CENTRE for MEDICINES DISCOVERY

NUFFIELD DEPARTMENT of MEDICINE

UNIVERSITY OF OXFORD

Centre for Artificial Intelligence in Precision Medicine (CAIPM)

Drug Discovery

Knowledge Exchange Programme

2024

9th to 18th September 2024

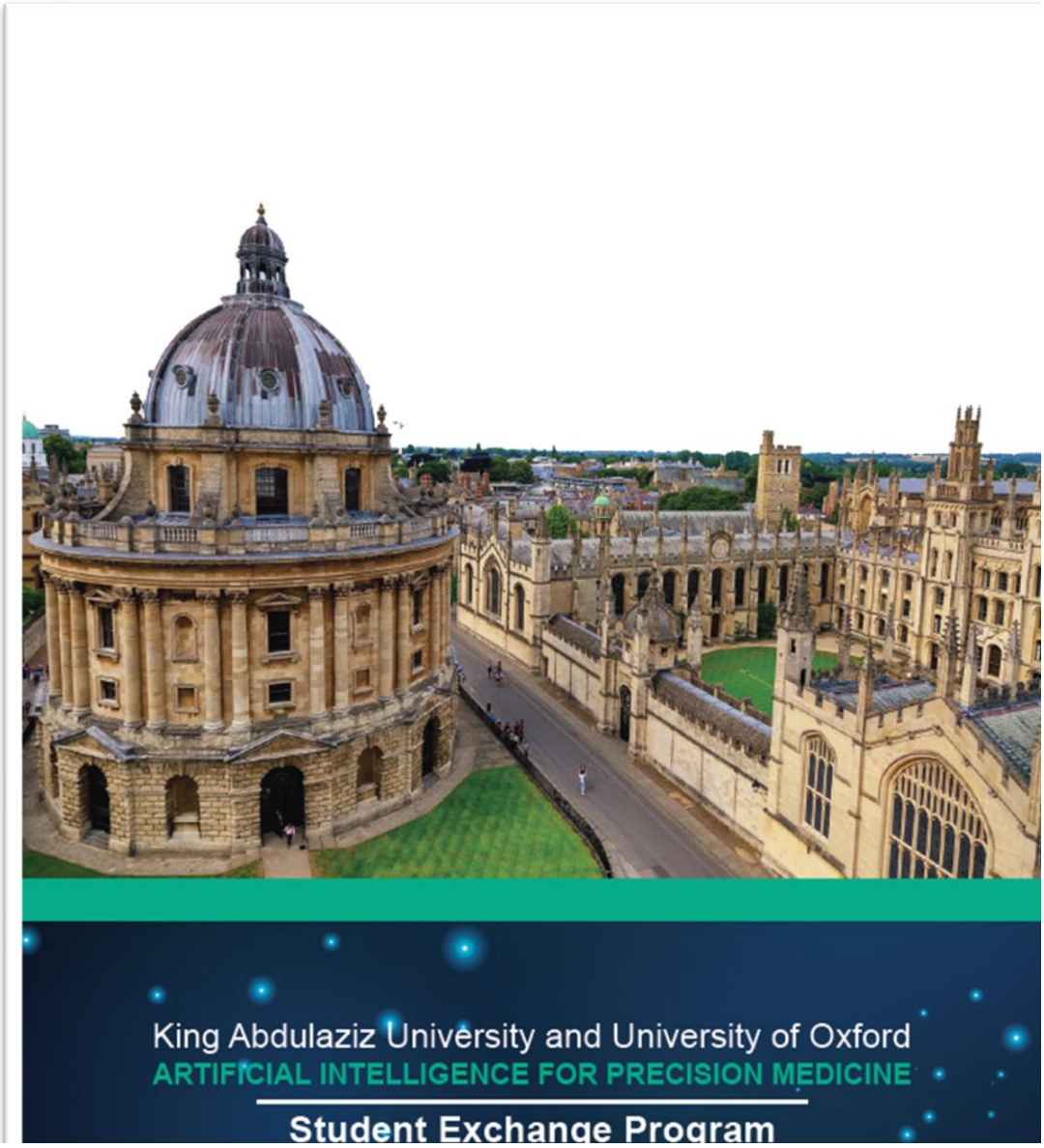
Centre for Artificial Intelligence in Precision Medicines
مركز الذكاء الإصطناعي في العلاجات الدقيقة

UNIVERSITY OF OXFORD | KING ABDULAZIZ UNIVERSITY

Contents

Overview

From Monday September 9th to Thursday September 18th the Centre for Medicines Discovery (CMD), University of Oxford, will host 20 students from Kind Abdulaziz University for an intensive 2-week course of online seminars. The content of the course will cover a wide range of topics related to the work of the Centre for Artificial Intelligence in Precision Medicine (CAIPM), which is a collaborative research Centre co-founded



Programme Content

The principal aim of the programme is to give students an insight into the field of Drug Discovery and how it is developing with the help of new AI technologies. The curriculum will draw on the wide range of world-class expertise possessed by members of the CMD, colleagues elsewhere in Oxford working in similar fields, and colleagues in industry.

Seminar topics will include discussion of early stage drug discovery, insights into Neural Network (NN) technology and its application to drug discovery, drug development in the pharmaceutical industry, and more.

Alongside the series of seminars, students will complete a research project focussing on drug discovery & bioinformatics. Students will use real resources and methods based on the principles followed by researchers at the CAIPM.

Programme – 1st week

Day	Date	Chair	Start	Activity	Title	Speaker(s)
Mon	09-Sep	Karen Froud	09:00	Introduction	*Welcome: Innovation and the Future of Drug Discovery*	Prof Paul Brennan
			09:30	Seminar	*Effective Data Management Approaches and Early Pipeline Target Tractability'*	Prof Brian Marsden
			11:00	Break		
			11:15	Seminar	*Functional characterisation of Type 2 Diabetes (T2D) – associated genes in beta cells.*	Dr Benoit Hastoy
Tues	10-Sep	Dr Gamma Chi	09:00	Seminar	*Post-modern epidemiology: analysis of real world complex data*	Prof Cornelia van Duijn
			10:30	Break		
			10:45	Seminar	*Protein Production & Expression*	Dr Eleanor Williams
			11:45	Break		
			12:00	Seminar	*Opportunities for data science and machine learning in drug discovery*	Prof John Overington
Wed	11-Sep	Dr Cass Adams	09:00	Seminar	*Artificial intelligence for the analysis of genomics data*	Prof Alejo Nevado-Holgado
			10:00	Break		
			10:15	Seminar	*Medicinal Chemistry in Drug Discovery*	Prof Paul Brennan
			11:15	Break		
			11:30	Seminar	*Deep topographic proteomics in the brain*	Prof Roman Fischer
Thurs	12-Sep	Dr Tryfon Zarganis-tzizikas	09:00	Seminar	*Structural mechanism of drug lead molecules targeting human Kv3.1 for neurological disorders*	Dr Gamma Chi
			10:00	Break		
			10:15	Seminar	*Membrane Transporters as new Therapeutic Targets*	Dr David Sauer
			11:15	Lunch		
			11:30	Seminar	*Hidden in plain sight : aggregating community data for biomarker discovery.*	Dr Wen Hwa Lee

Programme – 2nd week

Day	Date	Chair	Start	Activity	Title	Speaker(s)
Mon	16-Sep	Dr Darragh O'Brien	09:00	Seminar	*Functional Genomics using CRISPR-Cas9 Screening*	Prof Daniel Ebner Dr Sneha Anahd
			10:00	Break		
			10:15	Seminar	Omics profiling of the interferon induced ubiquitin-like response in cancer cells	Prof Benedikt Kessler
			11:15			
			11:30	Seminar	*MedChemica platform for Moonshot*	Dr Ed Griffen
Tues	17-Sep	Dr Beth McLean	09:00	Seminar	*Anti-viral drug discovery & development*	Dr Annette Von Delft Dr Lizbe Koekemoer Dr Jasmin Aschenbrenner
			10:00	Break		
			10:15	Seminar	*Structural biology, genetic diseases & drug discovery*	Dr Wyatt Yue
			11:15	Break		
			11:30	Talk	*Innovation at Oxford*	Prof Chas Bountra
Wed	18-Sep	Dr Lizbé Koekemoer	09:00	Seminar	*Modern Methods of Drug Discovery for Alzheimer's*	Dr Emma Mead
			10:00	Break		
			10:15	Seminar	*Translating genetic hits into drugs and clinical trials*	Prof Alex Bullock
			11:15	Break		
			11:30	Talk	*NDM DPhils in Clinical Medicine - Application Process Summary and Q&As*	Sally McKendrick
			12:00	Closing Session	*Wrap Up: Learnings and Discussion of Drug Discovery and Development*	Prof Paul Brennan

Nuffield Department of Health Research Building NDMRB – Seminars

The Nuffield Department of Medicine (NDM) is one of the largest and most highly regarded departments of medicine in Europe and noted for the wide range and excellence of its basic and clinical research (rated 5* in research assessment exercises). Home for the CAIPM & CMD team. Most of your seminars will be based out of this building.

NDMRB – home for Oxford CAIPM team

Biographies

Professor Chas Bountra is Pro-Vice Chancellor for Innovation at the University of Oxford; Professor of Translational Medicine, and Head of Impact and Innovation in the Nuffield Department of Clinical Medicine; Director, Oxford University Innovations; Professorial Fellow at Keble College, Oxford. Prior to coming back to Oxford in 2008, Chas was Vice President and Head of Biology at GlaxoSmithKline. Chas is an invited expert on several government and charitable research funding bodies, and an advisor for many academic, biotech and pharma drug discovery programmes. In 2012 he was voted one of the "top innovators in the industry", in 2014 received the "Rita and John Cornforth Award" from the Royal Society of Chemistry, in 2017 and 2018 was voted "Master of the Bench" from the Medicine Maker Power List, and in 2018 was awarded the "Order of the British Empire" in the New Year's Honours List.

Prof John Overington is Chief Technology Officer at Exscientia and has over 35 years experience of drug discovery and design, data science and machine learning; encompassing innovation and leadership positions in pharma, academia, and biotech sectors. After a degree in Chemistry, a Ph.D. in protein structure prediction at Birkbeck College, University of London, and a postdoc at Imperial Cancer Research Fund (now CRUK), John joined Pfizer. Here he established and led a department integrating structural biology, target analysis and prioritisation, and CADD. This was followed by increasingly more senior leadership positions at Inpharmatica Ltd., EMBL-EBI, BenevolentAI. Prior to joining Exscientia, John worked at the U.K.'s Medicines Discovery Catapult supporting the U.K. AI SME sector. John has a broad and extensive track record of innovation in applied pharmaceutical data sciences and machine learning/AI - spanning from genomics/genetics through to real world data. He has long track record in software engineering and product delivery and has developed several of the foundation data resources and tools that established the field of AI-based drug discovery.

Dr Wyatt Yue is a structural biologist with an MA (Biochemistry) from University of Oxford, and a PhD (Crystallography) from Birkbeck College, University of London. In 2008 he joined the Structural Genomics Consortium (SGC), University of Oxford as a Senior Scientist and in 2012 established the Metabolism & Organelle Biogenesis team. Wyatt specializes in the use of structural, biochemical and chemical biology approaches to decipher the molecular mechanism of inherited diseases

at the protein level, and address the challenges in drug discovery for autosomal recessive disorders. His team has to date deposited >180 human crystals structures in the Protein Data Bank (PDB). Through an extensive network of clinician and industry partnerships, his team aims to translate basic science into design of small molecule therapeutics for rare diseases.

Dr Benoit Hastoy is currently a Diabetes UK R.D Lawrence Fellow at the Oxford Centre for Diabetes Endocrinology and Metabolism (OCDEM) funded for 5 years. Benoit investigates the impact of Type 2 Diabetes (T2D) risk variants on pancreatic β-cell secretory capacity. He started as a PhD student in Professor Jochen Lang's group in Bordeaux in 2008. His project was on the molecular mechanisms promoting exocytosis of insulin. In 2012, Benoit moved to Oxford and joined Professor Patrik Rorsman's team for his first postdoctoral position where he learnt electrophysiology and broadened his skills on live cell imaging. He characterised using electrophysiology the first human glucose responsive β-cell lines EndoC-βh1/-βh2. During this time, he also investigated the impact of T2D associated genes such as *SOX4* on exocytosis. In January 2015, Benoit joined Professors Anna Gloyn's and Mark McCarthy's teams as a postdoctoral researcher working on an MRC Experimental Challenge Grant (DIVA) awarded to Professors McCarthy, Gloyn, Karpe and Rorsman. As a member of the DIVA consortium, he investigated the cellular physiology that underlies genetic predisposition for diabetes such as those associated with *PAM* and *SLC30A8* genes. In September 2019, he started his R.D Lawrence fellowship funded by Diabetes UK for 5 years. In 2022, he became the scientific director of the CAIPM taking part in the selection of targets and their characterisations in the human beta cell line, EndoC-βH1 and human pancreatic islets of Langerhans.

Prof Cornelia Van Duijn is a full professor of Genetic Epidemiology at the Nuffield Department of Population Health, University of Oxford and a Fellow of St Cross College, University of Oxford. She is a leader in several international consortia CHARGE (Cohorts for Heart & Aging Research in Genome Epidemiology), ENGAGE (European Network for Genetic and Genomic Epidemiology), EAGLE (Early Genetics and Life course Epidemiology), IGAP (International Genomics of Alzheimer's Project) and IGGC (International Genetic of Glaucoma Consortium). Over the years, she has served on various European/global scientific committees; these include for example the ERC (European Research Council) Advanced Expert committee, the European Society for Human Genetics (ESHG), the European Molecular Epidemiology Group, and the international Society for Genetic Epidemiology.

At the national level Cornelia has been the principal investigator of two large NGI (Netherlands Genomic Initiative) excellence centers: the CMSB (Center for Medical Systems Biology) and NCHA (Netherlands Consortium on Health Aging) and member of the steering committee of BBMRI-NL (Biobanking and BioMolecular resources Research Infrastructure).
Cornelia initiated an international education and training program in genetic epidemiology at the ErasmusMC Rotterdam, which turned into the MSc and PhD program in Genetic Epidemiology of the Erasmus University Medical Center. For 25 years, Cornelia has been directing the program.
She has published over 1000 scientific papers and graduated 52 PhD students.

Professor Alejo Nevado-Holgado an Associate Professor of the Department of Psychiatry and the Big Data Institute, and part of Dementia Research Oxford. He supervises the AI team in the TNDR, formed by 10 excellent machine learners and bioinformaticians. His group's focus is on the applications of machine learning and bioinformatics to mental health care. In addition, Alejo also hold a position at the Big Data Institute, with whom he collaborates on the application of machine learning to genomics and target discovery. He is also consultant to a number of AI companies.
The main technologies that his group applies and develops in his laboratory are bioinformatics, artificial intelligence and high performance computing, and they apply these to data coming from biotech laboratories (i.e. genomics, transcriptomics, proteomics and metabolomics from human samples and iPSC cells) and hospitals or GP practices (i.e. Electronic Health Records and cohorts of volunteer patients). His group combines biotech and hospital/GP data to validate laboratory results with real world evidence, such that any target or treatments proposed increases its chances of succeeding in the final stages of clinical trials. In all cases, high performance computing is the software (e.g. concurrent programming, threading or CUDA) and hardware (e.g. 40 GPUs computational cluster) of choice to perform all these calculations in hours rather than years.
In summary, Alejo believes in the benefits that information technologies can bring (and are bringing) to health care and drug discovery, and actively works towards implementing these methods in the lab and the clinic, and on developing the very computational methods that make this possible.

Upamanyu Ghose is a member of the bioinformatics team in the Translational Neuroscience and Dementia Research Group, specialising

in deep learning applied to genomic data. Ghose completed his MSc in Computer Science at Oxford. While computer science and deep learning are the areas he specialises in, neuroscience is the area that deeply fascinates him. Ghose believes that bridging the two fields together has the potential of novel and interesting findings that can better explain unanswered questions of neuroscience.
Ghose's current work revolves around using artificial neural networks (ANNs) to better understand the genetic factors contributing to neurodegenerative diseases like Alzheimer's disease. Traditional methods of GWAS using linear models have successfully identified several risk loci for a wide range of diseases and other phenotypes, but a large part of the missing heritability of diseases like Alzheimer's remains unexplained. To circumvent this issue, ANNs can be used to identify and incorporate non-linear patterns that are present in genomic data, such as the interaction between different genetic loci, allowing them to understand such diseases better than linear models.

Dr Gamma Chi is a membrane protein biochemist/biophysicist with particular interest in uncovering the regulation mechanism of solute carriers (SLCs) and ion channels. As a senior scientist, Gamma employs various structural biology and biophysics techniques to understand the function of SLCs and ion channels at molecular level, and he also works on adapting these techniques for compound screening and lead optimisation for chemical probes and drug discovery programmes.
Prior to his current role, Gamma worked as a postdoctoral scientist at Structural Genomics Consortium at the University of Oxford, where he focused his efforts on determinations of high-resolution structures of human urea transporters, potassium/chloride transporters and voltage-gated potassium channels, each of these leading to publications. During his PhD at the University of Queensland in Australia, he studied the interaction between phospholipids and a bacterial mechanosensitive channel MscL using structural and biophysical techniques. For his Honours degree project at the University of Auckland (New Zealand), Gamma also determined a series of crystal structures of a bacterial salicylate synthase in complex with inhibitor molecules for a drug discovery programme.

Dr Michael Miller is a postdoctoral researcher working at the University of Oxford in the Centre of Medicines Discovery. He is currently developing phenotypic, cellular, and biochemical assays for both exploratory and compound screening purposes. Michael completed his doctorate at University of Newcastle, Australia where he was researching bacterial

transcription and developing compounds that target transcription for the purpose of creating new antibiotics.

Professor Paul Brennan received his PhD in organic chemistry from UC Berkeley. Following post-doctoral research at Cambridge University, Paul spent eight years working in the pharmaceutical industry at Amgen and Pfizer. After leaving Pfizer in 2011, Paul joined the Structural Genomics Consortium at the University of Oxford and led the chemical probes discovery effort on epigenetic targets. After leaving the SGC in 2019, Paul was Head of Chemistry and then CSO of the Alzheimer's Research UK Oxford Drug Discovery Institute where his research was focused on finding new treatments for dementia. Paul is currently Professor of Medicinal Chemistry and Director of the Centre for Medicines Discovery at the University of Oxford. Over the course of his career, Paul has worked on most major drug targets classes: kinases, GPCRs, ion-channels, metabolic enzymes, and epigenetic proteins. His current research is on target validation in neurodegeneration, oncology, virology, and rare diseases; and chemical probe discovery for E3 ligases and small GTPases.

Dr Tryfon Zarganis-Tzitzikas obtained his B.Sc. in Chemistry from the Aristotle University of Thessaloniki, Greece in 2010 and his M.Sc., summa cum laude, in Synthetic Organic Chemistry in 2012, under the guidance of Prof. J. Stephanidou – Stephanatou at the same University. In 2017 he obtained his Ph.D., cum laude, in Medicinal Chemistry under the guidance of Prof. Alexander Dömling in the Group of Drug Design at the University of Groningen, The Netherlands. His thesis focused on *Innovative Multicomponent Reactions and their Use in Medicinal Chemistry*.
After obtaining his Ph.D., Tryfon joined Syncom B.V. as a medicinal chemist working on an immuno-oncology project in close collaboration with the University of Groningen. Since 2014, he has been a co-founder and CSO of TelesisPharma B.V. in Groningen, a company focusing on exploring novel synthetic routes to APIs using multicomponent reactions. In Dec 2018, he joined Prof. Paul Brennan's group at the Oxford Drug Discovery Institute at the University of Oxford. Currently he is a Team Lead in medicinal chemistry focusing on Dementia, funded by Alzheimer's Research, UK.

Professor Brian Marsden leads the NDM Data Platform based in the Wellcome Centre for Human Genetics, the Research Informatics team in the Centre for Medicines Discovery and is Associate Head of the University's Medical Sciences Division for Digital and Information.

Brian and his teams work with researchers to provide multimodal data management, research computing and early drug discovery informatics solutions.
Brian's undergraduate degree was in Natural Sciences at the University of Cambridge before he studied for a DPhil in structural bioinformatics at Oxford. During his postdoctoral work at the Scripps Research Institute in La Jolla, California, he developed tools and methods to improve comparisons of protein homology models and also developed large-scale high-performance compute implementations. Following this, he worked in industry for several years developing novel small molecule libraries for druggable protein families. He returned to Oxford to help setup the Structure Genomics Consortium and joining the Kennedy Institute.

Karen Froud $CEng_{MCIBSE}$ received her degree in Mechanical Engineering from University of Strathclyde and Postgraduate in Manufacturing from the University of Cambridge. Karen's broad technical interests have a unifying foundation in Process Management & Improvement. A Chartered Engineer affiliated with CIBSE, Karen has specific expertise with Low Energy Building design and in-depth experience with complex and diverse New Build Project teams. With her strong foundations in project & process management she is relishing the chance to work within the CAIPM alongside international leaders in their fields of scientific discovery.

Dr Cassandra Adams is a translational scientist in the Centre for Medicines Discovery. She received her D.Phil. in Clinical Laboratory Sciences at the University of Oxford in 2010 under the supervision of Prof. Nick La Thangue. She then undertook post-doctoral research on radiation-induced tumorigenesis in the laboratory of Prof. Allan Balmain at the University of California, San Francisco (UCSF). During which time she was awarded a full fellowship from the Leukemia and Lymphoma Society. Subsequently she became a senior staff scientist in Genome Analysis Core Facility, UCSF where she launched and managed the new Single Cell Analysis Center.
Adams is currently working on a range of projects accelerating novel drug targets downstream in a variety of therapeutic areas; including rare disease, oncology and inflammatory disease.

Dr Sneha Anand is currently a postdoctoral scientist in the Cellular High Content Imaging Group led by Daniel Ebner at the Target Discovery Institute (TDI), Centre for Medicines Discovery, University of Oxford. Sneha is responsible for cell-based high-throughput functional genomic screens. Before joining TDI, Sneha worked in Prof. Terry Rabbitt's group

at University of Oxford, where she worked on establishing technologies to target cellular protein function using antibody fragments as drug surrogates. She has experience developing specific and potent reagents to study cancer development and drug-like molecules as leads for therapeutic drug development. Sneha also holds a PhD in infection biology focusing on vaccine development for infectious diseases.

Dr Jasmine Aschenbrenner joined the XChem Team at Diamond as a PDRA in January 2023 after her PhD with Dirk Opperman at the University of the Free State. Her PhD project focused on structural biology and biochemistry and addressed limitations of self-sufficient bacterial and fungal cytochrome P450 monooxygenases, especially for the production of diols and lactones. She completed her BSc and MSc in Biology at the Technical University of Munich.

Professor Alex Bullock is a professor of Structural and Chemical Biology at the Centre for Medicines Discovery, University of Oxford. Prior to this, he spent over 15 years as part of the Structural Genomics Consortium (SGC), where his group contributed novel structures, assays and chemical tools for protein kinases and E3 ligases, particularly those linked to cancer and rare diseases. His work has defined a novel disease mechanism and therapeutic target for a subtype of medulloblastoma, as well as a promising drug candidate for fibrodysplasia ossificans progressive which is currently in a phase II clinical study targeting ALK2 kinase gain of function. Alex received his degree and PhD from the University of Cambridge where he trained with Sir Alan Fersht determining how cancer-associated mutations disrupt p53 folding. He subsequently held a Wellcome Fellowship for positions with David Baker at the University of Washington, Seattle, where he used the Rosetta software for protein design, and later with the Noble Prize winner Sir Peter Ratcliffe at the University of Oxford for work on VHL and the hypoxia signalling pathway. He has appeared on radio, TV and film documentary to discuss his work.

Dr Annette von Delft works on the discovery and development of novel small molecule inhibitors against viruses, bacteria and fungi. Her work covers projects from early target validation, target enablement, molecule discovery and preclinical development.
Annette's current focus is the preclinical development of a novel antivirals for pandemic preparedness, targeting coronaviruses, flaviviruses and enteroviruses, as part of the global consortia COVID Moonshot and ASAP (https://asapdiscovery.org/). On these projects, she works in close collaboration with Drugs for Neglected Disease initiative (DNDi).

Annette joined the BRC team in 2018 as a translational scientist with a focus on inflammation and immunity, and has initiated a range of early target validation projects in immunology, infectious disease and neuroscience.
Annette trained as a medical doctor at University of Leipzig (Germany) and received her D.Phil in Clinical Medicine at the University of Oxford in 2010, working on HCV T cell immunology and vaccine development under the supervision of Prof Eleanor Barnes. She then completed her medical foundation programme at Oxford University Hospitals.

Professor Daniel Ebner is an Associate Professor and Principal Investigator at the University of Oxford and heads the TDI High Throughput Cellular Screening Facility and the Oxford CRISPR/Cas9 Screening Facility at the Target Discovery Institute (TDI), Centre for Medicines Discovery, Nuffield Department of Medicine. Daniel's main academic research, through a five year £7M CRUK funded grant in collaboration with researchers from the University of Edinburgh and MIT, is focused on identifying and advancing novel combinatorial therapeutics for the treatment of glioblastoma. As head of the cellular screening facility, Daniel has worked with academic and industrial collaborators to complete >150 research projects and has published >70 peer-reviewed papers in the past 5 years in high impact journals such as the Lancet, New England Journal of Medicine, Nature and Journal of the American Medical Association across a broad range of pathologies including on neurodegeneration, inflammation, autophagy, large-scale iPSC CRISPR/Cas9 screening methods, and novel more physiologically relevant screening models. Previous to his academic career at the University of Oxford, Daniel has worked for >10 years in the biotechnology and pharmaceutical industry.

Professor Roman Fischer In the Discovery Proteomics Facility of the Target Discovery Institute we provide advice in experimental design, sample preparation, sample analysis with state-of-the-art LCMS workflows and data analysis to researchers from Oxford University and national and international collaborators. We routinely use label-free quantitation, SILAC, TMT, SWATH and other methodologies on diverse samples (i.e. cells, tissues, immuno precipitates et al.) and have developed sample preparation techniques to access the deep proteome form little sample amounts using instrumentation such as Orbitrap Fusion Lumos or TimsTOF Pro.
My own interests evolve around clinical proteomics and applications for the spatial characterisation of the proteome in biological structures such as tissues and tumours. In addition, I am developing methodologies for

the proteome characterisation of clinical cohort samples at high-throughput

Dr Ed Griffen obtained his Ph.D. from Imperial College, London, and undertook postdoctoral research at the University of Waterloo-Kitchener, Canada. He joined Zeneca Pharmaceuticals in medicinal chemistry working in the CNS, infection, oncology, and chemical biology areas. Taking a secondment into the computational chemistry group, he co-developed matched molecular pair tools to quantify medicinal chemistry approaches. In 2012 he cofounded MedChemica Ltd.. He has taught medicinal chemistry courses at the University of Manchester and AstraZeneca courses in the U.K., France, and India. He is a named inventor on 16 patents and coauthored more than 15 articles, book chapters, and a textbook. His interests are in developing data driven methods to support decision making and medicinal chemistry education.

Professor Benedikt Kessler graduated from the Swiss Federal Institute of Technology ETH in Zurich, Switzerland in biochemistry in 1992. He received his PhD in immunology at the Ludwig Institute for Cancer Research at the University of Lausanne, Switzerland in 1998. He then joined the laboratory of Hidde L. Ploegh at the Pathology Department at Harvard Medical School in Boston, USA, to study the role of proteolysis in MHC I antigen processing and presentation. After three years, he established a research platform in proteomics at Harvard Medical School. Currently he is Professor of Biochemistry and Life Science Mass Spectrometry at the Target Discovery Institute (TDI), Centre of Medicines Discovery, Department of Medicine, University of Oxford, UK. His laboratory is focused on ubiquitin and protease biology with a specialty in mass spectrometry, proteomics and recently in metabolomics. Expertise in his laboratory is also used to define “molecular signatures” in disease processes and accelerate target discovery in translational research.

Dr Wen Hwa Lee is CEO and chief scientist at Action Against AMD, a research charity focused on tackling the leading cause of legal blindness in the developed world at its earliest stages with maximum affordability and accessibility. Lee is a molecular and structural biologist with a wide international network in drug discovery, including charities, academia, industry, and government agencies. Previously at the University of Oxford, Lee is an experienced leader in setting up partnerships and alliances with multiple stakeholders to accelerate discoveries for drug discovery. He designed and implemented several strategies in two of the largest and most successful international public-private partnerships for drug

discovery – the Structural Genomics Consortium and the European Lead Factory. Along with his scientific endeavours, Lee also advised high-level government representatives from different countries and charitable institutions on policy and strategy to integrate scientific, societal, and economic impact.

Professor Emma Mead received her PhD in Neuroscience from University College London, investigating the role of reactive oxygen species in modulating neuroinflammation in Alzheimer's disease. Following a post-doctoral research position at Cardiff University, where she studied the mechanism of action of naturally occurring anti-inflammatory compounds, Emma joined Eli Lilly as a senior scientist and team co-ordinator. Emma worked in target validation and early drug discovery for neurodegeneration. Emma joined the Alzheimer's Research UK Oxford Drug Discovery Institute (ODDI) in 2018 to lead the Neuroinflammation team, and became the CSO in 2023.

The Alzheimer's Research UK Oxford Drug Discovery Institute (ODDI) is one of three institutes forming the Alzheimer's Research UK Drug Discovery Alliance (DDA). Alongside the UCL Drug Discovery Institute and ALBORADA Drug Discovery Institute at the University of Cambridge, our goal is to couple the deep disease knowledge and biology expertise of the academic community with high quality, innovative drug discovery technologies. We aim to translate cutting edge academic science into drug discovery programmes and develop therapies for patients living with Alzheimer's disease and other neurodegenerative conditions.

The ODDI is a multidisciplinary team of >35 biologists, pharmacologists and chemists. We are focussed on evaluating novel dementia targets that modulate neuroinflammation and organelle dysfunction. Both of these areas have been identified by human genetic studies as being dysregulated in Alzheimer's and Parkinson's disease, and are implicated in the development of pathology. We have identified a number of potential points of therapeutic intervention in immune pathways in microglia, and mitochondrial and endo-lysosomal targets that may hold therapeutic potential. We validate these targets using novel *in vitro* assays utilising human iPSC macrophages, relevant cell lines and primary cells. Targets that hold potential for further drug development are prosecuted via screening assays, and the biology team have developed cell based, biochemical and biophysical screening assays to identify novel small molecule compounds. Hits from our screens are further profiled in appropriate cell based assays to facilitate drug development, which is performed by our Chemistry team. Using this model, we have successfully translated cutting edge academic research in neurodegeneration to drug

discovery programmes, and continue to explore ways to develop disease modifying therapies for patients

Dr David Sauer is a biophysicist focusing on the structure and function of membrane channels and transporters. As group leader at the University of Oxford since 2021, he has been studying the structure and function of membrane proteins for 16 years. David completed his graduate degree studying potassium channel structure and ion selectivity with Youxing Jiang at the University of Texas Southwestern Medical Center. This was followed by postdoctoral training with Da-Neng Wang at New York University School of Medicine. There he described the structure, transport mechanism, and chemical inhibition of SLC13/DASS membrane transporters.
Since joining the Oxford's CMD, David had lead a group studying membrane proteins' function, pathogenesis, and chemical targeting by small molecules. This has resulted in the first detailed study of proline import by the transporter SIT1, and its complex with the SARS-CoV2 (COVID-19) receptor ACE2. His group has also revealed the ping-pong reaction mechanism, and product-bound inhibited state of the ceramide synthase CerS6. Finally, in a collaborative study, David's group revealed the substrate binding and transport triggers for SPNS2, which exports the immunoregulatory sphingosine-1-phosphate.

Professor William Whyte Like all historians, I am interested in people, but unlike many I am also equally preoccupied by things and places. I'm especially intrigued by what the serious investigation of the built and natural environment does to existing accounts of modern history. My research has consequently often focused on architecture, and I have a special interest in institutions like schools, universities, and churches.
My first book, *Oxford Jackson: architecture, education, status, and style, 1835-1924* (OUP, 2006) explored the work of an influential university architect. My second, funded by a Philip Leverhulme Prize, was *Redbrick: a social and architectural history of Britain's civic universities* (OUP, 2015). My third, *Unlocking the Church: the lost secrets of Victorian sacred space* (OUP, 2017), grew out of my Hensley Henson Lectures. Now, as the final part of what's become a trilogy on university architecture, I am working on *The University: a material history*, for Harvard University Press. Along the way, I have edited or co-edited a dozen or so other books. Current projects include the *Oxford Illustrated History of England*, for OUP, and the six-volume *Cultural History of High Learning*, which I am editing with Ning de Coninck-Smith (Aarhus) and Julia Horne (Sydney). I chair the editorial board of the *Oxford Review of Education* and sit on the board of the Oxford Historical Monographs series. I am currently serving as Senior

Responsible Owner and Chair of Project Board for the Stephen A. Schwarzman Centre for the Humanities: the university's largest ever capital project, the result of the largest ever gift given to Oxford.
It is my immense good fortune to be involved in a large number of organisations outside the University. I am chair of the Oxford Preservation Trust, the Oxford Historical Society, and the Victoria County History of Oxfordshire. I am a Trustee of English Heritage and Chair the Blue Plaques Panel. I am also a member of the Fabric Commission of Westminster Abbey, the Heritage Committee of the British Academy, the Oxford Diocesan Advisory Committee, and serve on the International Commission for the History of Universities/Commission internationale pour l'histoire des universités.
As professor of social and architectural history I am very glad to discuss graduate supervision with anyone whose interests fall within these fields. In the past, I have been lucky enough to work with a score of doctoral students on subjects ranging from science in the nineteenth century to theology in the twentieth, and on architectural history from the eighteenth century onwards. Recent theses include Elena Porter on country houses, George Entwistle on interwar housing, and David McKinstry on the Italianate style.

Dr Eleanor Williams is a structural biologist with a background in ITC, NMR and crystallography. She has been heading up the protein production facility since 2021. Ellie obtained her PhD with Prof. John Ladbury and Dr. Mark Williams at University College London, looking at the chaperone Hsp90. She then moved to the SGC Oxford in 2010 where she worked with Prof. Alex Bullock, studying the ultra-rare disease fibrodysplasia ossificans progressiva (FOP). FOP is caused by a single point mutation in the protein ACVR1/ALK2, a ser/thr kinase and part of the BMP signalling pathway. She focused on understanding the ways the various mutations influenced the activity of ALK2 in parallel with characterising the binding of specific inhibitors, primarily through crystallography, to allow for improved inhibitor development.
In 2021 she took over running of the protein production facility within the CMD. The facility supports the work of the CMD but is also open to external customers providing high throughput cloning, protein expression (in e.coli, insect and mammalian cell systems) and protein purification services.
She is a keen supporter of public engagement in research and was the public engagement officer for SGC Oxford between 2015 and 2020. In 2020 she became a non-stipendiary lecturer in biophysics at St. Annes College, Oxford.

Recommended Reading List

- Intro to Python for data science:
  - https://www.youtube.com/watch?v=LHBE6Q9XlzI
- Intro to ML using Python:
  - https://www.youtube.com/playlist?list=PLg8h8Ej1e8l1fhKwMVMLtCaug8jLLT0U_
- Integrating the inputs that shape pancreatic islet hormone release
  - Glyn M. Noguchi & Mark O. Huising
- Medium-Throughput Production of Recombinant Human Proteins: Protein Production in *E. coli.*
  - Nicola A. Burgess-Brown, Pravin Mahajan, Claire Strain-Damerell, Opher Gileadi & Susanne Gräslund
- Medium-Throughput Production of Recombinant Human Proteins: Protein Production in Insect Cells
  - Pravin Mahajan, Claire Strain-Damerell, Opher Gileadi & Nicola A. Burgess-Brown
- Structural Biology: A Century-long Journey into an Unseen World
  - Stephen Curry
- Hit and lead generation: beyond high-throughput screening
  - Konrad H. Bleicher, Hans-Joachim Böhm, , Klaus Müller & Alexander I. Alanine
- Epileptic Disorders - 2016 - Nascimento - Myoclonus epilepsy and ataxia due to potassium channel mutation MEAK is caused
  - Fábio A Nascimento , Danielle M Andrade
- Principles of Early Drug Discovery
  - JP Hughes, S Rees, SB Kalindjian, KL Phillpot

- Ten Simple Rules for Selecting a Bio-ontology.
    - Malone J, Stevens R, Jupp S, Hancocks T, Parkinson H, Brooksbank C (2016)
- Ten Simple Rules for Creating a Good Data Management Plan.
    - Michener WK (2015)
- A review of big data and medical research.
    - Mallappallil M, Sabu J, Gruessner A, Salifu M.
- Advanced: HPCCT '22: Proceedings of the 2022 6th High Performance Computing and Cluster Technologies Conference, July 2022,Pages 14–24
    - Sebaastian Varrette, Hyacinthe Cartiaux, Sarah Peter, Emmanuel Kiefer, Teddy Valette, Abatcha Olloh

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