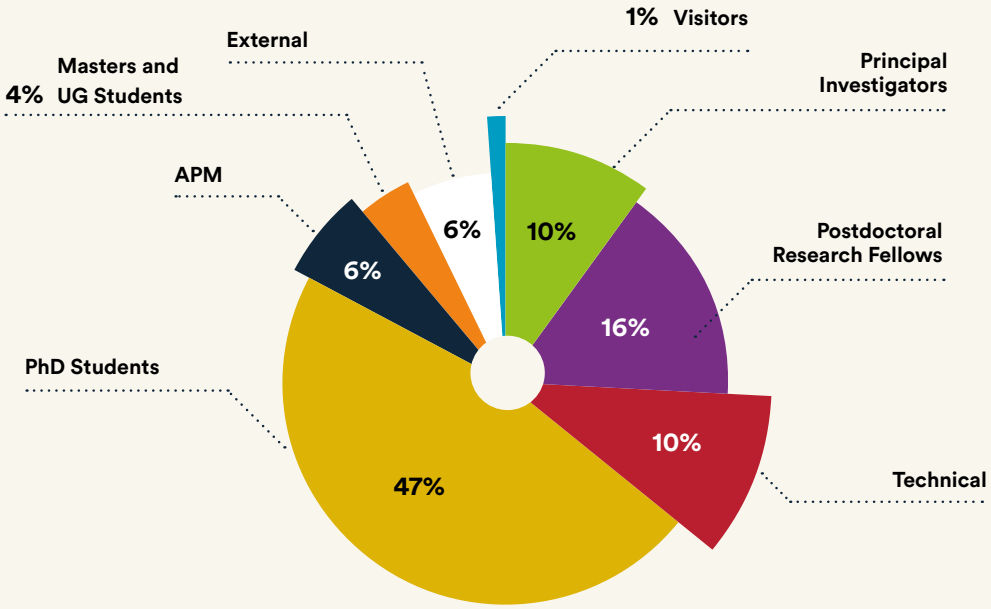
We actively participate in external outreach events including New Scientist Live and the Royal Society Summer Science Exhibition 2021, where we demonstrated research into 3D printing of personalised tablets that can deliver multiple medications to the body, at the correct dose and time. We regularly engage with the media; BDI researchers were featured on 'Pig to human heart transplant' on BBC Radio 4, and 'Undercover COVID' on the BBC Panorama programme. The 2022 Materials World report included BDI research focussing on surgical dressings to support the healing of melanoma wounds.

100,000

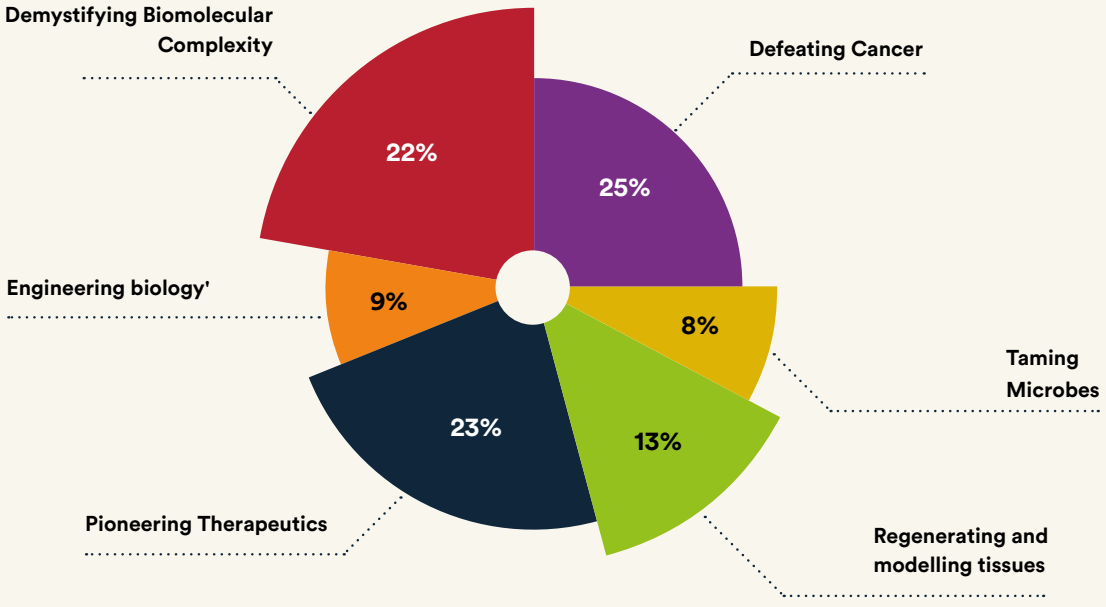
Engaged with over 100,000 members of the wider community face to face since 2018 and more than 5 million through online media and news broadcasts

Our research in numbers

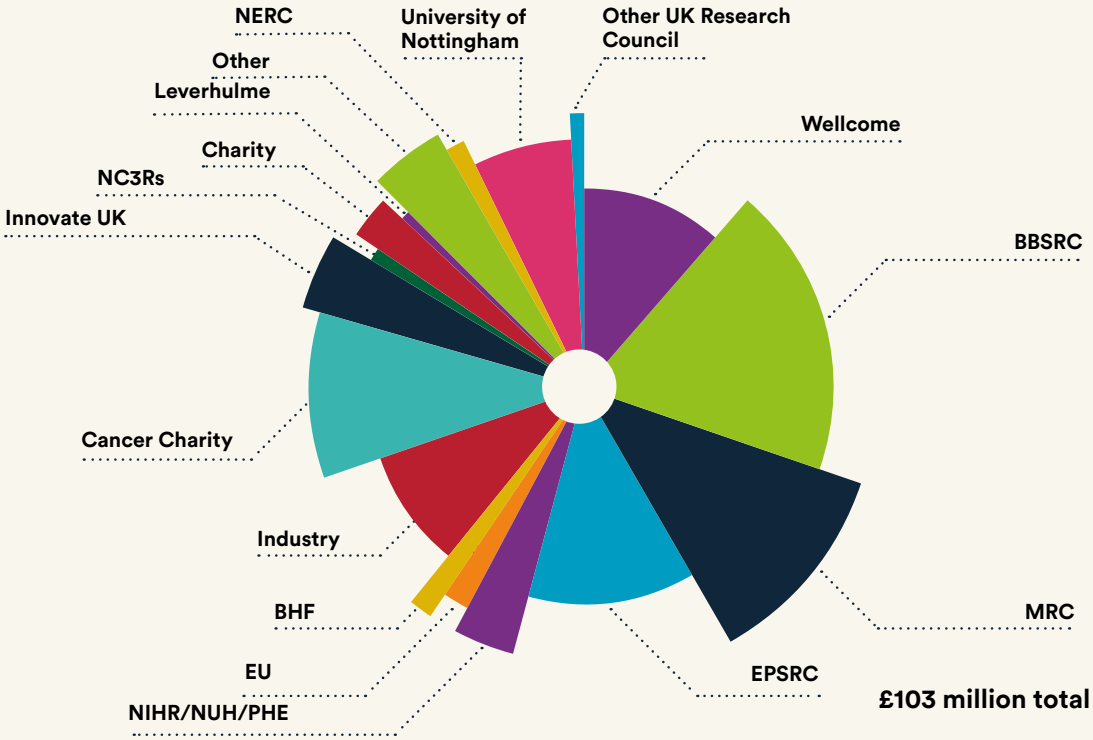
The Biodiscovery Institute community



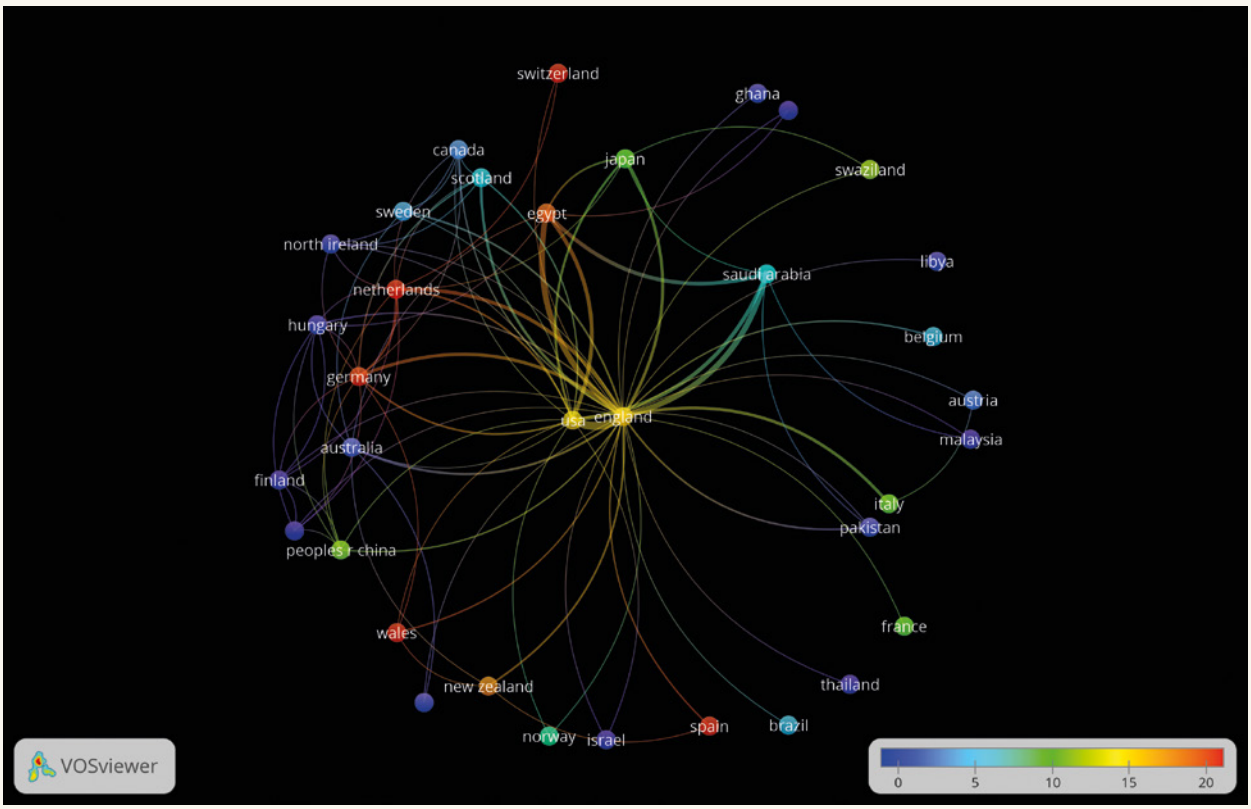
Biodiscovery Institute research activity by theme



Research funding 2015-2022



International Collaborations with the BDI



Our Research Leaders

Name	Research Themes	Research Keywords	Research Techniques
Cinzia Allegrucci		Cancer, stem cells, epigenetics, disease modelling, genetics	iPSC technology, 3D cell culture models, in vitro assays, epigenetic analysis
Kenton Arkill		Vascular permeability, endothelial glycocalyx, electron microscopy, correlative microscopy techniques	Functional permeability assays, 3D TEM, correlative microscopy techniques
Jennifer Ashworth		Biomaterials, fibrosis, cancer research, 3D in vitro models, imaging tissue	3D cell culture, biomaterials design and fabrication, primary cell/organoid culture, confocal imaging, micro-CT analysis
Steve Atkinson		Yersinia pestis, plague, black death, molecular genetic pathways, antibiotic resistance	Plague insect infection, soil infection, molecular genetics of plague
David Bates		Angiogenesis, vascular remodelling, cholangiocarcinoma, renal glomerular physiology, diabetes	In vivo imaging, RNA splicing, molecular and cellular biology, drug discovery
Andrew Benest		Endothelial cells, lymphatics, angiogenesis, vasculature, transcription factors	Transcriptomic, in vivo modelling, confocal imaging
Ben Blount		Synthetic genomics, synthetic biology, microbial strain engineering, genome engineering, yeast genetics	DNA assembly, CRISPR, chromosome design, SCRaMbLE
Dan Booth		Chromosomes, mitosis, advanced-imaging, cancer, cell-division	CLEM, electron microscopy, advanced proteomics, advanced imaging, light microscopy, volume microscopy
Tracey Bradshaw		Cancer, pharmacology, drug discovery, apoferritin, molecular mechanisms	Tissue culture, cell biology, MTT, western blot, flow cytometry
Lee Buttery		3D cell models, stem cells, osteoblasts, cell-materials interactions, tissue engineering	3D and ES cell culture, osteoblast culture, immunocytochemistry, optical tweezers for cell biology
Miguel Camara		Biofilms, quorum sensing, antimicrobials, microbial gene regulation, antimicrobial target discovery	Biofilm model design, biofilm imaging, bacterial transcriptomics, bioreporter design, HTP antimicrobial testing
Weng Chan		Antibiotic discovery, medicinal chemistry, chemical biology, anti-virulence, peptide chemistry	Solid-phase peptide synthesis, organic synthesis, in vitro microbial assay, drug design
Yan Chen		Artificial intelligence, quality assurance, digital screening, medical imaging	Programming, algorithms, artificial intelligence, DICOM image processing
Rachel Clifford		Respiratory, Epigenetics, Transcriptional regulation, DNA methylation, inhaled exposures	Primary cell culture, methylomics, histone modification analysis, transcriptomics, molecular biology
Beth Coyle		Paediatric brain tumours, resistance, metastasis, tumour microenvironment	3D cell culture, apoptosis, cytotoxicity, migration assays
Madhu Dandapani		Childhood cancer, brain tumours, cancer metabolism, clinical trials, global health	Immunohistochemistry, western blotting, cell culture, multi-omics, systematic reviews
Lodewijk Dekker		Drug discovery, cancer, thrombosis, protein kinase, protein interactions	Biochemical assays, cellular assays, enzyme assays, assay development, high throughput screening
Chris Denning		Human pluripotent stem cells (hPSCs), heart/cardiovascular disease, drug discovery and evaluation, regenerative medicine	Cardiovascular lineage differentiation, CRISPR engineering, phenotype-genotype correlations, automation
James Dixon		Gene therapy, gene editing, vaccines, nucleic acid delivery, regenerative medicine	Genetic engineering/editing, nanoformulation, reporter assays, particle characterisation, biomaterials
Ingrid Dreveny		Proteases in the ubiquitin system, protein structure, structure-aided drug design, enzyme specificity, proteins in biotechnology	Macromolecular X-ray crystallography, isothermal titration calorimetry, biochemistry, protein engineering

Name	Research Themes	Research Keywords	Research Techniques
Lindy Durrant		Cancer immunotherapy, vaccines, monoclonal antibodies, T cells, post-translational modifications	Production of antibodies, vaccine design, cancer animal models, T cell assays, ELISA
Isioma U. Egbuniwe		Bile duct cancer, tumour microenvironment, T and B cells, lymphatics, digital pathology	Primary cell isolation and culture, multi-parameter flow cytometry, 3D tumour-immune cell co-culture systems, histopathology, image analysis
Jonas Emsley		Structural biology, protein crystallography, protease structure, receptor structure, drug development	Protein crystallography, isothermal titration calorimetry, surface plasmon resonance, molecular docking
Mattea Finelli		Neurodegenerative diseases, redox mechanisms, oxidative and nitrosative stresses, proteomics, post-translational modifications of proteins	Quantitative/redox/PTMs proteomics, cell- and recombinant protein-based assays, stem cell derived disease models, various cell cultures (cortical, cerebellar, hippocampal, DRG, motor neurons)
Hester Franks		Cancer, immunotherapy, macrophages, tumour microenvironment, melanoma	Primary immune cell isolation and culture, flow cytometry, RNAScope
Kevin Gaston		Cancer, gene regulation, transcription, cell biology, protein-DNA interactions	RNA sequencing, ChIP sequencing, cell migration assays, cell viability assays, EMSA
Pavel Gershkovich		Biopharmaceutics, pharmacokinetics, drug delivery, intestinal lymphatic transport, targeted biodistribution	Bioanalysis, HPLC, in vivo pharmacokinetics, in vivo biodistribution, pharmacokinetic modelling and simulation
Amanda Goodwin		Fibrosis, development, lung repair	In vitro cell stretch (Flexcell), G protein knockdown studies, TMLC assays (TGFbeta signalling assay), ECM crossover studies
Anna Grabowska		Cancer models, tumour microenvironment, target validation, drug screening, drug delivery	Cancer modelling, 3D tissue culture, quantitative PCR, immunohistochemistry
Andrew Green		Breast cancer, molecular pathology, glutamine metabolism, genotype, phenotype	Immunohistochemistry, tissue microarrays (TMAs), laser microdissection, gene expression profiling, in situ hybridisation
Ruth Griffin		Oral vaccine delivery systems, infectious diseases	Gene cloning and protein purification, formulation, in vivo immunogenicity and challenge studies, antibody assays
Nick Hannan		Stem cells, disease modelling, respiratory disease, liver disease, inflammatory bowel disease	Stem cell differentiation, cell phenotyping, gene editing, CRISPR base editing, organoids
Kim Hardie		Biofilms, antimicrobial resistance, bacteria, pathogenicity, protein secretion	Fluorescent microscopy, infection models, microbiology, protein biochemistry, metabolite detection
John Heap		Engineering biology / synthetic biology, metabolic engineering, biotechnology, biocatalysis, enzyme evolution	Engineering biology / synthetic biology, metabolic engineering, biotechnology, biocatalysis, enzyme evolution
Stephan Heeb		Bacterial infections, virulence, quorum sensing, gene expression, antimicrobial strategies	Bacterial genomics, RNA-Seq, RNA-protein interactions, construction of bacterial vectors

Defeating Cancer

Demystifying Biomolecular Complexity

Engineering Biology

Pioneering Therapeutics

Regenerating and Modelling Tissues

Taming Microbes

Name	Research Themes	Research Keywords	Research Techniques
Mohammad Ilyas		Colorectal cancer, mutation analysis, liquid biopsy, cancer biomarkers, tissue modelling	Histopathology, PCR, co-culture models, gene cloning
Andrew M.Jackson		Cancer, immunotherapy, dendritic Cells (DC), T-cells, signalling	Isolation of rare primary leukocyte subsets, flow cytometry, small molecule kinase inhibitors, multi-cellular immune culture systems
Victoria James		Extracellular vesicles, RNA biology, cancer metastasis, epigenetics, inter-cellular communication	Nanoparticle biology, RNA biology, cell biology, epigenetics
Sheela Jayaraman		Gene expression, chromatin, PRH/HHEX, cell signalling, transcriptomics	RNAseq, western blotting, subcloning, ChIP Seq, tumour biology phenotypic assays, epigenetics, 3D models
Jennie Jeyapalan		Epigenomics, prostate cancer, transcriptional regulation, splicing	Genomics, RNA seq analysis, molecular biology, cell culture
Simon Johnson		Tissue remodelling, proteases, extracellular matrix, rare lung disease, drug repurposing	Protease assays, complex cell culture, molecular pathology
Barrie Kellam		Medicinal chemistry, fluorescent ligands, G protein-coupled receptors, drug discovery	Medicinal chemistry, molecular modelling, biospectroscopy, HPLC, fluorescence Imaging
Laura Kilpatrick		Molecular pharmacology, G protein coupled receptors, receptor tyrosine kinases, signalling complexes, protein-protein interactions	Bioluminescence resonance energy transfer (BRET), fluorescence correlation spectroscopy, fluorescence imaging, pharmacological assays
Katalin Kovacs		Engineering biology, metabolic engineering, autotrophic microorganisms, bioelectochemical synthesis, circular economy	Molecular biology, microscopy, microbial cultivation, electrofermentation, plastid engineering
Charlie Laughton		Biomolecular structure, molecular recognition, drug design, formulation design, molecular dynamics	Molecular dynamics simulations, protein structure prediction, virtual screening, machine learning, software development
Anbarasu Lourdusamy		Brain cancer, childhood cancer, systems biology, artificial intelligence, big data	Bioinformatics, NGS (RNAseq, ChIPseq, scRNAseq and ATAC-seq) data analysis, machine learning, statistics, high-performance computing
Srinivasan Madhusudan		Medical oncology, clinical trials, breast cancer, DNA repair therapeutics, drug discovery	DNA repair assays, immunohistochemical techniques, clinical trial methodologies
Anna Malecka		Cancer, immunology, macrophages, comparative oncology, immune-stromal interactions	Flow cytometry, stroma-Immune co-culture system, cell culture
Stewart Martin		Breast, brain and ovarian cancer, radiotherapy, metastasis, novel drugs, redox homeostasis, calpain proteases	Radiation biology, immunohistochemistry, cell and molecular biology
Alvaro Mata		Biomaterials, tissue engineering, regenerative materials, in vitro models, biomineralization	Self-assembly, bioprinting, electron microscopy
Alan Mcintyre		Cancer, hypoxia (low oxygen), acidosis, transcription, epigenetics, angiogenesis	CRISPR CAS9, RNA-SEQ, ChIP, tumour cell phenotype assays, hypoxia and acidosis investigations
Cathy Merry		Matrix biology, cancer research, disease modelling, glycobiology	Glycobiology, hydrogel development, stem cell culture and differentiation, matrix biology, in vitro disease models
Nigel Minton		Exploiting autotrophy, reducing carbon emissions, industrial biotechnology, microbial pathogenesis, anaerobes	Synthetic biology, metabolic engineering, gas fermentation, genome editing, therapeutic delivery systems
Shailesh Mistry		Drug discovery, chemical biology, medicinal chemistry, G protein-coupled receptors (GPCRs), allosteric modulators	Medicinal chemistry, compound purification, spectroscopic analysis, ligand / structure-based drug discovery

Name	Research Themes	Research Keywords	Research Techniques
Nigel Mongan		Bioinformatics, precision medicine, prostate cancer, breast cancer	Bioinformatics, epitranscriptomics
Abhik Mukherjee		Digital / molecular pathology, gastrointestinal and pancreaticobiliary cancers, translational therapeutics, inflammatory bowel disease	Histopathology and immunohistochemistry, digital pathology and image analyses, molecular pathology, functional biology
Paloma Ordeonez Moran		Stem cells, inflammation, differentiation, cancer, tumour heterogeneity	3D organoids, primary mouse and human cell culture, stem cell-based approaches, in vivo assays, gene expression
Ellis O'Neill		Natural products, algal biotechnology, biotransformation	Analytical chemistry, mass spectrometry, protein expression and purification, genome mining
Poulam Patel		Melanoma, renal cancer, cancer immunotherapy, clinical trials, translational medicine	Clinical trials, immune assays
Ruman Rahman		Brain cancer, cancer heterogeneity, cancer metabolism, biomaterial-based drug delivery, integrated genomics	Defeating Cancer, Pioneering Therapeutics
Emad Rakha		Breast cancer, pathology, classification, prognosis, digital pathology, AI, predictive and prognostic markers	Defeating Cancer, Demystifying Biomolecular Complexity
Judith Ramage		Cancer, immunology, T-lymphocytes, vaccines	Defeating Cancer, Pioneering Therapeutics
Frankie Rawson		Wireless bioelectronics, bioelectricity, electrochemistry, bionanotechnology, bioelectronic medicine	Regenerating and Modelling Tissues, Defeating Cancer, Pioneering Therapeutics
Timothy Ritzmann		Childhood brain tumours, brain tumour immunity, childhood cancer, ependymoma, cancer recurrence	RNA-sequencing, multiplex immunofluorescence, immunohistochemistry, clinical data analysis, childhood brain tumour clinical trials
Karen Robinson		Helicobacter pylori, antimicrobial resistance, infection and immunity, gastric cancer, bacterial virulence	Flow cytometry, real-time PCR, immunohistochemistry, antimicrobial sensitivity testing, immune cell purification and culture
Felicity Rose		Biointerfaces; biomaterials; peptide materials; hydrogels; computational material science	Surface modification and analysis; polymerisation kinetics; light and enzyme responsive materials; material characterisation
Ian Sayers		Molecular, genetic and cellular mechanisms underlying asthma and chronic obstructive pulmonary disease, virus-host interactions, stratified medicine	Gene discovery, primary airway cell and tissue models, functional genetics, transcriptomics, patient translational studies
Claire Seedhouse		Blood cancers, drug resistance, stem cells, dormancy, functional consequences of mutations	Quantitative PCR, flow cytometry, primary suspension cultures
Abdolrahman Shams-Nateri		Adult stem cells and cancer, precision oncology / personalized cancer treatments, intra-tumour heterogeneity, cell signalling and transcription, ubiquitin proteasome system and F-box proteins	3D Organoids and explants models, gene targeting and transgenics, CRISPR-Cas gene editing systems, epithelial and hematopoietic stem cells assays
Stuart Smith		High grade glioma, low grade glioma, childhood brain tumours, drug delivery, tumour heterogeneity	rtPCR, RNA methylation, IHC, FACS

Defeating Cancer

Demystifying Biomolecular Complexity

Engineering Biology

Pioneering Therapeutics

Regenerating and Modelling Tissues

Taming Microbes

Name	Research Themes	Research Keywords	Research Techniques
Philippe Soucaille		Metabolic engineering, system biology, synthetic biology, microbial physiology - CO_2 fixation	Enzyme evolution, bacterial genome editing, fluxomics, proteomics, transcriptomics
Panos Soultanas		DNA replication, DNA repair, replication-metabolism regulation, genome stability	Protein expression, purification, polymerase and helicase assays, analytical ultracentrifugation, SPR
Ian Spendlove		Controlling iTreg, engineering T cells, cloning TCRs from cancer patients, cancer survivors, anti cancer antibodies.	TCR cloning / transduction, CRISPR-Cas9 of primary leukocytes, flow sorting rare T cells, differentiating iTreg, autophagosome purification.
Michael Stocks		Medicinal chemistry, drug discovery, cancer, antimicrobial resistance, prodrugs	Synthesis, drug optimisation, drug delivery, medicinal chemistry
Sarah Storr		Cancer, breast cancer, DARPP-32, calpain, cell signalling	Cell culture, bioinformatics, immunohistochemistry, molecular biology, protein purification
Amanda Tatler		Respiratory disease, tissue remodelling, fibrosis, matrix, 3D models	Precision cut tissue slices, in vivo respiratory models, molecular biology, TGFb activation assays, immunohistochemistry / immunofluorescence
Neil Thomas		Enzyme mechanism, enzyme inhibitors, biopharmaceutics, silk and other protein-based biomaterials, nanobiotechnology	Bioconjugation, chemiluminescence, un-natural amino acid mutagenesis, enzyme activity assays, enzyme inhibitor design
Alexander Thompson		Blood cancer, stem cell technologies, pre-clinical evaluation, next-generation models, drug discovery	In vivo modelling, iPSC maintenance and differentiation, haematopoiesis, colony-forming assays, gene expression profiling
Lisa White		Regenerative medicine, biomaterials, extracellular matrix, hydrogels, microparticles	Decellularization, micro x-ray computed tomography, mammalian cell culture, biomaterials characterisation, supercritical CO_2
Huw Williams		NMR, molecular interactions, molecular structure, analytical, kinetics	NMR, molecular interactions, solid state NMR, molecular dynamics, molecular structure
Paul Williams		Quorum sensing, biofilms, bacteria, biomaterials, antimicrobial agents	Bacterial genetics, bacterial culture, antimicrobial assays, quorum sensing assays, microscopy / imaging
Klaus Winzer		Microbial metabolism, biological engineering, synthetic biology, bacterial carbon capture, quorum sensing	Anaerobic microbiology, gas fermentation, genetic modification of bacteria, adaptive laboratory evolution
Jing Yang		Biomaterials, 3D bioprinting, tissue engineering, regenerative medicine, immunomodulatory materials	3D printing, biomaterial preparation, chemical characterisation, mechanical testing, cell culture
Mischa Zelzer		Biointerfaces; biomaterials; peptide materials; hydrogels; computational material science	Surface modification and analysis; polymerisation kinetics; light and enzyme responsive materials; material characterisation
Ying Zhang		Industrial biotechnology, biological engineering, single-carbon utilising bacteria for carbon capture, sustainable bioproducts, biorecovery.	Synthetic biology, bacterial genome editing, metabolic engineering, protein engineering, strain improvement

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Find out more about these researchers here:

Companies that are or have been hosted by the Biodiscovery Institute

Scancell develops innovative cancer immunotherapies that stimulate the body's own immune system to treat or prevent cancer with minimal toxicity. Moditope® is a novel class of cancer vaccines, which is based on stress-induced post translational modifications. Alongside our ImmunoBody® platform, these two technologies provide complementary anti-tumour therapies. Our AvidiMab™ antibody platform provides a third method of attack against overexpressed tumour targets. The ImmunoBody® platform has been adapted to produce a cost-effective vaccine against the SARS-Cov-2 virus.
Scancell recently granted Genmab a worldwide license to its monoclonal antibody GlyMab® technology in a deal worth up to $624 million.

Visit: **scancell.co.uk**

Peripheral arterial disease (PAD) is a major global healthcare burden. IsomAb targets a mechanism that prevents regeneration of blood vessels in PAD (and coronary vascular disease). IsomAb is focused on the development of VEGF-A165b-specific therapeutic antibodies. The company is in pre-clinical development with lead compounds and intends to be in Phase I clinical trial by 2026. Founded by David Bates at the University of Nottingham and Steve Harper from the University of Bristol a pre-seed round of $1 million was completed in December 2022, with funds raised from Science Creates Ventures, Nottingham Technology Ventures, and some individual investors.

Visit: **isomab.bio/**

Current *in vitro* models of development and disease typically fail to recapitulate the complexities of native tissue environments, leading to a poor extrapolation of *in vitro* findings to *in vivo* relevance. Growing recognition of this has led to a recent interest in developing more sophisticated 3D *in vitro* models which allow for customisation of matrix stiffness and composition.
PeptiMatrix is a new University of Nottingham spinout company providing access to a fully synthetic and customisable peptide hydrogel platform for 3D cell culture. We have recently been awarded £270,690 in grant funding from Innovate UK to develop and launch a range of hydrogel products that aim to reduce, and eventually replace, the use of animals in research.

Visit: **peptimatrix.com**

Deep Branch and Chain Biotechnology were founded in the Biodiscovery Institute before moving to larger facilities elsewhere.

Visit: **deepbranch.com and chainbiotech.com**

Companies supported by the Synthetic Biology Research Centre's (SBRC) industrial collaboration model

Founded in 2018, Phenotypeca Ltd is a synthetic biology company combining yeast genomics technology developed by Professor Ed Louis, initially at the University of Nottingham and then in Leicester, with manufacturing expertise from the biopharmaceutical industry.
We use advance breeding of genetically diverse yeast to produce up to a billion novel strains for high-throughput screening. From these we select production strains with optimal phenotypes for future biomanufacturing processes.
Phenotypeca is a member of the Future Vaccine Manufacturing Research Hub (Vax-Hub) with Innovate UK funding, optimising biologics production processes for cost reduction and improved access to medicines, such as vaccines for developing countries.

Visit: **phenotypeca.com**

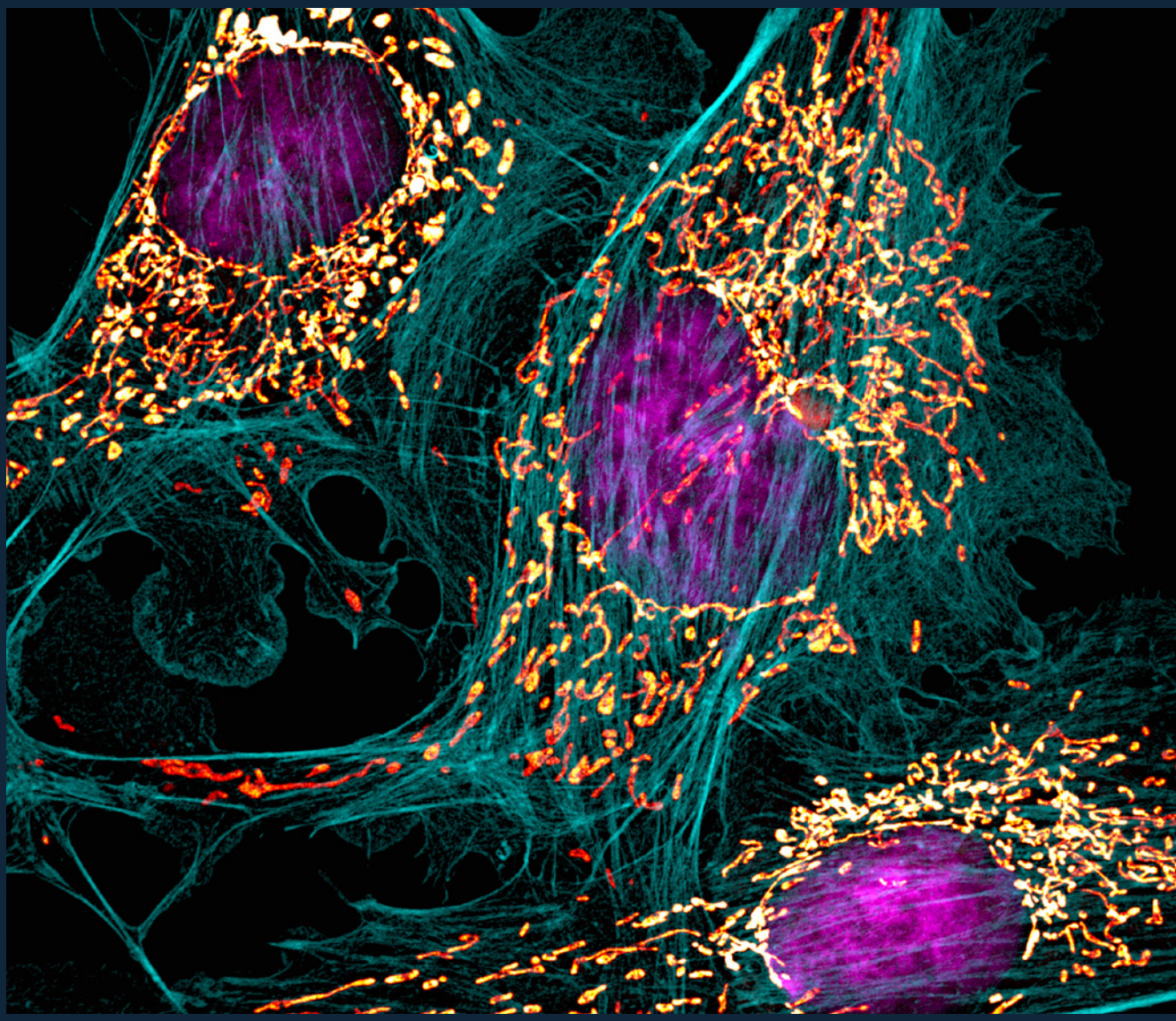
Launched in 2020, PHASE Biolabs makes carbon-negative chemicals from carbon dioxide (CO_2) using fermentation. Developing a technology that enables the conversion of CO_2 into sustainable solvents for the pharmaceutical, cosmetic, and paint industries, this helps to mitigate the effects of CO_2 emissions and enables our customers to generate new revenue streams from their waste CO_2. The company utilises engineering biology approaches to develop advanced biocatalysts which are able to convert CO_2 into products faster and more efficiently than is naturally possible. Collaboration with the SBRC has enabled access to world leading gas fermentation facilities to complete early development work, and resulted in Innovate UK government grants to continue this work.

Visit: **phasebiolabs.com/**

NetZeroNitrogen Ltd (NZN) activity focusses on the 'forgotten' element of greenhouse gases (GHG): nitrogen. Although gaseous N2O makes up just a fraction of global GHG emissions, its global warming potential is 298x greater than CO_2. Much of this N2O results from synthetic nitrogen fertilizer used in agriculture. NZN is developing natural nitrogen-fixing bacteria to replace synthetic nitrogen fertilizer. NZN will deliver its proprietary bacteria at the point of need in the plant, so that all the fixed nitrogen is used by the plant. Research and development will focus on using synthetic biology approaches and advanced genome engineering tools to better understand natural organisms and optimize strains for agricultural use.

Visit: **inms.international/nitrogen4netzero**

University of Nottingham
Biodiscovery Institute



Find out more
nottingham.ac.uk/go/biodiscovery-institute

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