UNIVERSITY OF LIVERPOOL

INSTITUTE OF SYSTEMS, MOLECULAR AND INTEGRATIVE BIOLOGY

RESEARCHER DIRECTORY

Professor Patrick Eyers

Head of Department

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Biochemistry, Cell and Systems Biology

Protein kinases ▪ pseudokinases ▪ redox signalling

Professor Eyers' research interests include protein phosphorylation and sulfation, redox-based analysis of protein kinase and sulfotransferase mechanisms, pseudoenzymes and kinome-wide mechanisms of acquired drug resistance in cells. He also teaches cell signalling, running modules explaining the biochemical mechanisms underpinning cell communication.

In 2022, he spun-out the biotech company Sulantrix (www.sulantrix.com) from the University of Liverpool, to develop a new generation of anti-cancer agents targeting pseudoenzymes such as pseudokinases. He serves on various panels at the BBSRC and Biochemical Society and is an Associate Editor of the Biochemical Journal.

Selected publications

Omar MH, Byrne DP, Shrestha S, Lakey TM, Lee KS, Lauer SM, Collins KB, Daly LA, Eyers CE, Baird GS, Ong SE, Kannan N, Eyers PA and Scott JD (2024) Discovery of a new Cushing's syndrome PKAc mutant that is retained within anchored type I holoenzymes. Science Advances adl1258.

Venkat A, Watterson G, Byrne DP, O'Boyle B, Shrestha S, Gravel N, Fairweather EE, Daly LA, Bunn C, Yeung W, Aggarwal I, Katiyar S, Eyers CE, Eyers PA*, Kannan N* (2023) Mechanistic and evolutionary insights into isoform-specific 'supercharging' in DCLK family kinases. eLife 87958

Byrne DP, Harris JA, Shrestha S, Ramakrishnan K, Daly LA, Eyers CE, Kannan N and Eyers PA* (2023). Evolutionary and cellular analysis of the 'dark' pseudokinase PSKH2. Biochemical Journal 480: 141-60.

Dr Svetlana Antonyuk

Reader

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Biochemistry, Cell and Systems Biology

Understanding catalysis in denitrification enzymes and search for a cure for malaria and liver disease

For denitrification enzymes that use redox centres we are utilizing the advanced Synchrotron and X-ray laser -based crystallographic approaches (at DIAMOND, UK and SACLA, Japan) as well as high resolution cryoEM approach to define enzyme mechanism of these life-sustaining enzymes. The cryoEM revolution has allowed us to combine it with our crystallographic studies of cytochrome bc1, a complex of the electron transport chain, and a validated antimalarial target. The use of cryoEM facilities at Leeds and DIAMOND is allowing visualization of drug candidates in solution of bc1 at high resolution. X-ray and cryoEM approaches are also utilized for studying MAT enzymes and complexes, a key enzyme associated with Liver disease.

Selected publications

A 2.2Å cryoEM structure of a quinol-dependent NO Reductase shows close similarity to respiratory oxidases Flynn, A. J., Antonyuk, S. V., Eady, R. R., Muench, S. P., & Hasnain, S. S. (2023). NATURE COMMUNICATIONS, 14(1). doi:10.1038/s41467-023-39140-xDOI: 10.1038/s41467-023-39140-x

The expanding toolkit for structural biology: synchrotrons, X-ray lasers and cryoEM Muench, S. P., Antonyuk, S. V., & Hasnain, S. S. (2019). IUCRJ, 6(2), 167-177. doi:10.1107/S2052252519002422

Catalytically important damage-free structures of a copper nitrite reductase obtained by femtosecond X-ray laser and room-temperature neutron crystallography. Halsted, T. P., Yamashita, K., Gopalasingam, ...Antonyuk, S.V.,Yamomoto, M., Hasnain, S. S. (2019). IUCRJ, 6, 761-772. doi:10.1107/S2052252519008285

Dr Igor Barsukov

Reader in Biomolecular NMR

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Biochemistry, Cell and Systems Biology

Structure and dynamics of proteins in cell adhesion and cell migration. Analysis and engineering of biotechnological materials

Igor Barsukov's main research field is protein NMR spectroscopy, focusing on the structure and function of proteins in cell adhesion systems, and structural enzymology. He studies molecular mechanisms that define protein dynamics, interactions and phase separation. His structure of the key adhesion protein talin contributed into the understanding talin role in mechanosensitivity of integrin adhesion complex. His structural analysis of neuronal protein shank3 revealed novel signalling pathway and defined the effects of the autism-related mutations.

Igor Barsukov has a strong interest interest in industrial biotechnology and NMR analysis of biomaterials. He developed an NMR-based approach for the analysis of complex polysaccharides and lipid mixtures. He has strong industrial collaborations in the biotechnology area supported through UKIR funding. In his research he applies a wide range of biophysical methods for molecular analysis, including ITC, BLI, DSF and DLS.

Selected publications

Atherton, P., R. Konstantinou, S.P. Neo, E. Wang, E. Balloi, M. Ptushkina, H. Bennett, K. Clark, J. Gunaratne, D. Critchley, I. Barsukov, E. Manser, and C. Ballestrem, Tensin3 interaction with talin drives the formation of fibronectin-associated fibrillar adhesions. J Cell Biol, 2022. 221(10): p. e202107022

Atherton, P., F. Lausecker, A. Carisey, A. Gilmore, D. Critchley, I. Barsukov, and C. Ballestrem, Relief of talin autoinhibition triggers a force-independent association with vinculin. J Cell Biol, 2020. 219(1): p. e201903134

Lilja, J., T. Zacharchenko, M. Georgiadou, G. Jacquemet, N. De Franceschi, E. Peuhu, H. Hamidi, J. Pouwels, V. Martens, F.H. Nia, M. Beifuss, T. Boeckers, H.J. Kreienkamp, I.L. Barsukov, and J. Ivaska, SHANK proteins limit integrin activation by directly interacting with Rap1 and R-Ras. Nat Cell Biol, 2017. 19(4): p. 292-305.

Dr Dominic Byrne

Tenure Track Fellow

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Biochemistry, Cell and Systems Biology

Eukaryotic and Prokaryotic Protein kinases ▪ Redox signalling

Dr Byrne's primary interests include understanding the regulatory mechanisms that underpin and coordinate various aspects of cellular signalling, such as the modulation of enzymes by co-factors, small molecule ligands and post translational modifications (phosphorylation, sulfation, cysteine oxidation). In particular, his research focuses on the biochemical characterisation of eukaryotic and prokaryotic protein kinases, pseudokinases and sulfer transferring enzymes, as potential targets for therapeutic intervention in a variety of human disease.

Selected publications

Bendzunas GN, Byrne DP, Shrestha S, Daly LA, Oswald SO, Katiyar S, Venkat A, Yeung W, Eyers CE, Eyers PA*, Kannan N* (2024) Redox Regulation of Brain Selective Kinases BRSK1/2: Implications for Dynamic Control of the Eukaryotic AMPK family through Cys-based mechanisms. bioRxiv: doi: https://doi.org/10.1101/2023.10.05.56114

Venkat A, Watterson G, Byrne DP, O'Boyle B, Shrestha S, Gravel N, Fairweather EE, Daly LA, Bunn C, Yeung W, Aggarwal I, Katiyar S, Eyers CE, Eyers PA*, Kannan N* (2023) Mechanistic and evolutionary insights into isoform-specific 'supercharging' in DCLK family kinases. eLife 87958

Byrne DP, Harris JA, Shrestha S, Ramakrishnan K, Daly LA, Eyers CE, Kannan N and Eyers PA* (2023). Evolutionary and cellular analysis of the 'dark' pseudokinase PSKH2.Biochemical Journal 480: 141-60.

Dr Daniel Canniffe

Senior Lecturer

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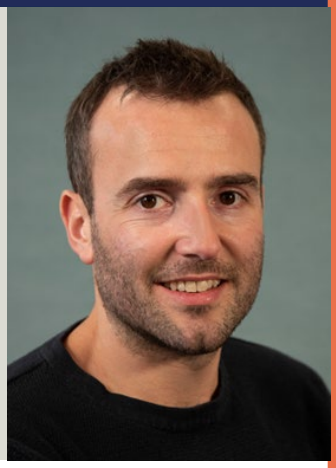

Biochemistry, Cell and Systems Biology

Improving photosynthesis – exploiting underutilised regions of the solar spectrum

My group aims to improve the efficiency of photosynthesis by enhancing light capture in unused regions of the spectrum. We do this by genetically engineering phototrophs to produce non-native or novel pigments with unique absorption properties – and by modifying the proteins that bind them – generating new strains with broadened spectral coverage. The long-term impact of this research will be in the development of new solar-powered platform organisms for biotechnological exploitation, and the modification of plants to improve crop yields and season length.

Selected publications

Globally distributed *Myxococcota* with photosynthesis gene clusters illuminate the origin and evolution of a potentially chimeric lifestyle. Nature Communications 14:6450 (2023) 10.1038/s41467-023-42193-7

The role of the γ subunit in the photosystem of the lowest-energy phototrophs. Biochemical Journal 479:2449 (2022) 10.1042/BCJ20220508

Cryo-EM structure of the Blastochloris viridis LH1–RC complex at 2.9 Å. Nature 556:203 (2018) 10.1038/s41586-018-0014-5

Dr Stephen Chapman

Lecturer in Computational Biology and Statistics

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Biochemistry, Cell and Systems Biology

Computational modelling of complex biological systems

Dr Chapman's research involves integrating multi-omics data to quantitative and qualitative predictive mathematical models and has expertise with genome scale metabolic modelling and logical modelling of cellular signalling. Stephen completed his PhD at the University of Manchester and previously worked as a Teaching Fellow at Aberystwyth University and as a Post doctorate at Aix-Marseille University.

His research spans photosynthetic regulation, the bioeconomy, understanding how dysregulated cellular signalling contributes to disease and the mitochondrial role in aging.

Selected publications

Chapman, S. P., et al (2023). Logical modelling of myelofibrotic microenvironment predicts dysregulated progenitor stem cell crosstalk. Biosystems, 231, 104961..

Chapman, S. P., et al. (2023). MitoMouse is a model reconstruction of murine mitochondrial metabolism. bioRxiv, 2023-01.

Guo, M., Wu, C., Chapman, S., et al. (2023). Advances in biorenewables-resource-waste systems and modelling. Carbon Capture Science & Technology, 100142.

Stiles, W. A., Styles, D., Chapman, S. P., et al. (2018). Using microalgae in the circular economy to valorise anaerobic digestate: challenges and opportunities. Bioresource technology, 267, 732-742

Dr Andrew Chetwynd

Tenure Track Fellow

Kidney Research UK Senior Non-Clinical Research Fellow

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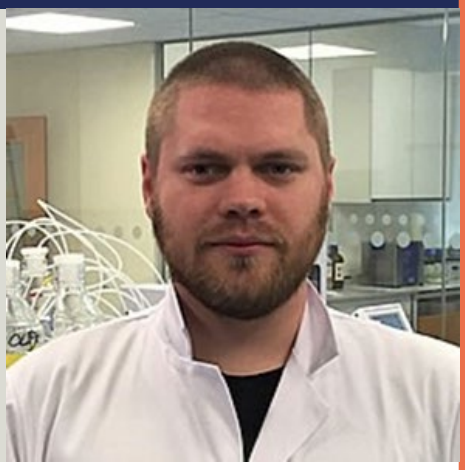

Biochemistry, Cell and Systems Biology

Glycan profiling in IgA mediated kidney disease

Primarily investigating the role of immunoglobulin and complement pathway glycosylation in IgA mediated kidney disease.

Interest in the development of novel separation and mass spectrometric methodologies in particular in the application of capillary electrophoresis to proteomics and metabolomics.

Strong background and interest in the bio-nano interface of nanomaterials and their biological environment.

Selected publications

Drouin, N., van Mever, M., Zhang, W., Tobolkina, E., Ferre, S., Servais, A. -C., . . . Ramautar, R. (2020). Capillary Electrophoresis-Mass Spectrometry at Trial by Metabo-Ring: Effective Electrophoretic Mobility for Reproducible and Robust Compound Annotation. ANALYTICAL CHEMISTRY, 92(20), 14103-14112.

Marro, J., Chetwynd, A. J., Hawkes, J., Northey, S. J., & Oni, L. (2023). Urinary markers of the alternative and lectin complement pathway are increased in IgA vasculitis nephritis.. Clinical kidney journal, 16(12), 2703-2711. doi:10.1093/ckj/sfad236

Guo, Z., Zhang, P., Xie, C., Voyiatzis, E., Faserl, K., Chetwynd, A. J., . . . Lynch, I. (2023). Defining the Surface Oxygen Threshold That Switches the Interaction Mode of Graphene Oxide with Bacteria. ACS NANO. doi:10.1021/acsnano.2c10961

Professor Michael Clague

Professor of Molecular and Cellular Physiology

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Biochemistry, Cell and Systems Biology

Ubiquitin and organelle biology

Our interests cover aspects of membrane trafficking (endocytosis, autophagy, mitochondrial dynamics) and cell signaling with a view to understanding mechanisms that lead to pathologies such as cancer and neurodegeneration (Parkinson's Disease). We have a strong interest in the deubiquitylase (DUB) family of enzymes. We contribute to drug discovery programmes in this area together with other academic centres and industry partners. My laboratory is codirected with Sylvie Urbé. I am currently a Royal Society Industry Fellow.

Selected publications

Elcocks, H., Brazel,A.J., McCarron,K.R, Kaulich,M., Husnjak,K., Mortiboys,H., Clague,M.J. and Urbé,S. (2023) FBXL4 ubiquitin ligase deficiency promotes mitophagy by elevating NIX levels. EMBO Journal 42: e112799.

Clancy, A., Heride,C. Pinto-Fernández, A., Elcocks,H., Kallinos,A., Kayser-Bricker,K.J., Wang, W., Smith,V. Davis,S., Fessler,S., McKinnon,C., Katz,M., Hammonds,T., Jones, N.P., O'Connell,J., Follows,B., Mischke, S., Caravella,J.A., Ioannidis,S., Dinsmore,C., Kim, S., Behrens,A., Komander,D., Kessler,B.M., Urbé,S, Clague,M.J. (2021) The deubiquitylase USP9X controls ribosomal stalling. J. Cell Biol. 220 (3): e202004211.

Clague, M.J., Urbé,S. and Komander,D. Breaking the chains: deubiquitylase specificity begets function. (2019) Nature Reviews in Molecular Cell Biology, 20, 338-352.

Dr Nicola Darling

Tenure Track Fellow

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Biochemistry, Cell and Systems Biology

Regulation of mast cell granule formation and degranulation

Inappropriate activation and release of mast cell content by degranulation contributes to both allergic and non-allergic diseases. Identifying and characterising intracellular signalling pathways that regulate granule formation and degranulation is critical to understanding mast cell biology and may help to inform new therapeutic approaches.

To underpin this research, we also characterise mast cell activation models to establish robust and relevant systems for signalling research and with potential clinical applications.

Selected publications

Salt-inducible kinases are required for the IL-33-dependent secretion of cytokines and chemokines in mast cells. NJ Darling, JSC Arthur, P Cohen. J. Biol. Chem. (2021) 296 doi: 10.1016/j.jbc.2021.100428

Salt-inducible kinase (SIK) inhibition is protective in a mouse model of asthma. M van Gijsel-Bonnello, NJ Darling, L McDonald, M Sime, J Clark, M Mezna, A Schuettelkopf, C Mackay, J Bower, H McKinnon, P Cohen, JSC Arthur. bioRXiv (2021) preprint doi: 10.1101/2021.06.07.447230

Inhibition of SIK2 and SIK3 during differentiation enhances the anti-inflammatory phenotype of macrophages. NJ Darling, R Toth, JSC Arthur, K Clark. Biochem. J. (2017) 474:521-537 doi: 10.1042/BCJ20160646

Professor Caroline Dart

Chair of Cardiovascular Physiology

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Cardiovascular signalling ▪ Ion channels ▪ Second messengers

I am interested in the cellular signalling mechanisms involved in the control of vascular smooth muscle contractility and thus blood flow/pressure. This is important for understanding both normal physiology and the progression of diseases such as hypertension and diabetes. I am particularly interested in the signalling roles played by ion channel proteins and have extensive expertise in the structure/function and regulation of potassium (K+) channels.

My group uses a variety of functional approaches to look at the behaviour and interaction of signalling molecules in real-time within live cells. Our techniques include: patch-clamp electrophysiology; calcium imaging; FRET-based biosensor imaging and biochemical/ molecular biological techniques.

Selected publications

Manning D, Barrett-Jolley R, Evans RL and Dart C (2023). TRPC1 channel clustering during store-operated Ca2+ entry in keratinocytes. Front. Physiol. 14:1141006.

McCormick LF, Wadmore K, Milburn A, Gupta N, Morris R, Held M, Prakash O, Carr J, Barrett-Jolley RA, Dart C and Helassa N (2023). Long QT syndrome-associated calmodulin variants disrupt the activity of the slow delayed rectifier potassium current. Journal of Physiology 601(17) 3687-3974

Celik N, O'Brien F, Brennan S, Rainbow RD, Dart C, Zheng Y, Coenen F, Barrett-Jolley RA (2020). Deep-Channel uses deep neural networks to detect single-molecule events from patch-clamp data. Communications Biology 3: 1-10

Parker T, Wang K, Manning D & Dart C (2019). Soluble adenylyl cyclase links store-operated Ca2+ entry (SOCE) to Ca2+/cyclic AMP-response element binding protein (CREB) activation in human coronary artery smooth muscle. Scientific Reports 9:7317

Dr Francesco Del Carratore

Lecturer in Computational Biology

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Biochemistry, Cell and Systems Biology

Research summary

Dr Del Carratore's research focuses on the statistical analysis of big datasets coming from multi-omics experiment, the mathematical modelling of biological systems (e.g., genome-scale metabolic models), and processing LC/MS-based untargeted metabolomics data with a particular emphasis on metabolites annotation.

Francesco completed his PhD in 2018 at the University of Manchester and previously worked as a Postdoc and Research Fellow on projects focusing on the genetic engineering of bacterial chassis for antibiotic production and on the molecular signalling governing soil microbiome interactions.

Selected publications

Del Carratore, F., et al. ipaPy2: Integrated Probabilistic Annotation (IPA) 2.0—an improved Bayesian-based method for the annotation of LC–MS/MS untargeted metabolomics data. Bioinformatics 39.7 (2023): btad455.

Del Carratore, F., et al. Biotechnological application of Streptomyces for the production of clinical drugs and other bioactive molecules. Current Opinion in Biotechnology 77 (2022): 102762.

Del Carratore, F., et al. Multi-omics study of Planobispora rosea, producer of the thiopeptide antibiotic GE2270A. Msystems 6.3 (2021): e00341-21.

Del Carratore, F., et al. Integrated probabilistic annotation: a Bayesian-based annotation method for metabolomic profiles integrating biochemical connections, isotope patterns, and adduct relationships. Analytical Chemistry 91.20 (2019): 12799-12807.

Professor Warwick Dunn

Professor of Analytical and Clinical Metabolomics

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Biochemistry, Cell and Systems Biology

Understanding and applying metabolism in human health and disease

Development and application of metabolomics and targeted metabolite assays to study human health, disease, ageing and circadian rhythms.

Development of metabolomics workflows focus on chromatography- mass spectrometry assays, QA/QC and metabolite identification applying laboratory and computational workflows.

Applications are focused on the development of precision medicine approaches to understand metabolic changes during disease development, to stratify patients based on risk and treatment success and to develop new treatments (both drug and lifestyle).

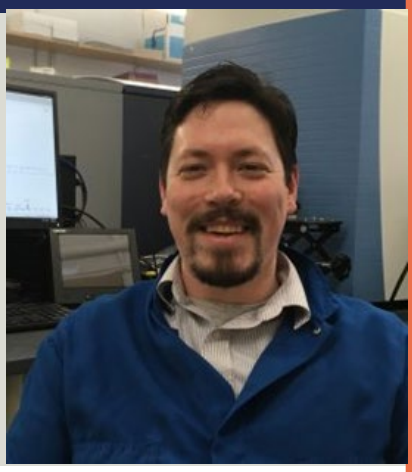
Selected publications

Dunn, W. B., Broadhurst, D., Begley, P., Zelena, E., Francis-McIntyre, S., Anderson, N., . . . Goodacre, R. (2011). Procedures for large-scale metabolic profiling of serum and plasma using gas chromatography and liquid chromatography coupled to mass spectrometry. NATURE PROTOCOLS, 6(7), 1060-1083. doi:10.1038/nprot.2011.335

Dunn, W. B., Broadhurst, D. I., Deepak, S. M., Buch, M. H., McDowell, G., Spasic, I., . . . Neyses, L. (2007). Serum metabolomics reveals many novel metabolic markers of heart failure, including pseudouridine and 2-oxoglutarate. METABOLOMICS, 3(4), 413-426. doi:10.1007/s11306-007-0063-5

Corbin, L. J., Hughes, D. A., Chetwynd, A. J., Taylor, A. E., Southam, A. D., Jankevics, A., . . . Timpson, N. J. (2020). Metabolic characterisation of disturbances in theAPOC3/triglyceride-rich lipoprotein pathway through sample-based recall by genotype. METABOLOMICS, 16(6). doi:10.1007/s11306-020-01689-9

Dr Edward Emmott



Reader

Wellcome Career Development Award Fellow

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Biochemistry, Cell and Systems Biology

Proteomics to understand RNA virus replication and virus-host interactions

My lab is interested in the study of virus-host interactions and virus replication for RNA viruses, especially where the replication of these viruses is governed by proteolytic cleavage and the impact of viral proteases on the host cell. These include the coronaviruses and noroviruses. We develop and apply mass spectrometry-based proteomic methods in support of this research. An example would be the development and application of single-cell proteomics by mass spectrometry methods, having helped develop the SCoPE2 carrier/reference approach being adopted internationally across different single-cell proteomics approaches.

The ultimate goal of our research is to identify and characterize virus-host interactions and replication mechanisms that can be targeted to inhibit virus replication as an antiviral strategy.

Selected publications

Gatto, L., Aebersold, R., Cox, J. et al. Initial recommendations for performing, benchmarking and reporting single-cell proteomics experiments. Nat Methods 20, 375–386 (2023). https://doi.org/10.1038/s41592-023-01785-3

Petelski, A.A., Emmott, E., Leduc, A. et al. Multiplexed single-cell proteomics using SCoPE2. Nat Protoc 16, 5398–5425 (2021). https://doi.org/10.1038/s41596-021-00616-z

Meyer, B., Chiaravalli, J., Gellenoncourt, S. et al. Characterising proteolysis during SARS-CoV-2 infection identifies viral cleavage sites and cellular targets with therapeutic potential. Nat Commun 12, 5553 (2021). https://doi.org/10.1038/s41467-021-25796-w

Professor Claire Eyers

Professor of Biological Mass Spectrometry

Associate Pro Vice Chancellor for Research, Faculty of Health and Life Sciences

Director, Centre for Proteome Research

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Biochemistry, Cell and Systems Biology

Research summary

Professor Eyers' research focuses on the development and application of biochemical and biophysical techniques (mass spectrometry (MS), ion mobility (IM)) to study global signal transduction and post-translational modifications (PTMs), particularly protein phosphorylation, but also sulfation, redox modifications and glycosylation. The ultimate goal of her research is to permit detailed characterisation (qualitative and quantitative) of cellular signalling systems and a better mechanistic understand of regulated cell signalling networks.

Her group's outputs are primarily used to investigate human biology and disease, although they are relevant to all organisms, and have impacted how mass spectrometry is both taught and practised.

Claire won the 2022 RSC Jeremy Knowles Award and is an Associate Editor at the Journal of Proteome Research.

Selected publications

Daly LA, Byrne DP, Perkins S, Brownridge PJ, McDonnell E, Jones AR, Eyers PA and Eyers CE (2023) Custom Workflow for the Confident Identification of Sulfotyrosine-Containing Peptides and Their Discrimination from Phosphopeptides Journal of Proteome Research 22: 3754–3772

Daly LA, Clarke CJ, Po A, Oswald So and Eyers CE (2023) Considerations for defining +80 Da mass shifts in mass spectrometry-based proteomics: phosphorylation and beyond Chem Commun 59: 11484-11499

Byrne DP, Clarke CJ, Brownridge PH, Kalyuzhnyy A, Perkins S, Campbell A, Mason D, Jones AR, Eyers PA and Eyers CE (2020) Use of the Polo-like kinase 4 (PLK4) inhibitor centrinone to investigate intracellular signalling networks using SILAC-based phosphoproteomics Biochem J 477: 2451–2475

Professor David Fernig

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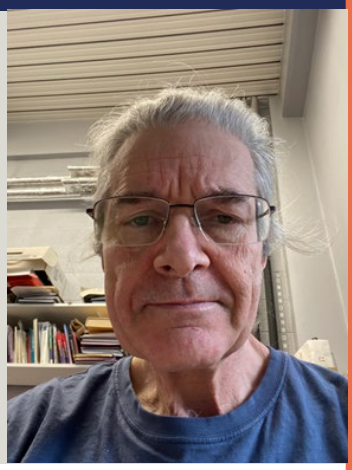

Biochemistry, Cell and Systems Biology

Growth factors ▪ sulfated polysaccharides ▪ extracellular matrix

Professor Fernig's research is focussed on communication between cells mediated by growth factors and its control by sulfated polysaccharides in the extracellular matrix. This encompasses development and homeostasis, non-communicable diseases (cancer, inflammatory conditions) and communicable diseases where such systems are exploited by pathogens. To tackle the challenge, he has a led substantial efforts in developing new tools in fields ranging from single molecular microscopy and new materials, to assays for sulfotransferases and other enzymes and high throughput screens for inhibitors and engineered enzymes. The associated understanding of the structure and function of polysaccharides of enzymes modifying their structure provides a platform for the development of new materials and therapeutics targetting, for example P. aeruginosa infections and conditions such as pancreatitis.

Selected publications

Foulkes, D. M., McLean, K., Sloniecka, M., Rustidge, S., Byrne, D. P., Haneef, A. S., . . . Kaye, S. B. (2022). Impact of fluoroquinolones and aminoglycosides on P. aeruginosa virulence factor production and cytotoxicity. BIOCHEMICAL JOURNAL, 479(24), 2511-2527. doi:10.1042/BCJ20220527

Lima, M. A., Rudd, T. R., Fernig, D. G., & Yates, E. A. (2022). Phosphorylation and sulfation share a common biosynthetic pathway, but extend biochemical and evolutionary diversity of biological macromolecules in distinct ways. JOURNAL OF THE ROYAL SOCIETY INTERFACE, 19(193). doi:10.1098/rsif.2022.0391

Foulkes, D. M., McLean, K., Zheng, Y., Sarsby, J., Haneef, A. S., Fernig, D. G., . . . Kaye, S. B. (2021).). A pipeline to evaluate inhibitors of the Pseudomonas aeruginosa exotoxin U. BIOCHEMICAL JOURNAL, 478(3), 647-668. doi:10.1042/BCJ20200780

Professor Roy Goodacre

Professor of Biological Chemistry

Centre for Metabolomics Research

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Biochemistry, Cell and Systems Biology

AMR ▪ chemometrics ▪ food security ▪ MS-based metabolomics ▪ VOCs ▪ infrared & Raman spectroscopy ▪ SERS ▪ single cell imaging

Trained as a microbiologist and analytical chemist, Roy's research develops metabolomics and spectroscopy to address interesting biological questions. He has helped establish mass spectrometry-based metabolomics for long-term studies and is employing these methods for clinical/health and plant studies, as well as for understanding microbial systems. He has developed a variety of different Raman spectroscopy approaches for bioanalysis with a particular focus on metabolite quantification and image analysis of single cells.

Roy helped establish the Metabolomics Society and is its current President, is Editor-in-Chief of the journal Metabolomics, and on the Editorial Advisory Boards of four other journals. Among other significant prizes and honours, in 2021 Roy was awarded the Nils Foss Excellence Prize, and the RSC Robert Boyle Prize for Analytical Science.

Selected publications

Lima, C., Muhamadali, H., & Goodacre, R. (2023). Monitoring Phenotype Heterogeneity at the Single-Cell Level within *Bacillus* Populations Producing Poly-3-hydroxybutyrate by Label-Free Super-resolution Infrared Imaging.. Analytical chemistry, 95(48), 17733-17740. doi:10.1021/acs.analchem.3c03595

Rattray, N. J. W., Trivedi, D. K., Xu, Y., Chandola, T., Johnson, C. H., Marshall, A. D., . . . Goodacre, R. (2019). Metabolic dysregulation in vitamin E and carnitine shuttle energy mechanisms associate with human frailty. NATURE COMMUNICATIONS, 10. doi:10.1038/s41467-019-12716-2

Langer, J., Jimenez de Aberasturi, D., Aizpurua, J., Alvarez-Puebla, R. A., Auguié, B., Baumberg, J. J., . . . Liz-Marzán, L. M. (2019). Present and Future of Surface-Enhanced Raman Scattering.. ACS nano. doi:10.1021/acsnano.9b04224

Aharoni, A., Goodacre, R. & Fernie, A.R. (2023) Plant and microbial sciences as key drivers in the development of metabolomics research. Proceedings of the National Academy of Sciences 120: e2217383120.

Professor Ben Goult

Chair of Mechanistic Cell Biology

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Biochemistry, Cell and Systems Biology

Talin ▪ mechanobiology ▪ cell signalling ▪ materials

Professor Goult's research interests are in understanding the cell's mechanical computation machinery, how physical and mechanical forces are sensed by cells to control cellular processes. His main focus is on the protein talin, which he has defined as a major mechanosensitive signalling hub. More recently he showed that talin has "molecular memory" and so provides organisms with a way to store data, through persistent alterations in protein conformation.

In 2023, he co-invented a new type of SynBio material based on talin. These Talin Shock Absorbing Materials (TSAMs) are being developed into a new type of armour.

Selected publications

Doolan JA, Alesbrook LS, Baker KB, Brown IR, Williams GT, Hiscock JR* and Goult BT* (2023) Next-generation protein-based materials capture and preserve projectiles from supersonic impacts. Nature Nanotechnology 18(9):1060-1066

Gallego-Paez LM, Edwards WJS, Chanduri M, Guo Y, Koorman T, Lee C-Y, Grexa N, Derksen P, Yan J, Schwartz MA, Mauer J and Goult BT* (2023) TLN1 contains a cancer-associated cassette exon that alters talin-1 mechanosensitivity. J. Cell Biol 222(5):e202209010

Barnett SFH and Goult BT* (2022) The MeshCODE to scale—visualising synaptic binary information. Front. Cell. Neurosci. 16:1014629

Goult BT*, Brown NH and Schwartz M. (2021) Talin in mechanotransduction and mechanomemory at a glance. J. Cell Sci. 134(20):jcs258749

Dr James Hartwell

Senior Lecturer in Plant Metabolism

Programme Co-Director MRes Advanced Biological Sciences

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Biochemistry, Cell and Systems Biology

Research summary

Dr Hartwell's research interests span the fields of plant molecular biology, plant biochemistry, and whole plant physiology. The focus of his research is understanding the molecular and biochemical basis for the circadian clock control of the metabolic adaptation of photosynthetic CO2 fixation called Crassulacean acid metabolism (CAM). He also has interests in the development of novel non-food CAM crops as biofuel feedstocks suited to seasonally dry lands, and the use of the latest plant synthetic biology approaches to re-engineer crop photosynthesis.

Currently, a key research focus is on the model CAM genus Kalanchoë and his group leverages multi-omics datasets ranging from whole genomes to metabolomes. The in-depth view of CAM and its control by the circadian clock that is gained from these 'omics datasets facilitates functional genomics approaches in Kalanchoë that are helping to build a ground-truthed molecular-genetic blueprint for CAM. Such comprehensive knowledge of the CAM system will in turn facilitate the forward engineering a drought-inducible CAM system into crops, leading to more water-use efficient varieties that can be leveraged for climate resilient agriculture.

Selected publications

Ludwig, M., Hartwell, J., Raines, C.A. and Simkin, A.J. (2024) The Calvin-Benson-Bassham cycle in C4 and Crassulacean acid metabolism species, Semin. Cell Dev. Biol., 155: 10-22.

Boxall, S.F., Kadu, N., Dever, L.V., Kneřová, J., Waller, J.L., Gould, P.J.D. and Hartwell, J. (2020) Kalanchoë PPC1 Is Essential for Crassulacean Acid Metabolism and the Regulation of Core Circadian Clock and Guard Cell Signaling Genes, The Plant Cell, 32(4): 1136–1160.

Ferrari, R.C., Bittencourt, P.P., Rodrigues, M.A., Moreno-Villena, J.J., Alves, F.R.R., Gastaldi, V.D., Boxall, S.F., Dever, L.V., Demarco, D., Andrade, S.C.S., Edwards, E.J., Hartwell, J. and Freschi, L. (2020) C4 and crassulacean acid metabolism within a single leaf: deciphering key components behind a rare photosynthetic adaptation. New Phytologist, 225: 1699-1714.

Professor Samar Hasnain

Max Perutz Professor of Molecular Biophysics

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Biochemistry, Cell and Systems Biology

Understanding catalysis in denitrification enzymes and search for a cure for motor neurone disease

For understanding of catalysis in redox enzymes we are utilizing and developing state-of-the art approaches using facilities for Synchrotron-based X-ray crystallography (at DIAMOND and SPring-8), coupled with on-line single crystal spectroscopy, Neutron-based crystallography (at ILL(Grenoble) and J-Parc (Japan)), and femtosecond X-ray crystallography at SACLA (Japan). For membrane proteins, such as nitrite oxide reductases we are using state of the art cryoEM facilities at Leeds and DIAMOND.

For motor neurone disease, we have an interdisciplinary programme involving medicinal chemistry (Prof Paul O'Neill), Cell Biology (Dr Raheela Awais), PROTAC approach (Prof Ciulli, Dundee) and transgenic mice (Prof Yamanaka, Nagoya).

Selected publications

A 2.2Å cryoEM structure of a quinol-dependent NO Reductase shows close similarity to respiratory oxidases Flynn, A. J., Antonyuk, S. V., Eady, R. R., Muench, S. P., & Hasnain, S. S. (2023). NATURE COMMUNICATIONS, 14(1). doi:10.1038/s41467-023-39140-xDOI: 10.1038/s41467-023-39140-x

Frontiers in metalloprotein crystallography and cryogenic electron microscopy Gopalasingam, C. C., & Hasnain, S. S. (2022). CURRENT OPINION IN STRUCTURAL BIOLOGY, 75. doi:10.1016/j.sbi.2022.102420DOI: 10.1016/j.sbi.2022.102420

Single crystal spectroscopy and multiple structures from one crystal (MSOX) define catalysis in copper nitrite reductases Rose, S. L., Baba, S., Okumura, H., Antonyuk, S. V., Sasaki, D., Hedison, T. M., . . . Hasnain, S. S. (2022). PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 119(30). doi:10.1073/pnas.2205664119DOI: 10.1073/pnas.2205664119

Dr Nordine Helassa

Senior Lecturer

British Heart Foundation Research Fellow

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Biochemistry, Cell and Systems Biology

Calcium signalling ▪ Biosensors ▪ Cardiovascular disease

Dr Helassa's research interests include calcium signalling in the context of cardiovascular diseases and the development of fluorescent biosensors for imaging small molecules (e.g. calcium, glucose, glutamate). He is a British Heart Foundation Intermediate Basic Science Research Fellow since 2018.

He teaches contractility, cell signalling and protein production for undergraduate and postgraduate students. He is an elected member of Senate, the Institute Academic Lead for Public Engagement and serves on the Physiological Society Conference/Event panel.

Selected publications

Yaganoglu S, Kalyviotis K, Vagena-Pantoula C, Jülich D, Gaub BM, Welling M, Lopes T, Lachowski D, Tang SS, Del Rio Hernandez A, Salem V, Müller DJ, Holley SA, Vermot J, Shi J, Helassa N, Török K, Pantazis P (2023). Highly specific and non-invasive imaging of Piezo1-dependent activity across scales using GenEPi. Nat Commun. 14(1):4352.

Prakash O, Gupta N, Milburn A, McCormick L, Deugi V, Fisch P, Wyles J, Thomas NL, Antonyuk S, Dart C, Helassa N (2023). Calmodulin variant E140G associated with long QT syndrome impairs CaMKIIδ autophosphorylation and L-type calcium channel inactivation. J Biol Chem 299(1):102777.

Dürst CD, Wiegert JS, Schulze C, Helassa N, Török K, Oertner TG (2022). Vesicular release probability sets the strength of individual Schaffer collateral synapses. Nat Commun. 13(1):6126.

Professor Andy Jones

Professor of Bioinformatics

Joint Director Computational Biology Facility

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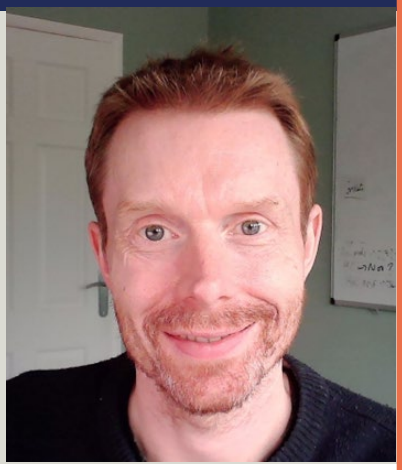

Biochemistry, Cell and Systems Biology

Computational biology applied to multi-omics data

Our team uses data science approaches to understand large-scale biological data sets, particularly from omics technologies. We are especially interested in understanding protein regulation across multiple species, including conservation, crosstalk and evolution of post-translational modifications. We develop approaches to perform structural and functional annotation of genomes and contribute to data standards and public databases (eukaryotic pathogens, plants and human immune genes). We also use and develop machine learning / AI pipelines for discovery of biomarkers.

Selected publications

Amos, B., Aurrecoechea, C., Barba, M., Barreto, A., Basenko, E. Y., Bazant, W., . . . Zheng, J. (2022). VEuPathDB: the eukaryotic pathogen, vector and host bioinformatics resource center. NUCLEIC ACIDS RESEARCH, 50(D1), D898-D911. doi:10.1093/nar/gkab929

Prakash, A., Garcia-Seisdedos, D., Wang, S., Kundu, D. J., Collins, A., George, N., . . . Vizcaino, J. A. (2023). Integrated View of Baseline Protein Expression in Human Tissues. JOURNAL OF PROTEOME RESEARCH, 22(3), 729-742. doi:10.1021/acs.jproteome.2c00406

Kalyuzhnyy, A., Eyers, P. A., Eyers, C. E., Bowler-Barnett, E., Martin, M. J., Sun, Z., . . . Jones, A. R. (2022). Profiling the Human Phosphoproteome to Estimate the True Extent of Protein Phosphorylation. JOURNAL OF PROTEOME RESEARCH, 21(6), 1510-1524. doi:10.1021/acs.jproteome.2c00131

Professor Douglas Kell

Chair in Research Biology

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Biochemistry, Cell and Systems Biology

Systems, Synthetic and Computational Biology

Development and exploitation of novel analytical methods, both computational and experimental, Evolutionary computing and machine learning; experimental metabolomics, including in the use of evolutionary, closed-loop methods for optimization; metabolic network biology; role of cellular transporters in effecting xenobiotic uptake. Bioenergetics. Microbial dormancy. Flow cytometry. Pre-eclampsia. Ergothioneine. Long COVID.

Selected publications

Roberts, I., Wright Muelas, M., Taylor, J. M., Davison, A. S., Winder, C. L., Goodacre, R., & Kell, D. B. (2023). Quantitative LC-MS study of compounds found predictive of COVID-19 severity and outcome.. Metabolomics : Official journal of the Metabolomic Society, 19(11), 87. doi:10.1007/s11306-023-02048-0

Turner, S., Laubscher, G. J., Khan, M. A., Kell, D. B., & Pretorius, E. (2023). Accelerating discovery: A novel flow cytometric method for detecting fibrin(ogen) amyloid microclots using long COVID as a model. Heliyon, 9(9), e19605. doi:10.1016/j.heliyon.2023.e19605

Kenny, L. C., Brown, L. W., Ortea, P., Tuytten, R., & Kell, D. B. (2023). Relationship between the concentration of ergothioneine in plasma and the likelihood of developing pre-eclampsia. BIOSCIENCE REPORTS, 43(7). doi:10.1042/BSR20230160

Dr Niall Kenneth

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Biochemistry, Cell and Systems Biology

The biochemistry of hypoxia: examining the role of oxygen sensing in normal function and disease

Hypoxia signalling is crucial in normal physiological function as it orchestrates adaptive responses to low oxygen levels, promoting the activation of key pathways that regulate cellular metabolism and ensure tissue survival. Conversely, its dysregulation of is implicated in various diseases, including cancer, cardiovascular disorders, and neurodegenerative conditions, highlighting its potential as a therapeutic target for mitigating pathological processes.

Our work is aimed at defining hypoxia-dependent signalling pathways to uncover new biomarkers and drug targets for human disease.

Selected publications

COLLINS, A., SCOTT, R., WILSON, C. L., ABBATE, G., ECCLESTONE, G. B., BIDDLES, D., OAKLEY, F., MANN, J., MANN, D. A. & KENNETH, N. S. 2023. UCHL1-dependent control of Hypoxia-Inducible Factor Transcriptional Activity in Liver Disease. bioRxiv, 2023.01.08.523142.

BATIE, M., FASANYA, T., KENNETH, N. S. & ROCHA, S. 2023. Oxygen-regulated post-translation modifications as master signalling pathway in cells. EMBO Rep, e57849.

HUNTER, J. E., MCHUGH, O., ECCLESTONE, G. B., CHILD, F., MEARNS, H., ROBSON, G., DADZIE, M., ROCHA, S., PERKINS, N. D. & KENNETH, N. S. 2022. Disruption of HIF1A translational control attenuates the HIF-dependent hypoxic response and solid tumour formation in vivo. bioRxiv, 2022.11.02.514731.

Dr Paraskevi Kritsiligkou

Tenure Track Fellow

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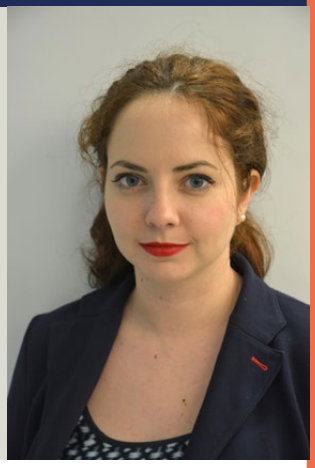

Biochemistry, Cell and Systems Biology

Redox biology ▪ Stress responses ▪ Organelle homeostasis

Dr Kritsiligkou's research is focused on redox biology and redox signalling, protein folding, and organelle homeostasis. She is particularly interested in understanding how cells respond to external and internal challenges, including metabolic, oxidative, ER, and protein misfolding stress.

She developed biosensor platforms that reveal the extent of intracellular redox heterogeneity, and she is now using this technology to study how highly localised oxidant generation can modulate protein post-translational modifications, phase transitions and oxidative damage.

Dr Kritsiligkou is a passionate advocate for early career researchers and has been involved in a number of committees to increase the inclusion and visibility of young investigators and promote their research output. She is currently the co-chair of the ECR committee and a member of the council of the Society of Free Radical Research Europe (SFRR-E).

Selected publications

Kritsiligkou P.*, Bosch K.*, Tsu-Keng S., Mauer M., Knop M., Dick T.P. (2023) Proteome-wide tagging of proteins with an H2O2 biosensor reveals highly localized and dynamic redox domains. PNAS

Denolly S., Stukalov A., Barayeu U., Rosinski A.N., Kritsiligkou P., Joecks S., Dick T.P., Pichlmair A., Bartenschlager R. (2023) Zika virus remodelled ER membranes contain proviral factors involved in redox and methylation pathways. Nature Communications

Cunningham J., Sfakianos A.P., Kritsiligkou P., Kershaw C.J., Whitmarsh A.J., Hubbard S.J., Ashe M.P., Grant C.M. (2023) Paralogous translation factors target distinct mRNAs to differentially regulate tolerance to oxidative stress in yeast. Nucleic Acids Res

Professor Luning Liu

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Synthetic Biology, Biotechnology, Biological Membrane, Protein Assembly, Molecule dynamics, High-resolution Imaging, Photosynthesis, Carbon Fixation, Environmental Adaptation

The Liu lab aims to uncover the molecular mechanisms underlying the biosynthesis and function of supramolecular systems, e.g. protein assemblies, biological membranes and energetic machinery, by applying and developing interdisciplinary approaches in biology, chemistry, physics, and engineering.

The long-term goal is to provide mechanistic insight into the development of self-assembling biological systems, and harness the knowledge to underpin the engineering of functional biological systems and promote biotechnological applications in energy and food production as well as therapeutics.

Biochemistry, Cell and Systems Biology

Selected publications

Nature Commun, 2023, 14: 2118. DOI: 10.1038/s41467-023-37490-0

Nature Commun, 2023, 14: 5512. DOI: 10.1038/s41467-023-41211-y

Nature Commun, 2022, 13: 2920. DOI: 10.1038/s41467-022-30608-w

Science Advances, 2021, 7(25): eabf8864. DOI: 10.1126/sciadv.abf886

Nature Commun, 2021, 12: 3475. DOI: 10.1038/s41467-021-23680-1

Nature Commun, 2020, 11: 5448. DOI: 10.1038/s41467-020-19280-0

Nature Plants, 2020, 6(7): 869-882. DOI: 10.1038/s41477-020-0694-3

Nature Commun, 2020, 11: 1976. DOI: 10.1038/s41467-020-15888-4

Dr Jill Madine

Senior Lecturer

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Biochemistry of amyloid protein diseases and aortic pathologies

Investigating the role of amyloid proteins and cofactors in neurodegenerative, cardiovascular and systemic diseases. Including the relationship between diseases, potential involvement of cross-seeding and inhibition methods.

As a founding member of Liverpool Aortic Biomechanics and Biochemistry Research Group (LABB) working towards increased understanding of aortic dissection and aneurysm. Evaluating future potential of biomarkers and developing point-of-care testing approaches for aortic surgery.

Selected publications

J. Wagner, K. Degenhardt, M. Veit, N. Louros, K. Konstantoulea, A. Skodras, K. Wild, P. Liu, U. Obermüller, V. Bansal, A. Dalmia1 L.M. Häsler, M. Lambert, M. De Vleeschouwer, H.A. Davies, J. Madine, D. Kronenberg-Versteeg, R. Feederle, D.K. Del Turco, P.R. Nilsson, T. Lashley, T. Deller, M. Gearing, L.C. Walker, P. Heutink, F. Rousseau, J. Schymkowitz, M. Jucker, J.J. Neher Medin promotes vascular amyloid-β aggregation in Alzheimer's disease, Nature, 2022, 612, 123–131, doi:10.1038/s41586-022-05440-3

H.A. Davies, E. Caamaño-Gutiérrez, YH. Chim, M. Field, O. Nawaytou, R. Akhtar, J. Madine, Idiopathic degenerative thoracic aneurysms are associated with increased aortic medial amyloid, Amyloid, 2019, 26, 148-155, doi:10.1080/13506129.2019.1625323

H.A Davies, E. Caamano-Gutierrez, J. Sarsby, O. Nawaytou, A. Harky, R. Akhtar, M. Field, J. Madine, Exploring the potential of rapid evaporative ionization mass spectrometry (Intelligent Knife) for point-of-care testing in aortic surgery, European Journal of Cardio-Thoracic Surgery, 2021, doi:10.1093/ejcts/ezab166

Dr Urszula McClurg

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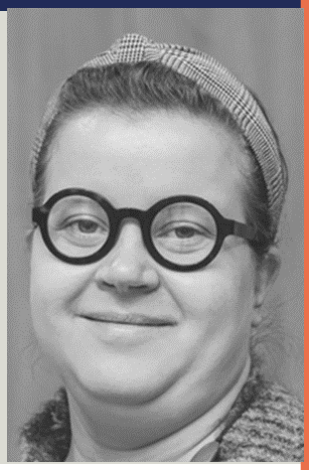

Biochemistry, Cell and Systems Biology

Germ cell cancer genes ▪ Meiosis ▪ Synaptonemal complex

During meiosis initiation expression of meiotic genes distributed across 46 chromosomes is turned on in a concerted, synchronised fashion. It is still unclear how mammalian cells control and regulate this process across the genome. Importantly, half of cancer patients aberrantly express these meiotic genes. Multiple studies demonstrate that expression of meiotic genes in somatic cells has oncogenic consequences and contributes to more aggressive disease, relapse and therapy resistance. However, it is unclear why and how cancer cells turn on meiotic genes. In our laboratory we develop novel tools and approaches to answer this question.

Selected publications

Cancer and meiotic gene expression: Two sides of the same coin? Sou, I. F., Hamer, G., Tee, W. -W., Vader, G., & McClurg, U. L. (2023). Current Topics in Developmental Biology, Vol. 151, pp. 43-68.

Centrosome dysfunction associated with somatic expression of the synaptonemal complex protein TEX12. Sandhu, S., Sou, I. F., Hunter, J. E., Salmon, L., Wilson, C. L., Perkins, N. D., . . . McClurg, U. L. (2021). Communications Biology, 4(1371).

Meiosis initiation: a story of two sexes in all creatures great and small. Sou, I. F., Pryce, R. M., Tee, W. -W., & McClurg, U. L. (2021). Biochemical Journal, 478(20), 3791-3805.

Towards inclusive and sustainable scientific meetings. Chalmers, S. B., Madgwick, S., Lloyd-Lewis, B., McClurg, U. L., Elias, S., Andersen, P., . . . Davis, F. M. (2023) Nature cell biology, 25(11), 1557-1560.

Dr Kirsty McMillan

Tenure Track Fellow

(starting August 2024)

ORCID: https://orcid.org/0000-0002-4619-3309

Endosomal system ▪ Membrane trafficking ▪ Neurodegeneration

Dr McMillan is interested in the molecular mechanisms driving neurodegeneration. In particular her research focuses on understanding the role of the endosomal system in neuronal and glial function in health and disease. Kirsty was awarded a BBSRC Industrial Collaborative PhD from the University of Bristol in 2014 for her research in Professor Maeve Caldwell's laboratory investigating the role of microRNAs in alpha synuclein regulation and Parkinson's pathology. During her postdoctoral research in Professor Peter Cullen's laboratory at the University of Bristol, she was instrumental in driving forward a new avenue of exploration for the laboratory into the role of the endosomal system in neuronal function and neurodegenerative disease.

Selected publications

McMillan KJ1*, Banks PJ1, Hellel FL, Carmichael RE, Clairfeuille T, Evans AJ, Heesom KJ, Lewis P, Collins BM, Bashir ZI, Henley JM, Wilkinson KA*, Cullen PJ* (2021) Sorting nexin-27 regulates AMPA receptor trafficking through the synaptic adhesion protein LRFN2. Elife. Jul 12;10:e59432. 1 co-first and * co-corresponding author.

McMillan KJ, Korswagen HC, Cullen PJ (2017) The emerging role of retromer in neuroprotection. Curr Opin Cell Biol. Aug;47:72-82.

McMillan KJ, Gallon M, Jellett AP, Clairfeuille T, Tilley FC, McGough I, Danson CM, Heesom KJ, Wilkinson KA, Collins BM, Cullen PJ (2016) Atypical parkinsonism-associated retromer mutant alters endosomal sorting of specific cargo proteins. J Cell Biol. Aug 15;214(4):389-99.

Dr Tarang Mehta

Lecturer in Bioinformatics

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Biochemistry, Cell and Systems Biology

Gene regulation ▪ Genome evolution ▪ Health and biodiversity

Dr Mehta's research broadly explores the genetic underpinnings of vertebrate adaptive traits and disease response, with an outlook towards preserving organismal health and biodiversity. Since much of his work utilises multi-omics data to characterise genetic diversity and identify markers of economically important traits, he also focuses on developing novel omics, systems, and algorithmic approaches for analysing complex genomes.

Tarang completed his PhD at the National University of Singapore, studying vertebrate genome evolution, and then postdoctoral work at the Earlham Institute focused on characterising gene regulatory networks associated with adaptive traits.

Selected publications

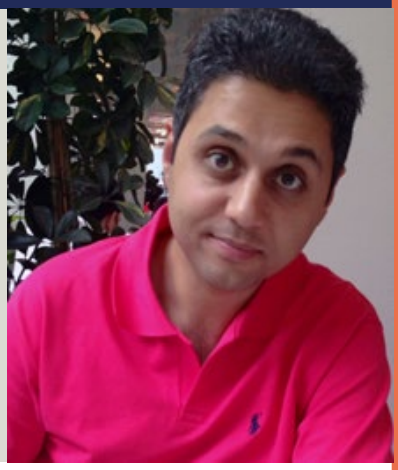
Mehta, T. K., et al. Chromatin accessibility in gill tissue identifies candidate genes and loci associated with aquaculture relevant traits in tilapia. Genomics (2023) 115, 4: 110633.

Etherington, G. J. *, Nash, W. *, Ciezarek, A. *, Mehta, T. K. * et al. Chromosome-level genome sequence of the Genetically Improved Farmed Tilapia (GIFT, Oreochromis niloticus) highlights regions of introgression with O. mossambicus. BMC Genomics (2022) 23: 832.

Mehta, T. K., et al. Evolution of miRNA-Binding Sites and Regulatory Networks in Cichlids. Mol. Biol. Evol. (2022) 39: msac146.

Mehta, T. K., et al. Evolution of regulatory networks associated with traits under selection in cichlids. Genome Biol. (2021) 22:25.

Dr Howbeer Muhamadali



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Biochemistry, Cell and Systems Biology

Using metabolomics and molecular imaging to investigate AMR in bacteria

Howbeer's group is focused on the application of mass spectrometry and spectroscopy-based metabolomics strategies to reveal the underlying molecular mechanisms of the bacterial response to various antimicrobial interventions.

He is also using metabolomics approaches and instrumentations (GC-MS, LC-MS, FT-IR, and Raman) combined with multivariate statistical analysis techniques for optimisation, enhancement and better understanding of various environmental and industrially relevant bioprocesses, such as recombinant protein, and secondary metabolite production.

Selected publications

Muhamadali, H., Chisanga, M., Subaihi, A. & Goodacre, R. (2015a) 'Combining Raman and FT-IR Spectroscopy with Quantitative Isotopic Labeling for Differentiation of E. coli Cells at Community and Single Cell Levels', Analytical Chemistry, vol. 87, no. 8, pp. 4578-4586.

Muhamadali, H., Xu, Y., Ellis, D.I., Allwood, J.W., Rattray, N.J.W., Correa, E., Alrabiah, H., Lloyd, J.R. & Goodacre, R. (2015b) 'Metabolic Profiling of Geobacter sulfurreducens during Industrial Bioprocess Scale-Up', Applied and Environmental Microbiology, vol. 81, no. 10, pp. 3288-3298.

Muhamadali, H., Xu, Y., Morra, R., Trivedi, D.K., Rattray, N.J.W., Dixon, N. & Goodacre, R. (2016) 'Metabolomic analysis of riboswitch containing E. coli recombinant expression system', Molecular Biosystems, vol. 12, no. 2, pp. 350-361.

Shams, S., Lima, C., Xu, Y., Ahmed, S., Goodacre, R. & Muhamadali, H. (2023) 'Optical photothermal infrared spectroscopy: A novel solution for rapid identification of antimicrobial resistance at the single-cell level via deuterium isotope labeling', Frontiers in Microbiology, vol. 14.

Dr Antonius Plagge

Lecturer

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Biochemistry, Cell and Systems Biology

Physiological functions and epigenetic regulation of imprinted genes

We are analysing a mouse model for a human neurodevelopmental disorder caused by mutations in Trafficking protein particle complex subunit 9 to elucidate disease mechanisms and cellular functions of the protein [1]. We are also investigating the epigenetic regulation of a cluster of neuronal genes to understand how promoter-enhancer interactions are regulated by DNA methylation and histone modifications [2] and [https://doi.org/10.1101/2023.09.26.559498].

Other collaborative work includes stem cell research and cell tracking via pre-clinical imaging [3].

Selected publications

[1]Microcephaly with a disproportionate hippocampal reduction, stem cell loss and neuronal lipid droplet symptoms in Trappc9 KO mice. S Aljuraysi*, M Platt*, M Pulix, H Poptani‡, A Plagge‡ bioRxiv, (preprint), (2023). Link: doi: https://doi.org/10.1101/2023.11.20.567859

[2]Variable allelic expression of imprinted genes at the Peg13, Trappc9, Ago2 cluster in single neural cells. M Claxton, M Pulix, MKY Seah, R Bernardo, P Zhou, S Aljuraysi, L Liloglou, P Arnaud, G Kelsey, DM Messerschmidt, A Plagge Front. Cell Dev. Biol., (2022) 10:1022422. Link: doi: 10.3389/fcell.2022.1022422

[3]Multimodal cell tracking from systemic administration to tumour growth by combining gold nanorods and reporter genes. J Comenge, J Sharkey, O Fragueiro, B Wilm, M Brust, P Murray, R Lévy, A Plagge. eLife (2018)7:e33140 . https://doi.org/10.7554/eLife.33140

Professor Daniel Rigden

Professor of Protein Bioinformatics

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Biochemistry, Cell and Systems Biology

Exploiting protein structural bioinformatics for function and more

We exploit protein bioinformatics methods, up to and including AlphaFold 2 (AF2), across targets of all kinds and in diverse collaborations. There are two distinct directions

1. As part of CCP4 and CCPEM, we produce software for structural biologists, especially for Molecular Replacement and structure validation

2. We use protein structure models, of single and multiple chains, to interpret and predict function. This assigns roles to genomic dark matter, sheds light on structure-function relationships, allows for rational protein redesign and enables ligand discovery. [2,3]

Selected publications

[1] Slice'N'Dice: Maximising the value of predicted models for structural biologists. Simpkin AJ, Elliott LG, Stevenson K, Krissinel E, Rigden DJ, Keegan RM. bioRxiv. 2022. 2022-06.doi: 10.1101/2022.06.30.497974

[2] Tertiary structure assessment at CASP15. Simpkin AJ, Mesdaghi S, Sánchez Rodríguez F, Elliott L, Murphy DL, Kryshtafovych A, Keegan RM, Rigden DJ. Proteins: Structure, Function, and Bioinformatics. 2023. doi: 10.1002/prot.26593

[3] From protein structure to function with bioinformatics (2nd edition)

Rigden DJ, editor. Berlin: Springer; 2017. doi: 10.1007/978-94-024-1069-3

Professor Sonia Rocha

Executive Dean of the Institute of Systems, Molecular and Integrative Biology

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Biochemistry, Cell and Systems Biology

Mechanisms controlling gene expression in hypoxia and inflammation

Our work investigates how cells sense and respond to low oxygen or hypoxia and how this intersects with inflammation.

From chromatin to cell cycle and autophagy, our work is collaborative and multidisciplinary using as diverse technologies as possible.

Selected publications

Regulation of Hypoxia Inducible Factor-1alpha by NF-kappaB. P van Uden, NS Kenneth, S Rocha Biochem J. (2008) 138, 477-484. link: https://doi.org/10.1042/BJ20080476.

Potent and selective chemical probe of hypoxix signalling downstream of HIF-alpha hydroxylation via VHL inhibition. J Frost, C Galdeano, P Soares, MS Gadd, KM Grzes, L Ellis, O Epemolu, S Shimamura M Batscheff, P Grandi, KD Read, DA Cantrell, S Rocha, A Ciulli. Nature Comms, (2016) 7, 13312. link: https://www.nature.com/articles/ncomms13312

Hypoxia induces rapid changes to histone methylation and reprograms chromatin. M Batie, J Frost, M Frost, JW Wilson, P Schofield, S Rocha. Science., (2019) 363, 1222-1226. link: DOI: 10.1126/science.aau587.

Dr Natalia Sanchez-Soriano

Reader

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Biochemistry, Cell and Systems Biology

Mechanisms of neuronal growth and ageing

The way in which neurons wire up into circuits or networks determines the flow of electrical messages in the nervous system, relevant for behaviour including movement, learning and memory. Aberrations of neuronal networks have debilitating effects and can be caused by developmental or neurodegenerative diseases or physiological ageing.

Neurons face great challenges due to their extreme morphology, demanding metabolism, and the fact that they are postmitotic cells that must survive an entire organism's lifetime. Across the animal kingdom, neurons display gradual axonal and synaptic decay when they age. Age remains the highest risk factor for neurodegeneration - yet the underlying mechanisms and cell biology of ageing remain little understood.

My research aims to understand the genetic and molecular mechanisms regulating the formation of neuronal networks during development and their maintenance during ageing. For this, we use the genetic model organism Drosophila melanogaster, and developed cellular models for the study of the cell biology that underpins axonal growth and processes of ageing. We have a key interest on the cytoskeleton of neurons and the processes regulated by microtubules and actin. Work carried out so far has started to reveal important roles of microtubules contributing to nervous system decay and provide promising new ideas for future therapies.

Selected publications

Microtubule decay is a driver of neuronal ageing and a promising target for intervention. Pilar Okenve-Ramos, Rory Gosling, Monika Chojnowska Monga, Kriti Gupta, Samuel Shields, Natalia Sánchez-Soriano*. bioRxiv 2023.01.11.523590; doi: https://doi.org/10.1101/2023.01.11.523590

Tau, XMAP215/Msps and Eb1 jointly regulate microtubule polymerisation and bundle formation in axons. Hahn, I., Voelzmann, A., Parkin, J., Fuelle, J., Slater, P.G., Lowery, L., Sanchez-Soriano, N*., Prokop, A*. (2021) PLOS Genet 17, e1009647ff. https://doi.org/10.1371/journal.pgen.1009647

Tau and spectraplakins promote synapse formation and maintenance through Jun kinase and neuronal trafficking. Voelzmann, A., Okenve Ramos, P., Qu, Y., Chojnowska-Monga, M., del Caño-Espinel, M., Prokop, A., Sánchez-Soriano, N*. (2016). eLife 5, e14694.

Dr Natasha Savage

Lecturer

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Biochemistry, Cell and Systems Biology

Building bespoke mathematical models used to predict biological mechanism

Work with experimentalists to build predictive mathematical models, designed to understand and uncover specific biological mechanisms. Design mathematical frameworks to best represent the biological data available.

Selected publications

Describing the movement of molecules in reduced-dimension models. Savage, N. (2021). Communications Biology. doi:10.1038/s42003-021-02200-3

Mechanistic mathematical model of polarity in yeast. Savage, N. S., Layton, A. T., & Lew, D. J. (2012). Molecular Biology of the Cell, 23(10), 1998-2013.

A Mutual Support Mechanism through Intercellular Movement of CAPRICE and GLABRA3 Can Pattern the Arabidopsis Root Epidermis. Savage, N. S., Walker, T., Wieckowski, Y., Schiefelbein, J., Dolan, L., & Monk, N. A. M. (n.d.). PLoS Biology, 6(9), e235. doi:10.1371/journal.pbio.0060235

Professor Richard Scheltema

Royal Society Wolfson Fellow

Co-Director, Centre for Proteome Research

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Biochemistry, Cell and Systems Biology

Structural proteomics ▪ Protein structure ▪ PTMs

Professor Scheltema's research interests revolve around the development of novel chemistry, analytical assays, and data analysis software for the analysis of protein structures. Richard commercialized novel reagents and software, which are in use in laboratories worldwide. New developments include the interpretation of PTMs like disulfide bridges and citrullination and placing the findings in a structural context.

His biological interests lie within 2 pillars, human diseases (lung diseases and diabetes) and photosynthesis.

Selected publications

A.B. Barroeta, P. Albanese, J.A. Marquart, J.C.M. Meijers, R.A. Scheltema; Thrombin activation of the factor XI dimer is a multi-staged process for each subunit; JTH (IF: 17.8), 2024

S. Heissel, Y. He, A. Jankevics, Y. Shi, H. Molina, R. Viner, R.A. Scheltema; Fast and accurate disulfide bridge detection; MCP (IF: 7.4), 2024

M. Gemmer, M. Chaillet, D. Vismpas, R. Cuevas Arenas, J. van Loenhout, M. Gröllers-Mulderij, P. Albanese, R.A. Scheltema, J. Fédry, F. Förster; Molecular snapshots of translation and protein translocation at the ER membrane; Nature (IF: 64.8), 2023

P. Albanese, S. Tamara, G. Saracco, C. Pagliano, R.A. Scheltema; How paired PSII-LHCII supercomplexes mediate the stacking of plant thylakoid membranes unveiled by integrative structural mass-spectrometry; Nature Communications (IF: 16.6), 2020

Dr Massimiliano Stagi

Lecturer

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Biochemistry, Cell and Systems Biology

Microscopy, molecular biology, lysosomal, mitochondrial and neuronal physiology

My expertise lies in high-throughput image-based screening and the development of image-based sensors to probe neuronal physiology. I have been at the forefront of developing novel methods to measure lysosomal pH through genetically encoded biosensors, enhancing our understanding of autophagy and its stability across cell types. I continue to build upon this foundation, aiming to bridge basic science with drug discovery by employing my custom-designed analysis software and culture devices. These tools not only facilitate high-throughput imaging but also ensure greater precision and consistency in neuronal culture systems, thereby advancing our knowledge of neuronal physiology and its alteration in age-related diseases.

Selected publications

Ponsford, A. H., Ryan, T. A., Raimondi, A., Cocucci, E., Wycislo, S. A., Fröhlich, F., . . . Stagi, M. (n.d.). Live imaging of intra-lysosome pH in cell lines and primary neuronal culture using a novel genetically encoded biosensor. Autophagy, 1-19. doi:10.1080/15548627.2020.1771858

Stagi, M., Klein, Z. A., Gould, T. J., Bewersdorf, J., & Strittmatter, S. M. (2016). Lysosome size, motility and stress response regulated by fronto-temporal dementia modifier TMEM106B. Molecular and Cellular Neuroscience, 61, 226-240. doi:10.1016/j.mcn.2014.07.006

Um, J. W., Nygaard, H. B., Heiss, J. K., Kostylev, M. A., Stagi, M., Vortmeyer, A., . . . Strittmatter, S. M. (2012). Alzheimer amyloid-β oligomer bound to postsynaptic prion protein activates Fyn to impair neurons. NATURE NEUROSCIENCE, 15(9), 1227-1U85. doi:10.1038/nn.3178

Dr Laura Swan

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Biochemistry, Cell and Systems Biology

Research summary

Dr Swan's lab studies membrane traffic- the process by which cells export, sort and remodel cellular membranes and their cargoes. This process is essential for cellular function, regulating how individual cells react to their neighbours and their environment and consequentially, cellular signalling and growth. One of the key determinants of membrane identity is a class of lipids called phosphoinositide lipids (PIPs). Failure of proper conversion of one PIP species to another causes defects in membrane trafficking with highly specific and serious consequences, from cancers, psychiatric disorders and congenital disorders of the nervous system.

Her lab studies membrane traffic in general, concentrating on PIP metabolising enzymes, using live cell imaging, optogenetics, biochemistry, lipid enzymology, systematic 'omics and genetic models, to identify trafficking nodes that can be modulated for therapeutic effect.

Selected publications

Dall'Armellina, F., Stagi, M., & Swan, L. E. (2023). In silico modeling human VPS13 proteins associated with donor and target membranes suggests lipid transfer mechanisms. PROTEINS-STRUCTURE FUNCTION AND BIOINFORMATICS, 91(4), 439-455. doi:10.1002/prot.26446

Hathazi D*, Cox D*, D'Amico A, Tasca G, Charlton R, Carlier RY, Baumann J, Kollipara L, Zahedi RP, Feldmann I, Deleuze JF, Torella A, Cohn R, Robinson E, Ricci F, Jungbluth H, Fattori F, Boland A, O'Connor E, Horvath R, Barresi R, Lochmueller H, Urtizberea A, Jacquemont ML, Nelson I, Swan LE, Bonne G*, Roos A* INPP5K and SIL1 associated pathologies with overlapping clinical phenotypes converge through dysregulation of PHGDH Brain 2021.

Ponsford AH, Ryan TA, Raimondi A, Cocucci E, Wycislo SA, Fröhlich F*, Swan LE*, Stagi M * Live Imaging of Intra-Lysosome pH in Cell Lines and Primary Neuronal Culture Using a Novel Genetically Encoded Biosensor Autophagy 2020

Professor Sylvie Urbé

Professor of Molecular and Cellular Physiology

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Biochemistry, Cell and Systems Biology

Ubiquitin and organelle biology

Our research covers aspects of membrane trafficking (endocytosis, autophagy, mitophagy, pexophagy), organelle biology (mitochondria and lysosomes) and cell signaling with a view to understand mechanisms that lead to human pathologies (cancer, neurodegeneration).

Central to our research is the small protein modifier, Ubiquitin, and the enzymes that add (E3 ligases) and remove (deubiquitylases, DUBs) ubiquitin from proteins. We have a particularly strong interest in DUBs and their role in protein and organelle homeostasis.

We use systematic approaches to catalogue these enzymes and study the cell biology of individual family members. We contribute to drug discovery programmes in this area together with other academic centres and industry partners. My laboratory is co-directed with Michael Clague.

Selected publications

Elcocks, H., Brazel, A. J., McCarron, K. R., Kaulich, M., Husnjak, K., Mortiboys, H., . . . Urbé, S. (2023). FBXL4 ubiquitin ligase deficiency promotes mitophagy by elevating NIX levels.. The EMBO journal, e112799. doi:10.15252/embj.2022112799

Clague, M. J., Urbe, S., & Komander, D. (2019). Breaking the chains: deubiquitylating enzyme specificity begets function. NATURE REVIEWS MOLECULAR CELL BIOLOGY, 20(6), 338-352. doi:10.1038/s41580-019-0099-1

Marcassa, E., Kallinos, A., Jardine, J., Rusilowicz, E., Martinez, A., Kuehl, S., . . . Urbe, S. (2018). Dual role of USP 30 in controlling basal pexophagy and mitophagy. EMBO Reports, 19(07), 14 pages. doi:10.15252/embr.201745595

Dr Peter Walley

Lecturer in Genetics

Crop Genetic Improvement Group

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Biochemistry, Cell and Systems Biology

Developing genetic resources to help feed the future

As a group, our aim is to decipher the genetic basis of plant adaptions to their environment, particularly stress, and to use this information to enhance the growth and quality of our crops. We develop genetic resources that help establish and feed into pre-breeding programmes. This includes new germplasm, genetic markers, genetic maps, and genetic markers linked to genetic variation for favourable characteristics.

National and International recognition:

Member of Scientific Committee: Plant Biotechnology scientific panel (2018 - Present). Congress for Young Researchers in Agri-Food Sciences Universidad de Almería.

Member of Management Board for UKRI-BBSRC Quality and Food Loss Network in Horticulture 2020 – 2024.

EC registered expert (Plant breeding, agricultural biotechnology) for Horizon 2020. Expert: EX2014D18024

Contributed to the CAAS-FAO-CGIAR 'Chengdu Declaration' announced at GLAST 2019, Chengdu.

Selected publications

Bianchi, G., Picchi, V., Tava, A., Doria, F., Walley, P. G., Dever, L., Concetta di Bella, M., Arena, D., Ben Hammar, H., Lo Scalzo, R., Branca, F. (2024). Insights into the phytochemical composition of selected genotypes of organic kale (Brassica oleracea L. var. acephala). Journal of Food Composition and Analysis, 125: 105721. doi.org/10.1016/j.jfca.2023.105721.

Walley, P. G., & Dever, L. (2021). Genotypic diversity in the BRESOV Brassica core collection (Version v1) [Data set]. Zenodo. https://doi.org/10.5281/zenodo.5764246. 676K Genotyping by Sequencing SNPs using 863 taxa for the Brassica research community.

Yalçın, H. A., Gutierrez, A. G., Steuernagel, B., Walley, P. G. and Ridout, C. J. (2021). Drought stress induces pattern-triggered immunity highly associated with quantitative disease resistance in Brassica oleracea. Molecular Plant-Microbe Interactions, 34(12):2-2.

Dr Edwin Yates

Senior Lecturer

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Biochemistry, Cell and Systems Biology

Biochemistry of carbohydrates and carbohydrate interactions

Developing and applying new tools to study complex carbohydrates and the means of elucidating their activities. This approach has been applied to a very wide-range of biological problems from Alzheimer's research [1] to nerve regeneration and from tropical disease biology [2] to cell signalling and host-virus interactions.

Pioneering and developing new analytical approaches for assessing the purity of the anticoagulant drug, heparin, which have been adopted by industry and regulatory bodies [http://dx.doi.org/10.1039/c0an00834f?].

Selected publications

[1] Stewart, K. L., Hughes, E., Yates, E. A., Akien, G. R., Huang, T. -Y., Lima, M. A., . . . Middleton, D. A. (2016). Atomic Details of the Interactions of Glycosaminoglycans with Amyloid-beta Fibrils. JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, 138(27), 8328-8331. doi:10.1021/jacs.6b02816

[2] Pagani, I., Ottoboni, L., Podini, P., Ghezzi, S., Brambilla, E., Bezukladova, S., . . . Vicenzi, E. (2022). Heparin Protects Human Neural Progenitor Cells from Zika Virus-Induced Cell Death While Preserving Their Differentiation into Mature Neuroglial Cells. JOURNAL OF VIROLOGY, 96(19). doi:10.1128/jvi.01122-22

[3] Mycroft-West, C. J., Su, D., Pagani, I., Rudd, T. R., Elli, S., Gandhi, N. S., . . . Skidmore, M. A. (2020). Heparin Inhibits Cellular Invasion by SARS-CoV-2: Structural Dependence of the Interaction of the Spike S1 Receptor-Binding Domain with Heparin. THROMBOSIS AND HAEMOSTASIS, 120(12), 1700-1715. doi:10.1055/s-0040-1721319

Professor Lu-Gang Yu

Professor of Glyco-oncology

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Biochemistry, Cell and Systems Biology

Galectins in cancer development, progression and metastasis

To understand the role and actions of carbohydrate binding proteins, particularly the galactoside-binding galectins, in cancer development, progression and metastasis. To develop galectin-targeted novel therapeutic agents from natural and synthetic sources for treatment of cancer

Selected publications

Zhao Q, Barclay M, Hilkens J, Guo X, Barrow H, Rhodes JM, Yu LG. (2010). Interaction between circulating galectin-3 and cancer-associated MUC1 enhances tumour cell homotypic aggregation and prevents anoikis. Molecular Cancer 9:154.

Barrow H, Guo X, Wandall HH, Pedersen JW, Fu B, Zhao Q, Chen C, Rhodes JM, Yu LG. (2011). Serum galectin-2, -3, -4 and -8 are greatly increased in colon and breast cancer patients and promote cancer cell adhesion to blood vascular endothelium. Clinical Cancer Research 17:7035-46.

Chen C, Duckworth CA, Zhao Q, Pritchard DM, Rhodes JM, Yu LG. (2013). Increased circulation of galectin-3 in cancer induces secretion of metastasis-promoting cytokines from blood vascular endothelium. Clinical Cancer Research 19:1693-704.

Professor Michael Schmid

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www,schmidlab.org

Molecular and Clinical Cancer Medicine

Stroma-immune-malignant cell crosstalk in pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) frequently metastasizes to the liver and ~80% of patients with PDAC present with non-resectable metastatic cancer at diagnosis. Fewer than 4% of patients with metastasis survive more than five years with current standard of care chemotherapy. There is an urgent need to inhibit metastasis or even reverse metastatic outgrowth in PDAC patients. Liver metastasis is accompanied by the generation of an extensive non-malignant stroma, rich in immune cells, that constitutes most of the metastatic tumour mass.

My laboratory studies the cross-talk between the metastasis associated stroma cells, immune cells, and disseminated PDAC malignant cells. We aim to better understand how these heterogenous cell populations cooperate together to promote metastatic disease progression and therapy resistance, with the goal to apply our knowledge to develop better treatments for metastatic PDAC patients. In our endeavour, we utilize a variety of approaches such as pre-clinical pancreatic cancer models, primary cell cultures, flow- and mass cytometry, proteomic and transcriptomic analysis, bioinformatics, and validation of findings in clinical samples.

Selected publications

Bellomo, G., Rainer, C., Quaranta, V., Astuti, Y., Raymant, M., Boyd, E., . . . Schmid, M. C. (n.d.). Chemotherapy-induced infiltration of neutrophils promotes pancreatic cancer metastasis via Gas6/AXL signalling axis. Gut. 10.1136/gutjnl-2021-325272

Quaranta, V., Rainer, C., Nielsen, S., Raymant, M., Ahmed, M., Engle, D., . . . Schmid, M. C. (2018). Macrophage-derived granulin drives resistance to immune checkpoint inhibition in metastatic pancreatic cancer. Cancer Research, 78(15), 4253-4269. 10.1158/0008-5472.CAN-17-3876

Schmid, M. C., Nielsen, S. R., Quaranta, V., Rainer, C., Mielgo, A., Emeagi, P., . . . Engle, D. (2016). Macrophage-secreted granulin supports pancreatic cancer metastasis by inducing liver fibrosis. Nature Cell Biology, 18(5), 549-560. 10.1038/ncb3340

Professor Paula Ghaneh

Deputy Head of Department

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Improving outcomes for patients with pancreatic cancer

Clinical and translational research in the diagnostic and management pathways for patients with pancreatic cancer. Evaluating adjuvant and neoadjuvant therapy in clinical trials of pancreatic cancer. Investigating the role of PET CT in the diagnostic accuracy and management of pancreatic cancer. Evaluating biomarkers for prognosis and stratification in the treatment of pancreatic cancer.

The findings from the PET-PANC and ESPAC-4 trials are standard of care and are part of the NICE Guidelines for Pancreatic Cancer and ESPAC 4 is part of the American Society of Clinical Oncology guidelines for resectable pancreatic cancer (JCO 2017; 35: 2324-2328).

Selected publications

Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable pancreatic cancer (ESPAC5): a four-arm, multicentre, randomised, phase 2 trial. 10.1016/S2468-1253(22)00348-X

PET-PANC: multicentre prospective diagnostic accuracy and health economic analysis study of the impact of combined modality ¹⁸fluorine-2-fluoro-2-deoxy-D-glucose positron emission tomography with computed tomography scanning in the diagnosis and management of pancreatic cancer. 10.3310/hta22070

Neoptolemos, J. P., Palmer, D. H., Ghaneh, P., Psarelli, E. E., Valle, J. W., Halloran, C. M., . Büchler, M. W. (2017). Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial.. Lancet (London, England), 389(10073), 1011-1024. 10.1016/s0140-6736(16)32409-6

Dr Paul Atherton

Lecturer

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Molecular and Clinical Cancer Medicine

How cells sense and shape oncological extracellular matrix

Cells throughout the body are supported by a complex and dynamic network of proteins that collectively form the extracellular matrix (ECM). The ECM provides mechanical support to tissues, while also acting as a source of biochemical and biophysical inputs that regulate cellular processes including proliferation, metabolism, migration, and differentiation. The ECM is continuously remodelled by cells as part of tissue homeostasis, and this often goes awry in cancer leading to profound changes in the amount and composition of ECM.

The ECM comes in many different compositional 'flavours', providing different signalling inputs for cells. Cells communicate with the ECM via a cluster of proteins at structures called focal adhesions (FA) where transmembrane receptors (integrins) bind to ECM proteins. These clusters connect directly to the actin cytoskeleton and indirectly to microtubules via an adjacent group of proteins that form cortical microtubule stabilising complexes (CMSC).

My research aims to understand how these two systems co-operate to function in ECM sensing and subsequent signalling and how this goes wrong in cancer. I am also particularly interested in how actin-microtubule crosstalk at adhesion sites regulates the remodelling of the ECM, and aim to understand how this part of tissue homeostasis goes wrong during tumour progression.

Selected publications

Atherton, P., Konstantinou, R., Neo, S.P., Wang, E., Balloi, E., Ptushkina, M., Bennett, H., Clark, K., Gunaratne, J., Critchley, D., Barsukov, I., Manser, E., Ballestrem, C. Tensin3 interaction with talin drives formation of fibronectin-associated fibrillar adhesions. Journal of Cell Biology (2022), 221(10): e202107022. 10.1083/jcb.202107022

Zuidema, A., Atherton, P., Kreft, M., Hoekman, L., Bleijerveld, O., Nagarjuna, N., Chen, N., Fässler, R., Sonnenberg, A. PEAK1 Y635 phosphorylation regulates cell migration through association with Tensin-3 and integrins. Journal of Cell Biology (2022), 221(8): e202108027. 10.1083/jcb.202108027

Atherton P., Lausecker F., Carisey A., Miskolczi Z., Gilmore A., Barsukov I., and Ballestrem C. Relief of talin autoinhibition triggers a force-independent association with vinculin. Journal of Cell Biology (2020) 219(1): e201903134. 10.1083/jcb.201903134

Dr Serena Chee

Senior Clinical Lecturer in Respiratory Medicine

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Molecular and Clinical Cancer Medicine

Research summary

Serena Chee was appointed as Senior Clinical Lecturer in Respiratory Medicine at the University of Liverpool and Consultant Respiratory Physician at the Liverpool Heart and Chest Hospital in 2021.

She completed her PhD, "Evaluating the effect of immune cells on the outcome of patients with mesothelioma" at the University of Southampton funded by the Mesothelioma Applied Research

Foundation. Her major academic interest lies in the immune response to Mesothelioma and Lung Cancer.

Selected publications

Severely ill COVID-19 patients display impaired exhaustion features in SARS-CoV-2 reactive CD8+ T cells Sci Immunol. 2021 Kusnadi A*, Ramírez-Suástegui C*, Fajardo V*, Chee SJ*, Meckiff BJ, Simon H, Pelosi E, Seumois G, Ay F, Vijayanand P, Ottensmeier CH. 10.1126/sciimmunol.abe4782

Imbalance of regulatory and cytotoxic SARS-CoV-2-reactive CD4+ T cells in COVID-19 Cell 2020 Meckiff, B J*, Ramírez-Suástegui C*, Fajardo V*, Chee SJ*, Kusnadi A, Simon H, Eschweiler S, Grifoni A, Pelosi E, Weiskopf D, Sette A, Ay F, Seumois G, Ottensmeier CH, Vijayanand P 10.1016/j.cell.2020.10.001

Single-cell transcriptomic analysis of tissue-resident memory T cells in human lung cancer Journal Experimental Medicine 2019 Clarke J, Panwar B, Madrigal A, Singh D, Gujar R, Wood O, Chee SJ, Eschweiler S, King E, Awad A, Hanley C, McCann K, Bhattacharyya S, Woo E, Alzetani A, Seumois G, Thomas G, Ganesan A-P, Friedmann P, Sanchez-Elsner T, Ay F, Ottensmeier CH, Vijayanand P 10.1084/jem.20190249

Professor Eithne Costello

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Key words: pancreatic cancer, early detection, diabetes, biomarker, NQO1

Understanding pancreatic cancer-related diabetes for earlier cancer detection

Individuals with new-onset diabetes (NOD) are the largest high-risk group for pancreatic ductal adenocarcinoma (PDAC; with 1/3 of PDAC patients experiencing NOD). The lack of an accurate screening test for this group delays PDAC detection. Diabetes mellitus (DM) secondary to pancreatic disease (type-3c diabetes) includes PDAC-related (and chronic pancreatitis-related) diabetes and exhibits features distinct from type-2 diabetes. Our research aims to develop a blood test, that when applied to individuals with NOD, distinguishes those with type-3c from type-2 diabetes, enabling the type-3c group to undergo screening for PDAC.

With programme funding from Cancer Research UK, we have begun a collection of individuals >50 years, newly diagnosed with DM (target 2,500) from diabetes centres and general practice. Biosamples and questionnaire/clinical data are collected. While recruitment is ongoing, biomarker development for the high-risk NOD group is underway, with protocols for biomarker discovery using NOD being developed/refined, and newly discovered biomarkers currently undergoing orthogonal validation. The sensitivity/specificity for the detection of PDAC by combined biomarker and epidemiological/clinical feature analysis will be evaluated in our NOD cohort (as well as international cohorts). The cost-effectiveness of diagnosing PDAC earlier is being assessed. Our work will enable stratification of individuals with new-onset DM for PDAC risk, making it feasible in future to screen for PDAC in individuals with new-onset DM.

The ability of pancreatic cancer to disrupt the normal regulation of blood glucose is not understood. At the time of cancer diagnosis, over 45% of patients have diabetes. With Pancreatic Cancer UK funding, we are undertaking single-cell gene expression analysis from pancreatic tumours, stratified by diabetes, and parallel analysis of blood protein profiles to identify genes and pathways dysregulated in pancreatic cancer-related diabetes is ongoing. We are applying extensive bioinformatic analysis followed by spatial transcriptomic for gene and pathway validation. The interrogation of the molecular pathways associated with pancreatic cancer-related diabetes is novel. Comparing newly obtained tissue and blood data will allow identification/explanation of potential biomarkers for early detection.

Finally, we are interested in role of NQO1 (a protein regulated by the cytoprotective transcription factor Nrf2) in predicting response to chemotherapy in pancreatic cancer

Selected publications

Oldfield L, Stott M, Hanson R, Jackson RJ, Reynolds W, Chandran-Gorner V, Van Der Meer R, Alison L, Tejeiro R, Purewal T, Ghaneh P, Palmer D, Greenhalf W, Halloran C, Costello E. United Kingdom Early Detection Initiative (UK-EDI): protocol for establishing a national multicentre cohort of individuals with new-onset diabetes for early detection of pancreatic cancer. BMJ Open. 2022;12(10):e068010. 10.1136/bmjopen-2022-068010

Oldfield L, Evans A, Rao RG, Jenkinson C, Purewal T, Psarelli EE, Menon U, Timms JF, Pereira SP, Ghaneh P, Greenhalf W, Halloran C, Costello E. Blood levels of adiponectin and IL-1Ra distinguish type 3c from type 2 diabetes: Implications for earlier pancreatic cancer detection in new-onset diabetes. EBioMedicine. 2022 Jan;75:103802. 10.1016/j.ebiom.2021.103802.

Barrera, L.N, Evans, A, Lane, B, Brumskill, S, Oldfield, F.E, Campbell, F, Andrews, T, Lu, Z, Perez-Mancera, P.A, Liloglou, T, Ashworth, M, Jalali M, Dawson R, Nunes, Q1, Phillips, PA, Timms, JF, Halloran, C. M, Greenhalf W, Neoptolemos J. P, and Costello, E. (2020). Fibroblasts from Distinct Pancreatic Pathologies Exhibit Disease-Specific Properties. Cancer Research 80, 2861-2873. 10.1158/0008-5472.CAN-19-3534

Professor Judy Coulson

Deputy Associate Pro-Vice-Chancellor for Technology, Infrastructure and Environment

Faculty Lead for Equality, Diversity and Inclusion

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Molecular and Clinical Cancer Medicine

Cancer cell signalling and ubiquitylation: discovery, translation, novel preclinical models

My cancer biology research group are interested in deciphering the interplay between cell signaling, transcription and ubiquitylation. We aim to translate discoveries towards therapeutic intervention in mesothelioma, uveal melanoma, breast, or lung cancer. To facilitate preclinical evaluation, whilst reducing the use of animals, we developed fertilised hens' egg xenograft models for cancer cells and patient-derived tissues (PDX) that are amenable to advanced preclinical imaging3. Recent and current research is supported by UKRI (EPSRC, NC3Rs) and UK charities (Breast Cancer Now, British Lung Foundation, Cancer Research UK, Fight for Sight, North-West Cancer Research, Wellcome).

Ubiquitylation regulates the stability and activity of proteins but can be removed by deubiquitylase enzymes (DUBs) to reverse phenotypes, with specific DUB inhibitors emerging1. Our discovery research maps DUBs to cancer-associated processes, including PI3 kinase and Hippo signalling, transcription, genome stability and cell division. Centrosome amplification promotes oncogenic phenotypes but presents a challenge, as supernumerary centrosomes must be clustered at mitosis to permit bipolar division and cell survival. Thus, centrosome clustering is a targetable cancer-specific vulnerability. We recently described centrosome amplification in uveal melanoma and have identified the first DUB that regulates the ubiquitylation of a key driver of clustering in triple negative breast cancer. Another focus is the DUB and tumour suppressor BAP1, which is frequently inactivated in two rare cancers, mesothelioma and uveal melanoma. Using gene-editing and multi-omics we uncovered BAP1-dependent therapeutic sensitivities in mesothelioma and are extrapolating findings to uveal melanoma. We discovered a new role for BAP1 in regulating the enzyme ASS1, which argues for expanding the eligibility of mesothelioma patients in clinical trials of arginine deprivation therapy2.

These projects are now entering preclinical phases in egg xenograft models, and in 2022 we established the LIV-SRF egg facility to enable colleagues and external researchers to also access these models. As UK leaders, we advise other HEIs establishing facilities, support major collaborative grant applications and attract income from external clients/collaborators. For example, as EPSRC IRC partners we are testing novel delivery systems in mesothelioma, including hydrogels and metal-organic frameworks.

Selected publications

Clague MJ, Barsukov I, Coulson JM, Liu H, Rigden D, Urbé S. Deubiquitylases from genes to organism. Physiological Reviews. 2013, 93(3):1289-1315. doi: 10.1152/physrev.00002.2013. (445 citations) 10.1152/physrev.00002.2013

Barnett SE*, Kenyani J*, Tripari M, Butt Z, Grosman RX, Querques F, Shaw L, Silva LC, Goate Z, Rusilowicz E, Marciniak SJ, Rassl D, Lian L-Y, Szlosarek P, Sacco JJ, Coulson JM. BAP1 loss is associated with higher ASS1 expression in epithelioid mesothelioma suggesting options for therapeutic stratification. Mol Cancer Res. 2023, 21(5):411-427. 10.1158/1541-7786.MCR-22-0635

Barnett SE, Herrmann A, Shaw L, Gash EN, Poptani H, Sacco JJ, Coulson JM. The chick embryo xenograft model for malignant pleural mesothelioma: a cost and time Efficient 3Rs model for drug target evaluation. Cancers 2022, 14(23):5836. 10.3390/cancers14235836

Dr David Criddle

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View staff profile

Molecular and Clinical Cancer Medicine

Understanding mechanisms of mitochondrial dysfunction and cell death in disease

Research is focussed on the elucidation of critical mechanisms that underlie pathophysiological changes in disease, with particular emphasis on cellular injury in acute pancreatitis. Our studies have demonstrated how alcohol and fatty acids, via non-oxidative metabolism, disrupt calcium signalling leading to mitochondrial dysfunction and cellular toxicity. Central to damage caused by precipitants of acute pancreatitis is formation of the calcium and ROS-dependent mitochondrial permeability transition pore (MPTP); impaired mitochondrial bioenergetics and rundown of cellular ATP modulate cell fate. Mechanisms of organellar dysfunction and cell death are currently being investigated using multiple approaches, including confocal microscopy and Seahorse bioenergetics analysis, with evaluation of novel approaches to ameliorate damage. Collaborative studies with Brazilian colleagues are directed towards elucidation of acute and chronic pancreatitis mechanisms, including visceral pain and lung injury.

Selected publications

Criddle, D.N., Gillies, S., Baumgartner-Wilson, H.K., Jaffar, M., Chinje, E.C., Passmore, S., Chvanov, M., Barrow, S., Gerasimenko, O.V., Tepikin, A.V., Sutton, R., Petersen, O.H. (2006) Menadione-induced reactive oxygen species generation via redox cycling promotes apoptosis of murine pancreatic acinar cells. J.Biol.Chem., 281(52):40485-92. 10.1074/jbc.M607704200

Criddle, D.N., Murphy, J.A., Fistetto, G., Barrow, S., Tepikin, A.V., Neoptolemos, .JP., Sutton, R., Petersen, O.H. (2006). Fatty acid ethyl esters cause pancreatic calcium toxicity via inositol trisphosphate receptors and loss of ATP synthesis. Gastroenterology; 130(3):781-93. 10.1053/j.gastro.2005.12.031

Criddle, D.N., Raraty, M.G.T., Neoptolemos, J.P., Tepikin, A.V., Petersen, O.H., Sutton R. (2004). Ethanol toxicity in pancreatic acinar cells: Mediation by non-oxidative fatty acid metabolites. Proc. Natl Acad Sci., 101 (29), 10738-10743. 10.1073/pnas.0403431101

Dr Carrie Duckworth

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Molecular and Clinical Cancer Medicine

Research summary

Dr Duckworth's research focuses on understanding the regulation of gastrointestinal architecture under homeostatic conditions and during disease processes. Her lab explores the mechanisms within the intestinal mucosa that modulate the susceptibility to the development of drug-induced gastrointestinal toxicity, inflammatory bowel disease and gastrointestinal cancers.

The ultimate aims of her research are to elucidate novel therapeutic approaches for gastrointestinal disease. To achieve these aims, the Duckworth lab specialises in the development and application of 3D and 2D in vitro adult stem cell-derived gastrointestinal organoid models which capture and recapitulate the dynamic nature of intestinal and gastric epithelia observed in vivo.

Selected publications

Jardi F, Kelly C, Teague C, Fowler-Williams H, Sevin DC, Rodrigues D, Jo H, Ferreira S, Herpers B, Van Heerden M, de Kok T, Pin C, Lynch a, Duckworth CA, De Jonghe S, Lammens L, Pritchard DM (2023). Mouse organoids as an in vitro tool to study the in vivo intestinal response to cytotoxicants. ArchToxicol 97(1): 235-254 10.1007/s00204-022-03374-3

Johnston LJ, Barningham L, Campbell EL, Cerovic V, Duckworth CA, Luu L, Wastling J, Derricott H, Coombes JL (2023). A novel in vitro model of the small intestinal epithelium in co-culture with 'gut-like' dendritic cells. Disc Immunol 2(1): kyad018 10.1093/discim/kyad018

Papoutsopoulou S, Tang J, Elramli AH, Williams JM, Gupta N, Ikuomola FI, Sheibani-Tezerji R, Alam MT, Hernández-Fernaud JR, Caamaño JH, Probert CS, Muller W, Duckworth CA*, Pritchard DM* (2022). Nfkb2 deficiency and its impact on plasma cells and on immunoglobulin expression in murine small intestinal mucosa. Am J Physiol 323(4): G306-G317 *share last authorship. 10.1152/ajpgi.00037.2022

Professor John Field

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Lung cancer aetiology, early detection and screening for improved outcomes

Early detection of lung cancer saves lives, as demonstrated by the introduction of low-dose CT screening for those at highest risk. Having produced the Liverpool Lung Project (LLP) lung cancer risk score and proven its worth in the UK Lung cancer screening trial (UKLS) led by Prof Field, it has now been incorporated into the NHS England Targeted Lung Health Checks, which will lead into the National Lung Cancer Screening Programme. We continue to focus on lung cancer screening implementation research. Currently our research has had major successes in understanding the nature of lung cancer at the molecular level, which is also fundamental to modern targeted treatments and can further improve early detection.

The LLP has been funded by the Roy Castle Lung Cancer Foundation (RCLCF) since 1996 and has established one of the largest prospective lung cancer case-control and cohort populations in Europe (>14,000) with epidemiological, clinical and outcome data, and a variety of blood and tissue specimens. These specimens and their associated data now form the LLP Biobank, managed by Dr Michael Davies, which is used by our collaborators around the world (both academic and industry) for lung cancer biomarker discovery and validation. Samples and data from the UKLS randomised controlled trial of LDCT, including imaging data, are particularly useful for studies on management of indeterminate pulmonary nodules. Both LLP and UKLS have long-term follow-up and provide pre-diagnostic plasma samples for a range of lung and other cancers.

Working with international partners through the NIH-funded INTEGRAL project and the International Lung Cancer Consortium (ILCCO), we continue to identify epidemiological/environmental and clinical risk factors, genetic predisposition and circulating biomarkers that can be used in conjunction with risk prediction models and imaging biomarkers to further improve the early detection of lung cancer and other smoking-related or thoracic diseases.

Selected publications

Davies, M. P. A., Sato, T., Ashoor, H., Hou, L., Liloglou, T., Yang, R., & Field, J. K. (2023). Plasma protein biomarkers for early prediction of lung cancer. EBIOMEDICINE, 93. doi:10.1016/j.ebiom.2023.104686

Field, J. K., Vulkan, D., Davies, M. P. A., Baldwin, D. R., Brain, K. E., Devaraj, A., . . . Duffy, S. W. (2021). Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis. LANCET REGIONAL HEALTH-EUROPE, 10. doi:10.1016/j.lanepe.2021.100179

Field, J. K., Vulkan, D., Davies, M. P. A., Duffy, S. W., & Gabe, R. (2021). Liverpool Lung Project lung cancer risk stratification model: calibration and prospective validation. THORAX, 76(2), 161-168. doi:10.1136/thoraxjnl-2020-215158

Mr Jason Fleming

Senior Clinical Lecturer, Liverpool Head and Neck Centre

Consultant Otolaryngologist, Head & Neck Surgeon, Liverpool University Hospitals NHS Foundation Trust.

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Molecular and Clinical Cancer Medicine

Precision radiotherapy, transoral robotic surgery, image-guided surgery, organ preservation surgery

Jason Fleming is an academic ENT/Head & Neck Surgeon, specialising in head and neck cancer and thyroid surgery. He defended his PhD thesis on tumour cell motility and metabolism in 2017 and following a surgical oncology Fellowship in the USA, he was appointed as a Senior Clinical Lecturer at the University of Liverpool in 2020. He has developed an active clinical trial and embedded translational research portfolio focussing on the innovation and development of new surgical technologies, and the evaluation of cancer therapies to improve outcomes and reduce long terms side effects of treatment for head and neck disease. He is leading three prospective clinical trials, including serving as Co-chief Investigator for the CRUK funded national phase III trial PROTIS (PROton beam Therapy versus Intensity-modulated radiotherapy for Sinonasal cancer), as well as leading on an international first Phase II trial evaluating a novel robotics platform for use in transoral surgery.

Mr Fleming is involved in a number of collaborations across the University of Liverpool campus, most notably with the Department of Chemistry, where he co-supervises a number of projects related to novel contrast agents for intraoperative imaging; the translational potential of this work has been recognised and supported through Translational Research access Programme (TRAP) funding. He regularly publishes on health outcomes research, authors a number of textbook chapters and recently produced the new UK guidelines for the management of sinonasal malignancy. He has an active teaching portfolio within the University of Liverpool, lecturing on a variety of University Masters modules (Frontiers in cancer, Cancer Clinical Trials). On a regional level he is an academic representative for the regional training committee, a member of the pan-Trust surgical robotic steering group and the Fellowship Director for the internationally renowned Shaun Jackson Head and Neck Surgical Fellowship at Aintree.

Selected publications

Mainsiouw L, Ryan ME, Hafizi S, Fleming JC, 2023. The molecular and clinical role of Tensin 1/2/3 in cancer. J Cell Mol Med; 27(13): 1763-1774. PMID: 37296531 10.1111/jcmm.17714

Fleming JC, Woo J, Moutasim K, Hanley CJ, Frampton SJ, Wood O, Ward M, Woelk CH, Ottensmeier CH, Hafizi S, Kim D, Thomas GJ, 2020. CTEN Induces Tumour Cell Invasion and Survival and is Prognostic in Radiotherapy-Treated Head Neck Cancer. Cancers (Basel); 12(10), 2963. PMID: 33066224 10.3390/cancers12102963

Fleming JC, Woo J, Moutasim K, Mellone M, Frampton SJ, Mead A, Ahmed W, Wood O, Robinson H, Ward M, Woelk C, Ottensmeier CH, King E, Kim D, Blaydes JP, Thomas GJ, 2019. HPV, tumour metabolism and novel target identification in head and neck squamous cell carcinoma. Br J Cancer; 120: 356-367. PMID: 30655616 10.1038/s41416-018-0364-7

Professor William (Bill) Greenhalf

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Research summary

Professor Bill Greenhalf is the scientific lead for the Liverpool Experimental Cancer Medicine Centre (LECMC) and the European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC). He is the Director of the Liverpool Good Clinical Practice Laboratory Facility (GCPLab) and the 2nd year assessment lead for Liverpool's MBChB. He is also the Institutional lead for the UK Reproducibility Network (UKRN).

His research focuses on pancreatic cancer and he was the president of the Pancreatic Society of Great Britain and Ireland (PSGBI) in 2019. His research has led to the introduction of the UK's largest research surveillance program for pancreatic cancer[1] and he led on the development of international guidelines for pancreatic cancer surveillance in chronic pancreatitis[2]. He has also published extensively on therapeutic biomarkers for pancreatic cancer[3].

His lab also carries out basic research on the molecular pathogenesis of the disease. During the COVID-19 crisis he directed his research towards this disease and maintains an interest in SARS-CoV2 and the consequences of long covid.

Selected publications

Sheel ARG, Harrison S, Sarantitis I, Nicholson JA, Hanna T, Grocock C, et al. Identification of Cystic Lesions by Secondary Screening of Familial Pancreatic Cancer (FPC) Kindreds Is Not Associated with the Stratified Risk of Cancer. Am J Gastroenterol 2018. 10.1038/s41395-018-0395-y

Greenhalf W, Levy P, Gress T, Rebours V, Brand RE, Pandol S, et al. International consensus guidelines on surveillance for pancreatic cancer in chronic pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the American Pancreatic Association, the Japan Pancreas Society, and European Pancreatic Club. Pancreatology 2020;20:910-8. 10.1016/j.pan.2020.03.014

Aughton K, Elander NO, Evans A, Jackson R, Campbell F, Costello E, et al. hENT1 Predicts Benefit from Gemcitabine in Pancreatic Cancer but Only with Low CDA mRNA. Cancers (Basel) 2021;13. 10.3390/cancers13225758

Dr Gabrielle Grundy

Lecturer

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Molecular and Clinical Cancer Medicine

ADP-ribosyltransferases in cancer biology and factors effecting the radioresistance of tumours

Radiotherapy remains a part of 50% of cancer treatments. Ionising radiation can be effective in destroying proliferating and genetically unstable cancer cells by overwhelming the cells with DNA breaks. However, many tumour types e.g. head and neck cancers and glioblastoma multiforme are inherently radioresistant, or acquire radioresistance, leading to treatment failure or recurrence. One strategy to overcome radioresistance is to target pathways that influence cell survival following radiation damage e.g. DNA repair, hypoxia or metabolism.

One area of research focus is the ADP-ribosyltransferases superfamily (also known as PARPs), which comprise 17 multifunctional enzymes that catalyse the post-translational addition of ADP-ribose to proteins often in response to DNA damage, oxidative stress, replication stress or viral infection. We have investigated certain PARP enzymes that are overexpressed in tumour cells that could be targeted to sensitize cancer cells to radiation using specific PARP inhibitors.

Selected publications

Zhou, C., M. R. Fabbrizi, J. R. Hughes, G. J. Grundy, and J. L. Parsons. "Effectiveness of Parp Inhibition in Enhancing the Radiosensitivity of 3d Spheroids of Head and Neck Squamous Cell Carcinoma." Front Oncol 12 (2022): 940377. https://doi.org/10.3389/fonc.2022.940377. https://www.ncbi.nlm.nih.gov/pubmed/36052247.

Grundy, G. J., and J. L. Parsons. "Base Excision Repair and Its Implications to Cancer Therapy." Essays Biochem 64, no. 5 (Oct 26 2020): 831-43. https://doi.org/10.1042/EBC20200013. https://www.ncbi.nlm.nih.gov/pubmed/32648895.

Grundy, G. J., L. M. Polo, Z. Zeng, S. L. Rulten, N. C. Hoch, P. Paomephan, Y. Xu, et al. "Parp3 Is a Sensor of Nicked Nucleosomes and Monoribosylates Histone H2b(Glu2)." Nat Commun 7 (Aug 17 2016): 12404. https://doi.org/10.1038/ncomms12404. https://www.ncbi.nlm.nih.gov/pubmed/27530147.

Professor Chris Halloran

Professor of Pancreatic Surgery

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Molecular and Clinical Cancer Medicine

Research summary

Main research areas

Early detection of pancreatic cancer

1. Early Detection Initiative of Pancreatic Cancer UK (EDI pancreatic Cancer), CRUK program grant with Costello
2. European Registry of Familial Pancreatic Cancer and Hereditary Pancreatitis (Europac)
3. Europe Beating Cancer plan

Surgical Trials

1. Dispact-2, Open vs Minimal Invasive for left pancreatectomy. CI for UK.
2. Vapor for pancreatic cancer, with Hanna (Imperial).

Selected publications

Dr Colin Hammond

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Molecular and Clinical Cancer Medicine

The fundamentals of histone homeostasis control in cancer biology

The chromatin landscape of a cell is subject to various “epigenetic” modifications that direct gene expression, allowing different cell-types to emerge from the same genetic information. Crucially, this epigenetic information must be inherited through cell division to allow specific cell lineages to propagate, modified to promote cellular differentiation, and protected from unscheduled changes that lead to complex diseases like cancer. Histone proteins wrap DNA to form nucleosomes, the basic repeating subunit of chromatin, and the post-translational modification of histones and their location in the genome is an important source of epigenetic information.

In my lab, we study a set of proteins called histone chaperones that support the supply of histones to chromatin for nucleosome assembly. We study how these proteins integrate with different cellular machinery and how they are organised to enable histone supply chains to streamline the delivery of histones to different processes and locations on chromatin. We are especially interested to study how these processes go wrong in cancer with the aim of translating our textbook discoveries into future therapeutics. We are a mechanistically minded laboratory that is multidisciplinary, and we recognise the strength that diversity brings to science.

Selected publications

Carraro M*, Hendriks IA*, Hammond CM*,#, Solis V, Völker-Albert M, Elsborg JD, Weisser MB, Spanos C, Montoya G, Rappsilber J, Imhof A, Nielsen ML#, Groth A#, “DAXX adds a de novo H3.3K9me3 Deposition Pathway to the Histone Chaperone Network” Mol Cell. 83(7):1075-1092 (2023). 10.1016/j.molcel.2023.02.009

Hammond CM*, Bao H*, Hendriks IA, Carraro M, García-Nieto A, Liu Y, Reverón-Gómez N, Spanos C, Chen L, Rappsilber J, Nielsen ML, Patel DJ, Huang H, Groth A, “DNAJC9 Integrates Heat Shock Molecular Chaperones into the Histone Chaperone Network” Mol Cell. 81(12):2533-2548 (2021). 10.1016/j.molcel.2021.03.041

Hammond CM*, Strømme CB*, Huang H, Patel DJ, Groth A, "Histone Chaperone Networks Shaping Chromatin Function" Nat Rev Mol Cell Biol. 18(3):141-158 (2017). 10.1038/nrm.2016.159

Professor Keith Hunter

Professor of Head and Neck Pathology

Academic Lead, Liverpool University Biobank

Consultant Cellular Pathologist, LUFT

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Molecular and Clinical Cancer Medicine

Research summary

I am Professor of Head and Neck Pathology and a Clinical Academic Histopathologist in Molecular and Clinical Cancer Medicine at the University of Liverpool, UK and Liverpool Universities NHS Foundation Trust, Working in the Liverpool Head and Neck Centre. I completed my PhD at the CRUK Beatson Institute for Cancer Research (Glasgow) and clinical training at Glasgow Royal Infirmary.

In 2009 I established a research group focussing on the transcriptional changes seen in the various stages in the development of oral precancer and cancer with a particular interest in the control of cellular immortalization of keratinocytes and aspects of the tumour microenvironment. I moved to the Liverpool Head and Neck Centre in 2022.

I am the author of over 130 peer reviewed articles and have also contributed to several books, including the 2022 WHO Classification of Tumours of the Head and Neck, and am a co-author of the 5th edition of Soames and Southam's Oral Pathology.

Selected publications

Mehanna H, et al. Developing and Validating a Multivariable Prognostic-Predictive Classifier for Treatment Escalation of Oropharyngeal Squamous Cell Carcinoma: The PREDICTR-OPC Study. Clin Cancer Res. 2024 Jan 17;30(2):356-367. 10.1158/1078-0432.CCR-23-1013

Essat M, Cooper K, Bessey A, Clowes M, Chilcott JB, Hunter KD. Diagnostic accuracy of conventional oral examination for detecting oral cavity cancer and potentially malignant disorders in patients with clinically evident oral lesions: Systematic review and meta-analysis. Head Neck. 2022 Apr;44(4):998-1013. 10.1002/hed.26992

Radhakrishnan R, Crane HL, Daigneault M, Padam KSR, Hunter KD. RARβ Expression in Keratinocytes from Potentially Malignant Oral Lesions: The Functional Consequences of Re-Expression by De-Methylating Agents. Cancers (Basel). 2021 Aug 12;13(16):4064. 10.3390/cancers13164064

Professor Philip Johnson

Professor in Translational Oncology

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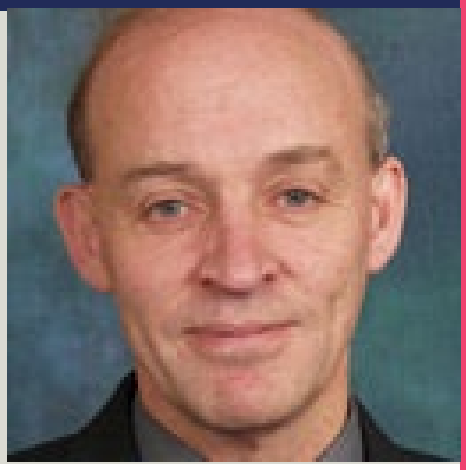

Molecular and Clinical Cancer Medicine

Research on chronic liver disease and liver cancer

We work on chronic liver disease (CLD) and primary liver cancer (hepatocellular carcinoma, (HCC)). Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and usually arises in patients with pre-existing CLD. It is a serious disease that is fatal if not detected and treated early. HCC poses a significant global health burden, ranking as the fifth most common cancer worldwide and the third leading cause of cancer-related death. In 2020 alone, HCC resulted in nearly one million deaths worldwide. The risk factors for CLD and HCC are well-known and include chronic hepatitis B virus (HBV), hepatitis C virus (HCV) infections, fatty liver disease and excessive alcohol consumption.

We build statistical models that predict outcomes of CLD and HCC in relation to several clinical settings. Having worked in this area for 50 years I have very extensive contacts around the world with former colleagues and collaborators, as well as industry. From this resource we have access to detailed datasets ('biomarkers') involving several hundred thousand cases, the great majority of which is provided without any financial support, often in exchange for high impact publications.

All these models are published in the international literature and include 'calculators' such that given a specific set of variables, a specific outcome can be predicted. Very specifically, we do not seek novel blood or 'molecular' tests, restricting ourselves to existing and routinely available 'liver tests' and other datasets. Likewise, our research is internationally, not locally, centred. By this approach our models are immediately and globally applicable. Any novelty arises from the breadth and quantity of CLD and HCC data that we have at our disposal and the statistical methodology that we apply. Previously we have used standard regression-based statistical methodology (and hence worked very closely with colleagues in statistics departments) but we are now moving to machine learning in collaboration with computer sciences departments.

Professor Terry Jones

Director, Liverpool Head and Neck Centre

Director of Research and Innovation, LUHFT
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Molecular and Clinical Cancer Medicine

Research summary

My research interests can be divided into four main themes

- Basic/translational research: including the molecular biology of the differential treatment response seen between HPV+ve and –ve oropharyngeal squamous cell carcinomas.
- Early and late phase Clinical Trials: Joint Chief Investigator respectively for three CR-UK funded H&N studies: PATHOS, PATHOS-T & EORTC 1420 and co –investigator for the CR-UK funded PROTIS clinical trial.
- Clinical outcomes research: with a particular interest in swallowing and voice outcomes following TLM
- Cancer Inequalities: and their impact on incidence and outcome for patients with head and neck cancer

Selected publications

Basyuni, Shadi; Nugent, Gareth; Ferro, Ashley; Barker, Eleanor; Reddin, Ian; Jones, Oliver; Lechner, Matt; O'Leary, Ben; Jones, Terry; Masterson, Liam; Fenton, Tim; Schache, Andrew (2022). Value of p53 sequencing in the prognostication of head and neck cancer: a systematic review and meta-analysis.. Scientific reports, 12(1), 20776. 10.1038/s41598-022-25291-2

Eschweiler, S., Ramírez-Suástegui, C., Li, Y. et al. Intermittent PI3Kδ inhibition sustains anti-tumour immunity and curbs irAEs. Nature 605, 741–746 (2022). 10.1038/s41586-022-04685-2

Dalton CL, Milinis K, Houghton D, Ridley P, Davies K, Williams R, Hamilton D, Wilkie MD, Markey A, Clarke K, Lofthouse M, Helliwell TR, Triantafyllou A, Rodrigues J, Bheemireddy K, Hanlon R, Wieshmann H, Haridass A, Brammer C, Husband D, Shenoy A, Loh C, Roland NJ, Bekiroglu F, Tandon S, Lancaster J, Jones TM. Transoral laser microsurgery and radiotherapy for oropharyngeal squamous cell carcinoma: Equitable survival and enhanced function compared with contemporary standards of care. Eur J Surg Oncol. 2020 Nov;46(11):2042-2049. 10.1016/j.ejso.2020.06.045

Professor Nagesh Kalakonda

Chair of Experimental Haematology

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Molecular and Clinical Cancer Medicine

Research summary

Having obtained his primary medical qualification from the University of Madras, Nagesh Kalakonda completed haematology training in Dundee and Manchester. Following a PhD from the Univ. of Manchester, and a postdoctoral fellowship at the Memorial Sloan-Kettering Cancer Centre in New York (2001-8), he joined the University of Liverpool. He leads a Cancer epigenetics lab focused on lymphoid and immuno-biology. His research is focused on epigenetic alterations in lymphoid cancers (Chronic lymphocytic leukemia and lymphomas). Understanding the role of such changes that impact overlapping hallmarks of cancer and ageing to compromise immune, transcriptional, and stress pathways is critical to develop new treatments to prevent cancer relapse. A major focus is on the epigenome (histones and non-coding (long and small) RNAs) by applying CRISPR-Cas9 gene-editing, mass cytometry-based PLAYR-CyTOF, and multi-omics to cell line models and primary patient samples.

He is a member of the CLL/lymphoma clinical service at the Clatterbridge Cancer Centre (CCC). He is a local and national principal/chief investigator for multiple clinical trials. Current and previous roles include Chair of the National working group for elderly/frail lymphomas, Lead physician for 'Teenage and Young Adults' (TYA) with haematological cancers (Cheshire and Merseyside), Member of the National High-grade and Lymphoma Science subgroups and Director for Clinical Research for CCC (2017-21). He has served on national and global peer-review, editorial, grant review and NICE panels.

He is the Founder Trustee and Hon. President of the regional 'Merseyside against Blood cancers-The Bloom Appeal' charity.

Selected publications

Fox CP, Chaganti S, McIlroy G, Barrington SF, Burton C, Cwynarski K, Eyre TA, Illidge T, Kalakonda N, Kuhnl A, McKay P, Davies AJ. The management of newly diagnosed large B-cell lymphoma: A British Society for Haematology Guideline. Br J Haematol. 2024 Jan 21. https://doi.org/10.1111/bjh.19273

Duckworth AD, Slupsky JR, Kalakonda N. Highly Multiplexed and Simultaneous Characterization of Protein and RNA in Single Cells by Flow or Mass Cytometry Platforms Using Proximity Ligation Assay for RNA. Methods Mol Biol. 2024;2752:143-165. 10.1007/978-1-0716-3621-3_10

Kalakonda N, Maerevoet M, et al., Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial. Lancet Haematol. 2020 Jul;7(7):e511-e522. 10.1016/S2352-3026(20)30120-4

Dr Aditi Kanhere

Reader

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Molecular and Clinical Cancer Medicine

Molecular mechanisms of non-coding RNAs and their applications in cancer medicine

Aditi Kanhere (AK) has over 20 years of experience in the fields of non-coding RNAs (ncRNAs) and transcription regulation. She has contributed a significant body of work to the field of ncRNAs with noteworthy citations (>2000) which has resulted in an international reputation in the ncRNA field. During her early years of research, she discovered how RNAs can influence the epigenome in immune cells. Recently, these non-coding RNAs have not only emerged as novel therapeutic targets but they also present untapped repertoire of biomarkers that can be effectively used in early diagnosis, an area of high importance in cancer medicine. Over last many years she has accelerated this line of research by successfully leading and completing many projects as reflected in publications in leading journals such as EMBO, Genome Research and Trends in Genetics. These efforts have led to identifying vital roles of RNAs in regulating the genome in early embryonic development and during oncogenesis. She is currently involved in multiple collaborations exploring the role of non-coding RNAs in ageing, drug sensitivity and metabolism, heamato-oncology and solid tumours. Through her association with three different international consortia, she has ventured into technologically ambitious ideas. AK currently leads a cross-disciplinary lab which seamlessly combines diverse techniques ranging from cell and molecular biology, transcriptomics to computational biology to understand mechanisms of ncRNAs in gene expression regulation and to develop ncRNA applications in cancer medicine. Moreover, AK has extensive experience in current transcriptomics methodologies such as RNA-seq, ChIP-seq, ATAC-seq and other next generation sequencing techniques. To date, she has supervised >10 PhD students and trained multiple fellows, a majority have secured postdoctoral positions in reputed labs as well as embarked on independent careers.

Selected publications

Pillay S, Takahashi H, Carninci P, Kanhere A. (2021) Antisense RNAs during early vertebrate development are divided in groups with distinct features. Genome Res. 31:995-1010. doi: 10.1101/gr.262964.120

Jones R, Wijesinghe S, Wilson C, Halsall J, Liloglou T, Kanhere A.(2021) A long intergenic non-coding RNA regulates nuclear localization of DNA methyl transferase-1. iScience. 24:102273. doi: 10.1016/j.isci.2021.102273.

Al-Raawi D, Jones R, Wijesinghe S, Halsall J, Petric M, Roberts S, Hotchin NA, Kanhere A. (2019) A novel form of JARID2 is required for differentiation in lineage-committed cells. EMBO J. 38:e98449. doi: 10.15252/embj.201798449.

Professor Tim Maughan

Chair in Oncology

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Molecular and Clinical Cancer Medicine

Research summary

Professor Maughan has recently joined the University of Liverpool to provide strategic leadership to the Cancer research programme in the University and across the city. He has previously held leadership positions in the Universities of Oxford and Cardiff and at the National Cancer Research Institute.

His research focuses on colorectal cancer where he has led four major national trials and the MRC stratified medicine consortium in colorectal cancer. His main focus in Liverpool will be to build the research programme in the tumour microenvironment to understand the factors inhibiting response to immunotherapy of cancer and to find ways to overcome them. Secondly he will be building a research team from several areas across Liverpool to evaluate approaches to early detection of cancer with a focus on overcoming the deprivation deficit.

Selected publications

Malla, S.B., Byrne, R.M., Lafarge, M.W. et al. Pathway level subtyping identifies a slow-cycling biological phenotype associated with poor clinical outcomes in colorectal cancer. Nat Genet (2024). https://doi.org/10.1038/s41588-024-01654-5

Beach C, MacLean D, Majorova D, et al . Improving radiotherapy in immunosuppressive microenvironments by targeting complement receptor C5aR1. J Clin Invest. 2023 Dec 1;133(23):e168277. doi: 10.1172/JCI168277

Sirinukunwattana K, Domingo E, Richman SD On behalf of S:CORT consortium, et al Image-based consensus molecular subtype (imCMS) classification of colorectal cancer using deep learning Gut 2021;70:544-554 10.1136/gutjnl-2019-319866

Dr Caroline McCarthy

Academic Clinical Lecturer in Oral Medicine

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Molecular and Clinical Cancer Medicine

Oral potentially malignant disorders and prevention of oral cancer

My research focuses on Oral Potentially Malignant Disorders (OPMD), particularly oral dysplasia and oral lichen planus. Patients with an OPMD have a greater risk of developing oral cancer compared to the general population. Therefore, by accurately diagnosing and managing these conditions, we aim to reduce the incidence of oral cancer. I am Principal Investigator for the SAVER chemoprevention trial at Liverpool University Dental Hospital, which is a trial investigating the use of Sodium Valproate in the prevention of cancer development for patients with oral dysplasia. I am also working with LightOx, a commercial partner, to develop light-based treatments for oral dysplasia. More recently, I have been awarded funding from the Academy of Medical Sciences to investigate the immune microenvironment in oral lichen planus, with a view to a wider programme of work in this area. I am the Patient and Public Involvement lead for a collaboration between colleagues in Physics and the Head and Neck Centre, aiming to develop a novel infra-red based diagnostic tool for the prediction of cancer development for patients with oral dysplasia. Finally, I am working with the Royal Pharmaceutical Society to develop educational tools for pharmacists with the aim of promoting early diagnosis of oral cancer where better patient outcomes are achieved.

Selected publications

McCarthy C, Fedele S, Ottensmeier C, Shaw RJ. Early-Phase Interventional Trials in Oral Cancer Prevention. Cancers (Basel). 2021 Jul 30;13(15):3845. doi: 10.3390/cancers13153845. PMID: 34359746; PMCID: PMC8345124. 10.3390/cancers13153845

McCarthy CE, Fedele S, Ho M, Shaw R. UK consensus recommendations on the management of oral epithelial dysplasia during COVID-19 pandemic outbreaks. Oral Oncol. 2021 Jan;112:105110. doi: 10.1016/j.oraloncology.2020.105110. Epub 2020 Nov 19. PMID: 33232878; PMCID: PMC7674996. 10.1016/j.oraloncology.2020.105110

Mccarthy CE, Bonnet LJ, Marcus MW, Field JK. Development and validation of a multivariable risk prediction model for head and neck cancer using the UK Biobank. Int J Oncol. 2020 Nov;57(5):1192-1202. doi: 10.3892/ijo.2020.5123. Epub 2020 Sep 22. PMID: 33491742. 10.3892/ijo.2020.5123

Dr Marisa Merino

Lecturer in Cancer Biology

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Molecular and Clinical Cancer Medicine

Research summary

I have always been passionate to understand how cells within tissues communicate to build up successful organisms. Indeed, my work shows for the first time that, Cell Competition is a physiological mechanism (Merino et al. 2013, Current Biology) which controls organismal lifespan (Merino et al. 2015, Cell & Merino et al. 2016, Trends in Cell Biology).

The difference between unfit and fit cells can be encoded by different levels of Dpp signalling. In the wing of flies and the pectoral fin of fish, the decay length (i.e. how far the morphogen reaches) of these morphogen gradients (Dpp and BMP) is proportional to the length of the growing tissue during development, namely they scale. Different levels of Dpp signaling are reminiscent of the steepness of the gradient that is-its decay length. In my recent work (Merino et al. 2022, Nature Cell Biology & Merino et al. 2022, Trends in Cell Biology). I have made a discovery of a novel phenomenon, Death-Mediated Scaling: the scaling of TGF-beta type growth factors (i.e. Dpp morphogen) is mediated also by Cell Death. On the other hand, disrupted TGF-beta signaling is one of the most common causes of tumorigenesis.

Death-mediated scaling machinery might provide a molecular toolbox exploited by cancer cells.

Selected publications

1M Merino, M., & Gonzalez-Gaitan, M. (2023). To fit or not to fit: death decisions from morphogen fields. Trends in cell biology, 33(2), 92-94. doi:10.1016/j.tcb.2022.09.00 10.1016/j.tcb.2022.09.003

Merino, M. M., Seum, C., Dubois, M., & Gonzalez-Gaitan, M. (2022). A role for Flower and cell death in controlling morphogen gradient scaling. Nature cell biology, 24(4), 424-433. 10.1038/s41556-022-00858-3

Merino, M. M., Rhiner, C., Lopez-Gay, J. M., Buechel, D., Hauert, B., & Moreno, E. (2015). Elimination of unfit cells maintains tissue health and prolongs lifespan. Cell, 160(3), 461-476. 10.1016/j.cell.2014.12.017

Professor Ainhoa Mielgo Iza

Molecular and Clinical Cancer Medicine

Professor in Cancer Biology

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www.mielgolab.org

Understanding how tumour-stroma interactions shape cancer progression, metastasis and response to therapies

Dr Ainhoa Mielgo is a cancer cell biologist who joined the University of Liverpool in 2013, funded by a career development award from the Wellcome Trust and the Royal Society.

Ainhoa performed her PhD at the University of Basel, Switzerland, followed by a post-doctoral training at the Moores Cancer Center, University of California San Diego.

Ainhoa's research team focuses on understanding the tumour-stroma interactions in cancer and how these affect cancer progression, metastasis, response to therapies and the immune response against cancer. To address these important questions, her laboratory uses a multi-disciplinary approach and a variety of cell-based assays, bioinformatics, omics technologies, pre-clinical tumour models and patient samples.

Ainhoa also has a keen interest in developing the next generation of cancer researchers and leads the MSc in Cancer Biology & Therapy course: Cancer Biology and Therapy MSc - Overview - Postgraduate Taught Courses - University of Liverpool

Selected publications

Lucy Ireland, Almudena Santos, Muhammad S. Ahmed, Carolyn Rainer, Sebastian R. Nielsen, Valeria Quaranta, Ulrike Weyer-Czernilofsky, Danielle D. Engle, Pedro Perez-Mancera, Sarah E. Coupland, Azzam Taktak, Thomas Bogenrieder, David A. Tuveson, Fiona Campbell, Michael C. Schmid, Ainhoa Mielgo. Chemoresistance in pancreatic cancer is driven by stroma-derived insulin-like growth factors. Cancer Research, 1;76(23):6851-6863 (2016). 10.1158/0008-5472.CAN-16-1201

Lucy Ireland, Almudena Santos, Fiona Campbell, Carlos Figueiredo, Lesley Ellies, Ulrike Weyer-Czernilofsky, Thomas Bogenrieder, Michael Schmid, Ainhoa Mielgo. Blockade of insulin-like growth factors increases efficacy of paclitaxel in metastatic breast cancer. Oncogene 37(15):2022-2036 (2018). 10.1038/s41388-017-0115-x

Lucy Ireland, Teifion Luckett, Michael C. Schmid, Ainhoa Mielgo. Blockade of stromal Gas6 alters cancer cell plasticity, activates NK cells and inhibits pancreatic cancer metastasis. Frontiers in Immunology, 11:297; doi: 10.3389/fimmu.2020.00297. eCollection 2020. 10.3389/fimmu.2020.00297

Dr Mark Morgan

Senior Lecturer / Research Team Leader

Chair ISMIB Equality, Diversity, Inclusion & Wellbeing

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Molecular and Clinical Cancer Medicine

Microenvironmental Sensation And Regulation In Cancer

The biochemical and mechanical properties of the tumour microenvironment drive cancer invasion and metastasis. The major goals of the Receptor Dynamic in Cancer Lab are to understand how tumour and stromal cells sense and interpret their extracellular microenvironment and how these mechanisms drive cancer progression and the response to targeted molecular therapeutics. We employ inter-disciplinary approaches incorporating proteomics, genomics, biophysical techniques and multi-modal live-cell imaging to dissect the impact of adhesion and growth factor receptor crosstalk mechanisms on cancer cell invasion, tumour-stromal interaction and drug resistance mechanisms.

The lab also has strong interests in how adhesion and growth factor receptor signalling networks and trafficking are dynamically integrated, spatially and temporally, to control mechanical force transmission, cell migration, wound healing and stem cell function and are dysregulated in fibrotic disease.

Selected publications

Maldonado H, Savage, BD, Barker HR, May U, Vähätupa M, Badiani RK, Wolanska, KI, Turner CMJ, Pemmari T, Ketomäki, T, Prince S, Humphries MJ, Ruoslahti E, Morgan MR* and Järvinen T* Systemically administered wound-homing peptide accelerates wound healing by modulating syndecan-4 function. Nature Communications, 14 (1). 8069 (2023) 10.1038/s41467-023-43848-1

Newman D, Young L, Waring T, Brown L, Wolanska KI, Macdonald E, Orszag AC, Caswell PT, Sakuma T, Yamamoto T, Machesky L, Morgan MR and Zech T 3D matrix adhesion feedback controls nuclear force coupling to drive invasive cell migration. Cell Reports, 42 (12): 113554 (2023) 10.1016/j.celrep.2023.113554

Maldonado H, Dreger M, Wolanska KI, Kyriakou T, Marotta V, Webster JM, Wang J, Rusilowicz-Jones EV, Marshall JF, Coulson JM, MacPherson IR, Hurlstone A, Morgan MR* A trafficking regulatory subnetwork governs αVβ6 Integrin-HER2 crosstalk to control breast cancer invasion and drug resistance. Research Square, 10.21203 rs-3318304 (2023) 10.21203/rs.3.rs-3318304/v2

Professor Christian Ottensmeier

Professor of Immuno-Oncology

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Molecular and Clinical Cancer Medicine

Research summary

Professor Ottensmeier joined the University of Liverpool and the Liverpool Head and Neck Centre as Professor of Immuno-Oncology in August 2020. His clinical commitments are to the Clatterbridge Cancer Centre NHS Foundation Trust, where his focus on early phase immuno-oncology (IO) studies to improve immunotherapy for patient benefit. His clinical practice is mainly works in head and neck cancer with early phase trials in this and other solid cancers; his group develop early phase IO trial and Christian has co-developed a number of national and international studies in head and neck and lung cancer.

Christian leads the Translational Immunology Group (TIG) together with Prof Natalia Savelyeva. His core academic interest reflects his clinical practice: to understand and to modulate adaptive immune responses in patients, to improve immunotherapies to treat solid cancers. His laboratory studies, which tumour-antigens are important for successful anti-tumour immune responses and how to overcome immune suppressive features of the tumour microenvironment. The laboratory focusses on three linked areas of investigation: the study of the tumour microenvironment and how this affects T cell responses at single cell resolution, the evaluation of antigen-specific immune responses in human tissue, and assay development and validation for use as endpoints in IO clinical trials. This work is underpinned by systematic tissue collection in lung cancer and head and neck cancer in collaboration with the head and neck surgical team at Liverpool University Hospitals NHS Foundation Trust and the thoracic surgical team in the Southampton University Hospitals and the Liverpool Heart and Chest Hospital; ~4000 patients have been recruited since 2014.

Selected publications

Eschweiler, S., Ramírez-Suástegui, C., Li, Y., King, E., Chudley, L., Thomas, J., Wood, O., von Witzleben, A., Jeffrey, D., McCann, K., Simon, H., Mondal, M., Wang, A., Dicker, M., Lopez-Guadamillas, E., Chou, T. F., Dobbs, N. A., Essame, L., Acton, G., Kelly, F., … Ottensmeier, C. H. (2022). Intermittent PI3Kδ inhibition sustains anti-tumour immunity and curbs irAEs. Nature, 605(7911), 741–746. https://doi.org/10.1038/s41586-022-04685-2

Ganesan, A. P., Clarke, J., Wood, O., Garrido-Martin, E. M., Chee, S. J., Mellows, T., Samaniego-Castruita, D., Singh, D., Seumois, G., Alzetani, A., Woo, E., Friedmann, P. S., King, E. V., Thomas, G. J., Sanchez-Elsner, T., Vijayanand, P., & Ottensmeier, C. H. (2017). Tissue-resident memory features are linked to the magnitude of cytotoxic T cell responses in human lung cancer. Nature immunology, 18(8), 940–950. https://doi.org/10.1038/ni.3775

McCann, K. J., Mander, A., Cazaly, A., Chudley, L., Stasakova, J., Thirdborough, S., King, A., Lloyd-Evans, P., Buxton, E., Edwards, C., Halford, S., Bateman, A., O'Callaghan, A., Clive, S., Anthoney, A., Jodrell, D. I., Weinschenk, T., Simon, P., Sahin, U., Thomas, G. J., … Ottensmeier, C. H. (2016). Targeting Carcinoembryonic Antigen with DNA Vaccination: On-Target Adverse Events Link with Immunologic and Clinical Outcomes. *Clinical cancer research : an official journal of the American Association for Cancer Research*, *22*(19), 4827–4836. https://doi.org/10.1158/1078-0432.CCR-15-2507

Professor Jo Patterson

Professor of Speech and Language Therapy

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Improving patient reported outcomes in head and neck cancer

Jo's work aims to optimise functional outcomes and quality of life in head and neck cancer, with strong collaborations regionally, nationally and internationally. Her research programme covers a range of topics, such as; holistic prehabilitation, enhanced recovery, psychosocial adjustment and support models, patient-directed consultations, patient-reported outcome measure development, functional assessments and novel swallowing intervention development. She works in close collaboration with the Liverpool Patient Forum, who provide a strong PPI foundation from research development to dissemination. In addition, Jo is highly committed to increasing research capability and capacity for Nurses, Midwives and Allied Healthcare Professionals, and expediting the translation of evidenced-based care into clinical practice.

Selected publications

Patterson JM, Lu L, Watson LJ, Harding S, Sharp L. Associations between markers of social functioning and depression and quality of life in survivors of head and neck cancer: findings from the Head and Neck Cancer 5000 study Psycho-oncology 10.1002/pon.5830

Stephen S, Murphy J, Goff, Paleri V, Patterson JM Early post-operative functional outcomes following minimally invasive surgery for oropharyngeal cancer: A systematic review Head and Neck 2022 10.1002/hed.26938

Starmer H, Drinnan M, Bhabra M, Watson LJ, Patterson JM. Development and testing of the Revised Patterson Edema Scale Clinical Otolaryngology 2021;00:1–6 10.1111/coa.13727

Dr Pedro Perez-Mancera

Research group leader

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Molecular and Clinical Cancer Medicine

Understanding the molecular pathogenesis of pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) is a virtually incurable disease, with a five-year survival rate of just ~10%. Activating mutations in KRAS are considered the earliest event in PDAC development, and induce the formation of preinvasive lesion, called pancreatic intraepithelial neoplasms (PanINs) that progress to invasive PDAC after the accumulation of additional genetic alterations, frequently involving inactivation of CDKN2A, TP53 and SMAD4. However, none of these mutations can be targeted therapeutically, and a better understanding of the molecular basis underlying the aggressive biology of PDAC is crucial for developing novel therapeutic strategies to improve overall prognosis.

Our laboratory combines mouse models of pancreatic cancer and mouse pancreatic (preneoplastic and neoplastic) organoids, with molecular biology techniques and omics approaches, to identify genes and molecular pathways that cooperate with oncogenic KRAS during pancreatic cancer progression and development. The lab maintains strong collaborations with clinicians to generate and make use of pancreatic patient-derived organoids for therapeutic studies. Our long-term goal is to identify drivers of pancreatic cancer progression and to use this knowledge to identify new options for therapeutic interventions to fight pancreatic cancer.

Selected publications

Gupta P et al., Chemotherapy Assessment in Advanced Multicellular 3D Models of Pancreatic Cancer: Unravelling the Importance of Spatiotemporal Mimicry of the Tumor Microenvironment. Adv Biol (Weinh). 2024 Feb 7:e2300580. 10.1002/adbi.202300580

Barrera LN et al., The role of microRNAs in the modulation of cancer-associated fibroblasts activity during pancreatic cancer pathogenesis. J Physiol Biochem. 2023 Feb;79(1):193-204. 10.1007/s13105-022-00899-0

Humpton TJ et al., Oncogenic Kras induces Nix-mediated mitophagy to promote pancreatic cancer. Cancer Discov. 2019 Jul 1. pii: CD-18-1409. 10.1158/2159-8290.CD-18-1409

Pérez-Mancera PA et al., The deubiquitinase USP9X suppresses pancreatic ductal adenocarcinoma. Nature. 2012 Apr 29;486(7402):266-70. 10.1038/nature11114

Professor Andrew Pettitt

Ronald Finn Professor of Experimental Medicine

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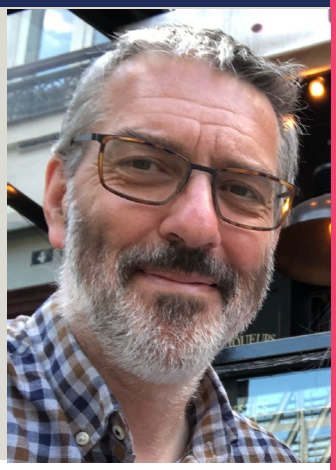

Molecular and Clinical Cancer Medicine

Clinical, laboratory and health data research in CLL and lymphoma

My research is focused on treatment optimisation in chronic lymphocytic leukaemia (CLL) and follicular lymphoma (FL) and includes clinical research, correlative science, and health data research. Funders include Cancer Research UK, Blood Cancer UK, MRC, NIHR and industry.

Clinical research. This research has two components: (1) recruiting patients into clinical studies and (2) leadership of national clinical trials evaluating different treatment approaches in CLL and FL. The latter studies, all of which are co-ordinated by the Liverpool Clinical Trials Centre and yet to be reported, include RIAltO (closed; n=521), PACIFICO (closed; n=369) and PETReA (open; n>500).

Correlative science. My laboratory research initially focussed on p53 dysfunction in CLL and led to the first clinical trial to intentionally circumvent the p53 pathway in patients with TP53 inactivation. More recently, I've focussed on unravelling the molecular basis of CLL heterogeneity and variable therapy response through the application of mass spectrometry and mass cytometry to clinical trial samples. To drive and enable this and other research, I established the UK CLL Biobank (n>2400) which functions as a central biorepository for multiple national CLL trials, as well as sample collections linked to national clinical trials and observational studies

Health data research. I am co-leading a two-part programme called "Understanding the impact of SARS-CoV-2 infection in patients with blood cancer (UnCoVer)". Part 1 aims to elucidate COVID-19 outcomes in patients with blood cancer during the different phases of the pandemic and identify risk factors for adverse outcomes, whereas part 2 aims to understand blood cancer pathways, treatments and outcomes and how they changed during the COVID-19 pandemic. Ten England-wide NHS cancer datasets, comprising ~400 variables across ~25 million healthcare episodes from all blood cancer patients diagnosed or treated in England since 2014, were transferred to Liverpool and have been merged and cleaned in preparation for analysis.

Selected publications

Pettitt AR, Jackson R, Carruthers S, et al. Alemtuzumab in combination with methylprednisolone is a highly effective induction regimen for patients with chronic lymphocytic leukemia and deletion of TP53: final results of the national cancer research institute CLL206 trial. J Clin Oncol. 2012;30(14):1647-1655. 10.1200/JCO.2011.35.9695

Hillmen P, Rawstron AC, Brock K, et al. Ibrutinib Plus Venetoclax in Relapsed/Refractory Chronic Lymphocytic Leukemia: The CLARITY Study [published correction appears in J Clin Oncol. 2020 May 10;38(14):1644]. *J Clin Oncol*. 2019;37(30):2722-2729. 10.1200/JCO.19.00894

Robbe P, Ridout KE, Vavoulis DV, et al. Whole-genome sequencing of chronic lymphocytic leukemia identifies subgroups with distinct biological and clinical features. *Nat Genet*. 2022;54(11):1675-1689. 10.1038/s41588-022-01211-y

Professor Harish Poptani

Chair of the Centre for Preclinical Imaging (CPI)

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View staff profile

Molecular and Clinical Cancer Medicine

Developing non-invasive imaging markers for assessing early treatment response in cancer

Professor Poptani is the Chair of the Centre for Preclinical Imaging (CPI) with a research focus on developing cutting-edge non-invasive imaging biomarkers for assessing early treatment response in cancer. His work is highly translational in nature and his group has been credited with identifying several markers for diagnosis or early treatment response which are currently used in the clinic. He completed his PhD in 1995 India, and after couple postdoc positions, he was appointed as an Assistant Professor in 2001 and Associate Professor in 2006 at the University of Pennsylvania, USA. He joined the University of Liverpool in December 2014. He has published 150 peer reviewed papers, and several book chapters and review articles. In 2021, he was awarded the Senior Fellowship from the International society of Magnetic Resonance in Medicine (ISMRM) for his significant contributions to the field. He currently serves as the Chair of the British and Irish chapter of ISMRM. His research has been funded by various grants including funding from the UKRI as well as UK based charities such as the Wellcome trust and the North West Cancer Research. As the module organiser of LIFE724 – MSc in frontiers of cancer research and treatment, he is heavily involved in both the undergraduate and postgraduate teaching at the University and he has successfully supervised four PhD students since 2015. As the academic lead of the CPI, which is a shared resource facility within the University, Professor Poptani has been developing cutting-edge multi-modal preclinical imaging methods for the benefit of students and staff interested in the use of imaging towards achieving their academic and research goals.

Selected publications

JM Hakumaki, H Poptani, A-M Sandmair, S Yla-Herttuala, RA Kauppinen. 1H MRS detects polyunsaturated fatty acid accumulation during gene therapy of glioma: implications for the in vivo detection of apoptosis. Nature Medicine 5:1323-1327,1999. 10.1038/15279

S Kim, LA Loevner, H Quon, E Sherman, G Weinstein, A Kilger, H Poptani. Diffusion-weighted magnetic resonance imaging for predicting and detecting early response to chemoradiation therapy of squamous cell carcinomas of the head and neck. Clinical Cancer Research 15:986-994, 2009. 10.1158/1078-0432.CCR-08-1287

Bhaduri S, Lesbats C, Sharkey J, Kelly CL, Mukherjee S, Taylor A, Delikatny EJ, Kim SG, Poptani H*. Assessing tumour heamodynamic heterogeneity and response to choline kinase inhibition using clustered dynamic contrast enhanced MRI parameters in rodent models of glioblastoma. Cancers (Basel). 14(5):1223, 2022. 10.3390/cancers14051223

Professor Ian Prior

North West Cancer Research Chair in Molecular Oncology

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Molecular and Clinical Cancer Medicine

Research summary

Professor Prior's research focuses on Ras biology. Ras is one of the most frequently mutated genes in cancer. He is interested in why different versions of Ras have different cancer-causing properties and how the communication networks that Ras controls are wired in different cell and tissue contexts.

The ultimate goal of his research is to inform models of cancer cell signalling networks that will allow better directed development and use of anti-cancer drugs targeting members of the Ras network.

He also directs an electron microscopy core facility that has led to a wide range of collaborations across the biomedical, chemistry and nanotechnology spectrum.

He is Director of LIV-SRF, the university oversight structure for 24 core facilities and led the introduction of a new career pathway for specialist technical staff working across the University.

Selected publications

Hood FE, Sahraoui YM, Jenkins, RE and Prior IA. (2023) Ras protein abundance correlates with Ras isoform mutation patterns in cancer. Oncogene 42:1224-1232. 10.1038/s41388-023-02638-1

Warren HR, Ross, SJ, Smith PD, Coulson JM and Prior IA. Combinatorial approaches for mitigating resistance to KRAS-targeted therapies. Biochemical Journal (2022) 479:1985-1997. 10.1042/BCJ20220440

Menzies GE, Prior IA, Brancale A, Reed S and Lewis PD. (2021) Carcinogen-induced DNA-structural distortion differences in the RAS gene isoform; the importance of local sequence. BMC Chemistry 15:51. 10.1186/s13065-021-00777-8

Prior IA, Hood FE, Hartley JL. The frequency of Ras mutations in cancer. (2020) Cancer Research 80:2969-74. 10.1158/0008-5472.CAN-19-3682

Professor D. Mark Pritchard

Professor of Gastroenterology

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Research summary

Prof Pritchard studied Medicine at Manchester University (BSc (1st class) in Medical Biochemistry, 1988, MB.ChB (Hons), 1991). After junior hospital posts (MRCP(UK) 1994), he returned to the University of Manchester to train in gastroenterology and to complete a PhD on the genetic regulation of apoptosis in the GI tract (Digestive Disorders Foundation and MRC Clinical Training Fellowships).

In 2000, he moved to the University of Liverpool as a clinical lecturer and in 2002 he was awarded an Advanced Clinical Fellowship for Clinicians from the Wellcome Trust to study apoptosis in the stomach. He was appointed Clinical Senior Lecturer in 2006, Professor in 2009 and Head of Department of Gastroenterology in 2010. He was awarded the ASNEMGE rising star award 2007 and the Sir Francis Avery Jones research medal from the British Society of Gastroenterology in 2008. He was Head of the Department of Cellular and Molecular Physiology 2016-20.

His current research focuses upon host factors which influence the development of gastrointestinal cancers and neuroendocrine tumours, in particular the importance of apoptosis, NF-κB signalling and the gastrin family of peptides.

Prof Pritchard is also an honorary Consultant Gastroenterologist at Liverpool University Hospitals NHS Foundation Trust where he leads the European Neuroendocrine Tumour Society (ENETS) Centre of Excellence for the management of patients with neuroendocrine tumours. He is also the current Chair of UKINETS (UK and Ireland Neuroendocrine Tumour Society).

Selected publications

Parsons, B.N., Ijaz, U.M., D'Amore, R., Burkitt, M.D., Eccles, R., Lenzi, L., Duckworth, C.A., Moore, A.R., Tiszlavicz, L., Varro, A., Hall, N. and Pritchard, D.M. (2017) Comparison of the human gastric microbiota in hypochlorhydric states arising as a result of Helicobacter pylori-induced atrophic gastritis, autoimmune atrophic gastritis and proton pump inhibitor use. PLOS Pathogens 13:e1006653 10.1371/journal.ppat.1006653

Lloyd, K.A., Parsons, B.N., Burkitt, M.D., Moore, A.R., Papoutsopoulou, S., Boyce, M., Duckworth, C.A., Exarchou, K., Howes, N., Rainbow, L., Fang, Y., Oxvig, C., Dodd, S., Varro, A., Hall, N., Pritchard, D.M. (2020) Netazepide Inhibits Expression of Pappalysin 2 in Type 1 Gastric Neuroendocrine Tumors. Cell Mol Gastroenterol Hepatol. pii:S2352-345X(20): 30017-5. 10.1016/j.jcmgh.2020.01.010

Khan, MS and Pritchard, D.M. (2020) Neuroendocrine Tumours – What Gastroenterologists need to know. Frontline Gastroenterology flgastro-2020-101431. 10.1136/flgastro-2020-101431

Professor Chris Probert

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Molecular and Clinical Cancer Medicine

The volatile metabolome and microbiome in gastrointestinal and urological disease

In my 30+ year research career, I have studied gastrointestinal diseases using a range of techniques. Initially, I studied epidemiology (describing the unexpectedly high incidence of inflammatory bowel disease (IBD) in South Asians migrants to the UK) in Leicester, then mucosal immunology (reporting personal and shared mucosal T cell receptor motifs in IBD) in Harvard, and then returned to UK. In Bristol, I continued on both these areas for a while and led several clinical trials in IBD. I subsequently embarked on ground-breaking research on the faecal volatile metabolome.

Volatile metabolomic studies in IBD and irritable bowel syndrome (IBS) have discovered unique biochemical signatures denoting these diseases. We have published several papers illustrating the changes in adults and children, in UK and overseas. Recently, we have undertaken microbiome studies and explored the links between the microbiome (who is the intestinal microbiome community), and the metabolome (which tells us what they are doing). Novel data is helping us to biochemically-define patients with IBS for the first time, and predict which patients will best respond to dietary treatments (see below).

Currently, we are completing similar studies in patients in colorectal and urological cancers.

Selected publications

1Raman M, Ahmed I, Gillevet PM, Probert CS, Ratcliffe NM, Smith S, Greenwood R, Sikaroodi M, Lam V, Crotty P, Bailey J, Myers RP, Rioux KP. Fecal microbiome and volatile organic compound metabolome in obese humans with nonalcoholic fatty liver disease. Clinical Gastroenterology and Hepatology 2013;11:868-75 ***Highly cited** https://doi.org/10.1016/j.cgh.2013.02.015

Brooklyn TN, Dunnill MGS, Shetty A, Bowden JJ, Williams JDL, Griffiths CEM, Forbes A, Greenwood R, Probert CS. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double-blind placebo-controlled trial. Gut 2006;55:505-509 10.1136/gut.2005.074815

Garner CE, Smith S, de Lacy Costello B, White P, Spencer R, Probert CSJ, Ratcliffe NM. Volatile organic compounds from feces and their potential for diagnosis of gastrointestinal disease. FASEBJ 2007;21:1675-1688 https://doi.org/10.1096/fj.06-6927com

Dr Joseph Sacco

Reader

Honorary Consultant in Medical Oncology

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Read staff profile

Molecular and Clinical Cancer Medicine

Research summary

Joe Sacco is a clinical academic with research interests spanning basic, translational and clinical domains. His main clinical speciality is in melanoma, with a subspecialist focus on uveal melanoma (UM); a rare cancer which frequently metastasises and for which there remain few treatment options.

Joe has led or contributed to a broad portfolio of clinical trials, including key trials in clinical development of tebentafusp, as well as the FOCUS clinical trial investigating percutaneous perfusion with melphalan; the only two therapeutic options to be licenced for metastatic uveal melanoma. He is UK lead for the OMNI study, an international natural history study of uveal melanoma as well as UK lead for the UM international rare cancer initiative.

His basic science interests include BAP1 signalling and targeting, and the development of a model of the tumour microenvironment of UM metastatic to the liver.

Selected publications

Barnett SE, Kenyani J, Tripari M, Butt Z, Grosman R, Querques F, et al. BAP1 loss is associated with higher ASS1 expression in epithelioid mesothelioma: implications for therapeutic stratification. Mol Cancer Res. 2023 10.1158/1541-7786.MCR-22-0635

Carvajal RD, Sacco JJ, Jager MJ, Eschelman DJ, Olofsson Bagge R, Harbour JW, et al. Advances in the clinical management of uveal melanoma. Nat Rev Clin Oncol. 2023;20(2):99-115. 10.1038/s41571-022-00714-1

Barnett SE, Herrmann A, Shaw L, Gash EN, Poptani H, Sacco JJ, et al. The Chick Embryo Xenograft Model for Malignant Pleural Mesothelioma: A Cost and Time Efficient 3Rs Model for Drug Target Evaluation. Cancers (Basel). 2022;14(23). 10.3390/cancers14235836

Professor Natalia Savelyeva

Professor

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View staff profile

Molecular and Clinical Cancer Medicine

Developing novel vaccines for cancer

Professor Savelyeva has focused on the development of novel immunotherapeutic interventions for head and neck cancer and lung cancer. She has developed several immunotherapeutic approaches including a number of cancer vaccine platforms. Her long-standing interest is in DNA vaccines. Having worked on several plasmid DNA vaccines, her current interest lies in unconventional non-plasmid-based DNA vaccine platforms. Currently her research group is actively pursuing optimisation of doggybone DNA vaccines to bring these novel, safe and efficacious candidate vaccines to the clinic.

Novel vaccines: Our novel vaccine candidate TGL-100 has been developed in collaboration with Cancer Research Malaysia and with our industrial partner Touchlight Genetics to utilise doggybone DNA technology. TGL-100 is targeting two novel antigens frequently expressed in a number of solid cancers including head and neck and lung cancers.

Cancer antigens: We are interested in targeting both, antigens which are shared between patients and antigens which are expressed in individual patient cancers but not elsewhere in the body. TGL100 vaccine targets shared antigens. The personalised approach deals with the identification of mutations expressed by patients' tumours, the "cancer mutanome" and we have focused on the developing of a robust pipeline for the identification of targetable epitopes. Our Neovacc trial will target individual patient's mutanomes and will also use the doggybone DNA platform to deliver antigen epitopes to patients with lung cancer.

Combinational approaches to cancer treatment: 50% of head and neck cancer cases contain cancer associated myofibroblast (CAFs) which impede the ability of cytotoxic T cells to attack cancer. Nox4 enzyme is critical for promoting and maintaining the myoCAF phenotype. Together with Prof Gareth Thomas's group at the University of Southampton, we recently showed that inhibition of this enzyme in fibrotic cancers helps cytotoxic T cells induced by vaccines migrate into cancer to mediate anti-cancer attack. One of the approaches which is being explored is targeting of myoCAFs with vaccines, once antigens expressed by myoCAFs have been fully characterised. We also continue to explore, further, how approaches to combine vaccination with CAF targeting can be harnessed to improve treatments for head and neck cancer and other fibrotic cancers.

Selected publications

Ford K, C.J. Hanley, M. Mellone, C. Szyndralewiez, P. Wiesel, Pa. Vijayanand, A-P. Ganesan, T. Fenton, A. Chakravarthy, O. Wood, M. Machado, M. Lopez, C. Wang, E. V. King, C.H. Ottensmeier, A. Al-Shamkhani, N. Savelyeva, G. J. Thomas (2020) Targeting cancer-associated fibroblasts through NOX4 inhibition overcomes immune exclusion and potentiates immunotherapy. Cancer Research Mar 2. 10.1158/0008-5472.CAN-19-3158

Savelyeva N., King CA., Vitetta E., & Stevenson FK. (2005) Inhibition of a vaccine-induced anti-tumor B-cell response by soluble protein antigen in the absence of continuing T cell help. PNAS USA, 102(31):10987-92. 10.1073/pnas.0505108102

Savelyeva N., Munday R., Spellerberg MB., Lomonossoff GP. & Stevenson FK. (2001). Plant viral genes in DNA idiotypic vaccines activate linked CD4+ T-cell mediated immunity against B-cell malignancies. Nat Biotechnol. 19(8), 760-4. 10.1038/90816

Professor Andrew Schache

Professor in Head and Neck Surgery

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Molecular and Clinical Cancer Medicine

Head & Neck Cancer – novel technologies and therapies

I am a clinical-academic Head & Neck Surgeon from an Oral & Maxillofacial Surgery background, providing cancer and reconstructive surgical care to Head & Neck patients.

Within my clinical role is as Consultant Head & Neck Surgeon at Aintree Hospital, I cover the breadth of Oral & Maxillofacial oncology surgery and reconstruction. I have a particular interest in virtual surgical planning technologies for complex custom composite reconstructions.

Offering all patients the opportunity and choice to be involved in clinical research/clinical trials is an ambition that I share with many of the Head & Neck team. LHNC has unique strengths in delivery of the national portfolio of clinical trials to our patients, with the aim to improve outcomes.

As a member of the Merseyside Head & Neck Oncology Research Group (MHNORG) I pursue both academic and surgical research interests, integrating "bench to bedside" research ambitions.

My research interests cover novel technologies and therapies, and ultimately how they can be incorporated into routine clinical care to achieve improvements in outcomes and provide tangible patient benefit. This includes translational research projects exploiting the rich bioresource generated via both clinical trials and research cohorts.

Within my academic role, I supervise several doctoral (PhD/D) students (both from clinical and basic science backgrounds) and I am departmental director for post-graduate research (DDPR) within cancer medicine.

Selected publications

Schache, A. G., Powell, N. G., Cuschieri, K. S., Robinson, M., Leary, S., Mehanna, H., Rapozo, D., Long, A., Cubie, H., Junor, E., Monaghan, H., Harrington, K. J., Nutting, C. M., Schick, U., Lau, A. S., Upile, N., Sheard, J., Brougham, K., West, C. M., Oguejiofor, K., … Jones, T. M. (2016). HPV-Related Oropharynx Cancer in the United Kingdom: An Evolution in the Understanding of Disease Etiology. Cancer research, 76(22), 6598–6606. https://doi.org/10.1158/0008-5472.CAN-16-0633

COVIDSurg Collaborative (2021). Head and neck cancer surgery during the COVID-19 pandemic: An international, multicenter, observational cohort study. Cancer, 127(14), 2476–2488. https://doi.org/10.1002/cncr.33320

Schache, A. G., Liloglou, T., Risk, J. M., Jones, T. M., Ma, X. J., Wang, H., Bui, S., Luo, Y., Sloan, P., Shaw, R. J., & Robinson, M. (2013). Validation of a novel diagnostic standard in HPV-positive oropharyngeal squamous cell carcinoma. British journal of cancer, 108(6), 1332–1339. https://doi.org/10.1038/bjc.2013.63

Dr Marco Sciacovelli

Tenure Track Fellow

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Molecular and Clinical Cancer Medicine

Investigating the role of metabolism and metabolites in cancer

Alterations of metabolism are a hallmark of cancer. It has been shown that tumours display a deep metabolic reprogramming, often orchestrated by activation of oncogenic signalling, that sustains the biosynthetic needs of cancer cells and their aberrant proliferation. Some of these alterations are shared by different tumour types while others are distinctive of specific tumours or are associated with a step of tumour progression. In our laboratory, we are interested in identifying the key metabolic pathways reprogrammed at different stages of tumour progression, how they are orchestrated, their impact on the malignant features of cancer cells, and uncover the role of metabolites as signalling molecules in cancer.

Selected publications

Sciacovelli, M., Dugourd, A., Jimenez, L.V. et al. Dynamic partitioning of branched-chain amino acids-derived nitrogen supports renal cancer progression. Nat Commun 13, 7830 (2022). https://doi.org/10.1038/s41467-022-35036-4

Sciacovelli, M., Gonçalves, E., Johnson, T. et al. Fumarate is an epigenetic modifier that elicits epithelial-to-mesenchymal transition. Nature 537, 544–547 (2016). https://doi.org/10.1038/nature19353

Sciacovelli, M., Guzzo, G., Morello, V. et al. The Mitochondrial Chaperone TRAP1 Promotes Neoplastic Growth by Inhibiting Succinate Dehydrogenase. Cell Metabolism, Volume 17, Issue 6, Pages 988-999 (2013). https://doi.org/10.1016/j.cmet.2013.04.019

Professor Richard Shaw

Professor of Head and Neck Surgery

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Research summary

Management of Oral Premalignant Lesions (OPMLs). I have authored national guidelines in clinical management of OPMLS. I lead the UK's first chemoprevention trial (SAVER, NIHR EME £1.2m 2019-2023), exploring the role of epigenetic reprogramming of high-risk lesions using HDACi. Most excitingly, I now collaborate with the newly appointed HN immuno-oncology team (Ottensmieir / Savalyeva) in order to develop novel early-phase mutanome vaccines for OPMLs.

Management of Late Radiation Toxicity, Osteoradionecrosis (ORN). I have led research exploring the genomic determinants of osteoradionecrosis (IJROBP papers, and current SNiP array study) but these studies are founded on tissue arising from my clinical trials. Firstly, HOPON RCT (CRUK £400k 2010-2015) explored the benefit of hyperbaric oxygen in prevention of ORN. Secondly an international collaboration (DAHANCA-21 RCT, CRUK £40k 2011-2016) explored the benefit of HBO in treatment of ORN. These trials established a new clinical standard of care, avoiding many millions of unnecessary NHS expense every year. More recently, I led the newly funded multicentre RCT (RAPTOR NIHR £1.1m 2021-24) looking at the role of repurposed drugs ("PENTOCLO") in resolution of ORN as well as NIHR RFPB PIT-STOP as a co-investigator.

COVID-19 and Surgery/ Head & Neck Cancer. I lead the COVIDSurg head and neck international cohort, which has so far recruited 5000 HN cancer patients since March 2020.. This surgical collaborative offers an entirely novel collaborative approach to recruitment and authorship in research, fuelled by the challenges presented by SARS-CoV-2.

Surgical Trials. I have held national roles such as chair of National Cancer Research Institute HN trials groups, chair of Royal College of Surgeons of England 'Future of Surgery Initiative' and have been the NIHR (National Institute for Health Research) National Specialty advisor for Surgical Oncology Trials since 2014. In this role I have developed a number of new initiatives to train the next generation of surgical trialists and to champion excellence in this field.

Liverpool Head & Neck Centre (LHNC) For the last 20 years, I have supported the development of a multidisciplinary head and neck cancer group in Liverpool. This has led to the formation of LHNC in 2018 which has specific strategies in translational research, education, clinical quality and patient involvement. I supported my longstanding ENT academic colleague Terry Jones as Director of LHNC, and I am research lead (chair of MHNORG) for the centre. The clinical academic appointments so far include ENT & OMFS, Medical Oncology, HN Pathology, Speech & Language therapy and we also have ambitions for HN Palliative Care and in Clinical Oncology

Selected publications

HOPON (Hyperbaric Oxygen for the Prevention of Osteoradionecrosis): A Randomized Controlled Trial of Hyperbaric Oxygen to Prevent Osteoradionecrosis of the Irradiated Mandible After Dentoalveolar Surgery. Shaw RJ, Butterworth CJ, Silcocks P, et al Int J Radiat Oncol Biol Phys. 2019 Jul 1;104(3):530-539. 10.1016/j.ijrobp.2019.02.044

Head and neck cancer surgery during the COVID-19 pandemic: an international, multicentre, observational cohort study. COVIDSurg Collaborative. Cancer; 2020 10.1002/cncr.33320

Brown J S, Shaw R J. Reconstruction of the maxilla and midface. Lancet Oncology. 2010 Oct;11(10):1001-8 10.1016/S1470-2045(10)70113-3

Professor Joseph Slupsky

Professor of Lymphocyte Biology

Academic Lead – Cell Sorting and Mass Cytometry SRF

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Research summary

Professor Slupsky's research is focussed on the biology of chronic lymphocytic leukaemia (CLL), an incurable common form of adult leukaemia. He is working to understand the mechanisms involved in malignant cell resistance to therapy in this disease. In this respect, deletion of the short arm of chromosome 17 (del17p) is a common aneuploidy in cancer and is associated with poor prognosis and resistance to therapy in CLL and other cancers. Prof Slupsky's lab is using CRISPR/Cas9 to build isogenic models with which to study the impact of del17p on the behaviour of the malignant cells in CLL and other lymphoid neoplasms. Professor Slupsky's lab is also developing mass cytometry, which is a high dimensional flow cytometry and imaging tool, to phenotypically characterise CLL cells at high resolution.

Selected publications

Duckworth AD, Gherardini PF, Sykorova M, Yasin F, Nolan GP, Slupsky JR, Kalakonda N. Multiplexed profiling of RNA and protein expression signatures in individual cells using flow or mass cytometry. Nat Protoc. 2019 Mar;14(3):901-920. PMID: 30728478. 10.1038/s41596-018-0120-8

Linley AJ, Karydis LI, Mondru AK, D'Avola A, Al Shmrany H, Cicconi S, Griffin R, Forconi F, Pettitt AR, Kalakonda N, Rawstron AC, Hillmen P, Steele AJ, MacEwan DJ, Packham G, Prior IA, Slupsky JR. Kinobead profiling reveals reprogramming of BCR signaling in response to therapy within primary CLL cells. Clin. Cancer Res. 2021 Oct 15;27(20):5647-5659. PMID: 34380642. 10.1158/1078-0432.CCR-21-0161

Talab F, Allen JC, Thompson V, Lin K, Slupsky JR. LCK is an important mediator of B cell receptor signalling in chronic lymphocytic leukaemia. Mol Cancer Res. 2013 11(May):541-554. PMID: 23505068. 10.1158/1541-7786.MCR-12-0415-T

Professor Alexei Tepikin

Professor of Physiology

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Molecular and Clinical Cancer Medicine

Ca2+ signalling, bioenergetics and physiology / pathophysiology of exocrine pancreas

Fundamental mechanisms of Ca2+ signalling (particularly store-operated Ca2+ influx). Interacting signalling cascades (Ca2+, reactive oxygen species and cAMP). Downstream effects of Ca2+ signalling cascade (including changes in bioenergetics, exocytosis and endocytosis). Ca2+ toxicity, mitochondrial damage, aberrant endocytosis, non-canonical autophagy and the initiation of acute pancreatitis.

Invited speaker and/or invited session chair at prestigious international meetings including Gordon Research Conferences (Ca2+ signalling), FASEB meetings (Ca2+ signalling) and the meetings of the European Pancreatic Club.

Primary collaborators are Dr David Criddle, Professor Robert Sutton and Professor Ian Prior.

Selected publications

De Faveri F, Chvanov M, Voronina S, Moore D, Pollock L, Haynes L, Awais M, Beckett AJ, Mayer U, Sutton R, Criddle DN, Prior IA, Wileman T, Tepikin AV. LAP-like non-canonical autophagy and evolution of endocytic vacuoles in pancreatic acinar cells. Autophagy 2020, 16 (7), 1314-1331. doi: 10.1080/15548627.2019.1679514 . PMID: 31651224.

Sherwood MW, Prior IA, Voronina SG, Barrow SL, Woodsmith JD, Gerasimenko OV, Petersen OH and Tepikin AV. Activation of trypsinogen in large endocytic vacuoles of pancreatic acinar cells. PNAS 2007, 27, 5674-5679. 10.1073/pnas.0700951104

Park M, Ashby MC, Erdemili G, Petersen O.H, Tepikin A.V. (2001) Perinuclear, perigranular and sub-plasmalemmal mitochondria have distinct functions in the regulation of cellular calcium transport. EMBO J. Apr 17;20(8):1863-74. 10.1093/emboj/20.8.1863

Mr Dale Vimalachandran

Reader in Colorectal Surgery

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Molecular and Clinical Cancer Medicine

Research summary

Dale Vimalachandran has a broad range of interests in the management of colorectal cancer and leads a research group that explores all aspects of the disease from screening, through to surgical and medical treatment and palliation. He has supervised a number of translational scientific projects that have examined the response of rectal cancer to radiotherapy and liver metastases to chemotherapy. More recently he has also collaborated with other scientific groups to understand the fundamental mechanisms contributing to tumour hypoxia and the use of metabolomics to assess response to treatment.

He also has an interest in clinical trials and has been the chief investigator on a number of national and international multicentre studies of both benign and malignant colorectal diseases. He is the RCS/ACPGBI national specialty lead for colorectal cancer and the NIHR national specialty lead for cancer surgery. He also established and runs the Northwest colorectal clinical academic research programme. He has also helped established and runs a pan-regional tissue collection programme to support pilot/feasibility translational cancer research studies.

Selected publications

Sekhar H, Dyer M, Khan M, Mitchell PJ, West NP, Moug S, Vimalachandran D; SF-CORNER collaborative study group. SF-CORNER (splenic flexure colorectal cancer): an international survey of operative approaches and outcomes for cancers of the splenic flexure. Colorectal Dis. 2024 Feb 12 10.1111/codi.16895

Jones RP, Mielgo A, Schmid M, Bury D, Andrews T, Burdak-Rothkamm S, Shackcloth M, J S Cross T, Fenwick S, Malik HZ, Diaz-Nieto R, Ottensmeier C, Palmer DH, Vimalachandran D. PINCER (A Platform Study for solId orgaN CancERs): an agile pan-network platform study to deliver high-quality translational research. Br J Surg. 2023 Aug 11;110(9):1108-1111. 10.1093/bjs/znad097

Vimalachandran D, Jones RP, Dickson E, Seehra J, Acheson A, Griffiths EA, Kamarajah S, Leung E, Torrance A, Ottensmeier C, Beggs AD, Whiteside E, Sanna H, Bury D, Youd E, Leopold G, Pugh M, Sundar S, Taylor GS. SARS-CoV-2 in the abdomen or pelvis: SAFE SURGERY study. Br J Surg. 2023 Feb 15;110(3):306-309. 10.1093/bjs/znac297

Dr Lorna Young

Lecturer

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Molecular and Clinical Cancer Medicine

Investigating the role of the cytoskeleton during cancer cell progression

My research focusses on the role of the cytoskeleton in cancer cell progression. I am particularly interested in how the cell "read" the extracellular environment and how this impacts the functions of the cell. My work is focussed on cell migration, invasion and metabolic reprogramming during cancer.

Awards

26/04/2019: Flash talk prize, NWCR Annual Symposium, Liverpool, UK

01/10/2018: DPCDA Professional Development Award, Dartmouth College

2016: MBoC paper of the year, "Cell type-dependent mechanisms for formin-mediated assembly of filopodia."

06/09/2015: Dartmouth E. Lucile Smith Award for Excellence in Biochemistry, Dartmouth College

Selected publications

Young, L.E, D Newman, T Waring, L Brown, K Wolanska, M Collins, E MacDonald, A Charles-Orszag, P Caswell, T Sakuma, T Yamamoto, L Machesky, M Morgan, T Zech (13/12/2024). 3D matrix adhesion composition facilitates nuclear force coupling to drive invasive cell migration. Cell Reports 10.1016/j.celrep.2023.113554

Young, L.E. & Higgs, H. N. (01/11/2018). Role for ENA/VASP proteins in FMNL3-mediated filopodia assembly. Journal of Cell Science. 10.1242/jcs.220814

Young, L.E. & Higgs, H. N. (08/07/2018). Focal adhesions are composed of discrete units of uniform width that can undergo longitudinal splitting, Current Biology. 10.1016/j.cub.2018.04.073

Mr Rasheed Zakaria

Senior Clinical Lecturer, Neurosurgery

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Molecular and Clinical Cancer Medicine

Translational brain tumour researcher and neurosurgeon

I am a translational brain tumour researcher, working jointly at the University of Liverpool and the Walton Centre NHS Foundation Trust where I am also employed as an Honorary Consultant Neurosurgeon. I see and operate on patients with brain tumours, conduct clinical research in the NHS and lead a preclinical research programme at the university.

I am interested in the mechanisms by which primary and secondary tumours invade brain tissue and the imaging and tissue biomarkers of this process. A better understanding of these mechanisms will improve our local control of brain tumours, extend survival and improve quality of life for patients.

Selected publications

Genomic Alterations and the Incidence of Brain Metastases in Advanced and Metastatic NSCLC: A Systematic Review and Meta-Analysis. Gillespie CS, Mustafa MA, Richardson GE, Alam AM, Lee KS, Hughes DM, Escriu C, Zakaria R. J Thorac Oncol. 2023 Jun 29:S1556-0864(23)00638-X 10.1016/j.jtho.2023.06.017

Immune checkpoint inhibitor treatment of brain metastasis associated with a less invasive growth pattern, higher T-cell infiltration and raised tumor ADC on diffusion weighted MRI. Zakaria R, Jenkinson MD, Radon M, Das K, Poptani H, Rathi N, Rudland PS. Cancer Immunol Immunother. 2023 Oct;72(10):3387-3393. 10.1007/s00262-023-03499-z

T-Cell Densities in Brain Metastases Are Associated with Patient Survival Times and Diffusion Tensor MRI Changes. Zakaria R, Platt-Higgins A, Rathi N, Radon M, Das S, Das K, Bhojak M, Brodbelt A, Chavredakis E, Jenkinson MD, Rudland PS. Cancer Res. 2018 Feb 1;78(3):610-616 10.1158/0008-5472.CAN-17-1720

Professor Tobias Zech

Director, Centre for Cell Imaging

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Molecular and Clinical Cancer Medicine

Research summary

Cell migration is fundamental to diverse aspects of the development and life of multicellular organisms. Angiogenesis, the immune system and neuritogenesis, to name but a few, all rely on the correct movement of cells to their destination in tissues in time and space.

During the progression of tumours, cells that were previously stationary re-acquire the ability to move through the adjacent tissue, a process known as cancer cell invasion. Cancer cell invasion often eventually leads to tumour cells entering the bloodstream (extravasation) and finally the colonisation of secondary tissues where metastatic secondary lesions of the primary tumour are formed. We are aiming to understand the mechanisms that enable cells to move and survive in a three dimensional tissue environment in health and during tumour progression

Selected publications

D Newman, L Young, T Waring, L Brown, K Wolanska, E MacDonald, A Charles-Orszag, P Caswell, T Sakuma, T Yamamoto, L Machesky, M Morgan, T Zech (2023), 3D matrix adhesion composition facilitates nuclear force coupling to drive invasive cell migration Cell reports, 42(12), 113554. 10.1016/j.celrep.2023.113554

Schnauß J, Kunschmann T, Grosser S, Mollenkopf P, Zech T, Freitag JS, Prascevic D, Stange R, Röttger LS, Rönicke S, Smith DM, Bayerl TM, Käs JA.(2021) Cells in slow motion: Apparent undercooling increases glassy behavior at physiological temperatures Advanced Materials, 2101840 2021 10.1002/adma.202101840

Ramkumar N.*, Farina F.*, Brown L., Samaner-Eweis D., Anstatt J., Waring T., Bithell J., Scita G., Thery M., Blanchoin L., Zech T., Baum B. (2019) Local actin nucleation tunes centrosomal microtubule nucleation during passage through mitosis. EMBO Journal 2019 Jun 3;38(11). 10.15252/embj.201899843

Professor Shampa Das

Head of Department

Chair of Antimicrobial Therapeutics

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Pharmacology and Therapeutics

Antimicrobial pharmacodynamics and therapeutics

Shampa Das is senior leader within the Antimicrobial Pharmacodynamics and Therapeutics group (APT), which focuses on the PK-PD of antimicrobial agents. The group has a strong track record in supporting the development of a number of antimicrobial and antifungal agents, where the outputs of this work has underpinned clinical dose selection. Shampa Das has 17 years industry experience in drug development which led to the registration of two recent antibiotics. Current APT projects are funded by the European Commission, the UK Medical Research Council, Global Antimicrobial Research and Development Partnership (GARDP) and the pharmaceutical industry (Pfizer, F2G, Bioversys, Bugworks, Spero).

APT's experimental platforms include mice and rabbit animal models of infection, hollow fibre infection model and state-of-the-art bioanalytical facilities. The group has strong mathematical modelling skills including population PK, and PK-PD modelling and Monte Carlo simulation.

Selected publications

Cristinacce, A., Wright, J. G., Macpherson, M., Iaconis, J., & Das, S. (2021). Comparing probability of target attainment against Staphylococcus aureus for ceftaroline fosamil, vancomycin, daptomycin, linezolid, and ceftriaxone in complicated skin and soft tissue infection using pharmacokinetic/pharmacodynamic models. doi:10.1016/j.diagmicrobio.2020.115292

Das, S., Fitzgerald, R., Ullah, A., Bula, M., Collins, A. M., Mitsi, E., . . . Hope, W. (2021). Intrapulmonary Pharmacokinetics of Cefepime and Enmetazobactam in Healthy Volunteers: Towards New Treatments for Nosocomial Pneumonia. doi:10.1128/AAC.01468-20

Das, S., Johnson, A., McEntee, L., Farrington, N., Kirby, A., Unsworth, J., .Hope, W. (2020). Pharmacodynamics of the Novel Metallo-β-Lactamase Inhibitor ANT2681 in Combination with Meropenem for the Treatment of Infections Caused by NDM-Producing Enterobacteriaceae.. Antimicrob Agents Chemother, 64(11). doi: 10.1128/AAC.01076-20

Dr Stephen Aston

Senior Clinical Lecturer

Honorary Consultant in Infectious Diseases

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Pharmacology and Therapeutics

Research summary

I undertake a portfolio of multidisciplinary and clinically-oriented research exploring strategies to mitigate the progression of antimicrobial resistance through optimised antibiotic prescribing in a variety of contexts - particularly in the management of suspected sepsis/serious bacterial infection and acute and chronic respiratory infection.

My current projects relate to three broad avenues of work: (1) Examining the use of artificial-intelligence and machine-learning enabled analysis of routinely collected electronic health record data to support data-driven diagnosis of infection at both individual patient and health system levels; (2) Pragmatic clinical trials of interventions to minimise unnecessary antibiotic prescribing in suspected sepsis/serious bacterial infection; (3) Optimising selection, delivery and monitoring of complex antibiotic regimens in chronic respiratory infections, in particular non-tuberculous mycobacteria.

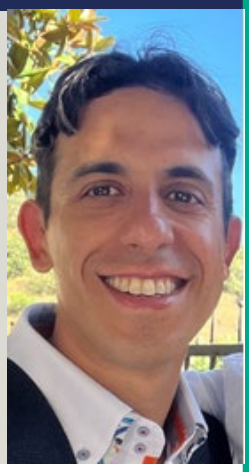
Selected publications

Howard A, Aston S, Gerada A et al. (2024). Antimicrobial learning systems: an implementation blueprint for artificial intelligence to tackle antimicrobial resistance. Lancet Digital Health, 6(1), e79-e86.

Howard A, Reza N, Aston S et al. (2024). Antimicrobial treatment imprecision: an outcome-based model to close the data-to-action loop. Lancet Infect Dis 24(1), e47-e58.

Euden J, Thomas-Jones E, Aston S et al. (2022). PROcalcitonin and NEWS2 evaluation for Timely identification of sepsis and Optimal use of antibiotics in the emergency department (PRONTO): protocol for a multicentre, open-label, randomised controlled trial. BMJ Open 12(6).

Dr Lawrence Barrera Briceno



Senior Lecturer

BSc Pharmacology Programme Director

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Pharmacology and Therapeutics

Tumour microenvironment, cancer progression, drug resistance

I specialise in studying the pancreatic tumour microenvironment and have a keen interest in exploring the role of Nrf2 transcription factor-regulated genes in chemotherapy resistance mechanisms. My research involves leveraging primary cells and various cell model systems such as co-culture, 3D spheroids and organoids to unravel the intricate communication between cancer cells and cancer-associated fibroblasts. I investigate their complex interactions with surrounding cells and molecules to better understand their impact on DNA methylation marks and microRNAs, all in pursuit of unravelling their implication in cancer progression. My current interest is focused on harnessing single-cell RNA sequencing technologies to dissect the heterogeneity within the tumour microenvironment, aiming to identify vulnerable cell populations and pave the way for the development of innovative treatments. I collaborate with Prof Eithne Costello and Dr Pedro Perez-Mancera within the Institute.

Selected publications

Barrera, L. N., Evans, A., Lane, B., Brumskill, S., Oldfield, F. E., Campbell, F., . . . Costello, E. (2020). Fibroblasts from Distinct Pancreatic Pathologies Exhibit Disease-Specific Properties.. Cancer Research, 80(13), 2861-2873. doi:10.1158/0008-5472.can-19-3534

Brumskill, S., Barrera, L. N., Calcraft, P., Phillips, C., & Costello, E. (2021). Inclusion of cancer-associated fibroblasts in drug screening assays to evaluate pancreatic cancer resistance to therapeutic drugs. JOURNAL OF PHYSIOLOGY AND BIOCHEMISTRY. doi:10.1007/s13105-021-00857-2

Abu-Alainin, W., Gana, T., Liloglou, L., Olayanju, A., Barrera Briceno, L., Ferguson, R., . . . Costello-Goldring, E. (2016). UHRF1 regulation of the Keap1-Nrf2 pathway in pancreatic cancer contributes to oncogenesis. Journal of Pathology, 238(3), 423-433. doi:10.1002/path.4665

Dr Dan Carr

Senior Lecturer

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Pharmacology and Therapeutics

Predicting, understanding and treating severe skin adverse drug reactions

The research of the group is focused on severe cutaneous adverse drug reactions, with a particular interest in Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis. SJS/TEN are rare, life-threatening skin blistering reactions which can be coursed by a diverse range of prescribed drugs.

We are trying to identify predictive biomarkers of SJS/TEN, both circulatory and skin-specific. In order to so, we have developed novel ex vivo models of the SJS/TEN pathology, which additionally afford us significant mechanistic insight into the pathogenesis. These insights have allowed us to identify valid therapeutic targets which we are investigating as putative novel treatment strategies for a reaction which currently has no targeted therapies.

We have established a network of: i) national and international academic collaborators in dermatology and pathology and ii) SJS/TEN survivors and patient advocates.

Selected publications

Olsson-Brown A Yip V, Ogiji E, Jolly C, Ressel L, Sharma A..., Carr DF. TNF-α mediated keratinocyte expression and release of matrix metalloproteinase 9: putative mechanism of pathogenesis in Stevens-Johnson syndrome/ toxic epidermal necrolysis. J Invest Dermatol. 2023. Jun; 143 (6):1023-1030.e7.

Nwikue G, Olsson-Brown A, Aboheimed N, Yip V, Jolly C..., Carr DF. TNF-α induced extracellular release of keratinocyte High Mobility Group Box 1 in Stevens-Johnson syndrome/ toxic epidermal necrolysis: biomarker and putative mechanism of pathogenesis. J Dermatol. 2023. 50(9):1129-1139

Carr DF, Wang CW, Bellón T, Ressel L, Nwikue G, Shrivastava V, Bergfeld W, Jorgensen AL, Chung WH, Pirmohamed M. Serum and blister-fluid elevation and decreased epidermal content of HMGB1 protein in drug-induced Stevens Johnson syndrome/toxic epidermal necrolysis. Br J Dermatol. 2019: 181(1); 166-174.

Dr Amy Chadwick

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Pharmacology and Therapeutics

Drug safety and the mitochondria: toxicological target to personal susceptibility factor

My research group, the "Bioenergetics Group", within the Department of Pharmacology & Therapeutics at the University of Liverpool, has a translational focus on investigating the role of mitochondria dysfunction in drug safety. We strive to develop physiologically and pharmacologically relevant 2D and 3D models and methods with which to define the molecular mechanisms of mitotoxins and their relative potential to induce human toxicity and have collaborated widely with the pharmaceutical industry in this area.

In addition, we also investigate how individuality in mitochondrial function and mitochondrial genotype may influence patient susceptibility to mitotoxins. Recently, we have performed innovative research to define variations in bioenergetic phenotype in human liver tissue in order to build a computational model to predict mitotoxicity. We have also created a panel of novel HepG2 transmitochondrial cybrids as a personalised model of mitochondrial genotype. Each cybrid line contains a different mitochondrial genome, against a stable nuclear background. Current projects in the group investigate the influence of mitochondrial function on drug safety across several organs including bone, muscle, kidney, heart and liver.

I have also established the Seahorse Respirometry Facility at Liverpool, which is a hub for collaborative projects across the University and externally, and we are at the forefront of pushing the boundaries of this technology into primary tissue interrogation and translational clinical studies. I believe that the influence of personal mitochondrial phenotype and genotype is an important and exciting new frontier in pharmacology & toxicology.

Selected publications

Ball, A. L., Jolly, C. E., Lennon, M. G., Lyon, J. J., Alfirevic, A., & Chadwick, A. E. (2023). The generation of HepG2 transmitochondrial cybrids to reveal the role of mitochondrial genotype in idiosyncratic drug-induced liver injury. eLife, 12, e78187. https://doi.org/10.7554/eLife.78187

Ball, A. L., Bloch, K. M., Rainbow, L., Liu, X., Kenny, J., Lyon, J. J., Gregory, R., Alfirevic, A., & Chadwick, A. E. (2021). Assessment of the impact of mitochondrial genotype upon drug-induced mitochondrial dysfunction in platelets derived from healthy volunteers. Archives of toxicology, 95(4), 1335–1347. https://doi.org/10.1007/s00204-021-02988-3

Jolly, C. E., Douglas, O., Kamalian, L., Jenkins, R. E., Beckett, A. J., Penman, S. L., Williams, D. P., Monshouwer, M., Simic, D., Snoeys, J., Park, B. K., & Chadwick, A. E. (2020). The utility of a differentiated preclinical liver model, HepaRG cells, in investigating delayed toxicity via inhibition of mitochondrial-replication induced by fialuridine. *Toxicology and applied pharmacology*, *403*, 115163. https://doi.org/10.1016/j.taap.2020.115163

Dr Derek Cocker

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Pharmacology and Therapeutics

Research summary

Derek is an infectious disease clinician and Academic Clinical Lecturer in Infectious Disease and Global Health currently working in the David Price Evans Infectious Disease and Global Health group at the University of Liverpool. He has clinical and research experience in Uganda, Tanzania and Malawi and works alongside international collaborators to undertake transdisciplinary research into the drivers of antimicrobial resistance (AMR), particularly focusing on resource limited settings.

His research is framed in a One Health context, most recently evaluating the relationship between water sanitation and hygiene (WASH) factors and environmental contamination with bacteria or chemicals on human health. He also evaluates the importance of the climate on AMR and considers putative mechanistic and preventative therapies to protect individuals and health systems from AMR.

Selected publications

Cocker, D., Chidziwisano, K., Mphasa, M., Mwapasa, T., Lewis, J. M., Rowlingson, B., . . . Feasey, N. A. (2023). Investigating One Health risks for human colonisation with extended spectrum β-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Malawian households: a longitudinal cohort study.. The Lancet. Microbe, S2666-5247(23)00062-9. doi:10.1016/s2666-5247(23)00062-9

Aiken, A. M., Rehman, A. M., de Kraker, M. E. A., Madrid, L., Kebede, M., Labi, A. -K., MBIRA study collaborators. (2023). Mortality associated with third-generation cephalosporin resistance in Enterobacterales bloodstream infections at eight sub-Saharan African hospitals (MBIRA): a prospective cohort study.. The Lancet. Infectious diseases, S1473-3099(23)00233-5. doi:10.1016/s1473-3099(23)00233-5

Sammarro M, Rowlingson B, Cocker D, Chidziwisano K, Jacob ST, Kajumbula H, et al. Risk factors, temporal dependence, and seasonality of human ESBL-producing E. coli and K. pneumoniae colonisation in Malawi: a longitudinal model-based approach. Clinical Infectious Diseases, 2023; ciad117. https://doi.org/10.1093/cid/ciad117

Professor Ian Copple

Professor of Pharmacology and Toxicology

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Research summary

After undertaking post-doctoral research at Leiden Universitiet (Netherlands) and Karolinska Institutet (Sweden), I was appointed as a Tenure Track Fellow in Liverpool in 2013, as a Lecturer in 2016, as a Senior Lecturer in 2019 and as a Professor in 2023. I was awarded a prestigious MRC Senior Non-clinical Fellowship in 2022. I am a Fellow of the British Pharmacological Society and Higher Education Academy.

Below is a simple explanation of my group's research interests. I am also academic co-lead for the Liverpool Human Liver Research Facility.

The different cell types within our bodies are protected against the damaging effects of daily stresses (e.g. ultraviolet radiation from sunlight, environmental pollutants) by proteins that help to remove toxic chemicals from the body and boost antioxidant levels. In fact, stimulation of these protective processes is one of the ways fruits and vegetables improve our health, by enhancing the 'stress tolerance' of our cells.

Evidence indicates that when the stress tolerance of our cells is hindered, there is an increased risk of developing certain diseases and of being sensitive to the toxic effects of some environmental agents. This can also influence susceptibility to the harmful side effects of some medicines. Hence, many pharmaceutical companies are now developing medicines that can boost our natural cell defences in order to treat certain diseases.

My research group focuses on: (1) understanding exactly how our cells sense and respond to different types of stress, (2) how this influences the adverse effects of medicines, (3) whether we can treat diseases by targeting stress response processes therapeutically, and (4) how to measure cell stress responses in patients.

Selected publications

Morgenstern, C., Lastres-Becker, I., Demirdöğen, B. C., Costa, V. M., Daiber, A., Foresti, R., Motterlini, R., Kalyoncu, S., Arioz, B. I., Genc, S., Jakubowska, M., Trougakos, I. P., Piechota-Polanczyk, A., Mickael, M., Santos, M., Kensler, T. W., Cuadrado, A., & Copple, I. M. (2024). Biomarkers of NRF2 signalling: Current status and future challenges. *Redox biology*, *72*, 103134. https://doi.org/10.1016/j.redox.2024.103134

Dinkova-Kostova, A. T., & Copple, I. M. (2023). Advances and challenges in therapeutic targeting of NRF2. *Trends in pharmacological sciences*, *44*(3), 137–149. https://doi.org/10.1016/j.tips.2022.12.003

Chan BKY, Elmasry M, Forootan SS, et al. Pharmacological Activation of Nrf2 Enhances Functional Liver Regeneration. *Hepatology*. 2021;74(2):973-986. https://doi.org/10.1002/hep.31859

Dr Michael Cross

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Research summary

Dr Cross's research focuses on the role endothelial cells in tumour angiogenesis and the role of cardiac endothelial cells in drug-induced cardiovascular toxicity. Dr Cross has developed a number of advanced in vitro cell models aimed at recapitulating in vivo cardiac physiology, allowing a better understanding of the adverse effects of drugs, such as anti-cancer drugs, on different cell types in the heart.

Dr Cross is also pursuing research in the area of cardioprotection, and has discovered that statins, which inhibit HMGCoA-reductase to lower LDL-cholesterol, also have pleiotropic effects on cardiac endothelial cells, activating a vasculoprotective pathway which ultimately preserves endothelial cell integrity. The aim of this research is to protect the cardiac endothelial cells against the damage that chemotherapy drugs can inflict, ultimately protecting cardiac function in patients receiving cancer chemotherapy.

Selected publications

Mondru, A.K., Aljasir, M.A, Alrumayh, A., Nithianandarajah, G.N., Ahmed, K., Muller, J., Goldring. C.E.P., Wilm, B., and Cross. M.J. (2023). VEGF Stimulates Activation of ERK5 in the Absence of C-Terminal Phosphorylation Preventing Nuclear Localization and Facilitating AKT Activation in Endothelial Cells. Cells. 2023 Mar 22;12(6):967 10.3390/cells12060967

Muñiz-García, A., Wilm, B., Murray, P., and Cross, M.J. (2023). Extracellular Vesicles from Human Umbilical Cord-Derived MSCs Affect Vessel Formation In Vitro and Promote VEGFR2-Mediated Cell Survival. Cells. 2022 Nov 24;11(23):3750 10.3390/cells11233750

Wilkinson, E.L., Sidaway, J.E and Cross, M.J. (2018). Statin regulated ERK5 stimulates tight junction formation and reduces permeability in human cardiac endothelial cells. Journal of Cellular Physiology 233:186-200. 10.1002/jcp.26064

Dr Lekh Dahal

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Pharmacology and Therapeutics

Research summary

Lekh's immunology group is interested in the basic immunobiology of soluble immune checkpoints; and innate immune sensing pathways as an interface between innate and adaptive immune systems. This stream of research is important to pharmacology department because of its focus on drug safety, immune-toxicology and personalised medicine. Currently embedded in his research are 3 key areas of investigation, the overarching aim of which are to identify refined approaches to more precise, less toxic therapy. First, regulation of immune system by soluble isoforms of immune checkpoints. Checkpoint receptors are crucial in maintaining immune tolerance and preventing inappropriate immune responses directed against self-tissues. Some of these receptors have been successfully targeted for cancer immunotherapy. However, many of these receptors also have overlooked isoforms, the role of which in immunotherapy or immune toxicity have been poorly investigated. Lekh's group has been pivotal in uncovering key role for the soluble isoform of CTLA-4 in regulation of immune responses, particularly its potential impact on cancer immunotherapy. Second, research on the intricate interplay between viral infections and innate immune sensing pathways in the context of cancers (Human papillomavirus in head and neck cancers and human cytomegalovirus in follicular lymphoma) to ultimately develop strategies to enhance immunotherapy aided by the benefit of patient stratification. And third, investigation of the immunogenicity of viral vectors (particularly AAV9) used in gene therapy. Gene transfer using AAV vectors is promising for treatment of rare diseases, but immune system mediated toxicity against the vector is a key challenge. The group is involved in EU Horizon 2020 ARDAT consortium, the overall objective of which is to develop and provide data and tools to fill gaps in our knowledge-base in the areas of immunology of viral gene/cell therapy.

Selected publications

Saulters E, Kennedy PT, Carter RJ, Alsufyani A, Jones TM, Woolley JF, Dahal LN, Differential Regulation of the Stimulator of Interferon Genes pathway in Human Papillomavirus positive and negative Head and Neck Cancers, Cancer Res Commun. 2023 Dec 26. https://doi.org/10.1158/2767-9764.CRC-23-0299

Kennedy PT, Saulters EL, Duckworth AD, Lim YJ, Woolley JF, Slupsky JR, Cragg MS, Ward FJ, Dahal LN, Soluble CTLA-4 attenuates T cell activation and modulates anti-tumor immunity, Mol Ther. 2023 Dec 5:S1525-0016(23)00661-5. 10.1016/j.ymthe.2023.11.028

Dahal LN, Dou L, Hussain K, Liu R, Earley A, Cox KL, Murinello S, Tracy I, Forconi F, Steele AJ, Duriez PJ, Gomez-Nicola D, Teeling JL, Glennie MJ, Cragg MS, Beers SA, STING Activation Reverses Lymphoma-Mediated Resistance to Antibody Immunotherapy, Cancer Res. 2017 Jul 1;77(13):3619-3631. 10.1158/0008-5472.CAN-16-2784

Dr David Dickens

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Pharmacology and Therapeutics

Research summary

His research interests lie at the interface of drug transporter pharmacology, psychopharmacology, BBB biology and molecular properties that determine the mechanism of transport by transporters. The BBB is considered a significant bottleneck to the development of new CNS treatments with the additional challenge of disease specific effects and inter-patient variability in drug response. With his broad base of skills, he is well equipped for the opportunities that are available in this exciting field of research.

Dickens lab recent novel findings include identifying a carrier-mediated process for the uptake of clozapine, interaction of transporters with an NMDA receptor antagonist, characterising gabapentin as a LAT1 substrate and LAT1s interactions with cholesterol.

David is an Elected Council Member of the British Association for Psychopharmacology and a Senior Academic for the steering committee of the UK & Ireland Early Career Blood-Brain Barrier Symposium series.

Selected publications

Patel W, Shankar RG, Smith MA, Snodgrass HR, Pirmohamed M, Jorgensen A, Alfirevic A, Dickens D. (2024) Role of transporters and enzymes in metabolism and distribution of 4-chlorokynurenine (AV-101). Mol Pharmaceut 21, 2, 550−563 10.1021/acs.molpharmaceut.3c00700

Bourque M, Grégoire L, Patel W, Dickens D, Snodgrass R, Di Paolo T. AV-101, a Pro-Drug Antagonist at the NMDA Receptor Glycine Site, Reduces L-Dopa Induced Dyskinesias in MPTP Monkeys (2022). Cells 11 (22), 3530 10.3390/cells11223530

Cappoli N , Jenkinson MD, Russo CD , Dickens D. LAT1, a novel pharmacological target for the treatment of glioblastoma Biochemical Pharmacology 2022. 201, 115103 https://doi.org/10.1016/j.bcp.2022.115103

Patel W, Rimmer L, Smith M, Moss L, Smith MA, Snodgrass HR, Pirmohamed M, Alfirevic A, Dickens D. Probenecid Increases the Concentration of 7-Chlorokynurenic Acid Derived from the Prodrug 4-Chlorokynurenine within the Prefrontal Cortex. Mol Pharmaceut. 2021. 18, 113-123. 10.1021/acs.molpharmaceut.0c00727

Dr Shiva Seyed Forootan

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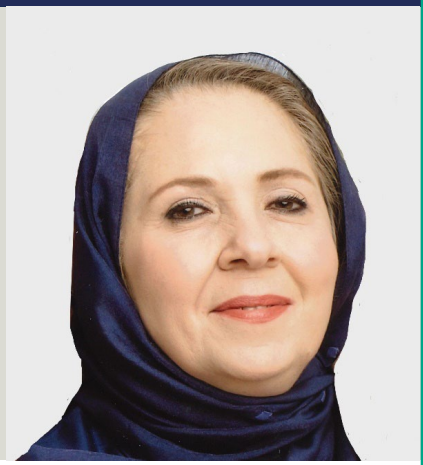

Research summary

I have completed my MD in Shahrekord University, Iran and my PhD in Department of Pathology, University of Liverpool. I have been working as a Research Associate in the Department of Molecular & Clinical Cancer Medicine and Pharmacology & Therapeutics at the University of Liverpool investigating the role of biomarkers in predication and progression of prostate cancer and Drug Induced Liver injury (DILI).

My current research in the group is focus on identifying more sensitive and specific panel of biomarkers for predication and detection of drug organ injury specifically liver injury using microRNAs (miRs) (non-coding RNAs of approximately 22 nucleotides in length) as potential circulating biomarker for DILI using chemotherapy drugs (e.g. methotrexate) and analgesic drug (e.g. paracetamol). My research involves using human and rodent primary cells, stem cells, different cell models (3D, co-culture), different in vivo models and state of art technologies such as next generation sequencing and pre-clinical imaging to understand the role of miRNAs in DILI and to investigate the different mechanism these miRNAs interact with. I am collaborating with Professor Chris Goldring, Prof Ian Copple and Dr Mike Cross.

Selected publications

A.L. Schofield, J.P. Brown, J. Brown, A. Wilczynska, C. Bell, W.E. Glaab, M. Hackl, L. Howell, S. Lee, J.W. Dear, M. Remes, P. Reeves, E. Zhang, J. Allmer, A. Norris, F. Falciani, L.Y. Takeshita, S. S. Forootan, R. Sutton, B.K. Park, C. Goldring. Systems analysis of miRNA biomarkers to inform drug safety. Arch Toxicol. 2021 Nov;95(11):3475-3495.. 10.1007/s00204-021-03150-9

B. K. Y. Chan*, M. Elmasry *, S. S. Forootan*, T.M. Bunday, F. Zhang, N. Brillant, P.J. Starkey-Lewis, R. Aird, E. Ricci, T.D. Andrews, R. L. Sison-Young, A. L. Schofield, Y. Fang, A. Lister, J.W. Sharkey, H. Poptani, N.R. Kitteringham, S.J. Forbes, H.Z. Malik, S.W. Fenwick, B. K. Park, C.E. Goldring, I. M. Copple. Pharmacological activation of Nrf2 enhances liver regeneration. Hepathology, 2021, 74 (2), 973-986. 10.1002/hep.31859

S.S. Forootan *, F.E. Mutter *, A. Kipar, T. Iwawaki, B. Francis, C.E. Goldring, B.K. Park, I.M. Copple. Real-time in vivo imaging reveals localised Nrf2 stress responses associated with direct and metabolism-dependent drug toxicity, Sci Rep. 2017 Nov, 22;7(1):16084. 10.1038/s41598-017-16491-2

Professor Christopher Goldring

Deputy Executive Dean of the Institute

Co-director, Human Liver Research Facility

Co-director, Joint Centre for Pharmacology and Therapeutics

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Pharmacology and Therapeutics

Models and biomarkers to Improve drug safety

Our research team aims to develop humanised biologically-relevant models to improve our ability to predict the safety of drugs in development, and those that are widely-used in patients but which possess some safety liability. In parallel we work on improving biomarkers that can allow a better definition of the safe use of medicines. The overarching goal of our research is to improve our understanding of adverse drug reactions from a human health perspective; therefore, we have established national and international links with academic scientists, clinicians and colleagues in the pharmaceutical industry, to ensure our work is relevant to patients and the process of drug development.

We have spent many years attempting to improve models of the human liver, and also other organs, for example leading the recent UKRI 3Dbionet project to enhance uptake of 3D in vitro models. Our philosophy in this endeavour is based on George Box's famous aphorism, "All models are wrong, but some are useful" - we try to understand what is actually pharmacologically-relevant in a given model. Working with clinical colleagues, and through the kind agreement of many patients, we established a pipeline for the use of human primary liver cells (>380 freshly-isolated archived liver tissue and cell culture since 2011), this allowed the evaluation of 3D models of the liver using patient-derived tissue, as well as creating a bank of patient-derived induced pluripotent stem cells. We led an industry-academic consortium to evaluate the reproducibility of such in vitro models – an absolute priority for industry drug development - and an examination of the physiological relevance of such liver models, largely through a proteomic approach. Alongside twelve industry partners, this led to the development of a roadmap, accepted by and now being used by a number of European Pharmaceutical companies, for the adoption of different models for the safety assessment of pharmaceutical compounds. Through further Innovative Medicines Initiative funding we led an evaluation of the role of systems toxicology models in drug safety assessment, which will now be developed into a new published roadmap.

Selected publications

Managing the challenge of drug-induced liver injury: a roadmap for the development and deployment of preclinical predictive models. Weaver et al. 2020 Nat Rev Drug Discov. 19:131-148. doi: 10.1038/s41573-019-0048-x.

Proteomic profiling of murine biliary-derived hepatic organoids and their capacity for drug disposition, bioactivation and detoxification. Howell L, et al. Arch Tox. 2021 95:2413-2430. doi: 10.1007/s00204-021-03075-3.

Genomic profiling of idiopathic peri-hilar cholangiocarcinoma reveals new targets and mutational pathways. Quinn LM et al. Sci Rep. 2023 13:6681. doi: 10.1038/s41598-023-33096-0.

Dr Dan Hawcutt

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Pharmacology and Therapeutics

Research summary

Dr Hawcutt is a Reader in paediatric pharmacology at the University of Liverpool, and honorary consultant in paediatrics at Alder Hey Children's Hospital. He is Director of Research at Alder Hey Children's Hospital, and Director of the NIHR Alder Hey Clinical Research Facility (CRF). Dr Hawcutt is also chair of the Royal College of Paediatrics and Child Health (RCPCH) / Neonatal and Paediatric Pharmacists Group (NPPG) joint standing committee on medicines, and a member of the Medicines and Healthcare Regulatory Agency Pharmacovigilance Expert Advisory Committees on both Pharmacovigilance and Paediatric Medicines. In addition, he is chair of the RCPCH training committee for Paediatric Clinical Pharmacology.

His research interests include Pharmacogenomics, Pharmacovigilance, and Early Phase Clinical Trials.

Selected publications

Hawcutt DB, Francis B, Carr DF, et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. Lancet Respir Med. 2018;6(6):442-450. https://doi.org/10.1016/S2213-2600(18)30058-4

Rugg-Gunn CEM, Dixon E, Jorgensen AL, et al. Factors Associated With Diabetic Ketoacidosis at Onset of Type 1 Diabetes Among Pediatric Patients: A Systematic Review. JAMA Pediatr. 2022;176(12):1248-1259. https://doi.org/10.1001/jamapediatrics.2022.3586

Nash, E., Bickerstaff, M., Chetwynd, A.J. et al. The readability of parent information leaflets in paediatric studies. Pediatr Res 94, 1166–1171 (2023). https://doi.org/10.1038/s41390-023-02608-z

Professor Alison Holmes

David Price Evans Chair in Global Health and Infectious Diseases

CAMO-Net Lead

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Pharmacology and Therapeutics

Interdisciplinary research on infection prevention and management, with a focus on antimicrobial therapy and addressing antimicrobial resistance

Professor Alison Holmes and her group undertake a range of research which aims to tackle the challenges of infection and antimicrobial resistance (AMR) within both UK and global contexts. Professor Holmes' interdisciplinary approach to research applies to social sciences as well as engineering, design, molecular medicine and the better use of technologies and data to improve the use of antimicrobials and the prevention, diagnosis, and management of infection.

The new Centres for Antimicrobial Optimisation Network (CAMO-Net), which Professor Holmes leads, is a unique global research partnership pursuing research themes in technology and innovation for optimised antimicrobial use, in understanding the role of context, culture, and behaviour; and in medicines management including supply chains and quality testing, and in considering comorbidities. Its aim is to address AMR through antimicrobial optimisation and to improve access to effective antimicrobial therapy. The network is underpinned by values of equity, local leadership, co-production, knowledge mobilisation, and shared learning.

Professor Holmes has established a new collaboration with Dr Abi Merriel from the Institute of Life Course and Medical Sciences. Dr Merriel is a Senior Clinical Lecturer in Obstetrics and Honorary Consultant Obstetrician Women's and Children's Health. Together, they are exploring how point of care biosensor technologies can be developed and applied to improve the management of labour, antimicrobial use, and clinical outcomes for mothers and babies.

Selected publications

Rawson, T. M., Gowers, S. A. N., Freeman, D. M. E., Wilson, R. C., Sharma, S., Gilchrist, M., . . . Holmes, A. H. (2019). Microneedle biosensors for real-time, minimally invasive drug monitoring of phenoxymethylpenicillin: a first-in-human evaluation in healthy volunteers. LANCET DIGITAL HEALTH, 1(7), E335-E343. doi:10.1016/S2589-7500(19)30131-1

Rawson, T. M., Wilson, R. C., O'Hare, D., Herrero, P., Kambugu, A., Lamorde, M., . . . Holmes, A. H. (2021). Optimizing antimicrobial use: challenges, advances and opportunities. NATURE REVIEWS MICROBIOLOGY, 19(12), 747-758. doi:10.1038/s41579-021-00578-9

Zhu, N. J., Rawson, T. M., Mookerjee, S., Price, J. R., Davies, F., Otter, J., . . . Holmes, A. (2022). Changing Patterns of Bloodstream Infections in the Community and Acute Care Across 2 Coronavirus Disease 2019 Epidemic Waves: A Retrospective Analysis Using Data Linkage. CLINICAL INFECTIOUS DISEASES, 75(1), E1082-E1091. doi:10.1093/cid/ciab869

Dr David Hong

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Research summary

The Hong group is focused on the discovery and development of drugs for infectious diseases with particular emphasis on using chemical tools to investigate and tackle antimicrobial resistance (AMR). My research covers a wide range of areas related to AMR at its broadest context, including: developing new therapeutics against some of the infectious diseases affect the most by AMR, such as chronic/resistant bacterial infections, malaria, tuberculosis, and human filariasis (neglected tropical diseases caused by filarial nematode infection), discovery of new insecticides against resistant vectors, and a cross-cutting theme of developing novel chemical tool molecules (chemical probes) to enable advanced AMR research.

I receive funding from UKRI research councils, such as BBSRC, MRC and EPSRC and charitable organisations, such as Global Heath Innovation Technology (GHIT) fund and Gates foundation, and work closely with pharmaceutical companies, such Astra Zeneca and Eisai.

Selected publications

Wu P, Tu B, Liang J, et al. Synthesis and biological evaluation of pentacyclic triterpenoid derivatives as potential novel antibacterial agents. Bioorg Chem. 2021;109:104692. https://doi.org/10.1016/j.bioorg.2021.104692

Hong WD, Benayoud F, Nixon GL, et al. AWZ1066S, a highly specific anti-*Wolbachia* drug candidate for a short-course treatment of filariasis. *Proc Natl Acad Sci U S A*. 2019;116(4):1414-1419. https://doi.org/10.1073/pnas.1816585116

Johnston KL, Cook DAN, Berry NG, et al. Identification and prioritization of novel anti-Wolbachia chemotypes from screening a 10,000-compound diversity library. Sci Adv. 2017;3(9):eaao1551. Published 2017 Sep 27. https://doi.org/10.1126/sciadv.aao1551

Professor William Hope

Dame Sally Davies Chair of AMR Research

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Antimicrobial pharmacodynamics, antimicrobial drug development and precision medicine to address the challenge of AMR

My research focusses on developing a deep understanding of antimicrobial dose-effect-response relationships that underpin effect, toxicity and emergence of resistance in bacteria and fungi. I use a combination of state-of-the-art bioanalysis, experimental platforms and mathematical modelling approaches to understand optimal regimens to address unmet medical needs and design mitigation strategies to minimise antimicrobial resistance. More recently, I have recognised that challenges in addressing AMR also require advanced data integration and AI approaches. As a result, I have worked in the past few years to build data science capabilities to address AMR at a national and international level.

An in depth understanding of antimicrobial pharmacodynamics and advanced information systems are simultaneously required to define:

- Optimal regimens of new antibacterial and antifungal agents
- Design of resilient regimens to prevent erosion of value by AMR
- The precise use of antimicrobials
- Antimicrobial regimens suitable for use in global health settings

I am the NIHR Specialty Co-Lead for Infection and advise multiple pharmaceutical companies, DNDi and GARDP. I am a Clarivate highly cited researcher. I was appointed Officer of the Order of the British Empire (OBE) in the 2021 Birthday Honours for services to Infectious Diseases research.

Selected publications

Abel, Kathryn & Agnew, Emily & Amos, James & Armstrong, Natalie & Armstrong-James, Darius & Ashfield, Thomas & Aston, Stephen & Baillie, Kenneth & Baldwin, Steven & Barlow, Gavin & Bartle, Victoria & Bielicki, Julia & Brown, Colin & Carrol, Enitan & Clements, Michelle & Cooke, Graham & Dane, Aaron & Dark, Paul & Day, Jeremy & Hope, William. (2024). System-wide approaches to antimicrobial therapy and antimicrobial resistance in the UK: the AMR-X framework. The Lancet Microbe. https://doi.org/10.1016/S2666-5247(24)00003-X

Howard A, Reza N, Aston S, et al. Antimicrobial treatment imprecision: an outcome-based model to close the data-to-action loop. Lancet Infect Dis. 2024;24(1):e47-e58. https://doi.org/10.1016/S1473-3099(23)00367-5

Reza N, Gerada A, Stott KE, Howard A, Sharland M, Hope W. Challenges for global antibiotic regimen planning and establishing antimicrobial resistance targets: implications for the WHO Essential Medicines List and AWaRe antibiotic book dosing. Clin Microbiol Rev. Published online March 4, 2024. https://doi.org/10.1128/cmr.00139-23

Professor Michael Jenkinson

Sir John Fisher Foundation and Royal College of Surgeons of England Chair of Surgical Trials

Professor of Neurosurgery

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Pharmacology and Therapeutics

Clinical trials in neurosurgery and neuro-oncology

His research interests include meningioma management (incidental tumours, seizures and quality of life), imaging and biology of brain metastases and interventional clinical trials in neurosurgery and neuro-oncology. He is the recipient of grants for basic science and clinical research from the MRC, Brain Tumour Charity and NIHR. He is the chief investigator on several NIHR-funded trials, including the multi-centre ROAM trial (Radiation versus Observation following surgical resection of Atypical Meningioma)[https://roam-trial.org.uk] and STOP 'EM (Surgeons Trial Of Prophylaxis for Epilepsy in Meningioma)[https://www.stopem-trial.org.uk]. He is a co-investigator on the NIHR funded SPRING, FUTURE GB and PROSSPER trials. He led a pilot study to investigate the use of Ketogenic diet for patients with glioblastoma (KEATING).

He was the co-chief investigator on the NIHR funded BASICS trial (The British Antibiotic and Silver Impregnated Catheters for ventriculoperitoneal Shunts randomized controlled trial) that showed that antibiotic catheters reduced the infection rate from 6% to 2% and save £135,000 per infection averted.

Selected publications

Mallucci CL*, Jenkinson MD*, Conroy EJ, Hartley JC, Brown M, Moitt T, Dalton J, Kearns T, Griffiths, M, Culeddu G, Solomon T, Hughes D, Gamble C. Antibiotic or silver versus standard ventriculoperitoneal shunts (BASICS): a multi-centre, single-blinded, randomised trial and economic evaluation. Lancet 2019 DOI 10.1016/S0140-6736(19)31603-4. 13 *Joint first authors

Goldbrunner R, Minniti G, Preusser M, Jenkinson MD, Sallabanda K, Houdart E, von Deimling A, Stavrinou P, Lefranc F, Lund-Johansen M, Moyal EC, Brandsma D, Henriksson R, Soffietti R, Weller M. EANO guidelines for the diagnosis and treatment of meningiomas. Lancet Oncol. 2016 Sep;17(9):e383-91. doi: 10.1016/S1470-2045(16)30321-7

Islim A, Kolamunnage-Dona R, Mohan M, Moon RDC, Crofton A, Haylock BJ, Rathi N, Mills SJ, Brodbelt AR, Jenkinson MD. A prognostic model to personalise monitoring regimes for patients with incidental asymptomatic meningioma. Neuro-Oncology 2020: 22 (2): 278-289. doi: 10.1093/neuonc/noz160.

Professor Simon Keller

Chair of Neuroimaging

Director of the Liverpool BRAIN lab

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View staff profile

Pharmacology and Therapeutics

Quantitative magnetic resonance imaging to study brain disorders and predict treatment outcomes

My main research interests are the use of advanced quantitative neuroimaging techniques, mainly magnetic resonance imaging, to understand aberrant brain mechanisms in neurological disorders, help improve imaging diagnostic accuracy and identify reliable imaging prognostic markers of medical and neurosurgical treatment. Epilepsy is of primary interest and my group works to understand how epilepsy impacts brain health and how we can use neuroimaging methods to improve evaluation of patients and predict their responses to treatment. Our work in epilepsy is supported by the Medical Research Council and the Epilepsy Research Institute.

The interests of my lab go beyond epilepsy and also include mapping patterns of brain alterations and predicting outcomes in movement disorders, neurodegenerative disorders, brain infections, and other acquired and developmental brain disorders. More information is provided in the lab website, above.

I am director of the Liverpool BRAIN (Brain Research using Advanced Imaging in Neurology) lab, recipient of the International League Against Epilepsy (ILAE) Europe Young Investigator award (2022, https://bit.ly/3RJqlRn), sit on the Scientific Advisory Committee for Epilepsy Research Institute UK (https://t.ly/KTwTz), and elected Fellow of the Anatomical Society (https://bit.ly/44dS3wq).

Selected publications

De Bezenac, C., Adan, G., Weber, B., Keller, S. S. 2021. Association of Epilepsy Surgery with Changes in Imaging Defined Brain Age. Neurology, 97(6):e554-e563.

Bryant, L., McKinnon, E., Taylor, J., A., Bonilha, L., Jensen, J., de Bezenac, D., Kreilkamp, B. A. K., Wieshmann, U. C., Adan, G., Biswas, S., Marson, A. G., Keller, S. S. 2021. Fiber ball white matter modelling in patients with focal epilepsy. Human Brain Mapping, 42(8):2490-2507.

Keller, S. S., Glen, G. R., Weber, B., Kreilkamp, B. A. K., Jensen, J. H., Helpbern, J., Wagner, J., Barker, G. J., Richardson, M. P., Bonilha, L. 2017. Preoperative automated white matter fibre quantification predicts postoperative seizure outcome in refractory TLE. Brain, 140:68-82.

Professor Saye Khoo

Professor

Honorary Consultant Physician in Infectious Diseases

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View staff profile

Research summary

Professor Khoo's research focuses on the pharmacology of antiviral and anti-tuberculous treatment, including early phase evaluation of novel compounds and formulations, characterisation of antimicrobial concentrations in relevant compartments for treatment and prevention, and drug interactions. Current research portfolio:

1. Leads the UK Early-Phase COVID-19 Antiviral Trials Platform (AGILE) which has undertaken dose-optimisation of molnupiravir, evaluation of high-dose nitazoxanide, first-into-human evaluation of VIR7832, first phase II evaluation of intravenous favipiravir, and first clinical study of nirmatrelvir/ritonavir combined with molnupiravir. Khoo is also Chief Investigator of the international DolPHIN consortium undertaking RCTs to establish safety and efficacy of HIV antivirals in pregnant women and their infants.
2. Leads the Liverpool Drug Interactions programme (www.drug-interactions.org) which has developed prescribing tools for managing drug interactions in HIV, hepatitis, Cancer and COVID-19 treatments. Collectively the tools returned over 14 million searches in 2022, and have been translated into Spanish, Portuguese and Japanese.
3. Professor Khoo has established the Liverpool Bioanalytical Facility, which undertakes GCP measurement of drug concentrations in plasma, cells, and tissue compartments.

Selected publications

Butler, C. C., Hobbs, F. D. R., Gbinigie, O. A., Rahman, N. M., Hayward, G., Richards, D. B., . . . Little, P. (2023). Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomised controlled trial. LANCET, 401(10373), 281-293. doi:10.1016/S0140-6736(22)02597-1

Heseltine, T., Hughes, E., Mattew, J., Murray, S., Ortega-Martorell, S., Olier, I., . . . Khoo, S. (2023). The association of epicardial adipose tissue volume and density with coronary calcium in HIV-positive and HIV-negative patients. JOURNAL OF INFECTION, 86(4), 376-384. doi:10.1016/j.jinf.2023.02.020

Hodge, D., Hodel, E. M., Hughes, E., Hazenberg, P., Granana Castillo, S., Gibbons, S., . . . Khoo, S. (2023). Prevalence of Potentially Clinically Significant Drug-Drug Interactions With Antiretrovirals Against HIV Over Three Decades: A Systematic Review of the Literature. JAIDS-JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, 92(2), 97-105. doi:10.1097/QAI.0000000000003122

Professor Neill Liptrott

Chair in Pharmacology and Immunocompatibility

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View staff profile

Pharmacology and Therapeutics

Investigating the biological interactions between advanced therapeutics, complex medicines and biomaterials,

Our research is aimed at investigating the biological interactions of conventional and complex medicines and therapeutics as well as other novel therapeutic strategies such as cellular therapies. This work encompasses the assessment of the immunocompatibility, and immunomodulatory potential, of these advanced therapeutics and complex medicines. An understanding of these, potential, interactions is vital to preclinical evaluation as well as enabling the future rational design of nanomaterials and therapies; and inflammation is key event in many Adverse Outcome Pathways (AOPs). In addition to immune and haematological systems, Dr Liptrott's team is also investigating impacts on cellular health and metabolism that may underpin these interactions, with a view to linking Critical Quality Attributes to biological performance using established, as well as novel, techniques and in vitro models. To date, the team's research has supported the successful translation of solid drug nanoparticle formulations, through GMP manufacture, towards healthy volunteer bioequivalence studies and the group continues to support developers of advanced therapeutics and complex medicines in their efforts to reach clinical studies. He was a founder member of the European Nanomedicine Characterisation Laboratory (EUNCL) and the Intracellular Drug Delivery Centre (IDDC).

Dr Liptrott is the coordinator for the Liverpool Nanotherapeutics Hub (NTH), Biocompatibility Theme Lead for the Centre of Excellence for Long-acting Therapeutics (CELT), member of the Intracellular Drug Delivery Centre (IDDC) steering committee and IDC taskforce, member of the Executive Board, Core Expert Team (CET) and Assay Group Leader (Immunotoxicity and Haematoxicity) for the European Nanomedicine Characterisation Laboratory (EUNCL) and platform manager for Nanotherapeutics within the Infection Innovation Consortium (iiCON).

Selected publications

Application of KU812 cells for assessing complement activation related effects by nano(bio)materials. Biomedicine and Pharmacotherapy. doi:10.1016/j.biopha.2023.114841

An inter-laboratory comparison of an NLRP3 inflammasome activation assay and dendritic cell maturation assay using a nanostructured lipid carrier and a polymeric nanomedicine, as exemplars. doi:10.1007/s13346-022-01206-6

Exposure of human immune cells, to the antiretrovirals efavirenz and lopinavir, leads to lower glucose uptake and altered bioenergetic cell profiles through interactions with SLC2A1. doi:10.1016/j.biopha.2022.112999

Professor David MacEwan

Chair of Molecular Pharmacology

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Pharmacology and Therapeutics

Research summary

Professor MacEwan's research investigates the signalling consequences of drug-induced alterations in clinically-relevant human cancers. Focussing on human leukaemias in particular, their efforts try to understand drug-resistant adaptations that allow cancers to fail chemotherapeutic destruction and evade therapy, so as to circumvent resistant cancers in future therapeutic strategies. Clinically-relevant mutations are introduced into human cancer cells using a variety of gene-manipulating techniques, such as CRISPR-Cas9 mutation, lentiviral knockdown or overexpression, siRNA, and miRNA manipulation. Adaptation upon signalling pathways and network are tested through a full range of molecular biological and multi-omic processes, with large dataset bioinformatic analyses performed. Pharmacological interests span all new drug types, but focus on many that are trialled in human leukaemias, covering tyrosine kinase inhibitors, checkpoint inhibitors, RAS oncogene and monoclonal antibody therapeutics.

Professor MacEwan is one of the authors of the global textbook 'Rang and Dale's Pharmacology', and a Senior Fellow of the Higher Education Academy.

Selected publications

Alexander SPH, Fabbro D, Kelly E, Mathie AA, Peters JA, Veale EL, ...MacEwan D et al,. (2023) The Concise Guide to Pharmacology 2023/24: Catalytic receptors British Journal of Pharmacology 180: S241-S288

Almutairi M, Lister A, Zhao Q, Line J, Adair K, Tailor A, Waddington J, Clarke E, Gardner J, Thomson P, Harper N, Sun L, Ostrov DA, MacEwan DJ, Pirmohamed M, Meng X, Zhang F, Naisbitt DJ (2023) Activation of Human CD8+ T Cells with Nitroso Dapsone-Modified HLA-B*13:01-Binding Peptides Journal of Immunology 210: 1031-1042

Stefanska B, Tucker SJ, MacEwan DJ (2022) New avenues in cancer prevention and treatment British Journal of Pharmacology 179: 2789-2794

Kilfoil P, Feng SL, Bassyouni A, Lee T, Leishman D, Li D, MacEwan DJ, Sharma P, Watt ED, Jenkinson S (2022) Characterization of a high throughput human stem cell cardiomyocyte assay to predict drug-induced changes in clinical electrocardiogram parameters European Journal of Pharmacology 912: 174584

Dr Gashirai Mbizvo

NIHR Academic Clinical Lecturer and Specialist Registrar in Neurology

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View staff profile

Pharmacology and Therapeutics

Health data approaches to epilepsy-related mortality and morbidity

The rise of digital care records has transformed treatment evidence generation by enabling both immediate and extensive analysis of national and international cohorts. This approach overcomes limitations in sample size, cost, and time associated with completing prospective studies while also facilitating exploration of previously unexamined patient outcomes.

Dr Mbizvo's research focuses on harnessing national and international health datasets to understand, predict and prevent mortality and morbidity in epilepsy. This builds on work completed during his PhD describing national trends in epilepsy-related mortality across Scotland using administrative health data, from which he built SEDS Score – the first ever risk prediction model for epilepsy-related deaths. Since then, he has begun working with causal inference and counterfactual prediction to understand risks related to discontinuation of sodium valproate. He is also looking at multistate models of epilepsy-related mortality and morbidity.

Dr Mbizvo was invited to present his work at Scottish Parliament in 2019 (www.epilepsy-institute.org.uk/eri/research/features/epilepsy-deaths-research-changing-policy/).

Selected publications

Mbizvo GK, Buchan I. Predicting seizure recurrence from medical records using large language models. Lancet Digit Health. 2023 Dec;5(12):e851-e852.

Mbizvo GK, Larner AJ. A treatable cause of dizziness: vestibular paroxysmia. Lancet. 2023 Jul 22;402(10398):e8.

Mbizvo GK, Schnier C, Simpson CR, Duncan SE, Chin RFM. Case-control study developing Scottish Epilepsy Deaths Study Score to predict epilepsy-related death. Brain. 2023 Jun 1;146(6):2418-2430.

Professor Peter McCormick

Associate Pro-Vice Chancellor for Postgraduate Affairs and International Partnerships

Chair in Pharmacology

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Pharmacology and Therapeutics

Cellular pharmacology for drug discovery

My lab studies the molecular underpinnings of disease. Our focus is on the role of the super family of G-protein coupled receptors (GPCR) in these mechanisms. Using a mix of biophysical, biochemical and cellular models, we study how GCPRs function as both monomers and oligomers and how they can be targeted to potentially treat numerous pathologies.

Selected publications

Tomas Bort, E., Joseph, M. D., Wang, Q., Carter, E. P., Roth, N. J., Gibson, J., . . . Grose, R. P. (2023). Purinergic GPCR-integrin interactions drive pancreatic cancer cell invasion. ELIFE, 12. doi:10.7554/eLife.86971

Israeli, H., Degtjarik, O., Fierro, F., Chunilal, V., Gill, A. K., Roth, N. J., . . . Shalev-Benami, M. (2021). Structure reveals the activation mechanism of the MC4 receptor to initiate satiation signaling. SCIENCE, 372(6544), 808-+. doi:10.1126/science.abf7958

Moreno-Delgado, D., Puigdellivol, M., Moreno, E., Rodriguez-Ruiz, M., Botta, J., Gasperini, P., . . . McCormick, P. J. (2020). Modulation of dopamine D1 receptors via histamine H3 receptors is a novel therapeutic target for Huntington's disease. ELIFE, 9. doi:10.7554/eLife.51093

Dr Xiaoli Meng

Lecturer

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View staff profile

Mechanistic understanding of drug-induced immunotoxicity

My main research interests are the use of advanced mass spectrometry-based multiomics techniques to investigate drug metabolism, explore drug-protein interaction/adduct, and discover HLA antigens that could lead to immunological reactions. My team has established a unique platform that integrates state-of the art analytical and immunological tools to address some of the most challenging questions in the field of drug hypersensitivity. We have developed analytical platforms to characterise drug-protein adducts in patients and within different cells including antigen presenting cells (B cells and dendritic cells), Keratinocytes, and hepatocytes. We were the first to show that drug-modified peptides can be presented by specific HLA alleles that can stimulate drug specific T cells. These studies will not only help understand the mechanisms of drug-induced immunotoxicity but also guide design novel therapeutics with improved efficacy and less toxicity.

Through collaborating with academic scientists, clinicians, and scientist in the pharmaceutical industry, we are developing novel assays for better diagnosis, prediction, and prevention of drug-induced immunotoxicity. Beyond drug-induced immunotoxicity, my group is also interested in developing novel T-cell based immunotherapies for the treatment of various diseases including cancer and autoimmune diseases.

Selected publications

Waddington, J. C., Meng, X*., Illing, P. T., Tailor, A., Adair, K., Whitaker, P., Hamlett, J., Jenkins, R. E., Farrell, J., Berry, N., Purcell, A. W., Naisbitt, D. J., and Park, B. K. (2020) Identification of Flucloxacillin-Haptenated HLA-B*57:01 Ligands: Evidence of Antigen Processing and Presentation. TOXICOL SCI 177, 454.

Amporndanai, K., Meng, X., Shang, W., Jin, Z., Zhao, Y., Rao, Z., Liu, Z. J., Yang, H., Zhang, L., O'Neill, P. M., Hasnain, S. S., and Rogers, M. (2021) Inhibition mechanism of SARS-CoV-2 main protease by ebselen and its derivatives. NAT COMMUN 12.

Meng, X*., Waddington, J. C., Tailor, A., Lister, A., Hamlett, J., Berry, N., Park, B. K., and Sporn, M. B. (2020) CDDO-imidazolide Targets Multiple Amino Acid Residues on the Nrf2 Adaptor, Keap1. J Med Chem 63, 9965.

Dr Ben Middlehurst

Tenure Track Fellow

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Pharmacology and Therapeutics

Research summary

have a keen interest in understanding the genetic underpinnings of neurodegenerative disorders, with a particular focus on motor neurone disease (MND) and Parkinson's disease (PD). These conditions considered as a growing concern within our society with awareness increasing each year, however, there has been a distinct lack of new therapeutics to treat them. One of our research interests aims to identify novel biomarkers within these diseases, utilising clinical data from studies such as the Trajectories of Outcome in Neurological Conditions (TONiC), which aims to improve the quality of life for people with MND. We can utilise the extensive clinical phenotypic data within TONiC and apply cutting edge genetic, epigenetic and transcriptomic analysis to identify novel biomarkers that predict disease progression. These approaches further our understanding of disease mechanisms and more importantly can lead to the identification of novel candidate drug targets to accelerate therapeutic development.

My other interests include the fundamental mechanisms that regulate the human genome, with a particular interest into the actions of retrotransposable elements. Retrotransposons make up nearly half of the human genome and have been implicated in a variety of diseases including neurodegeneration. They are active drivers of genome diversity and evolution through somatic mutation, acting through processes similar to that of retroviruses, often described as a 'copy and paste' mechanism. Our lab specialises in applying molecular biology techniques including PCR based genotyping, qPCR, CRISPR editing in established cell lines and iPSCs, anti-sense oligonucleotide knockdowns, transcription factor binding assays using ChIP, molecular cloning and luciferase-based reporter gene assays in cellular neuronal model systems.

Selected publications

Hall A, Middlehurst B, Cadogan MAM, Reed X, Billingsley KJ, Bubb VJ, Quinn JP. A SINE-VNTR-Alu at the LRIG2 locus is associated with proximal and distal gene expression in CRISPR and population models. Sci Rep. 2024 Jan 8;14(1):792. doi: 10.1038/s41598-023-50307-w. PMID: 38191889.

Fröhlich A, Hughes LS, Middlehurst B, Pfaff AL, Bubb VJ, Koks S, Quinn JP. CRISPR deletion of a SINE-VNTR-Alu (SVA_67) retrotransposon demonstrates its ability to differentially modulate gene expression at the MAPT locus. Front Neurol. 2023 Sep 29;14:1273036. doi: 10.3389/fneur.2023.1273036. PMID: 37840928; PMCID: PMC10570551.

Marshall JNG, Fröhlich A, Li L, Pfaff AL, Middlehurst B, Spargo TP, Iacoangeli A, Lang B, Al-Chalabi A, Koks S, Bubb VJ, Quinn JP. A polymorphic transcriptional regulatory domain in the amyotrophic lateral sclerosis risk gene CFAP410 correlates with differential isoform expression. Front Mol Neurosci. 2022 Sep 5;15:954928. doi: 10.3389/fnmol.2022.954928. PMID: 36131690; PMCID: PMC9484465.

Dr Anil Kumar Mondru

Teaching Fellow in Pharmacology

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Pharmacology and Therapeutics

Research summary

I completed B.Pharm, and M.Pharm in Pharmacology from Kakatiya University. I completed my PhD at the University of Liverpool in 2018. This was followed by postdoctoral training in the Department of Molecular & Clinical Cancer Medicine and Pharmacology & Therapeutics at the University of Liverpool in the area of chronic lymphocytic leukemia (CLL) and Malignant Melanoma to better understand cell signalling and drug resistance mechanisms.

My current research focuses on understanding the potential role of ERK5 in the development of drug resistance in melanoma. Melanoma is an aggressive form of skin cancer with increasing incidence and poor prognosis. In addition, drug resistance to various BRAFV600E inhibitors is a significant clinical challenge. My interest is to understand the role of ERK5 in BRAF inhibitor-induced resistance in melanoma cells. This involves co-culture and 3D spheroid cell models alongside pharmacological and genetic approaches to determine the complex mechanisms facilitating drug resistance. In addition, I investigate the role of ERK5 signalling pathway in acute myeloid leukemia (AML). Previous studies support the theory that targeting ERK5 signalling could have a therapeutic benefit in AML in the clinic as conjunctive therapy. I collaborate with Dr Michael Cross and Prof. Joseph Slupsky within ISMIB.

Selected publications

1Mondru AK, Aljasir MA, Alrumayh AA, Nithianandarajah GN, Ahmed K, Muller J, Goldring CEP, Wilm B, Cross MJ (2023). VEGF Stimulates Activation of ERK5 in the Absence of C-Terminal Phosphorylation Preventing Nuclear Localization and Facilitating AKT Activation in Endothelial Cells. Cells. 2023; 12, 967-985.

Roy S, Mondru AK, Chakraborty T, Das A, Dasgupta S. (2022). Apple polyphenol phloretin complexed with ruthenium is capable of reprogramming the breast cancer microenvironment through modulation of PI3K/Akt/mTOR/VEGF pathways. Toxicol Appl Pharm. 2022;434.

Linley AJ, Karydis LI, Mondru AK, D'Avola A, Al Shmrany H, Cicconi S, et al. (2021). Kinobead Profiling Reveals Reprogramming of BCR Signaling in Response to Therapy within Primary CLL Cells. Clinical Cancer Research. 2021;27(20):5647-59.

Professor Dean Naisbitt

Chair of Drug Safety Science

Director of the Immunopharmacology Lab

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View staff profile

Pharmacology and Therapeutics

Chemical and cellular basis of immunological drug reactions

I have developed practical and conceptual means to combine aspects of genetics, cell biology and chemistry in order to study the fundamental principles of drug and chemical hypersensitivity. This unique approach has allowed me to study immunological reactions from man to molecule and back again. A deeper understanding of such basic scientific principles can on the one hand inform clinical practice and on the other safe drug development in the Pharmaceutical Industry. Active innovative projects funded by the MRC and Pharma that highlight real-life impact include

i. Delivery of personalized drug treatment strategies to allergic patients. This allows us to make an impact clinically, by translating laboratory findings into patient care.

ii. Development of a toolbox of assays for drug immunogenicity prediction. Working alongside Pharma we have a pathway for application of the assays in a real-life setting.

iii. As leaders in mechanistic immunopharmacology, we are regularly approached by Pharma to explore the immunogenicity of drugs undergoing clinical trials.

Selected publications

Thomson P, Fragkas N, Kafu LM, Aithal GP, Lucena MI, Terracciano L, Meng X, Pirmohamed M, Brees D, Kullak-Ublick GA, Odermatt A, Hammond T, Kammüller M, Naisbitt DJ. Patients with naproxen-induced liver injury display T-cell memory responses toward an oxidative (S)-O-Desmethyl Naproxen metabolite but not the acyl glucuronide. Allergy. 2023 Jul 29. doi: 10.1111/all.15830.

Almutairi M, Lister A, Zhao Q, Line J, Adair K, Tailor A, Waddington J, Clarke E, Gardner J, Thomson P, Harper N, Sun Y, Sun L, Ostrov DA, Liu H, MacEwan DJ, Pirmohamed M, Meng X, Zhang F, Naisbitt DJ. Activation of Human CD8+ T Cells with Nitroso Dapsone-Modified HLA-B*13:01-Binding Peptides. J Immunol. 2023 Apr 15;210(8):1031-1042. doi: 10.4049/jimmunol.2200531.

Thomson PJ, Illing PT, Farrell J, Alhaidari M, Bell CC, Berry N, O'Neill PM, Purcell AW, Park KB, Naisbitt DJ.Modification of the cyclopropyl moiety of abacavir provides insight into the structure activity relationship between HLA-B*57:01 binding and T-cell activation. Allergy. 2020 Mar;75(3):636-647. doi: 10.1111/all.14057. Epub 2019 Oct 9

Dr Adeniyi Olagunju

Senior Lecturer

Wellcome Career Development Award Fellow

Centre of Excellence for Long-Acting Therapeutics (CELT)

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View staff profile

Pharmacology and Therapeutics

Research summary

Dr Adeniyi Olagunju is a member of the Centre of Excellence for Long-acting Therapeutics (CELT) where ongoing cutting-edge innovative research will transform drug delivery strategies for major disease burdens. He leads the Perinatal Pharmacology Group within CELT. The perinatal period represents a critical developmental window during which the health and wellbeing of future generations is laid down. Research within the Perinatal Pharmacology Group is focused on broadening our understanding of drug safety and efficacy during pregnancy and lactation. Working across three domains (human-relevant in vitro modelling, in silico modelling and clinical research), our goal is to generate actionable knowledge that will facilitate early recommendations for safe use of medicines during the perinatal period. In previous projects we elucidated the impact of maternal adaptations, host genetics and/or drug-drug interactions on drug exposure during pregnancy and lactation.

Dr Olagunju's vision for his research programme is to transform the assessment of drug safety during human pregnancy by developing a platform that will generate human pregnancy-relevant safety information early in drug development. This will facilitate decisions about situations where pregnant women can be safely included in early-phase clinical trials, enabling evidence-based, pregnancy-specific recommendations for potentially life-saving therapeutics. Ongoing work within the group is primarily funded by the Wellcome Trust.

The group is also leading new open access initiatives, including: (1) LAPaL(https://lapal.ch), the Long-acting Therapeutics Patents and Licences platform which tracks the clinical development, regulatory approval status and patents landscape of long-acting therapeutics globally; and (2) the PKRxiv (https://pkrxiv.org), a managed open access database and data visualization platform for post-print collaborative sharing of individual-level pharmacokinetic data and associated covariates, its early version focusing on pregnancy and postpartum.

Selected publications

Olagunju A, Mathad J, Eke A, Delaney-Moretlwe S, Lockman S. Considerations for the use of long-acting and extended-release agents during pregnancy and lactation. Clin Infect Dis. 2022 75(Supplement_4), S571-S578.

Atoyebi SA, Rajoli RKR, Adejuyigbe E, Owen A, Bolaji O, Siccardi M, Olagunju A. Using mechanistic physiologically-based pharmacokinetic models to assess prenatal drug exposure: Thalidomide versus efavirenz as case studies. European Journal of Pharmaceutical Sciences. 2019; 140:105068.

Olagunju A, Bolaji O, Amara A, Else L, Okafor O, Adejuyigbe E, Oyigboja J, Back D, Khoo S, Owen A. Pharmacogenetics of pregnancy-induced changes in efavirenz pharmacokinetics. Clinical Pharmacology & Therapeutics. 2015; 97(3):298-306.

Professor Paul O'Neill

Chair of Medicinal Chemistry

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View staff profile

Pharmacology and Therapeutics

Medicinal chemistry, drug discovery, organic synthesis and chemical biology

The O'Neill group operates at all stages of the drug discovery pipeline including hit triaging, hit to lead optimisation, lead optimisation to preclinical candidate selection with several active programmes ongoing at all of these stages. Currently the main target diseases of the group include malaria, Tb and human filariasis in collaboration with the Liverpool School of Tropical Medicine (LSTM). At Liverpool, Paul's group has candidate selected three novel antimalarials with one of these, Isoquine, entering clinical trials in 2008 in partnership with GSK. Since 2021, Paul has also been working with the Medicines's for Malaria Venture (MMV) on the discovery and development of novel 4-aminoquinolines without the herg liabilities or toxicity liabilities associated with currently used drugs such as amodiaquine.

In the last five years the Medicinal Chemistry group have undertaken research into novel antibacterial drugs for the treatment of filariasis as part of the Anti-Wolbachia (AWOL)Consortium, a drug discovery initiative run out of the Liverpool School of Tropical Medicine (LSTM). Within the Dept of Chemistry, medicinal chemistry optimisation of a screening hit led to a first in class drug candidate AWZ1066 which entered Phase 1 trials in 2022 in collaboration with Eisai Ltd. In related infectious disease drug discovery Paul's Group is working with the Biagini group at LSTM on anti-tubercular drug discovery and this collaboration has already made a strong impact through several MRC funded drug discovery projects. The most recent major research activity within the drug discovery group has been in the area of development of small molecule treatments of snake venom envenomation in a project funded by the Wellcome Trust (2.6 M funding, with Prof Nick Casewell, LSTM) .In addition to medicinal chemistry, Paul's group also works in the area of chemical biology and has contributed multiple papers on elucidation of the mechanisms of action of various classes of anti-infective agent with a particular focus on small molecule probe design. Paul has supervised 52 PhD students to completion, published 191 papers (WOS h-index =55, Google Scholar h-index = 70) and was awarded the Royal Society of Chemistry (RSC) Malcom Campbell Award for his antimalarial drug discovery research in 2011.

Selected publications

Amporndanai, K., Meng, X., Shang, W., Jin, Z., Zhao, Y., Rao, Z., . . . Rogers, M. (2021). Inhibition mechanism of SARS-CoV-2 main protease by ebselen and its derivatives. Nature Communications, 12(1). doi:10.1038/s41467-021-23313-7

Hong, W. D., Benayoud, F., Nixon, G. L., Ford, L., Johnston, K. L., Clare, R. H., . . . O'Neill, P. M. (2019).AWZ1066S, a highly specific anti-Wolbachia drug candidate for a short-course treatment of filariasis. PNAS,116(4), 1414-1419. doi:10.1073/pnas.1816585116

O'Neill, P. M., Amewu, R. K., Charman, S. A., Sabbani, S., Gnädig, N. F., Straimer, J., .et al. . A. (2017). A tetraoxane-based antimalarial drug candidate that overcomes PfK13-C580Y dependent artemisinin resistance. Nature Communications, 8. doi:10.1038/ncomms15159

Professor Sir Munir Pirmohamed

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View staff profile

Pharmacology and Therapeutics

Improving the benefit-risk ratio of medicines by understanding variability

Variability is the law of life – unfortunately this impinges on the effectiveness and safety of medicines we use in everyday clinical practice. Our research is therefore aimed at understanding the reasons for variability, and taking those findings into clinical practice to improve the benefit-risk ratio of medicines. Our work also includes evaluation of multimorbidity, and the complications associated with polypharmacy which is so prevalent in our population. To achieve this, we have a comprehensive research program which covers the whole spectrum from discovery to translation to application to implementation. This comprehensive approach has led to international recognition of our work in clinical pharmacology, pharmacogenetics, drug safety and personalised medicine. We use genomic and other omic techniques, as well as data science approaches to discover new genetic and clinical determinants of variability in drug action. Such discovery work is often followed by different studies, including laboratory studies and clinical trials, to further understand the mechanisms of variability, and develop solutions to overcome the variability. We have been actively trying to improve the diversity of the populations involved in our studies to ensure that our solutions are equitable for all populations, irrespective of ethnicity, geography and deprivation. We have extensive network of collaborations in the UK and worldwide, and also collaborate with industry partners.

I am Director of the Centre for Drug Safety Science, the Wolfson Centre for Personalised Medicine and HDR-North. I am Chair of the Commission on Human Medicines, and current President of the Association of Physicians. I am immediate Past President of the British Pharmacological Society, and am on the Scientific Advisory Boards of the Qatar Precision Medicine Initiative (Vice Chair), the Bosch Health Campus International Advisory Board in Germany, and Our Future Health. I am a Non-Executive Director for NHS England, a member of the MRC Council and a Medical Trustee for the British Heart Foundation. I am an honorary Fellow of the British Pharmacological Society, a Fellow of the Academy of Medical Sciences and an inaugural NIHR Senior Investigator. I am also highly cited researcher according to Clarivate.

Selected publications

Pirmohamed M, Burnside G, Eriksson N, Jorgensen AL, Toh CH, Nicholson T, Kesteven P, Christersson C, Whalstrom B, Stafberg C, Zhang JE, Leathart JB, Kohnke H, Maitland-Van Der Zee AH, Williamson PR, Daly AK, Avery P, Kamali F, Wadelius M. (2013). A Randomized Trial of Genotype-Guided Dosing of Warfarin. New England Journal of Medicine, 369(24):2294-303.

Thompson A, Cook J, Choquet H, Jorgensen E, Yin J, Kinnune T, Barclay J, Morris AP, Pirmohamed M. Functional validity, role, and implications of heavy alcohol consumption genetic loci. Sci Adv. 2020;6(3):eaay5034.

Swen, J. J., van der Wouden, C. H., ... Patrinos, G. P., Pirmohamed, M., Sunder-Plassmann, G., Toffoli, G., Guchelaar, H. J., & Ubiquitous Pharmacogenomics, Consortium. (2023). A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. Lancet, 401, 347-356.

Dr Sudeep Pushpakom

Lecturer in Pharmacology

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Pharmacology and Therapeutics

Pharmacogenetic and mechanistic studies to improve drug safety

I have a background in pharmacy and pharmacology with a PhD in disease genetics from the University of Manchester. I did my postdoctoral training in the National Genetics Reference Laboratory, Manchester and the Wolfson Centre for Personalised Medicine, University of Liverpool. My research interests are in personalised medicine (Pharmacogenetics) and drug safety with a focus on metabolic disease. I use in vitro, pharmacogenetic and clinical models alongside electronic health and omics data to understand the mechanistic basis of drug toxicity; to identify predictive biomarkers and; to develop therapeutic strategies to improve drug safety. My work on the metabolic toxicity of anti-HIV drugs has led to the identification of toxicity biomarkers and a phase II drug repurposing trial.

I am a Deputy Programme Director for the Pharmacology BSc programme; supervise Masters and PhD students and; holds a Fellowship of the Higher Education Academy (FHEA). I am a Board member for the Joint Centre for Pharmacology & Therapeutics established between the University of Liverpool and Xi'an Jiaotong-Liverpool University, Suzhou, China. I am also a member of the British Pharmacological Society (BPS) and UK Pharmacogenetics & Stratified Medicine Network.

Selected publications

Pushpakom S, Kolamunnage-Dona R, Taylor C, Foster T, Spowart C, García-Fiñana M, Kemp GJ, Jaki T, Khoo S, Williamson P, Pirmohamed M; TAILoR Study Group. TAILoR (TelmisArtan and InsuLin Resistance in Human Immunodeficiency Virus [HIV]): An Adaptive-design, Dose-ranging Phase IIb Randomized Trial of Telmisartan for the Reduction of Insulin Resistance in HIV-positive Individuals on Combination Antiretroviral Therapy. Clin Infect Dis. 2020; 70: 2062-2072. 10.1093/cid/ciz589

Sadiq S, Owen E, Foster T, Knight K, Wang L, M Pirmohamed, Clark RE, Pushpakom S. Nilotinib-induced metabolic dysfunction: insights from a translational pilot study using in vitro adipocyte models and patient cohorts. Leukemia. 2019; 33: 1810-1814. 10.1038/s41375-018-0337-0

Pushpakom S, Iorio F, Eyers PA, Escott KJ, Hopper S, Wells A, Doig A, Guilliams T, Latimer J, McNamee C, Norris A, Sanseau P, Cavalla D, Pirmohamed M. Drug repurposing: progress, challenges and recommendations. Nat Rev Drug Discov. 2019; 18:41-58. 10.1038/nrd.2018.168

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Pharmacology and Therapeutics

Research summary

Retrotransposons, which constitute almost 50% of our genome, are biomarkers of disease risk and progression. They are also functional regulatory domains which mechanistically are involved in diseases spanning cancer to neurodegeneration. Our current work focuses on their role in Motor Neuron and Parkinson's Disease. Mobilisation of retrotransposons, which has resulted in these elements being termed jumping genes, has resulted in the introduction of new regulatory domains throughout the human genome. Both germline and somatic de novo retrotransposition events have been involved in a range of human diseases. We are defining both the retrotransposon signatures underpinning neurodegeneration and their functional role in altering cell phenotype via epigenetic and transcriptional modulation. This is aided not only by molecular studies but also by the application of bioinformatics and machine-learning approaches to large data sets to better understand their role in the modulation of gene expression, epigenetic marks, cellular signalling, acting as regulatory RNA, immune modulation and chromatin 3D organization driving cellular phenotypic changes associated with neurodegeneration. Current therapeutics targeting somatic mobilisation include the repositioning of cancer drugs, RNA therapeutics and HIV drugs.

Our current work is integrated with International Consortia including ProjectMinE and the International Parkinson's Disease Genomic Consortium. More locally we have collaborations with Professor Young and her colleagues on studies addressing quality of life in motor neuron disease, entitled Trajectories of Outcome in Neurological Conditions (TONiC). This has expanded and now involves collaboration with Kings College London, Perron Institute in Perth and Xiangya Hospital, Changsha. Our focus on how the environment shapes gene expression led to highly successful collaborations in mental health with the 'Wirral Child Health and Development Study: First Steps' in the Institute of Population Health.

Selected publications

Billingsley, K. J, et al., Genome-Wide Analysis of Structural Variants in Parkinson Disease. Ann Neurol (2023). May;93(5):1012-1022. 10.1002/ana.26608

Pfaff, A.L., Bubb, V.J., Quinn, J.P. and Koks, S. (2021) Reference SVA insertion polymorphisms are associated with Parkinson's Disease progression and differential gene expression. NPJ Parkinsons Dis, 7, 44. 10.1038/s41531-021-00189-4

Savage, A.L., Schumann, G.G., Breen, G., Bubb, V.J., Al-Chalabi A., Quinn J. P. (2018) Retrotransposons in the development and progression of Amyotrophic Lateral Sclerosis. Journal of Neurology, Neurosurgery & Psychiatry; 90: 284-293. 10.1136/jnnp-2018-319210

Dr Laura Randle

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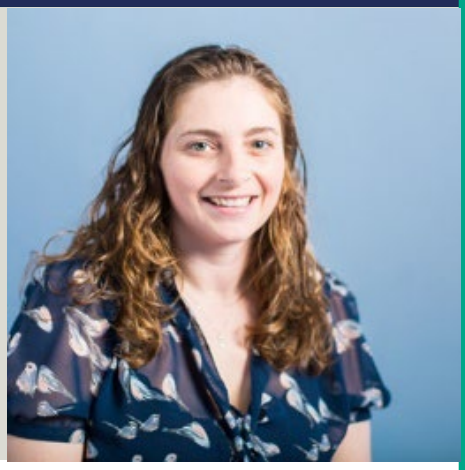

Pharmacology and Therapeutics

Investigating cholangiocarcinoma in precision-cut tumour slices to improve therapeutic response

Cholangiocarcinoma (CCA) is an aggressive hepatobiliary malignancy with increasing incidence and persistently poor prognosis. Late-stage diagnosis often precludes curative resection and chemoresistance means therapeutic options are limited. Since 2020, I have secured external funding from NC3Rs and North West Cancer Research to establish Precision cut tumour slices (hPCTS) in Liverpool. This has been facilitated by fruitful collaborations with colleagues at Liverpool University Hospital Trust, University of Liverpool, University of Surrey, Liverpool John Moores University and Astra Zeneca.

These patient derived, ex vivo 3D cellular structures can recapitulate critical aspects of cancer biology and crucially retain all aspects of the tumour microenvironment. I believe this translational model can bridge the gap from in vitro / in vivo models and man. Implementation of hPCTS has enabled me to begin to investigate hepatobiliary cancers to explore therapeutic drug response, cellular bioenergetics, the tumour immune-phenotype, validation of novel drug targets and aid in biomarker discovery. The versatility of this technique also means that it can easily be adapted for use on healthy and disease tissue from a variety of organs and species providing ample avenues for future exploration and collaboration.

I also have a keen interest in furthering our understanding of the chemical, biochemical and molecular mechanisms of drug-induced liver injury, particularly focusing on cellular defence and hepatoprotective mechanisms alongside developing novel safe anti-malarials.

Selected publications

Chidlow, S.J., Randle, L.E*. and Kelly, R.A., 2022. Predicting physiologically-relevant oxygen concentrations in precision-cut liver slices using mathematical modelling. PloS one, 17(11), p.e0275788 https://doi.org/10.1371/journal.pone.0275788

Eakins,R.*, Walsh, J.*, Randle, L*., Jenkins, R.E., Schuppe-Koistinen, I., Rowe, C., Starkey Lewis, P., Vasieva, O., Prats, N., Brilliant, N., Auli, M., Bayliss, M., Webb, S., Rees, J.A., Kitteringham, N.R., Goldring, C.E. and Park, B.K. (2015) Adaptation to acetaminophen exposure elicits major changes in expression and distribution of the hepatic proteome. Scientific Reports, 5: 16423. 10.1038/srep16423

Kitteringham, N.R., Abdullah, A., Walsh, J., Randle, L*., Jenkins, R.E., Sison, R., Goldring, C.E., Powell, H., Sanderson, C., Williams, S., Higgins, L., Yamamoto, M., Hayes, J. and Park, B.K. (2010). Proteomic Analysis Of Nrf2 Deficient Transgenic Mice Reveals Cellular Defence And Lipid Metabolism As Primary Nrf2-Dependent Pathways In The Liver. J. Proteomics, 73(8):1612-31. 10.1016/j.jprot.2010.03.018

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Antimicrobial Drug Discovery and Development and Medicinal Chemistry

Vision: "We aspire to bring new hope to improve and save lives currently lost due to antimicrobial resistance. We aim to achieve this by discovering and developing innovative molecules to refresh the AMR pipeline and provide new therapeutic options to tackle antimicrobial resistance."

Global media engagements on antimicrobial research with potential global impact: Invited interviews on antimicrobial research, featured in The Biomedical Scientist Magazine "Revolutionary thinking, Sky News, Sky News: Antibiotic could save millions of lives from superbugs after study eradicates MRSA in mice; The Independent: UK scientists' breakthrough could save millions from drug-resistant infections BBC Look North TV, ITV Calendar, BBC Radio Lincolnshire, Daily Mail, The Times, The Telegraph, Observer (Guardian), Chemistry World, China Daily, Geographical magazine, Eastern Eye

Collaborate locally and globally in AMR space some examples are **PK-PD:** Professor Das and Professor Hope, **Machine Learning / AI:** Professor Neil Berry, **Antimicrobial Surfaces:** Professor Rasmita Raval, Department of Chemistry, University of Liverpool, different aspects of AMR research (The Netherlands, Belgium, Italy, Germany, Singapore, and India.

Full member of EPSRC Peer Review College, Editorial board member, Molecules

Selected publications

Parmar, A. et al. Singh, I.... (2023) Development of teixobactin analogues containing hydrophobic, non-proteogenic amino acids that are highly potent against multidrug-resistant bacteria and biofilms. European Journal of Medicinal Chemistry. Available from : https://doi.org/10.1016/j.ejmech.2023.115853

Shukla, R. et al...Singh, I... (2020) Mode of action of teixobactins in cellular membranes. [Online] Nature Communications : https://doi.org/10.1038/s41467-020-16600-2

Parmar, A. et al. Singh, I..... (2018) Design and Syntheses of Highly Potent Teixobactin Analogues against Staphylococcus aureus, Methicillin-Resistant Staphylococcus aureus (MRSA), and Vancomycin-Resistant Enterococci (VRE) in Vitro and in Vivo. Journal of Medicinal Chemistry, 61(5), pp. 2009–2017: https://pubs.acs.org/doi/10.1021/acs.jmedchem.7b01634

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Pharmacology and Therapeutics

Research summary

Reecha Sofat is interested in making and using medicines better using a data science approach and by embedding research within routine clinical care.

Target discovery can be challenging and often because of failures in the drug development pipeline some disease areas continue be neglected. One way to overcome this but also enhance drug discovery is to identify targets in humans. I am interested in using the clinical contact as the point of recruiting to disease case collections and collecting repeat samples incorporating all multi-omics as well as linking bespoke clinical data to routine health data. This will enable us to understand the cause and consequence of disease in greater detail and understand appropriate molecular mechanisms to target at different stages of disease. Such an approach can enable enhanced drug and biomarker discovery.

Once in clinical use, it is essential to know that medicines are being used as intended and are having the effect that is intended, as well as being safe. Access to electronic health records linked to medicines data are now becoming increasingly available. I am interested in using such data sets to understand the clinical and cost-effectiveness of medicines, but also to begin to use causal inference methods in these and other (e.g. genetic) data sets to demonstrate reproposing opportunities as well as prioritisation of randomised controlled trials. To explore this area I have been awarded an NIHR Research Professorship.

Selected publications

Dale, C.E., Takhar, R., Carragher, R. et al. The impact of the COVID-19 pandemic on cardiovascular disease prevention and management. Nat Med 29, 219–225 (2023). https://doi.org/10.1038/s41591-022-02158-7

Sanghvi, S., Ferner, R. E., Scourfield, A., Urquhart, R., Amin, S., Hingorani, A. D., & Sofat, R. (2023). How to assess pharmacogenomic tests for implementation in the NHS in England. *British journal of clinical pharmacology*, *89*(9), 2649–2657. https://doi.org/10.1111/bcp.15820

Sofat, R., Hingorani, A. D., Smeeth, L., Humphries, S. E., Talmud, P. J., Cooper, J., Shah, T., Sandhu, M. S., Ricketts, S. L., Boekholdt, S. M., Wareham, N., Khaw, K. T., Kumari, M., Kivimaki, M., Marmot, M., Asselbergs, F. W., van der Harst, P., Dullaart, R. P., Navis, G., van Veldhuisen, D. J., … Casas, J. P. (2010). Separating the mechanism-based and off-target actions of cholesteryl ester transfer protein inhibitors with CETP gene polymorphisms. *Circulation*, *121*(1), 52–62. https://doi.org/10.1161/CIRCULATIONAHA.109.865444

Dr Katharine Stott

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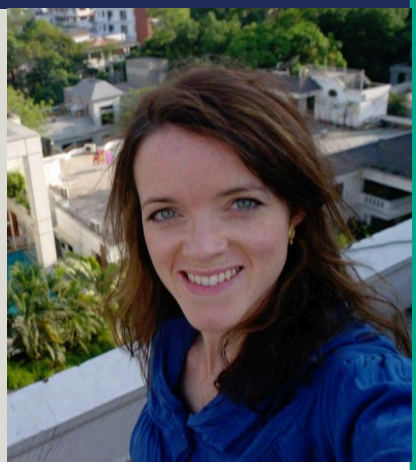

Pharmacology and Therapeutics

Optimising therapeutics for infectious diseases of unmet clinical need, including invasive fungal disease and antimicrobial resistance.

Dr Stott is an NIHR Clinical Lecturer in Infection Pharmacology at the University of Liverpool and a Specialist Medical Registrar in Clinical Pharmacology and General Internal Medicine. She undertook a Wellcome Trust-funded PhD fellowship to address health priorities in resource limited settings between 2017 and 2021. Dr Stott was awarded her PhD entitled The Pharmacokinetics and Pharmacodynamics Antifungal Agents for HIV-Associated Invasive Fungal Infections, from the University of Liverpool and in collaboration with Malawi-Liverpool Wellcome Trust Clinical Research Programme in 2021. She is currently working on in vitro and in vivo models of cryptococcal meningitis and invasive candidiasis to understand optimised treatment regimens including mitigating against antifungal resistance. She has ongoing collaborations at the University of Exeter, St George's hospital London, Duke University USA and the Broad Institute at Harvard, USA.

Dr Stott leads the Malawi-Liverpool Clinical Pharmacology Working group. She serves as a member of the British Infection Association Early Career Researcher Committee. She has teaching roles at the University of Liverpool, Liverpool School of Tropical Medicine, London School of Tropical Medicine and Hygiene and the University of Exeter.

Selected publications

Stott KE, Ahmadu A, Kajanga C, et al. Population pharmacokinetics and CSF penetration of flucytosine in adults with HIV-associated cryptococcal meningoencephalitis. The Journal of Antimicrobial Chemotherapy. 2023 Apr;78(4):1015-1022. 10.1093/jac/dkad038

Stott KE, Loyse A, Jarvis JN Alufandika M, Harrison T, Mwandumba HC, Day J, Lalloo DG, Bicanic T, Perfect JR, Hope W. Cryptococcal meningoencephalitis: time for action. The Lancet Infectious Diseases 2021; 21: e259-e71. 10.1016/S1473-3099(20)30771-4

Stott KE, Moyo M, Ahmadu A, et al. Population pharmacokinetics of liposomal amphotericin B in adults with HIV-associated cryptococcal meningoencephalitis. The Journal of Antimicrobial Chemotherapy. 2022 Dec;78(1):276-283. 10.1093/jac/dkac389

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Pharmacology and Therapeutics

Understanding of host responses to disease and pharmaceutical intervention with the aim to develop diagnostic tools and optimise treatments

We live in the era of artificial intelligence and large data collection and medicine is no exception. Pharmacogenomics are key to identifying the uniqueness of each patient and personalising clinical care, but our knowledge of the molecular world is still very limited. Hence, my choice to focus my research in understanding immune responses at the molecular level and from an individual patient perspective. This knowledge can help identify new targets for medical intervention, optimise current treatments and reduce drug toxicities.

Selected publications

Tsakiroglou M, Evans A, Pirmohamed M. Leveraging transcriptomics for precision diagnosis: Lessons learned from cancer and sepsis. Front Genet. 2023 Mar 10;14:1100352. 10.3389/fgene.2023.1100352

Cole C, Tsakiroglou M, Waitt C. Communication is crucial: Lessons from COVID-19 vaccination and pregnancy. Br J Clin Pharmacol. 2023 Feb;89(2):582-593. 10.1111/bcp.15578

Geretti AM, Tsakiroglou M. HIV: new drugs, new guidelines. Curr Opin Infect Dis. 2014 Dec;27(6):545-53. 10.1097/QCO.0000000000000106

Professor Catriona Waitt

Professor of Clinical Pharmacology and Global Health

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Pharmacology and Therapeutics

Safe effective use of medication in complex and understudied populations

Everybody deserves access to evidence needed to make informed decisions about their health. This is not possible when the evidence does not exist. Understanding of relative risks and benefits requires data. Worldwide more than half of all pregnant and breastfeeding women require treatment with medication at some point, and there are very scarce studies exploring the transfer of drug from mother to baby. Since 2015 I have been based in Uganda at the Infectious Diseases Institute, Makerere University College of Health Sciences to undertake my Wellcome Clinical Research Career Development Fellowship, MILK: Maternal and Infant Lactation pharmacoKinetics. This, and additional projects funded by EDCTP, Gates, Unitaid, NIHR and MRC, has built a research portfolio exploring pharmacokinetics, drug-drug interactions and medication safety in a range of understudied populations, primarily pregnant and breastfeeding mothers and their babies. This work includes pharmacometrics, clinical trials, bioanalytical methodology, public engagement and involvement and stakeholder engagement. We have published extensively on antiretrovirals, with more recent work investigating tuberculosis treatment (drug sensitive and drug resistant), antimalarials and antibiotics. I have a wide network of international collaborators and am part of the WHO HIV, Hepatitis and STIs Pregnancy and Breastfeeding Therapeutics Working Group.

Pharmacokinetic modelling techniques (both PBPK and population PK) are used to predict and understand drug exposure to the infant. I am on the Scientific Advisory Board for Pharmacometrics Africa. My work brought increased capacity in this area to Uganda and in 2021 my team launched the Uganda Chapter of Pharmacometrics Africa.

Community engagement and involvement is essential to ensure dialogue with the ultimate beneficiaries of our work at all stages. We have established a regular Community Advisory Board focussing on maternal and child health, social media channels, have produced several films accessible via our YouTube channel (At The Equator - YouTube), regular newsletters and have increasingly adopted participatory methodology.

Selected publications

Safety and pharmacokinetics of dolutegravir in pregnant mothers with HIV infection and their neonates: a randomised trial (DolPHIN-1 study) Waitt C et al, PLoS Med. 2019 Sep 20;16(9):e1002895. PMID: 31539371 10.1371/journal.pmed.1002895

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings. Waitt C et al Lancet HIV. 2018 Sep;5(9):e531-e536. PMID: 29960731 10.1016/S2352-3018(18)30098-5

A systematic review on maternal-to-infant transfer of drugs through breast milk during the treatment of malaria, tuberculosis, and neglected tropical diseases. Ojara FW, Kawuma AN, Waitt C.PLoS Negl Trop Dis. 2023 Jul 13;17(7):e0011449. 10.1371/journal.pntd.0011449

Dr Lauren Walker

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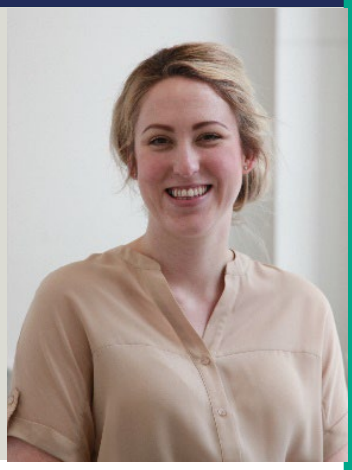

Develop, easy-to-use, artificial intelligence (AI) tools that support Healthcare professionals to manage complex polypharmacy

Dr Lauren Walker co-leads the DynAIRx programme, funded by the NIHR AI in multimorbidity stream and her research interest involves utilising existing health record data to understand how multiple long-term conditions, and their associated prescriptions, evolve over time and how these relationships between drugs and diseases lead to harm. She is very interested in predicting risk and examining patient journeys to identify at what point the harm of a medicine outweighs the potential for benefit. Lauren has co-developed a machine learning approach to identify disease and prescribing trajectories in people with complex care needs, utilizing existing health records (www.SERENDIP.org.uk).

She is also the Academic Director at the NIHR Clinical Research Facility at Liverpool University Hospitals NHS Foundation Trust and co-director of the Liverpool Early Phase Hub at the University of Liverpool. She is one of the senior investigators for the Agile trial,, the only UK Government-funded early-phase trial platform for Covid-19 therapeutics and chief investigator for repurposing high-dose nitazoxanide for Covid-19, a Unitaid-funded programme to ensure low-cost solutions worldwide.

Selected publications

Osanlou R, Walker L, Hughes DA, et al. Adverse drug reactions, multimorbidity and polypharmacy: a prospective analysis of 1 month of medical admissions. BMJ Open 2022;12:e055551. doi: 10.1136/bmjopen-2021-055551

Kuan, Valerie, Denaxas, Spiros, Patalay, Praveetha, Nitsch, Dorothea, Mathur, Rohini, Gonzalez-Izquierdo, Arturo, Sofat, Reecha, Partridge, Linda, Roberts, Amanda, Wong, Ian CK et al (show 5 more authors) (2023) Identifying and visualising multimorbidity and comorbidity patterns in patients in the English National Health Service: a population-based study. LANCET DIGITAL HEALTH, 5 (1). E16-E27. https://doi.org/10.1016/S2589-7500(22)00187-X

Walker LE, Abuzour AS, Bollegala D, et al. The DynAIRx Project Protocol: Artificial Intelligence for dynamic prescribing optimisation and care integration in multimorbidity. Journal of Multimorbidity and Comorbidity. 2022;12. 10.1177/26335565221145493

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Pharmacology and Therapeutics

Quantitative systems pharmacology, pharmacometrics, drug discovery and development

Antifungal Drug Discovery

Fungal diseases affect approximately 1.2 billion individuals worldwide with at least 1.5 million deaths each year. My interest is to discover and develop novel small molecule-based treatments with broad spectrum antifungal activity. This involves the assessment of novel targets, designing and screening small molecules, and drug development.

Cancer Patient Stratification

Tumour heterogeneity limits the efficacy of targeted cancer therapies and compromises treatment outcomes. My interest is to develop and validate novel algorithms which combine bioinformatics (genome-scale data characterising the patients, pre-treatments) with PK/PD modelling (tumour size changes in each patient, drug kinetics) to ultimately advise and optimise patient treatment outcomes.

Physiologically-based Pharmacokinetic Modelling of Vitamin D

Vitamin D is important for the prevention of osteoporosis and cancer. We have developed the world's first accurate PBPK model that predicts the serum pharmacokinetics profile of vitamin D3 and its active metabolite for an extremely wide range of doses of vitamin D3. This model predicts the population average behaviour. Currently, we are refining this model with the ultimate goal of accurately predicting individual serum profiles to advise clinical dose selection.

Selected publications

Agyeman AA, You T, et al. (2022) Comparative assessment of viral dynamic models for SARS-CoV-2 for pharmacodynamic assessment in early treatment trials. Br J Clin Pharmacol. doi: 10.1111/bcp.15518

Chinnery P, et al. (2021) Choosing drugs for UK COVID-19 treatment trials. Nat Rev Drug Discov. PMID: 34876668 DOI: 10.1038/d41573-021-00203-7

Huang ZH & You T. (2021) Personalise dose regimen of vitamin D3 using physiologically-based pharmacokinetic modelling. CPT Pharmacometrics Syst Pharmacol. 10.1002/psp4.12640

Professor Carolyn Young

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Pharmacology and Therapeutics

Research summary

Professor Young's two linked research programmes examine the varied clinical courses followed by people with multiple sclerosis and motor neuron disease, to develop insights which will improve care and quality of life (TONiC study) along with exploring the reasons for the differences in rate of progression and response to treatment (FINDeRS).

In addition, Professor Young is Principal Investigator in several drug treatment trials. Carolyn is deputy chair of NIHR MND CSG, a member of NIHR Neurosciences and NIHR Neurodegeneration Groups, Editor of the Cochrane MS Group, and the co-lead for NIHR CRN NWC in neurosciences. She leads a workstream in the UK MND Research Institute on integrating patient reported outcome measures into routine clinical care and improved clinical trial design.

Selected publications

Young CA et al. Multiple Sclerosis vision questionnaire (MSVQ-7): Reliability, validity, precision and discrimination. Mult Scler Relat Disord. 2023 Dec;80:105115. doi: 10.1016/j.msard.2023.105115

Young CA et al. Correlates and trajectories of relapses in relapsing-remitting multiple sclerosis. Neurol Sci. 2023 Nov 17. doi: 10.1007/s10072-023-07155-3

Young CA et al. Measuring disability in multiple sclerosis: the WHODAS 2.0. Qual Life Res. 2023 Nov;32(11):3235-3246. doi: 10.1007/s11136-023-03470-6

Young CA et al. Prevalence of depression in amyotrophic lateral sclerosis/motor neuron disease: multi-attribute ascertainment and trajectories over 30 months. Amyotroph Lateral Scler Frontotemporal Degener. 2023 Feb;24(1-2):82-90. doi: 10.1080/21678421.2022.2096410

Professor Susanne Voelkel

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Dean of the School of Biosciences

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Research summary

Professor Voelkel's research background and teaching is in the area of animal physiology. Her scholarship now focuses on educational research in the areas of student learning, assessment, and feedback. Her most recent work takes a nuanced look at the impact of lecture capture on student learning behaviours, finding that the availability of lecture recordings negatively influences a substantial subset of students.

As a member of the Society of Experimental Biology – Outreach, Education and Diversity Group, Professor Voelkel promotes scholarship and training for teaching focused academics. She holds a Masters in Learning and Teaching in Higher Education and was awarded the University of Liverpool Sir Alastair Pilkington Award for Teaching Excellence. Professor Voelkel is a National Teaching Fellow and a Principal Fellow (Advance HE).

Selected publications

1. Voelkel, S., Bates, A., Gleave, T., Larsen, C., Stollar, E. J., Wattret, G., & Mello, L. V. (2023). Lecture capture affects student learning behaviour. FEBS Open Bio. https://doi.org/10.1002/2211-5463.13548

2. Mello LV, Awais R, Sedghi G, Voelkel S (2022) Chinese students' awareness of and attitude towards employability skills. Developing Academic Practice. https://doi.org/10.3828/dap.2022.7

3. Voelkel S, Varga-Atkins T, Mello LV (2020) Students tell us what good written feedback looks like. FEBS Open Bio. 10(5), 692-7064. https://doi.org/10.1002/2211-5463.12841

4. Voelkel S, Mello LV, Varga-Atkins T (2016) Supporting students during their Undergraduate research projects using audio recordings. Innovations in Education and Teaching International. 55(4), 433-440. https://doi.org/10.1080/14703297.2016.1263233

Dr Fabia Allen

School of Biosciences

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Chief Editor, Insider Imprint student journal

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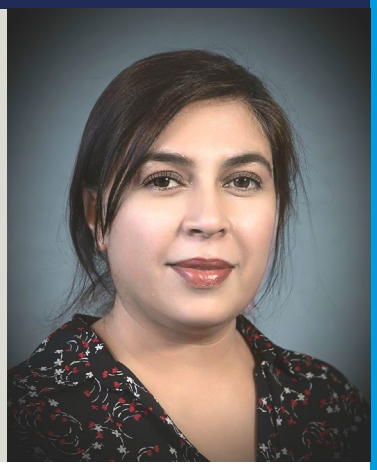
Research summary

Dr Allen's research background is protein structural studies using the technique X-Ray Crystallography. She undertook her PhD at the University of Sheffield, and her degree in Biochemistry at the University of Kent. She is interested in the role of diet in human health and disease.

Fabia has played a key role in the development of new MSc programmes at Liverpool and is programme director for the MSc in Biotechnology, delivering research-informed education to our students. She enjoys using innovative approaches to teaching, winning the Faculty Learning and Teaching prize for the course blog life-sciences-labs-explained.blogspot.com and the University of Liverpool Staff Award for Innovation of the Year for founding and sitting as chief editor of the student journal Insider Imprint.

Dr Raheela Awais

School of Biosciences



Senior Lecturer

Programme Director for integrated Master of Biological Sciences (MBiolSci)

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View staff profile

Unravelling the disease mechanisms and treatment strategies using optical tools

We develop *in-vitro* biochemical and functional assays based on advanced genetically- encoded fluorescent and bioluminescent reporters for imaging dynamic cellular signaling processes in real-time at the level of single living cells. Through these tools, we have advanced the understanding of the prolactin hormone regulation, inflammatory mechanisms through NF-kappaB signalling and cell death mechanism through p53, p63 and p73 family of proteins.

In a multidisciplinary project with the Molecular Biophysics group and the Department of Chemistry, we are currently exploring the pathophysiology of Amyotrophic Lateral Sclerosis (ALS) via superoxide dismutase misfolding and its inhibition as a treatment strategy. We are using genetically encoded optical tools such as Bimolecular Fluorescence Complementation techniques to monitor the engagement of target protein by the novel drugs for the treatment of ALS.

Selected publications

McNamara, A. V., Awais, R., Momiji, H., Dunham, L., Featherstone, K., Harper, C. V., . . . Davis, J. R. E. (2021). Transcription factor Pit-1 affects transcriptional timing in the dual-promoter human prolactin gene. Endocrinology. doi:10.1210/Endocr/bqaa249 DOI: 10.1210/endocr/bqaa249

Noda, N., Awais, R., Sutton, R., Awais, M., & Ozawa, T. (2017). Dynamic monitoring of p53 translocation to mitochondria for the analysis of specific inhibitors using luciferase-fragment complementation. Biotechnology and Bioengineering, 114(12), 2818-2827. doi:10.1002/bit.26407DOI: 10.1002/bit.26407

Ankers, J. M., Awais, R., Jones, N. A., Boyd, J., Ryan, S., Adamson, A. D., . . . White, M. R. H. (2016). Dynamic NF-kb and E2F interactions control the priority and timing of inflammatory signalling and cell proliferation. eLife, 2016(5). doi:10.7554/eLife.10473DOI:10.7554/eLife.10473

Dr Andrew Bates

School of Biosciences

Senior Lecturer in Biological Chemistry

Director of Admissions

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View staff profile

Research summary

Andy Bates is primarily a teacher and administrator in the School of Biosciences and is the School's Director of Admissions. He is a well-regarded lecturer, teaching biological chemistry and molecular biology to undergraduate students. He is an innovator in and enthusiast for teaching methodology, especially for flipped classrooms and the assessment of project work, and he heads the university's development of student evaluation of teaching.

In research, Andy is an expert in DNA topology, the understanding of the higher-order structures of DNA, including supercoiling, catenation and knotting, having written the definitive textbook in this area. He has worked extensively on the coupling of the free energy of ATP hydrolysis to the manipulation of DNA by type II topoisomerases, essential enzymes in all organisms and important targets for antibacterial and anticancer agents.

Selected publications

Bates, AD and Maxwell, A (2005) DNA Topology, Oxford University Press

Bates AD, Berger JM and Maxwell, A (2011) The ancestral role of ATP hydrolysis in type II topoisomerases: prevention of DNA double-strand breaks Nucleic Acids Res. 39: 6327-6339

Pyne, A.L.B., Noy, A., Main, K.H.S. et al. (2021) Base-pair resolution analysis of the effect of supercoiling on DNA flexibility and major groove recognition by triplex-forming oligonucleotides Nat Commun 2: 1053

Bednar, J, Furrer, P, Stasiak, A, Dubochet, J, Egelman,EH, Bates, AD (1994) The twist, writhe and overall shape of supercoiled DNA change during counterion-induced transition from a loosely to a tightly interwound superhelix: possible implications for DNA structure in vivo J. Mol. Biol. 235: 825-847

Dr Elinor Chapman

School of Biosciences

Lecturer

Programme Director for Biomedical Sciences

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View staff profile

Research summary

Dr Chapman is a lecturer in the School of Biosciences. She is Programme Director for Biomedical Sciences (C130) and is the Xi'an Jiaotong-Liverpool University (XJTLU) link tutor. Dr Chapman previously undertook research as a postdoctoral researcher on a number of biomedical projects including: the "Biology of dying", the "Molecular properties of neutrophil extracellular traps (NETs) in rheumatoid arthritis and systemic lupus erythematosus" and her PhD was in Chronic Lymphocytic Leukaemia. Dr. Chapman has wide ranging interests in blood sciences, cancer biology and therapy and immunology. She has an interest in proteomics, volatilomics and metabolomics.

Educationally, Dr Chapman is interested in assessment, practical classes and international student experiences. Dr Chapman plans to undertake some pedagogical / andragogical research in the near future.

Selected publications

GC-MS Techniques Investigating Potential Biomarkers of Dying in the Last Weeks with Lung Cancer (Journal article - 2023)

Optimisation of Urine Sample Preparation for Headspace-Solid Phase Microextraction Gas Chromatography-Mass Spectrometry: Altering Sample pH, Sulphuric Acid Concentration and Phase Ratio (Journal article - 2020)

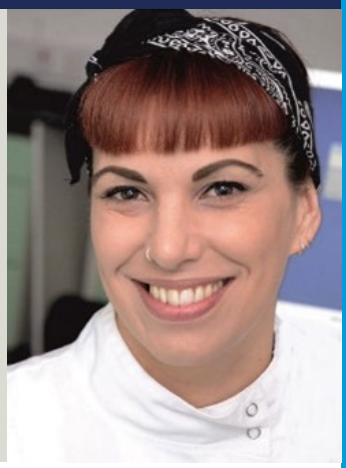
Caught in a Trap? Proteomic analysis of neutrophil extracellular traps in rheumatoid arthritis and systemic lupus erythematosus (Journal article - 2019)

Neutrophils and redox stress in the pathogenesis of autoimmune disease (Journal article - 2018)

Delineating the distinct role of AKT in mediating cell survival and proliferation induced by CD154 and IL-4/IL-21 in chronic lymphocytic leukemia (Journal article - 2017)

Dr Rachel Floyd

School of Biosciences



Senior Lecturer

Programme Director BSc Biological Sciences

Floyd78@liverpool.ac.uk

View staff profile

Virulence factors of uropathogens and identification of novel therapeutics

As a cellular and molecular physiologist and Programme Director for the Biological Sciences BSc undergraduate degree at the University of Liverpool, my research focuses on elucidating host-factors that modulate the pathogenicity and persistence of Gram-negative bacterial infections and how they might be manipulated therapeutically.

My current research focuses on the identification of novel therapeutics for Gram-negative infections, with a particular interest in the therapeutic application of lytic bacteriophage. My research combines molecular microbiology, genomics, cell biology and real-time live cell imaging in different in vitro models that recapitulate the in vivo environment.

Selected publications

Newman JN, Floyd RV, Fothergill JL. Invasion and diversity in Pseudomonas aeruginosa urinary tract infections. J Med Microbiol. 2022 Mar;71(3):001458. doi: 10.1099/jmm.0.001458. PMID: 35275806; PMCID: PMC9176269.

Floyd R, Upton M, Wray S, Hultgren S, Burdyga T, Winstanley C (2012 Journal of Infectious Diseases; doi: 10.1093/infdis/jis554. Escherichia coli-mediated impairment of ureteric contractility is UPEC-specific. IF 6.288 Editors pick

Floyd R, Winstanley C, Bakran A, Wray S, Burdyga T (2010). Modulation of ureteric Ca signalling and contractility in humans and rats by uropathogenic E. coli. Am J Physiol Renal Physiology 298(4):F900-8. IF 3.792

Dr Terry Gleave

School of Biosciences

Senior Lecturer

Education Lead for Institute of Systems, Molecular and Integrative Biology

tlgleave@liverpool.ac.uk

View staff profile

Research summary

Dr Gleave's scholarly activity and research has two main branches: the use of technology to enhance learning, and curriculum design and development. His technology branch focuses on the use of multimedia as blended learning resources, enhancing the learning environment and promoting engagement; Comparative Judgement analysis as a learning and feedback tool; promoting student engagement with feedback and reflection; development of learning communities to facilitate deeper learning; use of MOOCs to enhance student transitions, discipline engagement, and CPD; Lecture capture and its impact on student and educator engagement.

He is equally active in the design and development of strategies to facilitate a deep dive into curriculum review for effective change. In this he focuses on development of new curricula in partnership with employers, students and staff (from all areas of academia). He received the Sir Alastair Pilkington award in 2005, L&T award 2018 (MOOC), LTSE awards 2021 (Hybrid practicals) and 2022 (Science and Society Civic Service Award).

Selected publications

Gleave T, Goodman S. DON'T GO CHASING THE MARKS: A STUDY OF THE USE OF DIGITAL TOOLS TO ENCOURAGE LEARNER ENGAGEMENT WITH FEEDBACK AND REFLECTION 16th International Technology, Education and Development Conference, 07 Mar 2022 - 08 Mar 2022. INTED2022 Proceedings. IATED. Mar 2022 (Conference Paper)

Gleave T, Alston P, Prescott DE, Adamonyte V, Grubb B. B Supporting the transition to HE: Reflections and evaluation of the design, development and delivery of a MOOC to promote discipline engagement SOLSTICE, Edge Hill University, Ormskirk, 05 Jun 2019 - 06 Jun 2019. 05 Jun 2019 (Conference Paper)

Technologies in Biomedical and Life Sciences Education Approaches and Evidence of Efficacy for Learning, 2022. Published by Springer. ISBN-13: 978-3-0309-5632-5

Dr Kate Hammond

School of Biosciences

Senior Lecturer in Molecular Biology and Genetics

Programme Director Genetics BSc Hons

k.hammond@Liverpool.ac.uk

View staff profile

Research summary

Dr Hammond's research focusses on curriculum development within the field of genetics and molecular biology, particularly developing inclusive approaches to teaching and learning and enquiry-based learning during practical laboratory teaching.

Dr Hammond's recent focus has been on supporting autistic students during collaborative learning and in laboratory classes. She was also a member of the quality assurance agency for higher education (QAA) biosciences benchmark advisory group, leading the development of the equality, diversity and inclusivity sections of the biosciences benchmark statement, published in 2023.

Selected publications

Kate Hammond (in press). Sensory, communication & processing differences and collaborative learning. Don't forget about autistic students! Developing Academic Practice.

Helen Watson, Jonathan R Green, Jacqueline Nairn, Maureen Berg, Michael Ginger, Kate Hammond, Colin Hewitt, Janet Horrocks, Katharine Hubbard, Aisling Keane, Kevin Kendall, Gillian Knight, Georgina Manning, Sara Marsham, Lesley Morrell, Rana Parween, Richard Reece, Laura Roberts, Andrew Shore, Robert Watts, Salma Ali (2023). Subject Benchmark Statement (Biosciences) fifth edition. The Quality Assurance Agency for Higher Education. Subject Benchmark Statement: Biosciences (qaa.ac.uk)

Kate Hammond (2020). Precision medicine. Biological Sciences Review 33 (Nov), 22-26.

Dr Nigel Jones

School of Biosciences

Senior Lecturer in Genetics

N.J.Jones@liverpool.ac.uk

View staff profile

Research summary

Nigel's research interests lay primarily in the study of the DNA damage response (DDR) and the role that DNA repair mechanisms play in protecting against cancer. Specific areas of activity are the human genetic disorder Fanconi anaemia (e.g. DOI: 10.1016/j.molcel.2010.03.003) and the role of the dinucleotide Ap4A in the DDR (e.g. DOI: 10.1016/j.dnarep.2015.06.008). Fanconi anaemia (FA) is characterised by bone marrow failure, genetic instability and cancer predisposition. More than twenty FA genes have now been identified and the encoded proteins operate in a pathway to repair interstrand cross-links (ICL). The FA pathway protects cells from ICLs arising from endogenous aldehydes such as acetaldehyde and formaldehyde. Several of the FA genes are also breast cancer susceptibility genes, most notably FANCD1/BRCA2.

Nigel's research on FA has focused on the role of the proteins FANCG and FANCD2. In particular, how post-translational modifications modulate their activity, their protein binding partners and how they function in homologous recombination repair (DOI: 10.1038/sj.onc.1211034). Nigel's research has shown that FANCG & FANCD2 may have potential roles outside of the canonical FA pathway and are also likely to be involved in the development of a variety of cancers, including breast and cervical cancer (DOI: 10.2353/ajpath.2010.090779). Nigel is a Trustee of Fanconi Hope, a charitable trust set up by parents of Fanconi anaemia affected children and clinicians with an interest in FA

Selected publications

Thompson LH and Jones NJ (2010) Stabilizing and remodelling the blocked replication fork: anchoring FANCM and the Fanconi anaemia damage response Molecular Cell 37: 749-751

Rudland PS, Platt-Higgins AM, Davies LM, de Siva Rudland S, Wilson JB, Aladwani, A, Winstanley, JHR, Barraclough DL, Barraclough R, West CR and Jones NJ (2010) Significance of the Fanconi anaemia FANCD2 protein in sporadic and metastatic human breast cancer Am J of Pathology 171:1069-1072

Ferguson F, McLennan AG, Urbaniak MD, Jones NJ and Copeland NA (2020) Re-evaluation of Diadenosine Tetraphosphate (Ap4A): From a Stress Metabolite to Bona Fide Secondary Messenger Frontiers in Molecular Biosciences 7, 606807

Dr Carl Larsen

School of Biosciences

Senior Lecturer

C.Larsen@liverpool.ac.uk

View staff profile

Research summary

Dr. Larsen's research focuses on the function and evolution of facial bristles in birds. Dr Larsen also works in pedagogy and in particular, race equity, and is the PI of a study exploring the awarding gap between Black and White STEM undergraduates.

Selected publications

Voelkel, S., Bates, A., Gleave, T., Larsen, C., Stollar, E. J., Wattret, G., & Mello, L. V. (2023). Lecture capture affects student learning behaviour. FEBS OPEN BIO. doi:10.1002/2211-5463.13548 2022

Delaunay, M. G., Brassey, C., Larsen, C., Lloyd, H., & Grant, R. A. (2022). The evolutionary origin of avian facial bristles and the likely role of rictal bristles in feeding ecology. SCIENTIFIC REPORTS, 12(1). doi:10.1038/s41598-022-24781-7 2020

Delaunay, M. G., Larsen, C., Lloyd, H., Sullivan, M., & Grant, R. A. (2020). Anatomy of avian rictal bristles in Caprimulgiformes reveals reduced tactile function in open-habitat, partially diurnal foraging species. Journal of Anatomy, 237(2), 355-366. doi:10.1111/joa.13188 2019

Delaunay, M. G., Larsen, C., & Grant, R. A. (2019). Avian Facial Bristles, are they Analogous to Mammalian Whiskers?. In JOURNAL OF MORPHOLOGY Vol. 280 (pp. S107).

Dr Alice Maher

School of Biosciences

Lecturer

Alice.Maher@liverpool.ac.uk

View staff profile

The evolution, ecology and locomotion of vertebrate species

My research and interests are Zoology and Palaeontology based, with a desire to contribute to our understanding of animal ecology and evolution. In particular, my research focuses on how body shape has had a fundamental impact on organismal function in a wide array of vertebrate species.

Selected publications

Maher, A. E., Burin, G., Cox, P. G., Maddox, T. W., Maidment, S. C. R., Cooper, N., . . . Bates, K. T. (2022). Body size, shape and ecology in tetrapods. NATURE COMMUNICATIONS, 13(1). doi:10.1038/s41467-022-32028-2. DOI: 10.1038/s41467-022-32028-2

Biological Sciences Review. Maher, A. (2022). Biological Sciences Review.

Maher, A. E., Cox, P. G., Maddox, T. W., & Bates, K. T. (2021). The evolution of body shape in terrestrial tetrapods. In INTEGRATIVE AND COMPARATIVE BIOLOGY Vol. 61 (pp. E560-E561). Retrieved from https://www.webofscience.com/

Macaulay, S., Hoehfurtner, T., Cross, S., Marek, R., Hutchinson, J., Schachner, E., . . . Bates, K. (2023). Decoupling body shape and mass distribution in birds and their dinosaurian ancestors. Nature Communications, 14. doi:10.1038/s41467-023-37317-y. DOI: 10.1038/s41467-023-37317-y

Professor Luciane V Mello

School of Biosciences

Deputy Dean of the School of Biosciences

Professor of Bioscience Education

PGT Lead

Luciane.Mello@liverpool.ac.uk

View staff profile

Research summary

Professor Mello's research focuses mainly on Education where she explores teaching approaches helping with student engagement and employability skills development. She acts as the Editor-in-Chief for the Education section of the FEBS OpenBio. Luciane teaches bioinformatics at undergraduate and postgraduate levels. Her passion for teaching bioinformatics has been recognised by four Teaching Awards: 2013 and 2016 Excellence in Teaching and the 2015/16 Sir Alistair Pilkington, and 2019 Biochemical Society Teaching Excellence.

As part of the Biochemical Society, she leads the Training Theme Panel where she works with bioscientists and other academics across multiple institutions on the development of training in different areas of biochemistry and education. She also delivers training in association with FEBS.

Selected publications

Voelkel S, Bates A, Gleave, T, Larsen C, Stollar EJ, Wattret, G and Mello LV (2023). Lecture capture affects student learning behaviour. FEBS Open Bio. DOI: 10.1002/2211-5463.13548

Dusi DMA, Alves ER, Cabral GB, Mello LV, Rigden DJ, Silveira ED, Alves-Ferreira M; Guimarães LA, Gomes ACMM, Rodrigues JC, Carneiro VTC (2023) An exonuclease V homologue is expressed predominantly during early megasporogenesis in apomictic Brachiaria brizantha. Planta 258(5). DOI: 10.1007/s00425-023-04162-8

Horder JL, Connor A., Duggan AL, Hale JJ, McDermott FJ, Norris LE, Whinney SJD, Mesdaghi S, Murphy DL, Simpkin AJ, Mello LV, Rigden DJ (2023) Deep Learning-based structural and functional annotation of Pandoravirus hypothetical proteins. bioRxiv. DOI: 10.1101/2023.12.02.569716

Dr Chris Mitchell

School of Biosciences

Lecturer

Christopher.Mitchell@liverpool.ac.uk

View staff profile

Research summary

Dr Mitchell's research investigates the evolution of cognition in animals. This involves identifying and evaluating cross-species measures of cognitive complexity and using these measures to test hypotheses concerning the evolution of cognitive complexity. Historically this kind of research has been focused on primates. The principle aim of Dr Mitchell's research is to expand this focus beyond primates to test theories in other taxonomic groups. In his current work this includes cetaceans (whales, dolphins & porpoises), cephalopods (octopuses, cuttlefish and squid), insects and even non-avian dinosaurs amongst others. In order to study these groups, this research makes use of large comparative datasets and modern comparative methods.

Dr Mitchell leads the Comparative Research Group within the School of Biosciences. This group is made up of staff and students using phylogenetically controlled statistical methods for comparative research. The group provides training and resources for the use of phylogenetic controls in comparative research. Dr Mitchell also does pedagogic research seeking to improve the student experience in our statistics teaching provision and decolonising the Life Sciences curriculum.

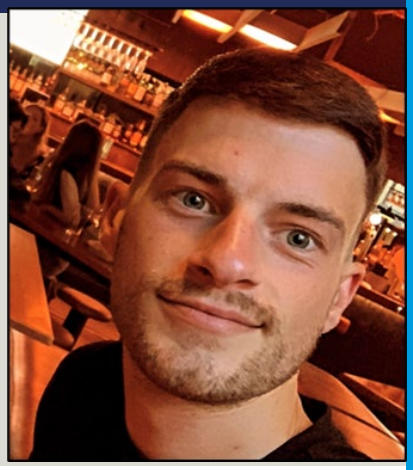
Selected publications

Mitchell C (2018) The evolution of large brains and advanced cognitive abilities in animals PhD Thesis, University of Liverpool

Mitchell C (2016) The evolution of brains and cognitive abilities Evolutionary Biology: Convergent evolution, evolution of complex traits, concepts and methods. pp73 – 87. Springer International Publishing

Dr Rob Morris

School of Biosciences



Lecturer

R.Morris10@liverpool.ac.uk

View staff profile

Research summary

Dr Morris' research is largely focused on the molecular biology of economically important nematodes, such as the parasitic threadworm (Strongyloides spp.) and beneficial nematodes (entomopathogenic nematodes). Strongyloides species are of particular interest due to their rare developmental switch that can produce parasitic and free-living offspring, offering a rather unique model to underpin the molecular basis of parasitism. Biological control of crop pests using beneficial nematodes that predate on insects are also of keen interest to Rob as they may provide effective biological control, replacing the need for harmful anti-insecticides. Molecular biology, genomics, transcriptomics and computational biology are his main teaching areas.

Selected publications

Morris, R., Wilson, L., Sturrock, M., Warnock, N. D., Carrizo, D., Cox, D. & Dalzell, J. J. (2017). A neuropeptide modulates sensory perception in the entomopathogenic nematode Steinernema carpocapsae. PLoS pathogens, 13(3), e1006185.

Warnock, N. D., Cox, D., McCoy, C., Morris, R., & Dalzell, J. J. (2019). Transcriptional variation and divergence of host-finding behaviour in Steinernema carpocapsae infective juveniles. BMC genomics, 20, 1-17.9

Viney, M., & Morris, R. (2022). Approaches to studying the developmental switch of Strongyloides–Moving beyond the dauer hypothesis. Molecular and Biochemical Parasitology, 249, 111477.

Dr Kelly Ross

School of Biosciences

Lecturer

Deputy Programme Director Biological Sciences

kelly.ross@liverpool.ac.uk

View staff profile

Research summary

Dr Ross' research centres on evolutionary respiratory physiology, focusing on haemoglobin (Hb) function in mammals. They have a specific interest in inter- and intraspecific variation in blood oxygen (O2) affinity. Their work explores the drivers that have shaped the O2 biding properties of the respiratory protein Hb, drawing upon a multidisciplinary approach that integrates physiology, ecology, genetics, and evolutionary biology. Using phylogenetic frameworks, information-theoretic methods and detailed studies of Hb-O2 binding characteristics, Dr Ross aims to shed light on the underpinning physiological demands that may drive variation in mammalian blood-O2 affinity, such as alternative O2 environments, mass-specific metabolic rate and early life history traits. They hope that their research will contribute to a more comprehensive understanding of the evolutionary dynamics that have shaped mammalian diversity, with potential implications for fields ranging from ecology and conservation biology and medicine.

Selected publications

Ross, K. (2023). Causes and consequences of evolved variation in mammalian blood oxygen affinity – effects of metabolic rate, environment, lifestyle and early life history parameters. Doctoral thesis, University of Liverpool.

Dr Alec Simpson

School of Biosciences

Senior Lecturer

Director MRes Biomedical Sciences and Translation Medicine

Awms@liverpool.ac.uk

View staff profile

Research summary

My research has mostly focused on various aspects of Ca2+ signalling and the use of novel tools to measure intracellular Ca2+, mitochondrial Ca2+ and most recently extracellular Ca2+. This work has included Ca2+ and platelet function, single cell measurements of Ca2+ and tension in smooth muscle and the regulation of mitochondrial Ca2+ using targeted recombinant aequorin. Current areas of interest include the role of extracellular Ca2+ in regulating epidermal function and cyclic-GMP mediated cyto-protection via activation of the PMCA (leading to a reduction in cytotoxic elevations of intracellular Ca2+). We have recently developed a series of novel probes to measure extracellular Ca2+ within tissues and tissue models.

Selected publications

Rizzuto, R., Simpson, A.W.M., Brini, M. and Pozzan, T. (1992). Rapid changes in mitochondrial Ca2+ revealed by specifically targeted recombinant aequorin.
Nature 358, 325-327

Ishii, N., Simpson, A.W.M. and Ashley C.C. (1989). Free calcium at rest during catch in single smooth muscle cells. Science 243, 1367-1368.

Green, A.K., Zolle, O. and Simpson A.W.M. (2002). Atrial natriuretic peptide attenuates Ca2+ oscillations in rat hepatocytes by modulating plasma membrane Ca2+ fluxes. Gastroenterol. 123, 1291-1203

.Voronina, S.G., Barrow, S.L., Simpson, A.W.M., Gerasimenko, O.V., Xavier, G.D., Rutter, G.A., Petersen, O.H., Tepikin, A.V. (2010) Dynamic changes in cytosolic and mitochondrial ATP levels in pancreatic acinar cells. Gastroenterology 138, 1976-U111

Professor Mike Speed

School of Biosciences

Personal Chair

Programme Director Human Physiology BSc

speedm@liverpool.ac.uk

View staff profile

Coevolution of defence and communication, computational measurement of evolutionary convergence

My research focuses on:

1) Animal Communication, with a focus on the stability of communication systems which are vulnerable to cheating. I use advertisement of prey defences as a case-study in communication, especially where animals use costly, bright colouration to signal to their enemies.

2) Evolutionary Bioinformatics Research: focuses on generating statistical measures to evaluate the predictability of phenotype evolution. It asks, are life's forms limited by the narrow range of engineering solutions to life's challenges?

3) Coevolution and plant secondary metabolites - seeks general explanations for the notorious diversification of plant metabolisms.

Selected publications

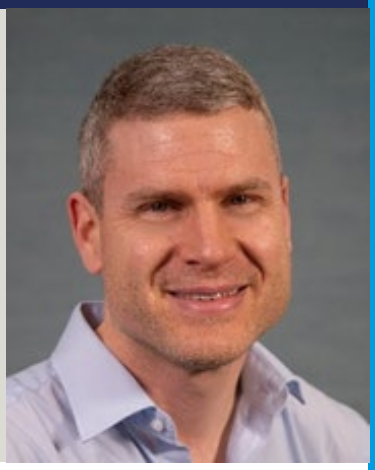
Ruxton, G.D., Allen, W.L., Sherratt, T.N. and Speed, M.P., 2019. Avoiding attack: the evolutionary ecology of crypsis, aposematism, and mimicry. Oxford university press.

Arbuckle, K. and Speed, M.P., 2015. Antipredator defenses predict diversification rates. Proceedings of the National Academy of Sciences, 112(44), pp.13597-13602.

Arbuckle, K., Bennett, C.M. and Speed, M.P., 2014. A simple measure of the strength of convergent evolution. Methods in Ecology and Evolution, 5(7), pp.685-693.

Dr Elliott Stollar

School of Biosciences



Senior Lecturer

Programme Director Biochemistry BSc and Mbiol

E.Stollar@liverpool.ac.uk

View staff profile

Uncovering protein structure, dynamics and interactions using SH3 domains

We use protein interaction domains as a model group of proteins to investigate the molecular basis of protein interaction specificity. We study the SH3 domain family in yeast which contains 28 family members in 24 proteins, with a particular focus on the SH3 domain from the yeast protein Abp1p.

Our experimental approaches range from basic molecular biology such as cloning/mutagenesis, through biochemistry including purification and quantitative analysis of binding equilibria (both in vitro and in vivo), to biophysical methods including nano differential scanning fluorimetry, isothermal titration calorimetry and NMR spectroscopies. Additionally, we employ complimentary bioinformatic approaches to study structural predictions and amino acid conservation patterns of SH3 domain paralogs and orthologs. By comparing the structural, functional and evolutionary features of many interactions, we hope to distill out the generalities that are essential for understanding the basis of molecular recognition. Our studies uncover the complexities of protein-protein interaction specificity, which, may also have impact in drug development.

Selected publications

KEY: 1 Undergraduates, 2 Master's students, 3 Secondary school students, *Corresponding Author

Jaramillo-Martinez V2, Dominguez MJ2, Bell GM1, Souness ME1, Carhart AH1, Cuibus MA1, Masoumzadeh E, Lantz BJ1, Adkins AJ1, Latham MP, Ball KA, Stollar EJ* (2023) How a highly acidic SH3 domain folds in the absence of its charged peptide target. Protein Science. Mar 29;e4635

Brown T, Brown N3, Stollar EJ* (2018) Most yeast SH3 domains bind peptide targets with high intrinsic specificity. PLoS ONE 13(2).

Stollar EJ*, Lin H, Alan R. Davidson AR , Forman-Kay JD* (2012) Differential dynamic engagement within 24 SH3 domain:peptide complexes revealed by co-linear chemical shift perturbation analysis. PLoS ONE 7(12).

Dr Rebecca Verspoor

School of Biosciences

Lecturer in Behavioural Ecology

Programme Director BSc Bioveterinary Sciences

Rebecca.Verspoor@liverpool.ac.uk

View staff profile

Research summary

Dr Verspoor's research focuses on anti-predator defences, focusing on parasite induced aposematism. This predominately takes place in the field but has included travel to Finland to work with avian predators in a laboratory setting. The ultimate goal of her research is to understand multi-modal anti-predator signalling and its evolution. Dr Verspoor has also started to investigate the impacts on her teaching on students as well through pedagogic research. Her research here focuses on the impact of teaching statistics via the programming language R on student assessment and understanding, as well as equality and diversity. Dr Verspoor has won the Sir Alistair Pilkington teaching prize for her work in this subject area.

Selected publications

Jones, R. S., Fenton, A., Speed, M. P., & Mappes, J. (2017). Investment in multiple defences protects a nematode-bacterium symbiosis from predation. Animal Behaviour, 129, 1-8.

Jones, R. S., Speed, M. P., & Mappes, J. (2016). Parameterising a public good: how experiments on predation can be used to predict cheat frequencies. Evolutionary Ecology, 30(5), 825-840.

Jones, R. S., Fenton, A., & Speed, M. P. (2016). "Parasite-induced aposematism" protects entomopathogenic nematode parasites against invertebrate enemies. Behavioural Ecology, 27(2), 645-651.

Dr Rudi Verspoor

School of Biosciences

Lecturer

R.Verspoor@liverpool.ac.uk

View staff profile

Research summary

Dr Verspoor's teaching and research focuses on the use of entomology, behaviour and the evolution of selfish genetic elements. In particular, his work in entomology explores the use of edible insects as food and feed.

Another role he is passionate about is outreach and public engagement. In this role, Rudi organises and leads events within the school aimed at engaging schools and the public about science, with a particular focus on disseminating research carried out at the University of Liverpool.

Selected publications

Lyth, S., Betancourt, A. J., Price, T. A. R., & Verspoor, R. L. (2023). The suppression of a selfish genetic element increases a male's mating success in a fly. Ecology and Evolution, 13(11).

Verspoor RL, Price TAR, Wedell N 2020 Selfish genetic elements and male fertility. Phil Trans Roy Soc B 375(1813), 20200067

Verspoor RL, ..., Landberg R 2020 Mineral analysis reveals extreme manganese concentrations in wild harvested and commercially available edible termites. Sci Reports 10(1), 1-9

Siozios S, Massa AR, Parr CL, Verspoor RL, Hurst GDD 2020 DNA Barcoding reveals uncertainty of identity labelling for insects sold as food in the UK. PeerJ 8, e8496.

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Research summary

Dr Wattret's research focuses on the development of transferrable skills and employability in students. As part of this she has evaluated the impact of implementing authentic assessments to develop students' skills such as video interviews and the impact of enterprise education. Gemma's research also focuses on widening participation, inclusivity and enhancing student success. Not only seeking to remove barriers and improve access to education for underrepresented groups, but also to improve success within higher education and improve progression to employment.

Gemma was awarded the 2021/22 Learning, Teaching and Student Experience Award and the 2021/22 Sir Alistair Pilkington Award for Developing Life Sciences Students' Digital Fluency and Employability at scale through authentic assessment. She was also awarded the 2022/23 Learning, Teaching and Student Experience Award for Enterprise in the Life Sciences Challenge. Gemma is also a member of the editorial advisory board for the Developing Academic Practice Journal.

Selected publications

Voelkel, S., Bates, A., Gleave, T., Larsen, C., Stollar, E. J., Wattret, G., & Mello, L. V. (2023). Lecture capture affects student learning behaviour. FEBS OPEN BIO. DOI: 10.1002/2211-5463.13548

Chaloner, G., Lacharme-Lora, L., Wedley, A., & Wigley, P. (2023). Use of Galleria mellonella as a Model for Insect Vector Transmission of the Foodborne Pathogen Campylobacter jejuni in Broiler Chickens: A Pilot Study. Poultry, DOI: 10.3390/poultry2010005

Wattret, G. and Delaney, J. (2022) Slivers of Silver Case Study: Developing Students' Digital Fluency and Employability at Scale Through Authentic Assessment : https://www.youtube.com/watch?v=QOF9L7QdhkA