

fusion

THE MAGAZINE OF THE SIR WILLIAM DUNN SCHOOL OF PATHOLOGY

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UNIVERSITY OF
OXFORD

**Support the
Centenary Campaign**

**Bugs not drugs: harnessing the gut
microbiome to prevent disease**

**A new children's book to
mark the Centenary**

**Celebrating the women
of the Dunn School**



Welcome...

Sitting down to write the annual introduction to Fusion always provides me with a moment of reflection. Another year of Dunn School life. Another opportunity to gently boast about the achievements of our fantastic community of scientists and staff. Honestly, though, it also sometimes induces slight anxiety about what the theme of the year's introduction will be. This year it's easy.

The 2027 Dunn School centenary has been in the background for several years, but is now reaching its crescendo, as the plans are finalised, the event bookings made, and guests invited. In fact, the greatest pleasure has been the contact with so many friends of the department and alumni, many of whom had been out of touch since they left. The oral and living history that we have gathered has added vivid colour to our understanding of past events.

Before I go further, I'd like to confess to liberal use of the 'royal we': almost all the work has been led by Catarina Vicente, Hannah Calkin and Lindsay Stimson. I know they have loved it, but it has been a huge effort. I want to express my personal thanks to them and hope that many of you will have your own chance to join me in expressing our gratitude over the next year.

There is a list of centenary events elsewhere in this issue as well as several relevant articles. Here, I will just highlight a few things. Perhaps most importantly, we will be holding a day-long symposium followed by a reception among the dinosaurs of Oxford's Natural History Museum on 14th July 2027. Mark your diaries: all alumni and friends will be very welcome to join current members of the department and a glittering guest list. Registration will soon go live, and I hope that many Fusion readers will be able to attend.

Other major events include the unveiling of a new blue plaque to celebrate the scientific and philanthropic impact of Edward Abraham and Guy Newton. Their landmark discovery and commercialisation of cephalosporin antibiotics, followed by extraordinary philanthropic generosity, have had huge impact on our future success.

Indeed, the three related trusts established by Edward Abraham have become models of supporting the people and the science that underpin medical advances. On a different note, in conjunction with Lincoln College, which is coincidentally celebrating its 600th anniversary in the same year, we have commissioned a new piece of music – an oratorio to celebrate the penicillin discovery. Composed by Lincoln alumna Emily Howard and with a libretto by Michael Symmonds-Roberts, next year's world premiere in Oxford will also be open to all.

Another centenary project of which I am particularly fond is the publication of a learning-to-read book, aimed at primary school children, about the discovery of penicillin and the role of the Dunn School. Written by Sam Gayton, it is part of an Oxford University Press reading series, has illustrations painted from life by Chiara Fedele, and will be the focus of an event at the 2027 Oxford Literary Festival. It will make a great souvenir and gift, and I love the idea of a new generation learning about the place of the Dunn School in medical history.

In among all the fun, there is also serious ambition. We have set ourselves the challenge of endowing new scholarships for Dunn School DPhil students. Students are, and have always been, the life blood of the department, and are central to all our scientific achievements. It is wonderful that every year we receive hundreds of outstanding applications and select a small and international cohort who represent the very best biomedical research students and future leaders. But we can only fund a small proportion of even the very highest achievers, and that means we turn away many who simply cannot afford to come.

We are working with many new donors who have already generously given to this cause and next year I hope to announce an outstanding result.

As part of this goal, we have decided for the first time to launch a mass donation project, with the aim of receiving gifts towards permanently endowing a Dunn School Centenary Scholarship. I am hugely grateful to the EPA Research Fund, the trustees of which have offered a 2:1 match to any donations that we receive. I hope that many of the readers of Fusion will agree that supporting brilliant students is the most significant impact we can have on the future of the Dunn School and therefore consider a gift of any size: and remember that every pound you give will be transformed into three by the additional generosity of the EPA Research Fund.

One of the many fascinating pieces in this issue of Fusion is an interview with Jane Sharps, who recently retired from a 40-year career at the Dunn School in a variety of technician and scientific support roles – working originally with Eric Sidebottom. This focus on Jane represents an important theme of our success and of the centenary: the famous scientists, whose names we all know, are not solely responsible for their achievements. They are always supported by teams who are often left out of the history of discovery. We are trying to redress that imbalance a little by, for example, curating an exhibition of some of our historic photos of the back-room researchers. A tiny taster:

we will be focusing on Ruth Callow, Claire Inayat, Betty Cooke, Peggy Gardner, Megan Lancaster, and Patricia McKegney, who rather embarrassingly are known to history and the world as simply ‘the Penicillin Girls’. We (the royal version again) have tried to learn more about them and we hope our exhibition

will help to give credit to them as individuals.

I hope you enjoy this issue as much as I do. Combined with next year’s official Centenary Fusion, it provides a foundation for a lasting celebration of this remarkable department, of which I am so

proud to lead. I also repeat and emphasise the invitation: we really hope that as many friends and alumni as possible will find some way of attending events next year. I much look forward to meeting you then, or indeed at any time.

Matthew Freeman

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Some arrivals and departures

In what may be a Fusion first, in the last year there have been no departures or arrivals of new groups in the Dunn School! We did, however, say goodbye to Andrew Souter, our Head of HR, who has returned to a career in law after 8 years at the Dunn School. Marina Katash is our interim HR Manager, supported by Sarah Barefield.

After 14 years as Lab Manager in the Tang Lab, and more recently as a member of the Centenary team, Lindsay Stimson has moved on to a new role as Deputy Head of Building Operations for the Medical Sciences Division.

Another notable departure was that of Jane Sharps, who retired after 41 years at the Dunn School in a variety of roles across several groups. You can read an interview with Jane on page 30.



News

A round-up of news from the last year. You can read these and other stories on our website www.path.ox.ac.uk

Honours for Dunn School researchers: some of the highlights



Anjali Hinch and **Girish Mali** were both awarded the prestigious Lister Research Prize, which recognises outstanding researchers in the early years of their independent career. Other recent Dunn



School recipients of this award include Tanmay Bharat and Alexander Borodavka.



Kevin Foster and **Emma Slack** were both accepted as members of EMBO, the leading European Molecular Biology Organisation.



Matthew Freeman, our Head of Department, was awarded the 2027 Biochemical Society Centenary Award, recognising his contributions in the field of intramembrane proteases and pseudoproteases, as well as his commitment to supporting and nurturing talent within the scientific community.

Teresa Thurston received the Pettenkofer Prize, awarded annually by the Pettenkofer Foundation, in recognition of her contributions to identifying how different bacterial effectors impact the outcome of infection.



Many congratulations as well to the Dunn School postdocs who recently started their independent groups: Iqbal Dulloo (Freeman lab)- University of Warwick; Carolin Kobras (Stracy group)- University of Birmingham; Yongxu Lu (Smith lab)- Shanghai Institute of Immunology and Infection, Chinese Academy of Sciences (Shanghai, China); João Monteiro (Raff lab)- Department of Biochemistry; Aakash G. Mukhopadhyay (Roberts Lab)- University of Cambridge; Marion Schuller (Ivan Ahel lab)- Max Planck Institute of Biochemistry (Munich, Germany); Rebecca Smith (Ivan Ahel's group)- St Vincent's Institute of Medical Research (Melbourne, Australia).



Top L-R – Carolin Kobras, Aakash G. Mukhopadhyay, Rebecca Smith. Bottom L-R: Iqbal Dulloo, Marion Schuller, Yongxu Lu, João Monteiro

In other news...

Phosphorylation fine-tunes viral condensates during rotavirus replication

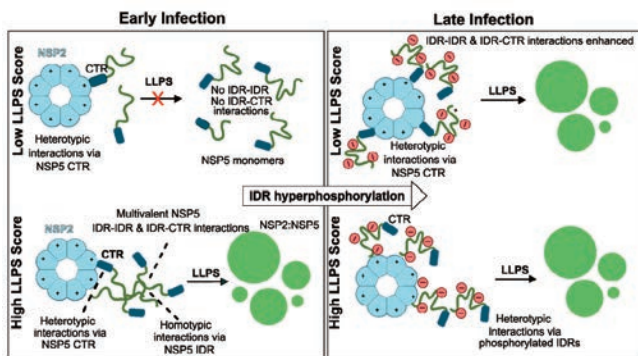
A recent study from the Borodavka lab reveals how rotaviruses use phosphorylation to control the formation of viral replication factories.

Published in *The EMBO Journal*, the work investigates how rotavirus strains assemble viroplasms, specialised membrane-less organelles where viral replication takes place. These structures form through liquid-liquid phase separation (LLPS), a process driven by weak interactions between viral proteins, particularly the intrinsically disordered protein NSP5 and the RNA chaperone NSP2.

Although NSP5 is essential for viroplasm formation, its sequence varies considerably between rotavirus strains. This raised an important question: do all rotaviruses use the same mechanism to build these organelles, or can different strains rely on distinct ways of forming condensates?

To address this, a machine learning approach was used to predict the phase-separation potential of hundreds of NSP5 variants. They found that most NSP5 proteins were predicted to have a high ability to phase separate. However, a small number of variants showed much lower predicted LLPS propensity. The team used these naturally occurring low-scoring sequences to engineer an NSP5 variant, 'SC_{Low}', designed to have reduced condensate-forming ability.

Surprisingly, although SC_{Low} could not efficiently phase separate with NSP2 *in vitro*, viruses carrying this variant were still able to replicate in cells and form viroplasms. These viroplasms were smaller and developed more slowly than those formed by wild-type virus, but they still contained viral RNA and supported productive infection. This suggested that additional factors could compensate for reduced intrinsic phase-separation ability.



Phosphorylation tunes protein condensation and interactions during rotavirus replication organelle assembly.

The authors found that phosphorylation is a key factor in condensate formation. NSP5 is known to become progressively phosphorylated during rotavirus infection, and phosphomimetic mutations, or phosphorylation by casein kinase II *in vitro*, restored the ability of low-LLPS NSP5 variants to form condensates with NSP2. In contrast, high-LLPS NSP5 variants could phase separate without phosphorylation, although phosphorylation still altered their condensate behaviour.

The team further showed that phosphorylation does more than simply 'switch on' phase separation. Instead, it rewires how NSP5 interacts with NSP2. In the unphosphorylated state, NSP5 relies more heavily on its C-terminal region (CTR), whereas phosphorylation of the disordered region creates new interaction modes with NSP2. This shifts the condensate from a more CTR-dominated network to a more distributed and adaptable interaction network.

Overall, this work highlights phosphorylation as a flexible mechanism that allows rotaviruses to maintain viroplasm formation despite sequence variation in intrinsically disordered proteins. By showing that different viral strains can use phosphorylation to tune condensate assembly, the study provides important insight into how viral replication factories are regulated and how similar condensate-forming systems might be targeted therapeutically.

Written by Zara Kaplan (Freeman Lab)

Funding success for Dunn School PIs

Congratulations to Sumana Sanyal, Matthew Freeman, Georgia Isom and Kevin Foster for securing prestigious Wellcome Trust Discovery Awards.

Sumana Sanyal - Redefining how flaviviruses build infectious virions

This project will uncover how mosquito-borne viruses such as dengue and Zika assemble infectious particles at specialised sites inside host cells. The interdisciplinary approach will include advanced proteomics and imaging to map the molecular composition and biogenesis of these sites, and investigate how epidemic outbreak variants adapt to exploit this machinery. By revealing the basic biology of how these globally important viruses are made, this research aims to expose new vulnerabilities that could inform interventions against dengue, Zika and related infections.

Matthew Freeman - Exploiting rhomboid-like proteins to control signalling

The Freeman lab discovered the rhomboid-like superfamily of membrane proteins and have spent years unearthing their fundamental mechanisms. This new Wellcome grant builds on the group's past discovery science while also changing direction. The new aim is to exploit the properties of rhomboid-like proteins to develop ways of re-engineering cell signalling.

If successful, this project will allow the fine tuning of signalling processes that control many aspects of disease, for example in inflammation, immunology, and cancer.

Georgia Isom - Enigmatic bacterial sphingolipids; elucidating their biosynthesis, transport and function within the host

Sphingolipids were previously thought to be exclusive to eukaryotic membrane components, with only a handful of unusual bacteria capable of producing them. Recent work has revealed that sphingolipid biosynthesis is widespread across diverse bacteria, and that they are key determinants of membrane homeostasis, antimicrobial resistance and host-pathogen interactions. The Isom lab will answer one of the biggest outstanding questions: how are sphingolipids transported to the bacterial cell surface?

This collaborative grant formalises an international collaboration to investigate bacterial sphingolipids, bridged between Georgia's lab and the laboratories of Prof Dominic Campopiano (University of Edinburgh), Dr Jon Marles-Wright (Newcastle University), Dr James Connolly (Newcastle University) and Prof Eric Klein (Rutgers University, USA).

Kevin Foster - RNAi in *Candida albicans*: adaptation, commensalism and pathogenesis

This collaborative project will study how the key fungal pathogen *Candida albicans* competes with our gut bacteria and capitalise on this research to identify communities that inhibit the growth and virulence of the fungus. The collaboration will

also investigate the role of RNAi based regulation in *Candida*, including its behaviour and ecological success in the gut microbiome. The project is a collaboration with the labs of Professor Alessia Buscaino (Quadram Institute, UK) who is leading the project, and Professor Ana Traven (Monash University, Australia).

Protection for newborns: new treatment to prevent meningitis

Emma Slack and collaborators have developed a preventive approach that stops harmful bacteria in their tracks before transmission occurs.

Newborn meningitis is one of the most dangerous childhood infections. It is often life-threatening and can cause serious and lasting damage, including developmental problems, in the children who survive. Although meningitis is rare in newborns, it is more common in premature babies, affecting one in every 500 such infants in industrialised economies and likely more in developing countries.

One of the leading pathogens responsible for these meningitis cases is the K1 form of the *E. coli* bacterium. Now, the Slack group (based at the University of Oxford and ETH Zurich), in collaboration with Médéric Diard (Biozentrum, University of Basel), have developed an approach that seeks to prevent transmission to newborns.

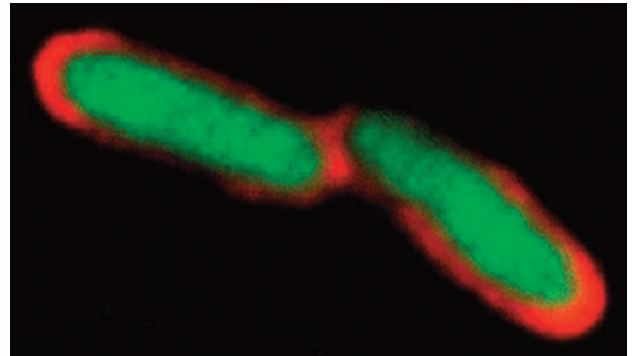
E. coli K1 is part of the intestinal flora in one in three healthy adults, with no normal adverse effects. This is a consequence of both interactions with other bacteria and a functioning immune system. However, if the pathogen is carried by an expectant mother, it can be transmitted to the child during birth and enter the intestine. In premature babies whose immune systems are still weak, the pathogen can enter the bloodstream and migrate to the brain, where it causes severe inflammation. The aim of the project was to stop this transmission by eliminating the pathogen in carrier pregnant women.

The two groups had previously developed a new concept for eradicating pathogens living in the intestine: combining an oral vaccination that weakens the pathogenic bacteria with a dose of harmless microbes that compete with the weakened pathogen. The researchers demonstrated that this approach can eliminate certain *Salmonella* and *E. coli* strains in the intestine.

However, the K1 form of *E. coli* provides an additional challenge, as it contains a polysaccharide capsule that makes it particularly resistant to antibodies generated by the oral vaccination. The researchers addressed this by including a third component to their previously developed approach: bacteriophages. Bacteriophages normally dock to the polysaccharide capsule, with lethal effects. However, bacteria can rapidly evolve to avoid bacteriophages, often by shedding their protective layer. This presented an opportunity.

“This is essentially a resistance mechanism that the bacteria deploy against the phages,” says Emma Slack. “We use this mechanism to our advantage: the antibodies formed by the oral vaccination are effective against K1 bacteria that no longer have their protective coating.”

The project involved searching for effective strains of phages, with a sample of wastewater from the treatment plant of the Lucerne region providing several phages that are particularly effective at attacking the bacterium *E. coli* K1.



GFP-expressing bacteria (green) coated with O-antigen-binding IgA (red) Image credit – Alyson Hockenberry, ETH Zürich

In experiments with pregnant mice, which the researchers had previously infected with pathogenic *E. coli* K1, they were able to demonstrate the effectiveness of their triple-pronged treatment. The researchers first gave the mice phages that forced the bacteria to cast off their protective shell. Second, they administered an oral vaccination that produced antibodies in the intestine to weaken the bacteria. Third, they gave them a harmless probiotic bacterium that could compete against the weakened bacteria and occupy their ecological niche in the intestine.

In the control experiment, *E. coli* K1 was transmitted to 83 percent of young animals at birth. By contrast, the triple-pronged treatment significantly reduced the level of *E. coli* K1 in the mothers' intestines, such that the pathogen was only transmitted to 23 percent of offspring.

“In a world in which effective antibiotics are becoming increasingly scarce, we need new therapeutic approaches”, says Slack. “Bacteria such as *E. coli* K1 are difficult to tackle. Our approach is potentially the only one that can be used to fight this pathogen and others without antibiotics.”

“Oral vaccinations, probiotics and even phages are all already used in medicine,” she says. It will also be possible, she adds, to pack all three components into a single capsule that people can simply swallow.

The researchers plan to continue developing this approach so that it might one day be used in the clinic. Moreover, projects are ongoing to use the same approach to tackle bacteria other than *E. coli* K1, including multi-resistant pathogens, against which many antibiotics are no longer effective.

Monika Gullerova recognised in the MIT-Royalty Pharma Faculty Founder Prize Competition

Monika is one of six Oxford finalists of a unique Oxford-MIT initiative that supports entrepreneurs in biotech.



The MIT-Royalty Pharma Faculty Founder Prize Competition is a collaboration between the University of Oxford and MIT, which aims to bridge the worlds of academia and entrepreneurship. The two-year initiative empowers faculty at both institutions to translate human health technologies – including diagnostics, therapeutics, devices, and AI driven digital health, into real-world impact.

The 12 finalists for its third prize competition have now been announced: six each from MIT and the University of Oxford. The initiative, recently renamed in recognition of a gift by Royalty Pharma, runs a two-year programme that supports biotech innovators and faculty entrepreneurs interested in commercialising their solutions.

Monika and the other finalists receive wide-ranging support to help advance and grow their biotech solutions into startups and companies ready for commercialization. This includes workshops, executive education classes, and mentorship from world-leading entrepreneurs and investors. The program culminates in the MIT-Royalty Pharma Prize Competition Showcase, scheduled for 2027.

Monika Gullerova is a Professor of Molecular Medicine at the Dunn School. One of her ongoing projects is on RAIDEN, an AI-driven drug discovery project developing small-molecule medicines that target RNA, unlocking entirely new ways to treat diseases long considered “undruggable.” By combining advanced machine learning with molecular biology and chemistry, RAIDEN is redefining how next-generation RNA-targeted therapies are developed.



Prof Natalia Gromak receives funding for Friedreich's Ataxia research

The funding will support research into the molecular mechanisms underlying potential therapeutic avenues for this rare disease.

Friedreich's Ataxia (FA) is a debilitating, life-shortening, degenerative

multisystem rare disease for which there is currently no cure. The Oxford-Harrington Rare Disease Centre ('OHC'), a partnership between the University of Oxford, UK and Harrington Discovery Institute at University Hospitals, Cleveland, Ohio, dedicated to creating new medicines for rare diseases, recently announced funding to five researchers from the University of Oxford, each of whom receive £100,000 and specialist support to advance pioneering research projects exploring novel approaches to discover treatments for FA.

Natalia's project will develop innovative approaches to uncover the proteins which recognise expanded GAA repeats in the frataxin gene, which cause FA. This project will help reveal how GAA repeats cause pathology and silence the frataxin gene, advancing the understanding of the precise molecular mechanisms of FA. This work is directly relevant to the identification of novel therapeutic targets and disease biomarkers, important for advancing FA drug discovery programmes.

The OHC coordinates the Friedreich's Ataxia Alliance at Oxford (FA Alliance), which brings together researchers and clinicians from across the University of Oxford, supported by philanthropic funding, to develop new therapies or cures for FA. The alliance comprises established experts in FA research together with emerging investigators at the forefront of developing advanced therapeutic modalities and novel delivery systems to ensure appropriate targeting to relevant tissues, which is critical in FA.

The Gromak group studies the role of R-loops in health and disease. These unusual nucleic acid structures are surprisingly common in genomes and are composed of an RNA/DNA hybrid and a single strand of DNA. Formed in all living organisms, they can occupy 10% of the human genome under physiological conditions. R-loops have emerged as important regulators in biological processes as diverse as transcription, DNA replication, generation of antibody diversity, epigenetics and DNA damage responses, and have been implicated in other rare neurodegenerative diseases such as Aicardi-Goutières syndrome.

Dunn School marks International Women's Day in partnership with Suffrage Science

The event also marked the department's 99th birthday and the countdown to our Centenary in 2027.

On Monday 9 March, the day after International Women's Day, the Dunn School hosted a reception to mark its 99th anniversary. The event was an opportunity to celebrate almost 100 years of women in the Dunn School, as well as the winners of this year's Suffrage Science Awards in Life Sciences.

The event included a presentation on the Women of the Dunn School, as well as a panel discussion on 'Global challenges and opportunities facing women scientists – is it getting better?'. The panel was moderated by the award-winning science writer

and presenter Dr Kat Arney and was composed of:

- Areej Abuhammad, School of Biochemistry, University of Bristol
- Kay Davies, Department of Physiology, Anatomy & Genetics, University of Oxford
- Ulrike Gruneberg, Dunn School, University of Oxford
- Edith Heard, The Francis Crick Institute
- Petra Hajkova, MRC Laboratory of Medical Sciences



The Suffrage Science Awards were founded in 2011 to celebrate women in science, for their scientific achievements and their ability to inspire others. Initially focusing on the Life Sciences, other award categories now include Engineering and Physical Life Sciences and Mathematics and Computer Sciences. The awards themselves are heirloom items of jewellery commissioned from students of the art and design college, Central Saint Martins-UAL, who worked with scientists to create pieces inspired by research and the Suffragette movement, from which the scheme takes its name. Winners are nominated by previous awardees, and the items of jewellery are passed on at each award ceremony.

This year's winners were:

- Chrystalina Antoniadis, University of Oxford
- Sarah Cooley, Earth Science Data Partners
- Cara Croft, Queen Mary University of London
- Camille Dion, MRC Laboratory of Medical Sciences
- Dima A. Hammoud, National Institutes of Health
- Karoline Kuchenbaecker, University College London
- Madeline Lancaster, MRC Laboratory of Molecular Biology
- Liset Menendez de la Prida, Cajal Institute (Madrid) and Cajal Neuroscience Center
- Arwen Pearson, University of Hamburg
- Kate Watkins, University of Oxford
- Dana Pe'er, the Sloan Kettering Institute

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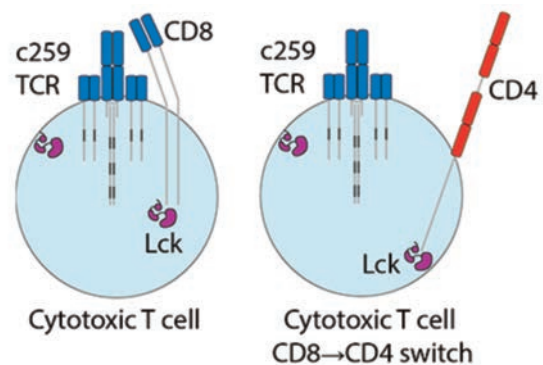
Rewiring T cell co-receptors to improve the safety of cancer immunotherapy

A new study from the Dushek and van der Merwe labs demonstrates a novel strategy to reduce dangerous off-target effects in engineered T cell therapies.

Published in *Nature Biomedical Engineering*, the work shows that T cell cross-reactivity can be finely controlled by engineering co-signalling receptors, offering a universal way to make adoptive T cell therapies safer without altering the T cell receptor (TCR) itself.

Adoptive T cell therapy, in which patient T cells are engineered to express tumour-specific TCRs, has shown remarkable promise in cancer treatment. However, a major limitation of this approach is TCR cross-reactivity: engineered T cells can mistakenly recognise healthy tissues, leading to severe and sometimes fatal autoimmune toxicities. Current strategies to mitigate this risk largely focus on painstakingly identifying TCRs with intrinsically low off-target activity, a process that is time-consuming and not always reliable.

In this study, Cabezas-Caballero and colleagues took a fundamentally different approach. Instead of modifying the TCR, they investigated whether T cell cross-reactivity can be tuned through co-signalling molecules that modulate TCR signalling strength. Focussing on CD5, CD8 and CD4, the authors systematically dissected how these receptors influence antigen sensitivity and specificity.



Schematic of CD8→CD4 co-receptor switch in cytotoxic T cells

A central finding from this work is that co-receptors CD8 and CD4 have opposing effects on ligand discrimination. CD8 lowers the activation threshold for low-affinity peptides, thereby reducing discrimination, whereas CD4, when expressed in a context where it cannot engage its canonical ligand, increases discrimination. By knocking out CD8 in cytotoxic T cells and expressing CD4 in its place, the authors implemented a co-receptor switch that substantially raises the activation threshold for lower-affinity, off-target peptides. Importantly, these engineered T cells retain strong on-target responses against their intended tumour antigens, maintaining cytotoxic potency while becoming far more selective.

By decoupling TCR specificity from co-receptor-mediated signal amplification, the authors show that it is possible to generate ‘super-selective’ T cells that are much less likely to trigger harmful autoimmune reactions. Because this strategy does not depend on altering the TCR sequence itself it could, in principle, be applied broadly across many different TCR-based therapies.

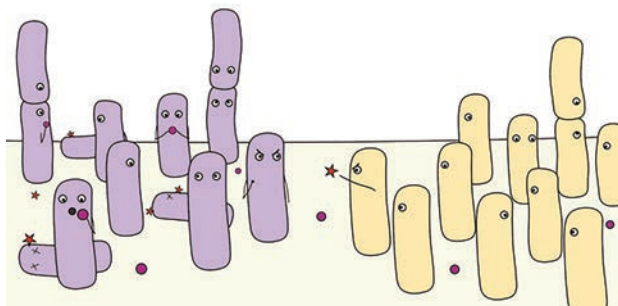
Overall, this work highlights co-receptor engineering as a powerful and generalisable tool to enhance the safety of T cell immunotherapies. By reducing the risk of lethal off-target cross-reactivity while preserving anti-tumour efficacy, the study opens new avenues for the clinical development of safer, more reliable TCR-T cell treatments.

Written by Zara Kaplan (Freeman lab)

More than just a food fight: what it takes to succeed in a bacterial community

An investigation carried out by the Foster lab sheds new light on life in diverse microbial communities. By capturing the interplay of nutrient competition and toxin warfare, the authors show what it takes to win against neighbouring bacterial strains – with important implications for antimicrobial resistance research.

The human body is a battleground for bugs. Across multiple fronts – from fuzzy teeth to the depths of our digestive systems – bacteria are waging an invisible war for the resources available. Aggressive strategies or ‘interference’ targeted at competing strains can manifest in different ways; from the use of ranged weapons like released toxins to melee attacks with the spear-like type six secretion system (T6SS). Whether producing these weapons is worth the cost for bacteria is a key question in antimicrobial resistance research, where work is ongoing to engineer beneficial strains capable of outcompeting and displacing problematic residents.



The mathematical model developed by the team predicts that tools like the TS66 are actually fairly useless for rare invaders. Success against overwhelming forces is instead determined by the ability to secure resources – especially ‘private nutrients’, which invaders enjoy but existing residents find unpalatable. Invaders must then survive any deadly interference in their new neighbourhood long enough for growth to outpace mortality.

With enough time and eventual rearmament, invading underdogs can even launch their own campaign of toxic interference and displace the resident strain.

These predictions played out across several experimental scenarios using both engineered *E. coli* and naturally occurring isolates with antimicrobial resistance. While antimicrobial resistance strains are metabolically diverse, a predicted nutrient niche difference to the resident strain was the consistent factor for successful invasion. Invaders able to gain a foothold and with the capacity to ramp up effective interference measures were also able to displace residents. Tellingly, these same resident-invader pairs behave very differently when their battle plays out in a neighbourhood of diverse communities; invasion is effectively blocked in the face of wide competition for what might otherwise be private nutrients.

This work builds on previous studies that suggest successful niche invasion ultimately comes down to obtaining the right nutrients. However, once strains are established, antimicrobial weapons can be used to devastating effect. These deceptively simple rules of engagement are of fundamental importance to researchers investigating complex questions around the gut microbiome and antimicrobial resistance, where effective biotherapeutic strains and tailored supplementation could be a powerful tool for ousting problematic bacteria.

Written and illustrated by Charlotte Melia
(Electron Microscopy Facility)

Converting a kinase through molecular mimicry Published in *EMBO Reports*, a new study by the Thurston Group reveals how a small virulence protein from *Salmonella* called SteE uses molecular mimicry to reprogramme host kinase specificity.

Kinases carry out phosphorylation, a diverse, reversible post-translational modification that mediates the precise regulation of diverse, core cellular processes, including cell cycle progression, metabolism and immune signalling. Paramount to the integrity of phospho-regulated signalling networks is the strict control of kinase substrate specificity; this refers to both the amino acid that is phosphorylated and the substrate that becomes phosphorylated. Conventional dogma assigns eukaryotic kinases to one of three groups according to the amino acid(s) they phosphorylate; serine/threonine kinases, tyrosine kinases and a rarer group that phosphorylate serine, threonine and tyrosine residues – the so-called dual specificity kinases (DSKs).

The Thurston group previously identified a novel phenomenon they called kinase reprogramming, whereby the amino acid and substrate specificity of a host kinase, called GSK3, is altered when bound by the small *Salmonella* virulence protein, SteE. That is, remarkably, when SteE interacts with GSK3, this otherwise strict serine/threonine kinase phosphorylates new substrates on tyrosine residues.

Until now, it was not known whether kinase reprogramming was specific to *Salmonella* or not. In this new study, led by postdoctoral researcher Ioanna Panagi, the team shows that the reprogramming of GSK3 happens in diverse Gram-negative bacteria, and is mediated by homologues of SteE found in those organisms. As the mechanism behind the switch in GSK3's activity remained enigmatic, they then investigated the molecular basis of how SteE targets GSK3 in *Salmonella*. They found that SteE-induced tyrosine activity conferred on GSK3 requires an L/xGxP motif found in SteE. Interestingly, this motif was previously shown to mediate GSK3 autophosphorylation on a tyrosine residue and is found in several kinases that undergo auto-tyrosine phosphorylation. Overall, they propose that a series of short linear motifs within SteE, which each mimic eukaryotic signalling motifs, mediate kinase selection, kinase reprogramming and substrate selection, ultimately driving kinase reprogramming.

Few kinases are *true* dual-specificity kinases that phosphorylate S/T and Y residues of substrates. This study suggests that kinase reprogramming allows an expansion of the kinome without the need for an entirely new kinase, representing a fourth class of kinases that are adaptable.

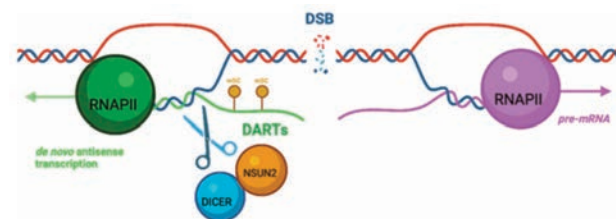


The findings of this work were summarised in artwork that was selected as the cover image for *EMBO Reports*. The image shows *Salmonella* wearing a mask to depict how it mimics the host cell (lady in blue). The bacterium is holding SteE (rope) which acts as a link to tie the host kinase GSK3 together with its substrate STAT3.

The 'DART' side of transcription: new role for NSUN2 in the RNA-dependent DNA damage response

A recent study from the Gullerova lab led by Adele Alagia reveals an important mechanism by which cells repair DNA damage.

Published in *Nature Communications*, the work highlights the importance of RNA modifications and how the NSUN2 protein is involved in the cellular response to DNA damage.



NSUN2 promotes RNA turnover at DNA breaks via DICER-dependent degradation of DARTs.

Cells produce a type of RNA called DARTs (damage-associated RNA transcripts) near the sites of the most toxic type of DNA damage, double-strand breaks. These RNAs can form R-loops, structures where RNA binds back to the DNA strand, leaving a displaced single strand of DNA. Such R-loops could be a double-edged sword: whilst they can facilitate DNA repair (e.g., by acting as binding platforms for repair factors), they can also cause further DNA damage (if single strand DNA remains exposed), increasing the risk of mutations, and are linked to various diseases including cancer.

Known for its role in adding methyl groups to RNA, NSUN2 influences RNA stability and its interactions with other proteins. Since similar proteins have known roles in repairing DNA damage where R-loops are present, and increased levels of NSUN2 are common in many cancers, this prompted the group to investigate the role of NSUN2 in DNA damage repair.

Employing a variety of state-of-the-art molecular biology techniques, including modified 5-AZA-chromatin immunoprecipitation and Oxford Nanopore Technology for direct RNA sequencing, the team demonstrated a clear interaction between NSUN2, DICER, and R-loops. The findings reveal that NSUN2 is essential for promoting the cleavage of R-loops by the DICER enzyme. When NSUN2 is depleted, cells accumulate DARTs and R-loops around break sites, and DNA repair is delayed. The authors also show that NSUN2's methylation activity is essential for efficient repair via homologous recombination, a high-fidelity repair pathway. Their results suggest that inhibiting NSUN2 activity and its associated RNA modifications could offer promising therapeutic strategies for conditions linked to DNA damage and R-loop accumulation.

Overall, this work underscores the intricate relationship between RNA modifications and DNA repair mechanisms, showcasing how cells maintain genomic integrity under stress. By highlighting the role of NSUN2 and RNA modifications, the Gullerova lab have opened new avenues for potential

treatments for diseases resulting from DNA damage, paving the way for innovative therapeutic approaches.

Written by Zara Kaplan (Freeman lab)

New funding to support research on children's cancer treatment

The funding by Alice's Arc will support a project co-led by Bass Hassan, to develop a new vaccine for Rhabdomyosarcoma.

Alice's Arc is delighted to announce that it will be investing £670K in an innovative, new Rhabdomyosarcoma research project with the University of Oxford.

The project aims to develop and test the efficacy of a bespoke neoantigen mRNA vaccine as an adjuvant therapy for multi-modality treated Rhabdomyosarcoma. The work will also focus on generating a therapeutic pipeline to test these vaccines in clinical trials for Rhabdomyosarcoma patients. It will be co-led by Doctor Felipe Galvez-Cancino, Group Leader, Kidani Fellow, Centre for Immune-Oncology, Nuffield Department of Medicine and Professor Bass Hassan, Group Leader, Professor of Medical Oncology, Sir William Dunn School of Pathology.

Rhabdomyosarcoma (RMS) is a rare and aggressive cancer of soft tissue e.g. muscle and fibrous tissue, that usually occurs in children but is also seen in teenagers and adults. For the majority of patients, the treatment of RMS includes intensive chemotherapy, surgery and radiotherapy. Treatment remains generic and progress devising new treatments has stalled. At the point of relapse, survival is a dismal 8%. New treatments are urgently needed.

Bass Hassan commented: "Over the last 30 years we have learnt about the molecular mechanisms that underly the development of Rhabdomyosarcoma, yet we have not translated these into new effective treatment strategies. I am excited by the leadership provided by the Alice's Arc charity in challenging and supporting the research and innovation community to take risks with new disruptive approaches. My lab and clinical team are excited to continue our work on this challenge with Felipe's team to bridge the gap between basic research and an informed development of mRNA vaccines in Rhabdomyosarcoma".

Felipe Galvez-Cancino commented: "It has been a pleasure to co-create this research with Bass' lab and Alice's Arc. It is imperative that we focus on devising new treatments for children with aggressive tumours such as Rhabdomyosarcoma. These children continue to be treated with the same, old, generic treatment protocols leaving those that do survive with serious long-term side effects. My laboratory is motivated to play a role to change this story for future patients."

Sara Wakeling (Alice's Arc co-founder) added: "Alice's Arc has a

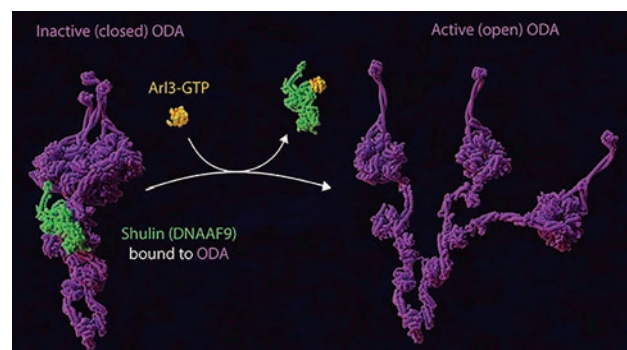
mission to help pave the way for new treatment options for Rhabdomyosarcoma patients to be available at frontline and relapse timepoints. The development of mRNA vaccines is a promising and relevant new avenue in the field of cancer research. We want to ensure children with Rhabdomyosarcoma are at the forefront of scientific research and discoveries in the field of mRNA vaccines as a treatment for cancer in the future. We are delighted to be working with the team at Oxford on this ground-breaking research"

Switching on dynein motors to power cilia motion

Published in *Nature Structural & Molecular Biology*, a new study by the Mali group reveals a mechanism for activating the dynein motors that power cilia motion.

Cilia are vital for human health, driving fluid movement in the airways, brain, and the reproductive system. Defective ciliary beating underlies devastating human diseases called motile ciliopathies. Ciliary movement relies on outer dynein arms (ODAs) which are powerful motor protein complexes. ODAs exert forces on ciliary microtubules to generate beating motion. ODAs must be carefully regulated to prevent premature activity as this can severely disrupt the cells' microtubule organisation.

In their inactive state, ODAs are packaged in the cell by an inhibitory protein called Shulin (known as DNAAF9 in mammals; green molecule in the figure). Shulin keeps ODAs "switched off" during their assembly and transport to the cilia. Once ODAs reach cilia, they must be activated i.e. Shulin must be released. This study reveals how the GTP-bound form of ARL3, an essential ciliary GTPase protein, binds to Shulin and displaces it from ODAs, unlocking the motors specifically inside cilia. This release allows ODAs to become active and power ciliary movement.



Using a combination of biochemical reconstitution, mutagenesis, and structural analyses, the group identified the binding region between ARL3 and DNAAF9. This work presents a unified model for ciliary dynein regulation – ODAs are assembled and kept inactive in the cytoplasm, transported into cilia via intraflagellar transport (IFT), and locally activated by ARL3-GTP within cilia to power motility.

The study uncovers a fine-tuned molecular switch in motor activity that is coupled to the GTPase cycle of an essential

ciliary protein, marking a significant step in our understanding of how motor proteins are spatially and temporally controlled. For their breakthrough work, the research team, led by Girish Ram Mali with support from the studies first author Karim Housseini, received the 2025 Ian and Barbara Gibbons Award (named after the pioneers who discovered the dynein protein).

Written by Siham Abdul Jaleel (Mali group)
and edited by Girish Ram Mali



Professor Emma Slack forges link with Botnar Institute of Immune Engineering

Professor Emma Slack, the Barclay-Williams Professor of Molecular Immunology at the Dunn School, has accepted a joint appointment at the newly founded Botnar Institute of Immune Engineering (BIIE). This marks the

start of an exciting partnership between this Basel-located institute and the University of Oxford.

With a focus on immunology, the BIIE aims to develop solutions for the diagnosis, treatment and prevention of disease, with a particular focus on global child and adolescent health.

Emma's joint appointment will link the Dunn School's mission of transforming health by discovering the underlying causes of disease with a new team of world-leading bioengineers working towards novel therapies, vaccines and diagnostics. It will provide opportunities for collaborations and synergy at all levels, including for postdocs and students.

A leader in the rapidly growing field of intestinal mucosal immunity, Emma's group investigates the interactions between bacteria and the gut immune system. Epitomising the overall strategy of the Dunn School, her twin goals are to discover fundamental immunological principles, and to pioneer oral vaccines and methods of engineering the microbiome to improve health and protect against disease.

"I am really excited about the possibilities this appointment opens up, particularly the interactions with expert bioengineers such as Chase Beisel, and the shared vision to drive our laboratory towards tangible change for the health of infants and children in low resource settings", said Emma.

An immunological spin on war poetry by Jemima Barton, Trinity College

All Quiet in the Necrotic Core

*It began with the swirling of blood, curling and whirling through arteries
the foreign army: apoprotein armour covering a cholesterol core,
slipping through endothelial defences, numbers building, building*

We Must Fight Back!

*we send in some of our finest, our best, most dedicated men
the Macrophage Unit, armed with pseudopodia and digestive enzymes,
the beating heart of the Innate Immune Division*

Find the Cholesterol Army that has breached our defences and destroy them, a simple task

*The macrophages advanced, taking up lipoprotein after lipoprotein, skilled fighters indeed
Unaware of the threat*

The lipoproteins had evolved. Oxidised by traitorous free radicals. Armed.

*The macrophages deployed their lysosomes, the final nail in the coffin
but the enemy were ready. One by one the lysosomes failed,
the lipoproteins prevailed*

Desperately, the macrophages tried again, gathering up lipoproteins and dignity, their reputation, their honour

Subverted, wearing a badge of shame labelling them Foam Cells

The firing squad would have been preferable

The ghosts of the once great Macrophage Unit can still be seen today

The fatty streak their place of death, the necrotic core their final rest

Fragments of brave soldiers surrounded by the enemy,

The atherosclerotic graveyard only growing

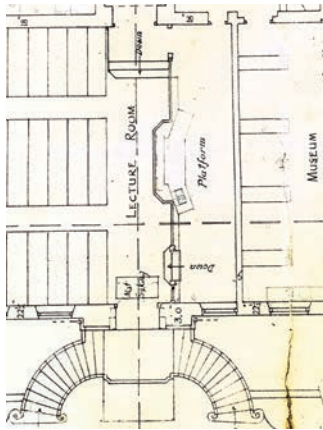
A warning of a battle lost that will never be heeded

In memoriam: Dr Eric Sidebottom 1938 – 2025

Simon Hunt

“Local boy from nowhere makes good”. He was the archetypal self-effacing team-player. A Lancashire lilt to his voice and a sympathetic smile formed the essence of a multifaceted and satisfying life. Here is an appreciation by his near-contemporary, Simon Hunt.

Transport your imagination back to the first week of the 1960 academic year on Monday 10th October, a cool, somewhat drizzly day. You are standing at the outside staircase of the Dunn School – not the main entrance facing the road but the one at its West end, opposite what was then the University’s Botany Department and Commonwealth Forestry Institute. You tally-count the 59 medical students who are arriving to hear their first lecture by Sir Howard Florey, PRS, at 9.15 a.m. They are in their fourth year¹, starting their “Path and Bact” course, having passed their Final Honours degree



Design for the lecture theatre entrance steps by Edward Warren, architect

in Animal Physiology in the summer. One of those bounding energetically up the stone steps directly into the Lecture Theatre² is Eric Sidebottom. Florey customarily began his lecture series with an exposition of the “history and scope of pathology”³. In 2017⁴, Eric described Florey’s lectures as “competent, very conscientious but not exciting”. That initial experience of the Dunn School did not, however, discourage him from later

returning to the department as a DPhil student in 1966 and then as University Lecturer in Experimental Pathology for two decades (1969-1989) and finally as de facto historian from the late 1990s onwards. Perhaps you may suspect, as I do, that Florey’s first lecture embedded itself into Eric’s deep subconscious. Could that explain why he subsequently became everyone’s go-to historian of the Dunn School? We’ll see later how he revealed the story of our early departmental foundation when a Scottish pathology lecturer, Dr James Ritchie, was appointed in 1897.

People with the family name Sidebottom in the mid-20th century were strongly clustered in the Lancashire-Derbyshire-Cheshire region. Eric was born bang in the centre, in Whaley Bridge, and he lived there and nearby as he grew up. His speech retained touches of a typical Lancashire lilt throughout his life. People associate that accent with character traits which are down-to-earth, no-nonsense but very sympathetic and supportive. Eric certainly exhibited all of those attributes. His father was a water-supply engineer who tragically lost his life at the age of 36 when Eric was only four years old, probably through occupational illness at Fernhill reservoir where he worked. Eric remained an only child, brought up by his widowed mother, a seamstress. She deeply felt the lack of a chance for her own higher education, so she was very



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Eric in 2022, viewing his own 1966 portrait photo

determined that Eric’s schooling should prosper and that he should aim high. “*She was responsible for my career*” said Eric later. He held a County Scholarship as a boarder at Kirkham Grammar School near Preston in Lancashire, an institution with a centuries-old heritage. The headmaster steered him to study medicine at Corpus Christi College, where he matriculated in 1957 having deferred the then-obligatory call-up to National Service⁵.

Eric enjoyed his Oxford undergraduate time to the full. He played plenty of team sports (photo) but also did the necessary to pass every exam first time. He completed his clinical medicine course in London⁶ at St Bartholomew’s medical school, 1961-3.



©Eric Sidebottom, own collection CC-BY-NC 4.0

Rugby players aspiring to be a Rowing Eight crew, Corpus Christi College, 1958

¹ It was in the 1970s that Pathology teaching was moved from the 4th to the 2nd year.

² The Lecture Theatre is now a lab, and the door to the exterior is now an impassable window

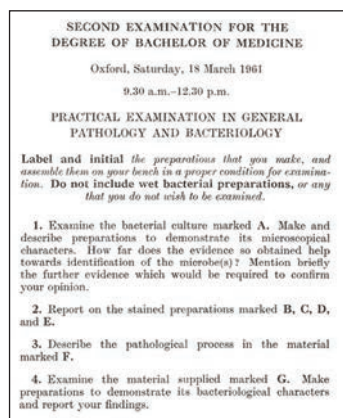
³ Read Chapter One of “*General Pathology*”, the textbook that Florey wrote and edited. Eric would have assiduously assimilated the contents of the 2nd edition in preparation for his BM exam at the end of Hilary Term – which he successfully passed first time. Only 44 of the 59 managed that, in those days!

⁴ Interview with Georgina Ferry, <https://podcasts.ox.ac.uk/eric-sidebottom>

⁵ Military National Service was abolished by the time he graduated.

⁶ At that time practically every Oxford medical undergraduate was obliged to study their clinical course at a medical school other than Oxford, usually London.

His Foundation Year ("House Jobs") included six months at a Bart's-associated hospital in Rochford which had a tuberculosis sanatorium where he treated TB patients. His seniors at Bart's and at the Pathology Department of the Radcliffe infirmary where he became Senior House Officer helped him further his interest in medical research. They put him in touch with the recently-appointed head of the Dunn School, Professor Harris, who awarded him a Philip Walker studentship for three years to undertake a DPhil.



Exam paper for Pathology practical which Eric sat and passed in 1961

sourced by Jim Kent from - where else? - the department's animal house. In essence, a dormant, transcriptionally inactive nucleus (hen) could be transferred into a metabolically active recipient cultured cell (mouse). Over the next few days, genes in the reactivating hen nucleus burst into new RNA synthesis. Henry had noticed that nucleoli, not previously visible within the hen nucleus, develop at the same time. Did nucleoli therefore play a necessary role in the synthesis of RNA and its transport to cytoplasm to be translated to chick-specific proteins? If so, what kind of RNA? It was Eric's task to zap the newly-arising nucleoli in heterokaryons with a powerful ultra-violet microbeam¹¹ to inactivate them, then measure the subcellular distribution of intracellular RNA synthesis by laborious autoradiography. Microscope systems with the appropriate optics (no UV lasers then!) had previously been described in the literature but the sophisticated instrumentation he needed had to be designed, constructed and tested in-house. The expert Dunn School workshop rose to the challenge, just as it had done previously for many other departmental research programmes. The vital contributions by Harry Stroud and his craftsmen specialists always enabled the Dunn School to undertake unmatched research. The department had a superb reputation as an exceptionally 'well-found' laboratory because of

the technical skills of the staff who worked in the workshop¹² and the animal house. Equally vital was the lab technician support. Joy Rawlins¹³, née Whiter, joined the microbeam lab from its outset, continuing for eight years with Eric until 1974. She has written about her time working conscientiously, successfully and happily together with him during the cell fusion days. She recollects the special dinner to mark her leaving that he generously gave for her in Lincoln College in gratitude for her service. Jane Sharps then replaced Joy as Eric's technician after 1984 (see an interview with Jane in page 30).

The results from the microbeam experiments, technically extremely difficult but successful, were open to a number of possible interpretations, discussed in his 1976 review co-authored with his first DPhil student, Ilan Déak¹⁴. To the question about the necessity for nucleoli in the transfer of genetic information from nucleus to cytoplasm, the answer could be summarised as "yes, partly, but...". Many of the suggestions they made can easily be embraced within modern-day models of gene transcription and expression. It cannot be claimed, however, that their nucleolar ablation experiments really forged an influential shaping of these models.

Having been appointed to his University Lecturership in 1969 immediately following his DPhil, Eric turned his research towards studying metastasis in experimental mice, continuing his collaboration with Henry Harris's lab group. They sought cell biological characteristics that might reliably distinguish metastasizing from non-metastasizing tumour cells. His studies, conducted mainly with his DPhil student Stephen Clark¹⁵ and with academic visitors over the next decade or so, showed that the simplifying hope that there might be a major prominent "marker" was over-optimistic for such a multi-step and intricate process as metastasis.

Eric's time and energy for research were substantially constrained by other competing demands. Not only had he been doing frontline teaching as departmental Demonstrator then Lecturer but, in addition, the Head of Department tasked him with organising all of the Pathology teaching contribution to the overall medical course. In 1970 his predecessor at the Dunn School in this role, Dr John French, died suddenly mid-career. French had initiated moves towards better coordination between all the preclinical departments, which traditionally had acted too independently. Eric vigorously took over the further development of this integration strategy and soon found himself on many faculty

⁷ The nucleolus is an eye-catching sub-structure within the nucleus of some but not all cells, described first by the Berlin-based microscopists of the 1830s. In 20th-century research, a high-magnification phase-contrast microscope would be used to visualise them in living cells.

⁸ Multinucleate cells that contain genetically different nuclei

⁹ Replaced later by polyethylene glycol, PEG, which remains to this day the standard fusogen.

¹⁰ Birds, reptiles, fish, amphibians all retain their nuclei. It is only mammalian erythrocytes that shed their nuclei when fully differentiated.

¹¹ Tschachotin's 1912 'radiopuncture' or 'micro-vivisection' experiments introduced a way to target intracellular destruction using UV. Zirkle, Uretz and Perry (1954, Oak Ridge, USA) and their colleagues engineered precision UV microbeam instruments to perform nucleolar ablation. Commercial instruments were not available in the 1960s. Eric, trained as a doctor not an engineer, supervised the building of his own bespoke instrument from their descriptions.

¹² The workshop was demolished to make way for the entrance hall of the EPA Building in the late 1990s

¹³ Joy returned part-time to Eric's lab in 1983 for one year, then moved on to become Henry Harris's own research assistant. The final phase of her Dunn School time was with Prof Jeff Errington 1997 – 2004.

¹⁴ E. Sidebottom, I.I. Déak (1976) "The Function of the Nucleolus in the Expression of Genetic Information: Studies with Hybrid Animal Cells" International Review of Cytology 44: 29-53. doi: 10.1016/S0074-7696(08)61646-0

¹⁵ Steve described his 41-year Dunn School journey in "With no particular place to go...": Fusion 11 (2012) page 14. He highlighted his great debt to the two Eric(h)s, Jost and Sidebottom, as he progressed while employed full-time first through an Open University degree, then a DPhil, strongly encouraged by them. "...I hope the Dunn School will continue to provide an environment which enables people from less conventional backgrounds to benefit from similar educational and professional development..."



Eric (L) and the author, Dunn School group photo 1988

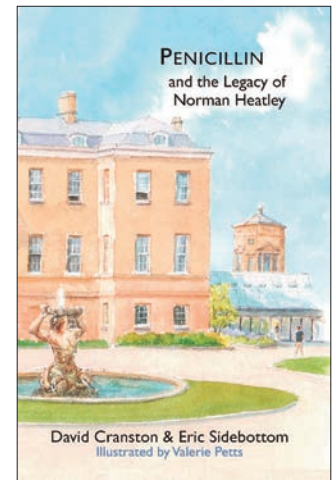
and sub faculty committees, often chairing them. He served on four curriculum review committees, chairing one. Further burdens – as well as plentiful satisfactions! – arose from his appointment in 1972 to a full Fellowship at Lincoln College as their Nuffield Research Fellow and Medical Tutor; from his University role as ‘Assessor’ (1979-80), whose specific remit was (and still is) student welfare; from his membership (1980-9) and acting chairmanship (1983-4) of the Committee for Scientific Collections in the University Natural History Museum; and most significantly as ‘Preclinical Adviser’ (1982-9). This latter job is now entitled ‘Director of Preclinical Studies’ with a substantial staff occupying one floor of the Medical Sciences Teaching Centre. In Eric’s time there was only a small office within the Physiology department, staffed by just one extremely capable secretary, Glenys Davies, who brought her Welsh background to her work. Eric was instrumental in cajoling, not banging, heads together to improve management of teaching resources, academic planning and cross departmental liaisons. The title ‘Adviser’ emphasised that any undergraduate medical student who was in a difficulty that was not soluble elsewhere could come to him through his open door for confidential assistance. The duo from Wales and Lancashire fully deserved their reputation for providing effective, helpful support. Over the decades, along with senior staff from other pre-clinical departments, the sequence French → Sidebottom → Goss → Vaux → Norbury, developed a highly-regarded framework for thought-provoking teaching and effective learning. The Dunn School should be proud of the pedigree of this leadership.

In 1989 Eric, by his own choice, resigned his University and College posts and moved to new pastures for his career progression. A sabbatical in the previous year had generated contacts with the clinical side of the major cancer charity ICRF¹⁶, especially with its clinical director, Dr (now Sir) Nick Wright. Eric’s post was Assistant Director of Research (Clinical Liaison). The work involved many visits around the UK to clinical oncologists and medical school Deans. He found enjoyment and satisfaction as a skilled and experienced administrator fostering the translation of basic research on malignancy and metastasis through to application in useful diagnosis and treatment. He researched and wrote ICRF reports, both internal and published, including for example the annual volumes of Cancer Surveys. He was involved in high

level-national reports on future medical manpower in the UK. But a deterioration in the ICRF’s funds meant that he had to leave their employment rather sooner than he had at first expected. In 1994 at the age of 57 he became an independent medical research and education consultant based in Oxford. He additionally taught as a medical tutor at St Hilda’s College and as a demonstrator in the BM pathology classes.

His new independence, worrying as it must have been for his financial income, gave him the chance to develop a professional interest in the history of pathology and of medicine at Oxford. He became a sought-after lecturer, for instance on cruise ships and to local lay public groups. In his presentations he often recounted the Dunn School’s part in the penicillin story. He was a master of the anecdote and painted convincing word-pictures of

Florey, Heatley and Abraham. After all, he had met them! In 1977 during the 50th anniversary celebrations of the opening of the Dunn School he had shared the lecture podium with A. D. ‘Duncs’ Gardner¹⁷, a co-author of the first penicillin publications.



The ‘Pathological Laboratory’ in the Science Area adjacent to the Pitt Rivers Museum. James Ritchie drew up the specification for it. It opened in 1901, was transferred to Pharmacology in 1927, then to Chemistry. It made way for the new Earth Sciences building in 2008

He took a particular interest in researching the birth of pathology and bacteriology as a discipline at Oxford in the late 1890s. Dr James Ritchie, appointed as the first University Lecturer in Pathology in 1897¹⁸, became Eric’s ‘hero’. Backed by the Regius Professor, Burdon-Sanderson, the very energetic Ritchie prepared plans to expand teaching accommodation near the University Museum: and he shaped and gave most of the first course of instruction in the subject. One of his first students, the Australian Ewan Frazer, generously donated £5,000¹⁹ towards the

¹⁶The Imperial Cancer Research Fund ICRF amalgamated with the Cancer Research Campaign to form CRUK in 2002.

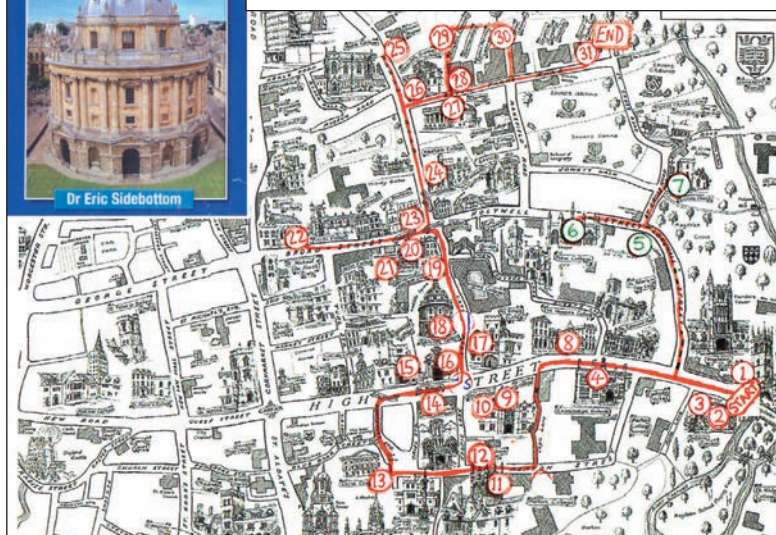
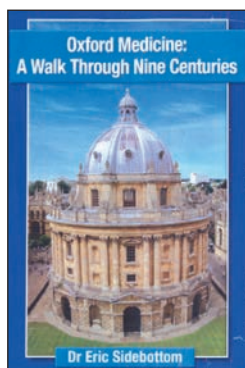
¹⁷Former bacteriology professor in the department and Regius Professor of Medicine 1948-56.

¹⁸And goodness, did he lecture?! He delivered three lectures per week for each and every term for seven years; plus practical classes and demonstrations in Pathology; plus approximately 200 reports per year on clinical pathology specimens as a service commitment to the Radcliffe Infirmary. He was soon promoted to Reader, and in his last year to Professor. The promotion was, however, insufficient to retain him at Oxford and he returned to Edinburgh for the rest of his career.

¹⁹Worth over £0.5mn nowadays. It was conditional on the University match-funding a further £5000.

construction of the “Pathological Laboratory”, on a site where Earth Sciences is now located. Later, the occupants of this building relocated when the Dunn School opened in 1927, leaving it instead to be used by Pharmacology. Eric greatly admired Ritchie and unearthed the relevant original University documents and correspondence. He wrote up this story in a short,

authoritative biography of Ritchie published to celebrate the centenary, in 2006, of the Pathological Society²⁰. Subsequently, Eric took every opportunity to publicise Ritchie’s



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talents and achievements and to raise his profile publicly. Eric also co-authored peer-reviewed biographies of Sir William Dunn²¹ and of Sir Henry Harris²². He devised, published and sold a successful book “*Oxford Medicine: a walk through nine centuries*”. Both natives of, and visitors to, our city greatly enjoyed his guided tours. With David Cranston he published in 2016 an authoritative and very readable book on the Penicillin story, slanting it towards the part played by Norman Heatley. He co-edited with Paul Fairchild the magazine you’re reading, *Fusion*, from Issue 6 to 19, 2007–2021²³. ‘History Corner’ was a special responsibility in each of these. His history instincts energised him, along with Lance Tomlinson when the latter retired as departmental photographer in 2002, to identify, sort through and index hundreds of Dunn School photos, papers and correspondence for permanent archiving in the Bodleian Library²⁴. What a valuable resource this will always be for both the casually interested and as serious primary course material for future academic historians delving into the history of education and research.

His range of contacts with Oxford medics, present and past, was inexhaustible. No wonder that he found himself organising the Oxford Medical Teachers Association (the ‘Bundle of His’) and

finding speakers for the Oxford Medical Lecture Club (OMLC). Like a snake-charmer, he managed to sweet-talk ten people per year into lecturing at OMLC over a period of a decade or more - testament to both to his persuasiveness and to the length of his contacts list.

This appreciation would be glaringly incomplete without a mention of Eric’s family. Eric married Margaret in 1964, having known each other since schooldays in Lancashire. By then he was a houseman on the way to becoming a fully-qualified doctor, while she had completed her training as a physiotherapist.

Although Eric once listed ‘Family’ under the ‘Hobbies’ section of his C.V., the rock-fast commitment of their 61 years of married life together proves that family provided a central foundation for him, come what may. As his mental powers declined towards the end, the sustaining comfort that Margaret and their family gave him was immeasurably reassuring. Their eldest child, Janet, leads the Public Engagement team at the University’s Museum of Natural History and is a Fellow of Reuben College. Their two sons are both medical doctors, consultants in radiology and in anaesthetics. Their seven grandchildren are a delight to them all – most of the time!

Thank you, Eric, for your friendship, for your collegiality, and for all the long-term benefits that those whose lives you improved now enjoy because of your service in your many engine-rooms of research, teaching, administration and family life.

Further resources:

Interview by Marisa Benoit: ‘Oxford Medicine’ magazine in 2015
His interview with Georgina Ferry in 2017:
<https://podcasts.ox.ac.uk/eric-sidebottom>

His full scientific bibliography and c.v. is in development.
Document is at Sustainable Digital Scholarship: doi:
10.25446/oxford.32820143



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Eric with his wife Margaret in 2022 on a visit to the roof of the Dunn School. They came to view aerially the tree in the University Parks under which Florey and Chain made the decision in 1938 to study the mould juice from *Penicillium*, to explore antibacterial properties that Fleming had documented in 1929

²⁰Sidebottom, E. “James Ritchie (1864–1923): The First General Secretary of the Society” www.pathsoc.org/_userfiles/pages/files/about/c01.pdf

²¹With Alison Paul (2006): “Sir William Dunn (1833–1912): The man, his trust and his legacy to science and medicine”. *Journal of Medical Biography* 14:46–53 doi: 10.1258/j.jmb.2006.04-24

²²With Sir Richard Gardner FRS. (2018). “Sir Henry Harris: 1925 – 2014”. *Biographical Memoirs of Fellows of the Royal Society*, 65, 133–150. www.jstor.org/stable/26774166

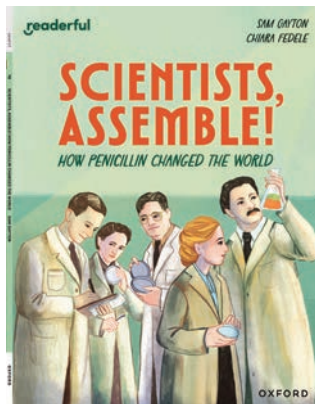
²³The archive of all *Fusion* issues is at www.path.ox.ac.uk/centenary_original/fusion-magazine/

²⁴They are catalogued at <https://archives.bodleian.ox.ac.uk/repositories/2/resources/3272>. They occupy six metres of shelving at the Bodleian’s Collection Storage Facility near Swindon: <https://blogs.bodleian.ox.ac.uk/oxfordtrainees/a-visit-to-the-collection-storage-facility/>

Scientists, Assemble! How Penicillin Changed the World

Catarina Vicente

To mark our upcoming Centenary in 2027, the Dunn School partnered with Oxford University Press to create a new children's book that celebrates core values of our scientific research: perseverance, interdisciplinarity and teamwork.



Rachel Exley first proposed the idea of marking the Centenary with a children's book in 2023. Rachel, and other members of the Tang lab, had for several years developed a series of outreach activities for schools that focused on the story of the development of penicillin. This experience had highlighted how the story of penicillin has the potential to inform and inspire

children, and also how it had relevance to several curriculum subjects: history, science and literacy (through storytelling).

This idea was enthusiastically received by everyone, but we were conscious that our expertise does not lie in children literature! Finding the right partner was, therefore, essential to ensure that our centenary children's book would have an impact and a legacy.

The obvious partner to approach was Oxford University Press (OUP), one of the leading publishers in educational literature. Established over 500 years ago, they undoubtedly had the track record we needed! Discussions started, and the project evolved. OUP proposed that the book should be aimed at children aged 9-10 years, a more mature primary school audience likely to be able to engage with the complexity of the penicillin story and its global medical impact. Another bonus was the natural links with both the science and the history curriculum for this age group.

OUP also proposed to develop the book as part of their new reading series, Readerful. Readerful is a whole school reading programme designed to build motivation, fluency, vocabulary, and knowledge through reading for pleasure. It offers carefully levelled books that strike the right balance between challenge and confidence, ensuring every child can experience success and enjoyment in reading. It places strong emphasis on inclusion and representation, presenting fully rounded characters, diverse lives, and global perspectives so that all children can see themselves reflected in books while also encountering experiences beyond their own. Alongside this, Readerful intentionally develops vocabulary through meaningful, repeated, and useful word choices, and builds



Sam Gayton



Chiara Fedele

knowledge in a structured, well scaffolded way that respects chronology, context, and multiple perspectives, ensuring children not only read more, but read more deeply and insightfully. And by selling to schools, the Readerful books reach children who may have never come across them otherwise. The series won an Educational Resources Award (ERA) in 2025. We were delighted and honoured by this proposal and also reassured that the book would also be available as a single, stand-alone title that Danners would be able to access.

This meant that this would no longer be "our" book, but rather an OUP project that we supported. However, OUP was enthusiastic in bringing us on board as scientific advisers. The Dunn School team was composed of myself, Christoph Tang and Rachel Exley, supported by several others who helped us find resources and check information, especially Lindsay Stimson.

Getting the text right

We started discussions with OUP in 2024, but it wasn't until early 2025 that working on the project began in earnest. The first step was to identify the right author for the book. OUP's expertise was invaluable, as for all other aspects of the project. They were keen to find an author that specialised in fiction books (and hence was skilled at engaging young readers) but also had a strong track-record in non-fiction, especially scientific topics, which are often complex and challenging to present to a young audience. Sam Gayton, a UK-based author that had worked with OUP before, including a book for the Readerful series on Dr Jon Snow and the cholera epidemic, was invited to join the project. His first task was to write a brief book synopsis. As soon as we read it, and discussed it with Sam, it was clear that he had invested a lot of time reading about the development of penicillin. There were also several important principles that Sam had picked on instinctively, and that we

thought were really important:

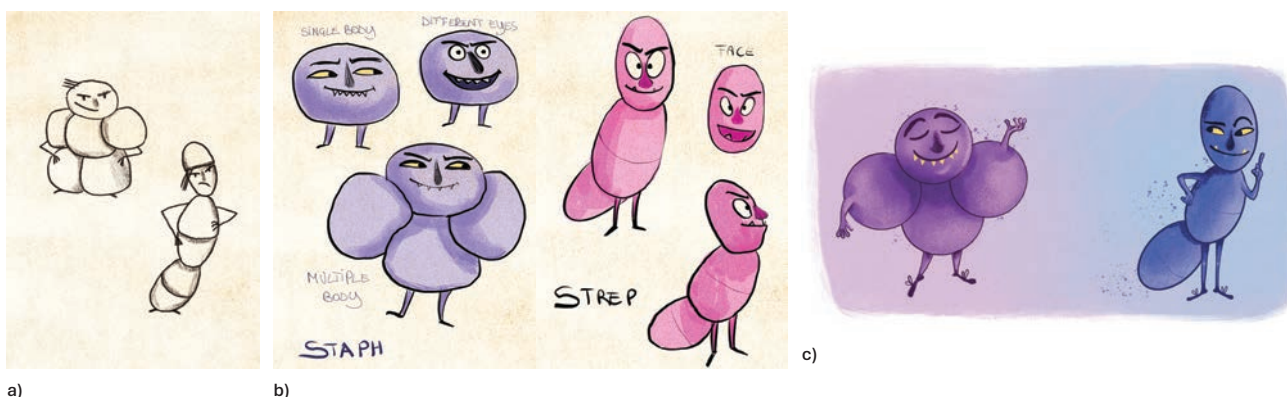
- Science is a collaborative endeavour, and the story should emphasise teamwork (acknowledging that scientists are human too, who sometimes disagree).
- A villain is important to draw a reader in, and we were pleased when Staph and Strep were cast in the role as the (albeit very cute) baddies! An idea also reflected in the Marvel-inspired book title!
- Big, world-changing breakthroughs do not appear out of nowhere. They are built on years of basic research.
- It should include the contribution of the various players across the world that helped make penicillin an invaluable therapeutic.

It was fascinating to see Sam's creativity shine through the text, but also how the text evolved through several iterations of feedback from us and the OUP team. For example, one of the points we were very keen on was that the story was inclusive, and featured a wide range of individuals who contributed to this work, in particular women. Meanwhile, OUP pointed out that some references to the Second World War were too complex for children, or that certain scientific terminology and concepts needed to be simplified for the target age group.

"When I was approached to write this book, I think I had the fairly typical understanding of how penicillin came about. I knew it was something to do with Alexander Fleming and mould, and that it happened sort of by accident. The truth - as ever - is far more fascinating! It involves mad inventions made from old dustbins, mouldy market melons, and a desperate race against time during the darkest hours of World War II.

There is so much to inspire and enthrall in this story. I see it as a kind of medical thriller. There are our heroes: an international team of talented scientists, who work together in spite of their personal differences. There are villains - bacterial infections, which before antibiotics meant that 'even a scratch from a rose thorn could kill'. And of course, as in all thrillers, there is a 'ticking clock' - the terrible battles of the Second World War, in which penicillin would save many thousands of lives."

Sam Gayton, author



The evolution of the villains a) The original sketch for Staph and Strep. Our feedback was that they were too 'insect-like' for bacteria b) An intermediate version c) The final villains, including the cute shoelaces! The bacteria were given a grape-like look and a purple-blueish colour to reference how they look like under the microscope.

Illustrating the story

For our target audience, illustrations are key, so finding the right illustrator was important. We were absolutely delighted when we heard that OUP had invited Chiara Fedele, an Italy-based illustrator, to work on the project. Chiara creates beautiful illustrations, and had worked on several projects with OUP before. Crucially, she had in the past illustrated books about historical figures, including scientists like Rosalind Franklin, and was skilled at ensuring that the characters were recognisable.

We sent Chiara and OUP a portfolio of current and archival images of the department, but with the Dunn School featuring so prominently in the story, we were keen that the Oxford-focused illustrations should be as accurate as possible. After all, the original building where the work took place is still our home today.

We therefore invited Chiara to travel from Milan to Oxford to sketch the Dunn School *in situ*. It was wonderful to meet Chiara, and to see how she creates images. For a project such as ours, she often sketches on her iPad using specialist software, but she also enjoys drawing on paper. In fact, as a thank you for our invitation, she kindly sent us a set of beautiful hand-drawn sketches of the Dunn School. These illustrations do not appear in the book, but feature in our new centenary postcards (see page 35 for full details on our centenary merchandise).

"When the Dunn School invited me to see the place, I was very honoured. It is not common for an illustrator to see the subject of the book in person. This helped me so much in the development of the illustrations, helping me create the right atmosphere."

Chiara Fedele, illustrator,
www.chiarafedeleillustrator.it



A selection of Dunn School characters and scenes from the book

a) A 'penicillin girl'

b) The P-patrol. Charles Fletcher, from the Radcliffe Infirmary, brings urine collected from patients treated with penicillin to Norman Heatley, so that it can be re-extracted

c) Ernst Chain hard at work in the original Dunn School library, sitting in an historically accurate chair

d) Florey in the Head of Department's office, mostly unchanged since the 1930s

a)



c)



b)



d)

Chiara's illustrations for the book reflect her versatility, and include cute/threatening looking bacteria, likenesses to the main characters of the story, as well as scenes featuring the inside and outside of the Dunn School.

We were grateful to be able to provide feedback on the illustrations, and how generous OUP was in incorporating our advice. Some of our feedback was very scientific, including fantastic detective work from Rachel in investigating original papers from the time to ensure the techniques were represented accurately. But we also had input on small details that made the illustrations more accurate, such as the chair in which Chain is sitting in the library scene (an original chair from the department still exists), or Florey's office (still our Head of Department's office). And sometimes our feedback was purely aesthetic, such as the little shoelaces for Strep and Staph, which we voted to keep despite the lack of any scientific basis!

Final reflections

Working on this project was a wonderful experience. Providing feedback on a children's book is so different from my day job, and I am sure that was also the case for Chris and Rachel, although both drew on their extensive experience engaging with school children on the penicillin story. From inception to publication, it was a 3-year project, and it was a delight to work with experts and professionals from such a range of areas, from writing to illustrating and editing.

The book is now published, and widely available to schools around the world. There are many ways you can get your own copy. It can be purchased from most online retailers, and you can also purchase it from our centenary online shop (with each copy including a special centenary sticker on the cover).

We will also showcase this project in a special temporary exhibition outside the Round Room, here in the Dunn School. It is a fantastic legacy of this centenary that the amazing story of the development of penicillin, which had such important milestones in our department, will live on in schools and homes. Through this story, we hope children encounter the importance of scientific collaboration, the transformative power of basic research, and the value of perseverance: principles that have shaped the Dunn School's work for over a century. We also hope it sparks curiosity and ambition, encouraging young readers to see science as something they could be part of and to consider futures in STEM related careers.

Acknowledgments

We would like to thank Jenny Campbell, Chris Lacey and everyone in the OUP team who enthusiastically supported this idea, welcomed and encouraged our feedback, and created such a fantastic book.

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The making of Scientists, Assemble!

Step 1: We had an idea that we knew would make a good children's book.

Step 2: We approached OUP and pitched the idea. We discussed aims, format, ways of working. They loved the idea and, luckily, had the perfect publishing opportunity for it!

Step 3: OUP asked its pool of children's authors with the right experience to submit synopsis ideas for the book.

Step 4: The author is sent a rough brief and submits a book synopsis. This is discussed and finessed before the first draft is developed.

Step 5: The author wrote several drafts of the manuscript, receiving feedback from OUP and us at each stage. The author also worked with editors to brief artwork and page layout.

Step 6: An illustrator was selected. The illustrator produced a sample, followed by feedback from OUP and us. Once a style had been agreed, the illustrator was commissioned.

Step 7: The text and artwork were developed further over the course of five proof stages. Slowly, all the elements of the book took shape.

Step 8: OUP presented us with several concepts for the front cover. After some back and forth, we arrived at a version we were all happy with. The cover was approved by OUP's editorial, design and sales teams.

Step 9: The final proof was approved and signed off, ready for publication.

The book was trialled with a Year 5 class and their teacher, who gave their honest opinions!

"It's rare to have the opportunity to collaborate so closely with the institution at the centre of an amazing story, and Scientists, Assemble! is all the better for it. It also felt special to bring this piece of local history to life, with the former Radcliffe Infirmary just a stone's throw from OUP.

Cat and the team's enthusiasm and attention to detail have baked a real sense of authenticity into every page. Whether it was the science itself, the Dunn School's furnishings in the 1930s, or imagining Staph and Strep as cartoon villains, their input was hugely valued by us and the author. Even access to Heatley's notebooks added another layer of authenticity to the page design (though his handwriting might have tested some readers!).

It was also a pleasure to share the book with children, who found it 'super interesting' and loved discovering things they hadn't known before. It's such a strong addition to our Readerful series, helping to get more children reading more, and will be a real asset to school libraries — hopefully inspiring children to pursue STEM-related careers."

Thoughts whilst writing an atherosclerosis essay (abridged) by Sunaina Raveesh, St Anne's College

Fatty streak inside of me, too young for detection by CT.

Small, yellow, and flat- but enough to unnerve
in my mind's eye I know where you are:
where my arteries branch, bifurcate, curve
where my blood flow is not laminar.

And there you remain, not clinically scary.
Is that all, small fatty streak?
Or will you inflame to a plaque- I am wary
Am I right, does my future look bleak?

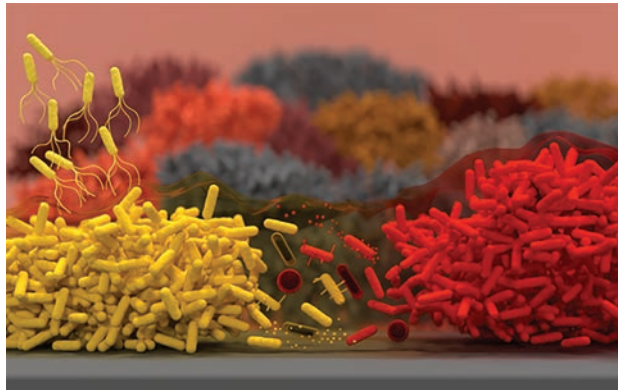
I'll do my part- avoid alcohol,
air pollution, and cigarettes.
I'll keep my lipid intake small
but it's not certain, I cannot bet.

I've learned your structure, aetiology
your public health burden I know.
To all fatty streaks, globally:
stay as you are, please do not grow.

Bugs not drugs: harnessing the gut microbiome to prevent disease

Kevin Foster

The human microbiome is rarely out of the news but we understand surprisingly little of how it works or how to control it. The Foster lab wants to change this and harness our own gut bacteria in the fight against antibiotic resistant infections.



Computer generated cartoon of two bacterial strains fighting with the type six secretion system and other toxins.

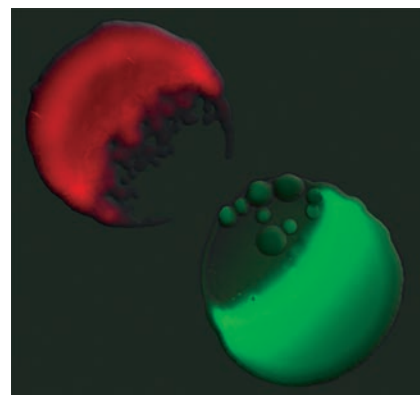
We are all host to massive and diverse communities of microorganisms, which are critical for our health. Our symbiotic microbes include bacteria, fungi, protists, viruses and archaea (the mysterious but ancient sister group to bacteria) and they form a complex living ecosystem that shapes our health and physiology. They live all over our bodies but it is in the large intestine that they reach the astonishing numbers that match that of our own cells. And the state of our gut microbiome has been implicated in everything from gastrointestinal and liver disease through asthma, arthritis and obesity to cancer and even mental health.

It is clear then that our gut microbiomes are central for our health and well-being. What is much less clear is what to do about it. Can we change and control our microbial symbionts in the pursuit of good health? This question has proved devilishly tricky to answer because of the sheer number of species that we each host. Indeed, you and I do not even harbour the same set of species. While there can be many overlaps, we each have our own characteristic communities; a 'microbial fingerprint' that is increasingly used in forensic science.

But I digress. The problem with all this diversity is that it makes it hard to know which member(s) of our microbiome cause a particular disease or even know if microbes matter at all. In some cases, your microbial fingerprint will be changed by a disease but not actually cause it, or at most exacerbate your symptoms. The difficulty in finding the causes of microbiome-associated diseases is particularly acute for conditions such as autoimmune disorders, cancer and psychological disorders where complex changes in our own physiology accompany any microbial shifts. For this reason, it made sense for my group to focus its first efforts in microbiome

engineering on the diseases that have the simplest of aetiologies (the fancy medical term I had to learn that translates roughly to 'stuff that made them ill').

What then *are* the microbiome diseases with the simplest aetiology? Perhaps there can be some debate but, for me, it is diseases caused by bacterial pathogens; such as *E. coli* and *Salmonella*. Strains of these species can enter our gut without adverse effects, but also have the capacity to invade the body via the gut wall and cause a range of symptoms including diarrhoea, nausea and fever. While these infections can resolve on their own, they can also have serious complications and even prove fatal. In the last century, these infections were routinely treated with antibiotics, but the rise of drug resistance has changed this. Indeed, *E. coli* and closely related species now cause the most deaths of any bacteria due to antibiotic-resistant infection, which number in the hundreds of thousands to millions worldwide.



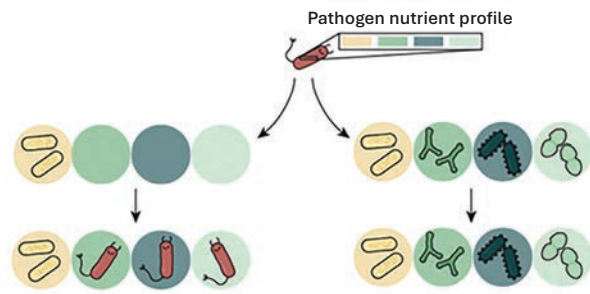
Two strains of *E. coli* fighting with protein-based toxins (colicins). While some *E. coli* strains are highly pathogenic, most are harmless and help to protect us against a wide range of pathogens, including other *E. coli* strains but also *Salmonella*, *Klebsiella*, *Shigella* and more.

Targeting bacterial pathogens with microbiome-based therapies makes sense, therefore, because the aetiology is clear but also because we are losing our ability to treat these infections with antibiotics. But what does a microbiome-based therapy look like? Here, we are building on something that has been known about microbiomes for decades: your resident microbes naturally protect you against incoming bacterial pathogens.

The human microbiome is, after all, an ecological system where bacteria and other microbe species must compete to persist and survive. That is, all incoming bacteria have to find space and nutrients to grow, which may have already been taken by

other species. A pathogen may also face a host of other hostile strategies from resident bacteria. It turns out that bacteria are probably the most aggressive organisms on the planet. They have evolved an amazing array of draconian mechanisms to kill and inhibit competing bacteria. This includes bacteria that make their own antibiotics, but also molecular machines like the type six secretion system whose dry name belies its fascinating biology: it is a tiny molecular speargun that fires into neighbouring cells to deliver lethal toxins.

Your resident gut microbes therefore combat incoming pathogens by starving them but also by stabbing and poisoning. The power of these mechanisms is such that some of our resident gut bacteria are starting to look like real alternatives to antibiotics. Can we replace (or at least augment) antibiotic drugs with friendly pathogen-killing bugs? We believe so. My lab has been growing many different species of human gut bacteria to find out which are the best at stopping pathogens. Typically, no one species alone will work but certain combinations are already showing the ability to stop some pathogens in their tracks. The reason lies in what we are calling ‘nutrient blocking’: while any one species typically leaves certain types of nutrients behind for others to consume (because each species will only eat certain types), the right combination of bacterial species can remove all of the resources that an incoming pathogen needs to grow and thereby block it from establishing. Add some species that also deploy toxins against a pathogen and you have the recipe for a microbial cocktail that can stop deadly bacteria in their tracks.



Nutrient blocking of bacterial pathogens. Left: if you have a depauperate microbiome with few species, there will be nutrient left for an invading pathogen to eat. Right: a diverse microbiome that contains the right species will use up all available nutrients and block an incoming pathogen from growing and causing disease.

There is plenty still to do but - in a field that has struggled to move beyond correlations - it is exciting to begin to see how to design microbiome communities for a particular goal. Another great advantage of working with living medicines is that we can make them evolve. When a bacterial pathogen evolves resistance to an antibiotic, the strategy has been to move to the next drug, and then the next one, until they run out. A live bacterial product is different, and we are developing ways to compete them against resistant pathogens and thereby evolve new products that are more effective. By harnessing both ecology *and* evolution, therefore, we are finding ways to harness the amazing biology of our own microbiomes for better health.

The curious case of the Dunn School Japanese garden

Louise Pankhurst

When visiting the Dunn School, people are often surprised by the fact, and curious as to why, we have a Japanese garden in our grounds. In this article, Louise Pankhurst (Foster Lab) gives us a short history of the Dunn School's Japanese garden.

Tucked away between the Dunn School and the EPA building, the Japanese garden has been a feature of the EPA entrance since around 2013. Measuring time in DPhils and Postdocs thirteen years is an eon; long enough ago that only a handful of Dunners now remember its creation.

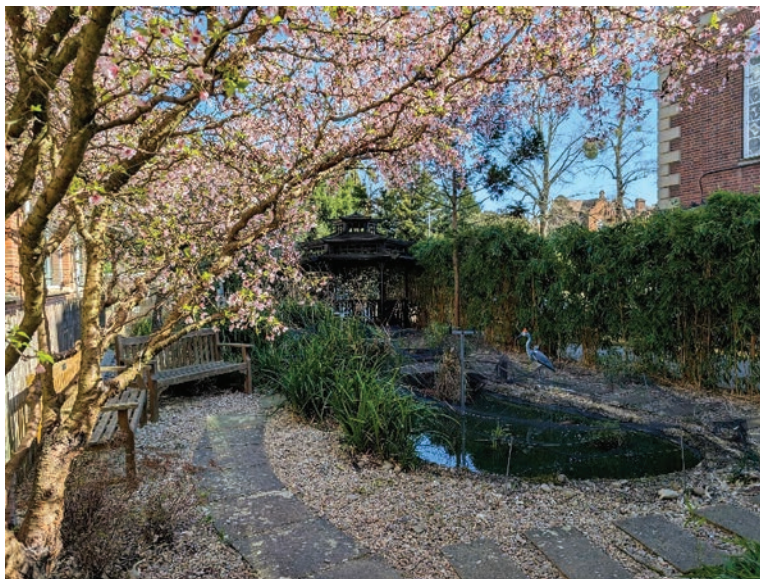
Previously the ‘muddy patch with bicycle parking’, the then Head of Department Herman Waldmann challenged Dunn School members to come up with a design for the area. Proving how artistry and science can go hand-in-hand, Quentin Sattentau (then a PI at the department, now at the Max Delbrück Center in Berlin) pivoted from immunology to garden design. A traditional British garden would not work, as the area does not receive enough sun. However, inspired by his travels, Quentin realised the muddy patch was ideal for a Japanese

scheme using plants that thrive in sheltered shade. Running with the idea, Quentin researched traditional Japanese garden design and sketched out some plans. Fumiko Esashi (Professor in Molecular Biophysics here at the Dunn School) provided guidance on the authenticity of the design, and finally, the garden was created as we see it today.

Centred around an hourglass shaped pool, the garden was populated with low maintenance and shade-loving plants and enclosed with bamboo. The garden has changed somewhat since 2013, when it was photographed for Fusion. Plants and trees have matured, and as I write the cherry tree is heavy with blossom, speaking of warmer days to come. Some plants, such as the irises, have been lost and fish (allegedly a gift from our esteemed current Head of Department) mysteriously appeared.



The Japanese garden nearing completion (photograph courtesy of Quentin Sattentau) and the 2013 Fusion magazine cover featuring the completed garden.



The Japanese garden today (March 2026); featuring the cherry tree in bloom and hungry, hopeful, local wildlife.

The presence of a garden and pond on-site is part of the Dunn School's heritage. The original garden with 'Molecular pools' was lost to the OMPI building and bicycle parking; although it is immortalised in the beautiful, tactile artwork 'Molecular Pools 2' (Ackroyd & Harvey) gracing the OMPI G entrance. The Japanese garden is safe from any new building, but time and usage have taken their toll. There is scope for some repair, tidying, and perhaps some new additions. These could be carefully chosen to remain faithful to the design but also contribute to supporting local wildlife. The University has an ambitious target to reach net biodiversity gain by 2035. At the Dunn School, we can contribute to this by making thoughtful

planting choices on our grounds and demonstrating how a biodiverse and wildlife rich garden is also beautiful.

Providing wildlife habitat is only a part of the garden's purpose, however. When designing the Japanese garden, Quentin created a haven where staff and students can grab a moment of peace during a busy day or meet colleagues to chat science. Amongst University departments, the Dunn School has an outstanding record when it comes to valuing the welfare of its members. The dedication of space to a garden is tangible evidence of this, as are the famed parties!



Painting of the original Dunn School 'Molecular Pools' (1999), their shape now echoed by 'Molecular Pools 2' (Ackroyd and Harvey); the artwork was constructed from slate salvaged from the original ponds. Photograph of painting courtesy of Lindsay Stimson.



The newly-minted Dunn School mascot.

One evolving tradition is the unwitting involvement of the Japanese garden and its residents in Dunn School celebrations. Legend has it the pond was once home to a flock of yellow rubber ducks. Intense internet sleuthing has turned up one suspicious photo of Susan Lea's laboratory (now at St Jude's Children's Research Hospital, Memphis), where yellow rubber ducks line the shelves - could it be they migrated from the Lea lab? The heron statue always adheres to guidance and wears PPE appropriate to the weather conditions, thanks to an unknown benefactor. However, it does sometimes sadly fail in its deterrence duties, as evidenced in the photos accompanying this piece; perhaps it's the hat? Regardless, it indulges in some classic Dunn School rest and relaxation and has been spotted in the Christmas dance floor conga line for the past two years; a timeline coinciding with the arrival of a somewhat boisterous lab on OMPI G. The author could not possibly comment.

Teaching Pathology at the Dunn School: a newbie's perspective

Teresa Thurston

One of our recent recruits, Associate Professor Teresa Thurston, who also holds a tutorial fellowship at Magdalen College, shares her experience of teaching her first series of practical classes for the department. The most important bit - the Dunn School community that supports behind the scenes.

It's nearly 2pm as I nervously await the arrival of the students for my first practical class. Today I'm teaching second year Biomedical Science students on the Infection and Immunity course. With some help (Greaves – what would I do without you!), I've successfully navigated the AV system, and the safety instructions are displayed across the lab. As the students start to filter in, I scan the classroom. There, ready and waiting, I spot

the team of demonstrators in their blue laboratory coats. My nerves start to calm. These early career researchers, PhD students and postdoctoral researchers, have, this week, put down their own pipettes to undertake a very important job: during these practical classes they will lead small group discussions and provide a supportive learning environment to the students in this classroom. From helping those who have

fallen behind, to skilfully answering any number of questions, they also provide invaluable support to the class leads. This allows me to focus on the overall delivery but to also have time to walk around and discuss with individual students.

Before long, my cue to start has arrived: like a well-oiled machine, a mini procession of Dunn School research technicians file out of the preparatory room, ready to hand out plates full of bacteria to the students. Throughout these practical classes, they will seamlessly help the class transition through the different experiments, providing freshly aliquoted samples and reagents.

In this first class, the students analyse the structure of bacteria. Not all bacteria are alike, and the composition of their cell wall is an important aspect when considering which antibiotics will successfully treat any given bacterial infection. Later this week, the students will attempt to kill bacteria with an antimicrobial peptide and get bacteria to take up DNA from their surroundings (some more successfully than others). This process, used by scientists all the time in the laboratory, can spread antimicrobial resistance genes in nature, contributing to the burden posed by bacteria to human health.

Before long, the now traditional Greaves Poetry Writing interlude has been completed (the outputs of which can be found throughout this Fusion issue) and, in a flash, the class is over. Yet the room is not empty: the aforementioned team of helpers in the preparatory room (Natalie Davis, Lucy Bryant and their new apprentice Jess Rushton, alongside Gonzalo Ramirez Roman) are already busy tidying up and getting the classroom ready for tomorrow.

The Biomedical Sciences Degree

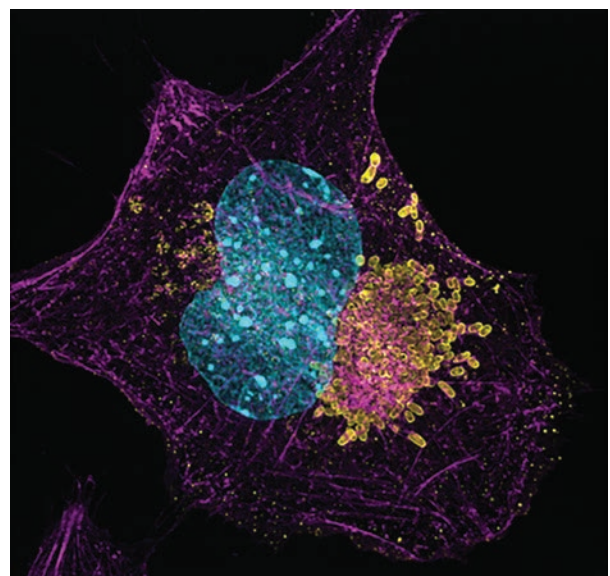
The Biomedical Sciences (BMS) course was launched in the academic year 2011-2012. The ~40 students study some topics alongside medical students with additional teaching delivered by biochemistry, experimental psychology and physics. The Dunn School provides bespoke teaching on Immunology in the first year (delivered by Emma Slack and Sumana Sanyal) with a dedicated BMS Infection and Immunity module in the second year. The baton for the practical classes and seminars, previously run by Rachel Exley, Christoph Tang and David Greaves, has now largely been handed over to me. Yet as you will see, I am far from alone.

After completing my first practical course, I have time to reflect on how the students see just the tip of the iceberg – the actual practical class. But now I know that underneath every class sits the sturdy pillars of the Dunn School community. From the handed down (amazingly organised and extensive) notes of the prior class lead (Rachel, you really are a star), to the admin teams and my trusty co-leads, Prof Greaves and Carolyn Nielsen, there is always help at hand. But that isn't it, there is also my trusty postdoc Ines Diaz-del-Olmo, who prepared the bacteria, the team of demonstrators and the prep team who, well, prepare everything from tubes to tips to water baths. All in all, it really does “take a village” to teach, to support and to grow a future generation of scientists.

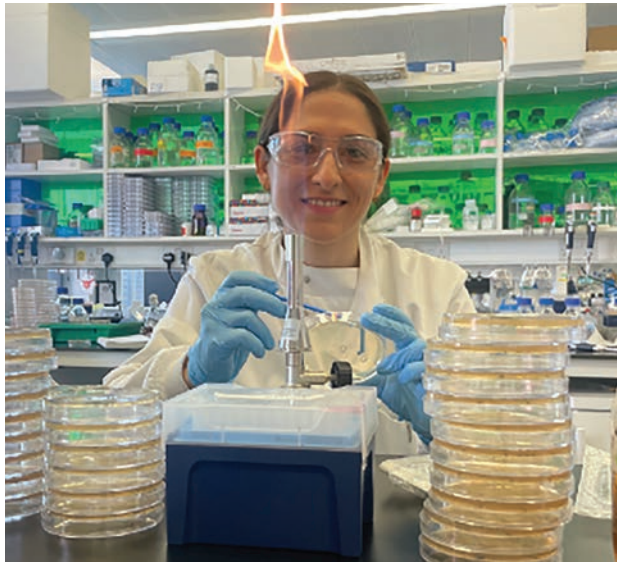


The prep team behind Dunn School practical classes.

Is it hard work? Maybe – but I can't think of a more rewarding and special place to teach than standing beside my fellow Dunn School colleagues and friends. I just can't promise to deliver any poetry.



Bacteria (yellow) taking over the cell from the inside.



Ines preparing the bacterial plates.

The Thurston Lab

Teresa moved to the Dunn School from Imperial College London in Sep 2024. Her group focuses on understanding both the host and pathogen determinants that impact the outcome of bacterial infections. They use a combination of cell biology, biochemistry, structural biology and molecular microbiology to study two intracellular pathogens: *Salmonella*, which represents a significant burden in sub-Saharan Africa, where it causes blood-stream infection; and *Burkholderia*, a pathogen with high lethality rates that is endemic in parts of Asia and Northern Australia.

Some Greaves Poetry

Which cell type are you?

You scatter light
Just like a lymphocyte.
FSC and SSC
But are you T, or are you B?

The only way to really tell
Is add fluorescent antibodies
To identify your most favourite cell.

The antibodies all have CD numbers.
For T cells try anti-CD3s and anti CD2s
With this combination of markers, you cannot lose (!)

Why not try some different antibodies
Like anti-CD19, anti-CD20; B lymphocyte-
specific markers – we've got plenty (!)

Don't forget Greaves' favourite – the monocytes

Anti-CD14, anti-CD68, and MHC Class II
This combination gives great myeloid insights.

For modern day Immunology
Flow cytometry is now obligatory

For clinical management
of blood cell malignancy
You *must* understand
Flow cytometry

With many thanks to Bobby from David Greaves

05 11 2025

Centenary events

We are marking our Centenary with an exciting programme of events throughout 2027, celebrating our past and future research, as well as the people who make our community.

The most up to date list of events can be found on our website: www.path.ox.ac.uk/centenary/events

15th January

Annual Departmental Symposium and Centenary Launch

Keynote speaker: Professor Benny Chain, on the life and research of Professor Sir Ernst Chain.

Internal event; keynote lecture will be live streamed

8th February

Legacy Donors Event in partnership with the Development and Alumni Engagement Office

Celebrating the history and legacy of the penicillin discoveries, and current research in bacteriology. *Internal event*

14th March

Woodsworth Lecture, in partnership with Lady Margaret Hall

Dunn School Associate Professor Mathew Stracy will present his work on antimicrobial resistance and tolerance, followed by tea and cake. *Registration available soon*

18th March

Annual Postdoc Symposium

Marking the opening of the department in March 1927.

Internal event

March 2027

Oxford Literary Festival

The Dunn School team behind our new children's book joins the author Sam Gayton for a lively discussion on the challenges of making medical history engaging and accessible for children.

Registration available soon

14th April

Celebrating Support Staff

Unveiling of a new exhibition celebrating the technical and administrative staff that supported our research endeavours and continue to do so. *Registration available soon*

14th May

Blue plaque unveiling

Celebrating Edward P. Abraham & Guy Newton, the researchers



and philanthropists who developed cephalosporins, the most prescribed class of antibiotics in the world.

Registration available soon

25th June

Annual Student Symposium

Including the Centenary departmental photograph.

Internal event

13th of July

The Dunn School Immunology Symposium, supported by the CIU trust

Celebrating the pioneering work on immunology at the Dunn School and its legacy in research and clinical practice.

Registration available soon

14th July

Centenary Symposium and Reception

Our flagship Centenary event will celebrate past and current research at the Dunn School, and explore the challenges and opportunities in our next 100 years of history. The symposium will be followed by a reception at the Oxford University Museum of Natural History.

Registration now available on the event's web-page

13th October

Penicillin Oratorio, in partnership with Lincoln College

Premiere of a new music piece, especially commissioned by the Dunn School and Lincoln College to celebrate our Centenary and Lincoln's 600th Anniversary.

Registration available soon

October – December

Dunn School Portraits Exhibition

A special temporary exhibition in the Weston Library, celebrating our unique collection of portraits, through the eyes of local school children.

Open to all

We're Net Worthy*

Helly Worsdell

In this article, Helly Worsdell continues the series exploring the Dunn School's professional service teams, this time focusing on the finance team and the vital role they play in ensuring the department runs smoothly and successfully.



I wrote about an amazing team of people - our workshop - in last year's Fusion Magazine (Pulitzer Prize incoming) and I'm delighted to be back again, writing about another fantastic group - our finance team.

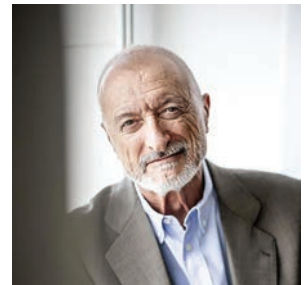
When I sat down to chat with James (Sturgess – Head of Finance) about this article, he used a rather wonderful expression – he described his colleagues as “the Goldilocks finance department”. Not too this and not too that, just perfect in every way. Money is a contentious topic at the best of times and now is certainly not the best of times by any measure when it comes to budget scrutiny, higher costs for everything and the pressure any establishment in further education is under. Our finance team have to balance these stresses and keep our show on the road. Millions of pounds worth of incomings and outgoings, payments that need making, sometimes immediately, clerical errors, funds and grants to manage, books to balance. It is a MAMMOTH task and one without room for error. They sit right in the middle of not only our expectations, but the expectations and demands of the University's central finance department – a department that often says “no” and it's down to James and his colleagues to find the money for science and discovery to continue unabated.

As you may know, James is a relatively new addition to the Dunn School – he's been here for just over a year, although he has a long career steering the finances of educational establishments, most recently at our South Parks neighbour, OU's Biology department. James has an academic background in Biology so he's in an environment that he's very interested



in and brings great energy to his role and an eternally curious mind. James is also an incredibly talented artist (see for yourselves) and somehow also finds the time to act as a trustee to a charity very close to his heart - Alfie's Wish.

Raquel Perez Marina is James's second in command and, jointly with Haydee Halfhide (more on Haydee later), ran the finance team when it was without leadership. She had a solid background in corporate accounting before coming to us via the Saïd Business School's finance team. Raquel is responsible for budgeting and forecasting, as well as our student's finances. Like every department, division and college at OU, our finances are under intense scrutiny in an effort to save a penny here and a pound there - Raquel runs the reports that need to withstand this scrutiny and does so with equanimity. She maintains balance by travelling to home to her beloved Northern Spain and loves reading crime fiction in both Spanish and English, her favourite author being Arturo Pérez-Reverte.



Arturo Pérez-Reverte
Image credit Alberto di Loli

James inherited, and I quote, “a great team, really invested in the Dunn School” despite their soldiering through a challenging few years before his arrival. And talking of the wider finance team, I have to lead with the longest serving member - Mark Hawkes, Finance Assistant, Accounts Payable, responsible predominantly for invoicing. An occasionally difficult balancing act between the demands of

the department and the demands of OU's central finance department, Mark has gently been dealing with our paperwork errors, goofs and bloopers for 21 years. I've certainly had several emails from

Mark, and he's always kindly steered me in the right direction. I greatly admire his patience. Mark is another great reader, counting Dostoevsky and Dickens amongst his favourite authors.



Mark shares an office with Sheji Bhaskaran. The other side of the accounts processing coin, Sheji is our Purchasing Manager (but they both know our complicated accounting systems inside out and cover each other's roles during absences). We will all recognise Sheji's beaming smile and, again, her patience at correcting our errors and managing our



expectations - she's been here for four years after working at OU off and on since 2004. What you might not know is that Sheji (along with Rachel Faulkes) also looks after all the beautiful indoor plants scattered throughout our buildings.

What does she love most about the Dunn School? The people and the outstanding parties. Well said, Sheji..!

Haydee Halfhide (Research Grants Manager) and Mervat Zen Aldin (Finance Officer) will be very familiar to anyone in the department who relies on funding. Haydee manages the life cycle of awarded grants - making sure monies aren't overspent or sometimes even underspent - and has oversight of well over 130 projects with funds ranging from the many thousand to the multi-million. Every grant has different terms, even within the same funding entity, so Haydee has to pay great detail to the small print and relay the dos and don'ts to the fundees. Haydee is one of OU's own - she graduated from Balliol College in Classics and then spent time in investment banking before returning here. Moonbeam is a very important being in Haydee's life (see photo).



As well as supporting Haydee, Mervat helps researchers with their grant and internal funding applications. Mervat has worked at OU since 2017 and has been at the Dunn School since 2024. When she moved to this department she found the friendliness and lack of hierarchy a wonderful surprise - something we can all appreciate - and really enjoys her role here, finding the potential of the funds, and the research they

will reap, really rewarding. Mervat is working her way through the various modules required to become ACCA qualified, and is an avid gardener and recently took over an allotment.

And there we have it. Another great team that we're lucky enough to count amongst our colleagues. We're really NOT worthy, they're a super smart bunch and a lovely group of people to boot.



Now for a quick quiz. I challenge you to match the little nuggets of secret information below with the right member of the finance team:

- who shares a birthday with the Dunn School?
- who skates with the Oxford Blackbirds Roller Derby team a couple of nights a week?
- who bakes delicious cakes?
- who spent a recent Halloween at Dracula's Castle in Romania?
- who walked the Camino de Santiago as a teenager?
- who has budgerigars at home (as well as a quite a few other animals)?

(answers on page 55 NO CHEATING!)

*If you're not familiar with the Wayne's World films (or indeed any of the "Bill and Ted" offerings) check them out and transport yourself to a pre-mobile, GenX world of ingenuity and, more importantly, absolute silliness.

A bacterial limerick by Maisie Burrow-Hills, Exeter College

There once was a little bacteria,
Which caused an enormous hysteria.
Intracellular infection
Of each intestinal section
Food poisoning all from Listeria.

An Interview with Jane Sharps

Lindsay Stimson

Jane Sharps joined the Dunn School in 1984 as a trainee technician and remained at the Dunn School for the next 42 years. Jane retired earlier this year from her most-recent role as lab manager in the Fodor Lab. Lindsay Stimson, lab manager in the Tang Lab, takes the opportunity to ask Jane about her time at the Dunn School.



Can you tell us a little bit about your background and what led you into science and the Dunn School?

I was never academic at school. I started A levels but didn't enjoy them. Luckily there was this fabulous biology teacher called Dr Wallace, who recommended a course in medical laboratory science at Oxford College. It was only one day a week,

so I started that alongside some A levels in college - one being statistics. One day, my statistics teacher came to me and said "My friend at the Dunn School, June Clark, has a trainee technician job open. Would you like me to recommend you for an interview?". The spooky thing was that my statistics teacher was also a Girl Guide leader. And many years previously, I had volunteered to go on a bike to the local village whilst we were on a Guide camp to get someone if she went into labour, as she was heavily pregnant at the time. My statistic teacher had remembered my willingness to help her all those years later, and that was the reason she asked if I wanted to come for an interview at the Dunn School.

For the interview itself, I had 10 minutes with Dr Eric Sidebottom, where he asked me questions about my likes and dislikes in labs and science. By the time I got back to reception, I was offered the job! I started the following Monday and having never worked in a lab before, it was quite an eye opener. I was put under the wing of Stephen Clark as Eric was heavily into his teaching at that point. The department allowed me to continue one day a week at Oxford College to complete my Ordinary National Certificate and then my Higher National Certificate.

Could you tell us what the labs were like when you started working at the Dunn School?

All the lab spaces were still mahogany. Even in the Leslie Martin building (which existed in the site where OMPI now is from the late 1960s to early 2000s) - where I was based - which was a big concrete block, the benches inside were still wood. We used something called bench coat, which had a plastic side you'd put on the benches to absorb anything and stop it from going into the wood. Things like incubators didn't exist at the time, so you had walk-in rooms. One cold and one hot. The hot room was set to 37 degrees - which was excellent in winter to dry your clothes or warm yourself up!

There was very little technology so much more time was spent preparing things, but I wouldn't say it delayed work - you just needed to plan things well. For example, if you were ordering supplies, you had to do it over the phone or via a fax machine rather than online. Nonetheless, orders probably arrived quicker then than they do now! It was also crucial to keep notes of all the work you were doing as there were no computer systems keeping records for you.

What was the department like as a whole when you started?

The department was much smaller, with probably around 15 research groups (compared to over 30 today) but, like today, everyone was very friendly. Being smaller allowed people to get to know each other well just by having coffee and tea together. We also had a really good photography department who photographed the images for papers, and a group of ladies who would type up theses.

The Heatley lecture was already taking place, but there were no other regular seminars: only one-offs if prestigious researchers were visiting.

Structurally, the space in the old building was used differently. The East wing included a lecture theatre, a library and also a museum which had shelves of biological specimens in containers. The museum was where you went for coffee breaks. But you couldn't go in the afternoons because that was when the PIs used it - with their lady with the tea trolley. You never, ever got invited to that. Thankfully, things are less hierarchical now!

During your career, how many roles did you have and with how many research groups?

I worked in four research groups during my time at the Dunn School: Eric Sidebottom's group 1984 - 1990, Henry Harris' group 1990 - 1996, George Brownlee's group 1997 - 2008 and Ervin Fodor's group 2001 - 2026. I started out as a trainee technician before becoming a graded technician and then later a research assistant and lab manager.

What would you say are your career highlights?

When I worked with Sir Henry Harris, who was Head of Department at the time, he was the first PI who encouraged me to get involved in research. That was a real turning point for me. One of the highlights from that time was having our

work with Joy Rawlins - A Different Approach to Tumour Suppression - published in *The Journal of Cell Science*.

Then, when I worked with George Brownlee, one of the things that really stands out was the outreach work we did with the Royal Society. I really enjoyed being involved in that. George also made sure I was included in a wide range of research projects, and as a result of my contributions I was fortunate to become an author on a number of scientific publications.

When working with Ervin Fodor, being included as a co-author on a paper published in *Nature* is something I am incredibly proud of. But I don't think of that as just a personal achievement - it was a highlight for the whole research group.

A social highlight of the Dunn School was the epic annual Christmas party! Mike Bramwell loved quizzes, and he would always do a treasure hunt where you'd be look for clues and then find a letter to make a word. The Christmas party would also be where we watched the movie that would be filmed sometime throughout the year. They were always funny. For example, one year we had new paper towels and they were this brownish beige colour and didn't absorb any liquid. So, people started making outfits and lab coats from these paper towels – which then turned into that year's movie!

Over your time at the Dunn School, technology has changed considerably. What would you say was the thing that revolutionized your work?

The electric pipette - it saved so much time! It used to be part of my job, at the end of the day, to wash all the glass pipettes then leave them to soak overnight before washing them again in the morning to use that day. Interestingly, even though it saved a lot of time, relying on plastic disposable pipettes has increased our waste hugely, so really we're coming full circle and we should go back to glass pipettes.

Reflecting on your time at the Dunn School, is there anything you'd change or any advice you would give to others?

I wouldn't change a thing. It is a great credit to the Dunn School to feel like that after 40 years. It is a great department with lovely people. I am very grateful to Henry, George and Ervin who supported me in doing research almost as a postdoc alongside my lab manager role. It kept things interesting!

I would advise anyone reading this interview to just do what makes you happy. I was lucky to have been happy here my whole career. The only other thing I wanted to do was to be a mother and I got to do that as well, so I am very pleased.

Getting things Dunn: fostering conversations for women in science

Sofia Bustamante Eguiguren and Michelle Fan

The ideas and enthusiasm of our students and postdocs fuel many of the initiatives and events that make the Dunn School such an engaging and vibrant place to work and study. In this piece, Sofia and Michelle reflect on the beginnings and impact of the Women in Science group, which for the last 2 years has organised panel discussions on a variety of topical issues of relevance to all.

This past winter, the Weston Library displayed renowned items from the Bodleian collections, in their exquisite collection *Treasured*. The mere suggestion of a gorgeous manuscript found in Agra from the 18th century featuring "Women in the lead" (piece 23) got our attention. It was an Indian court scene with shiny borders and rolling hills featuring Princess Mihir al-Nisa, a woman from the Mughal court, riding so fast that she stunned onlookers. Powerful historical depictions of women are hard to come by, amongst the many men that are featured in history books. We are inspired by Princess Mihir al-Nisa and the women who overcame the biases many of us face our whole lives. Women are often carefully nurtured to be soft and caring, and our leadership skills seldom fostered. Can we find the same inspiration in the Dunn School?

In February 2023, one of us (Sofia) and Tabea Elsener (Tang Lab, 2021) found ourselves on a train back from Manchester. During our conversation, we discovered that, despite having grown up in different continents, we had similar fears and frustrations regarding the gender imbalances in science. We had rarely met any female role models during our youth and were exposed to constant



Princess Mihir al-Nisa

belittling comments that discouraged us from following careers in STEM. Realising this, we decided to counter these biases and ask those who had successfully overcome them for advice. It only took a few weeks, and meetings with Anton van der Merwe (Director of Graduate Studies), Lucinda Risius (Graduate Studies Administrator), and Cat Vicente (Head of Scientific Strategy and Projects) to establish a working group. Armed with our questions, Laura de Nies (Stracy lab, 2023), Tabea, and Sofia organised the first Dunn School Women in Science panel discussion to explore the compatibility of a career in science and family. It felt natural to explore such a relevant topic that could interest many Dnners. The panelists shared their personal experiences and wisdom with

a seminar room full of curious Dnners from both sexes. The rest is history.

To date we have run eight panels - and have learnt that, regardless of the path you take, there will always be challenges. From deciding how to balance children with busy work schedules, personal finances to our public image, the one continuous thread was that everything is possible when you are empowered by a support network, such as the Dunn School. Every panel discussion sparked new conversations and strengthened our sense of belonging to both the Dunn School and the wider scientific community. We are grateful for all the time, wisdom, and discussions offered.

Topic	Panel
Compatibility of a career in science and family – the strategies of balancing them	Prof Ulrike Gruneberg (Gruneberg lab) Dr Hayley Lavender (Tang lab) Dr Annabelle Shaw (Gullerova lab, 2019)
Mobility in science – Is international movement essential for a scientific career?	Prof Shona Murphy (Murphy lab) Prof Emma Slack (Slack lab) Prof Geoffrey Smith (Smith lab) Dr Thomas Williams (Carvalho lab)
Publication as scientific currency? – do you need a Cell/Nature/Science for a successful career in academia	Dr Georgia Isom (Isom lab) Dr Ana Cehovin (Tang lab) Dr Catarina Vicente (Raff lab)
Mentorship - how to become a mentor and how to be a good mentee	Prof Anton van der Merwe (va der Merwe lab) Prof Teresa Thurston (Thurston lab) Dr Viktoriya Stancheva (Sanyal lab)
Do I stay or do I go? Career in academia vs elsewhere	Prof Sally Cowley (Cowley lab) Prof Mathew Stracy (Stracy lab) Dr. Dessislava Veltcheva (Amgen)
Social media in science – is it just a tool?	Prof Matthew Freeman (Freeman lab) Dr Luciano Marasco (Proudfoot lab) Vasiliki Tsioligka (Don Mason Flow cytometry facility)
Been there, Dunn that - a cross-generational conversation celebrating women in science at the Dunn School	Dr Penny Gilbert (Harris lab, 1982) Dr Abigail Stevenson (Norbury lab, 2002) Dr Ines Alvares Rodrigo (Raff lab, 2015)
Where is Science Going? The future with AI	Prof Monika Gullerova (Gullerova lab) Dr Katerina Toropova (Toropova lab) Clare De’ath (Isom lab, 2022)

As our panels evolved, so did we. The group slowly changed, and is currently being run by the two of us, Michelle and Sofia. We streamlined planning and developed efficient communication routes with both panelists and audience. With more panels, we also achieved more engaging conversations.

As we explored more topics, engagement across the Dunn School continued to grow. We soon began covering topics beyond gender issues, while always exploring a female perspective. The initiative expanded to benefit all members.

To mark the upcoming centenary, we planned a very special panel discussion. Spanning four decades of DPhils, we hosted

Penny Gilbert (Harris Lab, 1982), Abigail Stevenson (Norbury lab, 2002), and Ines Alvarez Rodrigo (Raff Lab, 2015). It was a rare window into the past. How had these three women experienced the same hallways we now walk? What has changed? What wisdom can be imparted to current students? On the day, we welcomed the speakers to our Old Building reception. Our excitement was mirrored in their eyes – yes, the Dunn School still had some of their spaces, yet many had changed over time. We expected to be the ones giving the tour, but instead the stories of their time here led us through the halls. We learned that old seminar rooms used to exist where the Greaves lab now is, how the professors managed their groups and their memories of all their fellow students. We

asked them to sign their theses and marveled at how, in Penny's time, it was a herculean effort to type and paste the data panels. Then Microsoft word came and now we even code in LaTeX!

After a meeting with our Head of Department, Matthew Freeman, our visitors enjoyed catching up over lunch with their previous supervisors and mentors. The EPA seminar room was filled with an expectant audience ready to hear about the past, current careers, and future of our guests. Online, alumni joined in to celebrate this moment with us. From diverse careers to student memories, it was clear that the Dunn School has always been the same welcoming and nurturing environment for fantastic science that it is today.

It also came to light that the frustrations Sofia and Tabea shared in that train ride back in 2023 also rang true in decades past. Women are still the minority in the most powerful positions, within and beyond science (for example, as we heard from Penny – now a Partner in a law firm specialising in Intellectual Property).

It is important to us that not only the audience, but also our panellists, find these events a worthwhile and exciting experience. The feedback from 'Been there, Dunn that' gives an insight into the panellists' experience:

"It was a really lovely opportunity to visit and to hear how the Dunn School is thriving."

Penny Gilbert

"Twenty years after I left, it was a weird feeling walking through the corridors of the Dunn, which still felt very familiar with the old faces of the alumni photos, but with the new addition of OMPI. After a warm welcome from Sofia, Hannah and Michelle, and an entertaining catch up over lunch with Profs Norbury, Cook and Raff - it was time for the panel. The hour went quickly, sharing stories of our time, our career paths and how things had changed (or not) for #WomenInScience!"

Abigail Stevenson

"It was truly special to come back to the Dunn School for this event. Penny and Abi had lots of interesting anecdotes about their days in the department; we touched on everything from rooms changing purpose to lost traditions. More critically, comparing our experiences as female PhD students, it was remarkable how so much has shifted since the 80s, yet key challenges like the "leaky" pipeline in academia stubbornly persist. Nevertheless, I was profoundly inspired by both the impressive careers of my fellow panellists and the passion and dedication of the current PhD students who organised such an insightful conversation."

Ines Alvarez Rodrigo

Our community is an optimal space to have complex discussions, and we strive to do them justice. Most importantly, we are at the cusp of finding new routes to change these inequalities, but current students are not alone, as alumni have been there and Dunn that. We hope groups like ours are staples in generations to come, with images of Indian princesses who take the lead in action.



Left to right:
Sofia Bustamante Eguiguren, Penny Gilbert, Abigail Stevenson, Ines Alvarez Rodrigo



Women of the Mughal court could be beautiful but they could also be powerful. Here, Princess Mihir al-Nisa, daughter of Emperor Aurangzeb and Nur Jahan, chief consort of Emperor Jahangir, rides so fast they leave stunned onlookers in their dust. Nur Jahan in particular was a force to be reckoned with having been de facto ruler of the Empire for nearly a decade.

Capturing the Dunn School

Hannah Calkin

To mark our Centenary, we wanted to create a range of merchandise as physical mementos of this important milestone. But what to choose as a visual representation of 100 years of history?

The Department of Pathology has existed at the University of Oxford since 1901. It was a gift of £100,000, by the trustees of Sir William Dunn, that enabled the construction of the ‘Old Building’, which opened in 1927. This led to a change of name to the Sir William Dunn School of Pathology or, as we fondly call it today, the Dunn School

Over the subsequent 100 years, many things have changed: different areas of research have been explored; the land behind the old building has been used in different ways (from the original animal building, to the current OMPI and EPA buildings). Through the years, the constant for all Duffers will have been the Old Building, the grand red brick building, once described by Nobel Prize winner (and Dunn School alum) Peter Medawar as “the splendid new building on the great South Parks campus”. To honour this legacy, we decided to place the Old Building front and centre of our centenary merchandise.

To capture the essence of this historical building, we were delighted to work with Nicola Durrant. Nicola is an Oxfordshire-based artist and created a striking ink illustration of the Dunn School: you will notice, however, that the full artwork also incorporates the newer OMPI and EPA buildings. Together, they represent not only the changing Dunn School’s architectural landscape, but also its continued growth in both research and scale. The Old Building may be iconic, but the inclusion of these newer spaces reflects something equally important: that the best of the Dunn School is still to come.

In Nicola’s words:

“I loved sketching the old building using my faithful barbeque stick and black ink to create slightly wonky lines. Drawing the two newer buildings needed a complete contrast in technique and for these I used dip pen and ruler.”

We then hit a stroke of luck when Chiara Fedele was chosen by Oxford University Press to illustrate their children’s book on the discovery of penicillin, published to commemorate our centenary (read more on page 17). Chiara, who trained at La Scuola del Fumetto in Milan, specialises in children’s illustration.

During her visit to the Dunn School to work on the illustrations for the book, Chiara took the opportunity to sketch the Old Building. She later kindly gifted us her original sketches. We chose our three favourites to feature in our set of centenary postcards, now available to purchase (see p35).



In Chiara’s words:

“When I visited the Dunn School, I had the opportunity to take tons of pictures and make some sketches. I later developed some of the photos into hand drawn sketches, keeping the memories of the visit in mind.”

Together, these pieces of artwork, and the merchandise they feature on, aim to capture the feel and look of the Dunn School, but also something more. We hope you see them not just as mementos, but also small reminders of a place that has shaped careers, advanced science, and inspired generations.



Centenary Shop

Our new Centenary merchandise is now available to purchase on the Oxford University Store!
Scan the QR code to access our shop.



Centenary sweatshirt

Navy sweatshirt with the Dunn School Centenary logo and sketch of the Old Building. Artwork by local artist Nicola Durrant, especially commissioned for the Centenary.

Price: £16.50

Centenary mug

Bone China mug with wrap-around sketch of the Dunn School's three buildings on a blue background. Artwork by local artist Nicola Durrant, especially commissioned for the Centenary.

Price: £9.00



Centenary pin-badges

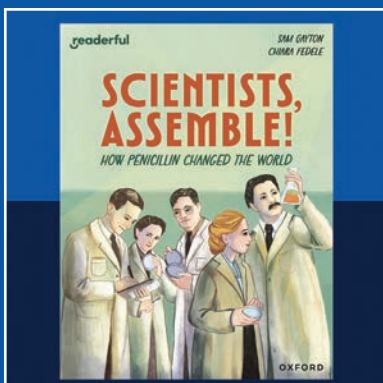
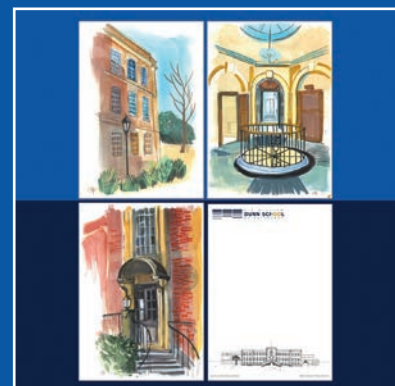
Set of two metal pin-badges: the Old Building and the Dunn School's Centenary logo.

Price: £4.00

Centenary prints

Set of three A6 coloured prints of the Dunn School. Original artwork by Italian artist Chiara Fedele.

Price: £2.00



Scientists, Assemble! How Penicillin Changed the World

A new children's book developed by the Dunn School in partnership with Oxford University Press to mark our centenary. Part of the award-winning Readerful Series, it is aimed at helping children aged 9 to 10 with their reading practice but is certain to make a special souvenir for Danners of all ages.

Price: £6.50



Driving discovery 'forward' for cancer

Bass Hassan

Bass Hassan originally joined the Dunn School as a Wellcome Clinical Research Training Fellow in 1991, to study for a DPhil with Peter Cook. After setting up his group in Zoology, then in Bristol and the WIMM, he returned in 2009. Until recently dividing his time between research and as a sarcoma medical oncologist, Bass reflects on current approaches to cancer research, with a specific focus on sarcoma, and the research questions his group is trying to tackle.

Development of single target and single molecule therapeutics, followed by subsequent testing in early phase cancer clinical trials, has progressed at scale over the last decades. We now have many hundreds of selective small molecules, protein degraders, antibodies with conjugates and fusions, many biotech companies developed and many agents have secured FDA licence approvals. The overall premise is, however, based on the assumption that a single target modification can result in enduring clinical benefit in patients, an outcome that is rarely achieved before multiple resistance and clonal escape mechanisms evolve. In effect, this 'reverse genetic' approach is still seen as the 'sweet spot' for the development of cancer drugs and the justification for the enormous scale of the associated investment. Continuing to develop single targets without fully understanding experimentally validated contexts continues to prematurely promote targets and agents with marginal gains, and only in the rare subset that clinically benefit. Continuing this approach also has other consequences: precious research funding can be misplaced, and the short-term biotechnology 'exits' ultimately fuel unaffordable high drug costs for healthcare systems without meeting basic requirements for health-years gained.

But where, if any, have there been successes in cancer, what can we learn from these and where should the future efforts now focus? The main successes are of course the polyclonal activation of T-cells and specific cytotoxic responses to the multiple endogenous MHC-presented neoantigen peptides (variants) following immune checkpoint blockade (ICB). Unleashing the impact of ICB on cancers with high variant (mutational) burdens has been a profound paradigm shift in cancer therapy for some, but not all, cancers. Further examples extend the principle of molecular and cellular delivered immune cytotoxicity, such as cell surface protein targeting with bispecific T-cell engagers and CAR T-cells. Of course, there are small molecule inhibitors and antibodies for many pathways that can also act selectively in certain contexts and so extend lifespan, such as PARP inhibitors that impede non-homologous end-joining in the context of BRCA1/2 loss of function, resulting in synthetic lethality. Do these lessons mean that we need to consider an alternative paradigm? The answer must be yes, probably.

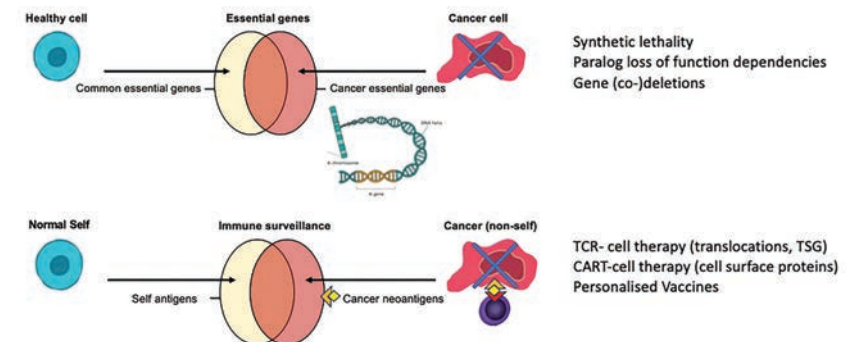


Figure 1: Two ways to cure cancer: molecular and cellular mechanisms for cancer cell selective lethality

One alternative paradigm is based on classical 'forward' genetic principles. Here, it is the 'phenotype' that is the central objective of the approach. This means that multiple interacting mechanisms may be required to achieve the phenotypic objective, rather than preoccupation with a single gene and its potential consequences. The best example is selection based on the phenotype of selective cancer cell lethality. The route to that phenotype may involve multiple mechanisms, for example, through synthetic lethality or through polyclonal T-cell neoantigen recognition mechanisms (Figure 1). The phenotypic outcome is likely to be context dependent and there may be tailoring across multiple interacting pathways to achieve selective lethality of any given cancer (personalisation). This approach can be extended through a wider range of phenotypic objectives, that also take into account the multi-factorial 'systems' context of cells. This 'forward' approach therefore directly appreciates the known complexity of an individual cancer and the many routes to reversing the phenotype. This is especially relevant if one is to fully understand with certainty the key multiple interactions (genetic, pathways, protein complexes) that will also define the potential interacting therapeutic strategies.

A Dunn School historical perspective

It will come as no surprise to readers of 'Fusion' that the 'forward' genetic principles for cancer were also promoted by the late great Sir Henry Harris, the former head of department between 1963 to 1993. One of his lifelong interests was on the mechanisms that reverse the cancer phenotype, specifically in later years, the regulation of cancer differentiation. In the 1969 *Nature* paper entitled '*Suppression of malignancy by cell fusion*', Harris and

colleagues used Sendai virus to generate fused cells (heterokaryons) of mouse sarcoma cells and a non-malignant mouse fibroblast. The malignant phenotype of the mouse sarcoma cells was completely suppressed following cell fusion, but as chromosomes were lost from the suppressed heterokaryons, the malignant phenotype returned. Implicit in these experimental observations was the appreciation that cancers arise because of mainly loss-of-function events, that is the loss of tumour suppressor genes. Complementing the whole genome reverted the phenotype as judged by xenograft growth of the heterokaryons. Gain-of-function events, such as oncogenic mutations, are overall rarer events in cancer, and may not be so critical when it comes to reversion of the phenotype, yet oncogenic proteins remain the focus of much of conventional ‘reverse’ drug development.

Sarcoma as a model

The focus of my laboratory is understanding the irreversible phenotype of cancer cell lethality, the main and unequivocal phenotype as a basis of ‘forward’ genetic and immunological screens. In my group, we have invested in establishing the use of enabling technologies, including computational bioinformatics of sequencing data, the evolution of multiplex sgRNA CRISPR with enhanced PAM directed Cas12a nuclease (enAsCas12) and selection and evolution of high affinity neoantigen-MHC specific T-cell receptors.

We focus on some of the 100 or so rare types of cancer that arise in bone and soft tissue, referred to collectively as ‘sarcoma’. Specific types of sarcoma reflect the major cancer genomic changes across all cancers, from somatic copy number, structural genomic and single nucleotide variants (Figure 2). For example, inheritance of disrupted alleles of the key tumour suppressor genes *Tp53*, *RB1* and *NF1* result in early onset cancers that frequently include sarcomas. Knowing both the germline and somatic genomic changes that arise in sarcomas is already impacting on the diagnostic stratification and potential therapeutic implications for those cancers. However, the data that underpins important multi-omic and cross cutting evaluation of technologies that could impact on sarcoma care remains poorly integrated. Through our major infra-structure project, the Oxford Precision Oncology for Sarcoma project (OxPOS), we have established seamless integration of laboratory

discovery into evaluation of material from sarcoma patients in real-time. Early adoption of an integrated science and clinical approach means that new findings and information are exchanged early, in the hope this will improve aspects of patient care and ensure the science is focused on the main relevant biological and experimental question. Here, sarcoma is a model system for cancer as a whole.

Tumour suppressor genes

In terms of lethality (perturbation) screens, enAsCas12a CRISPR is a relatively recent addition to the genome wide targeting field, exploiting the expression of multiple guide RNAs (gRNA) per gene (and gRNA targeting multiple genes) in cell lines. Importantly, the guide efficiency and developments in sgRNA library design have generated reagents that now allow for efficient screens at high depth of coverage, that can be performed in a regular laboratory. We have utilised this approach with a multiplex IN4MER library of four gRNA per gene, duplicated in two separate cassettes, with combined gene targeting of paralog pairs, triplets and quads. Efficient targeting of the major paralog gene families extends the utility of the screens from single genes to multiple genes. A further refinement of such experiments includes isogenic comparisons across the same cells that differ in defined manipulations. We have exploited this first in the use of an immortalised human Schwann cell-derived model of the multi-step development of malignant peripheral nerve sheath tumours (MPNST). These tumours are often the lethal endpoint for a significant number of the 25,000 people in the UK that have inherited *NF1* variants and have developed Neurofibromatosis. Identification of multiple gene-epigenome targets might identify the range of key genes that influence the growth and survival of MPNST cells.

We are continuing such approaches to understand which key pathways remain activatable in the context of restoration of another important tumour suppressor gene, *Tp53*. In this case we aim to restore expression of an intact wild-type *Tp53* in osteosarcoma cells with mutant *Tp53* derived from both human and canines. We are asking whether the resulting abrogation of the cancer phenotype can be accounted for by a limited number of reignited pathways. Interestingly, high grade primary bone osteosarcoma occurs more frequently in canine breeds, and these exactly phenocopy the rarer human disease with almost universal disruption of *Tp53*. By

developing our own canine specific enAsCas12a library, we can now conditionally restore *Tp53* in both human and canine cells and identify key dependency genes. In effect, this is a focused repeat of the Harris cell fusion experiments, but trying to define the key downstream pathways that execute cell dependent cell death.

Loss of function of another key tumour suppressor *CDKN2A/B* also results in activation of proliferation through abrogation of a G1/S cell cycle checkpoint. Interestingly, deletion of 9p21, the region where *CDKN2A/B* is located, is frequently a main mechanism of loss of function resulting to cell cycle activation. There is

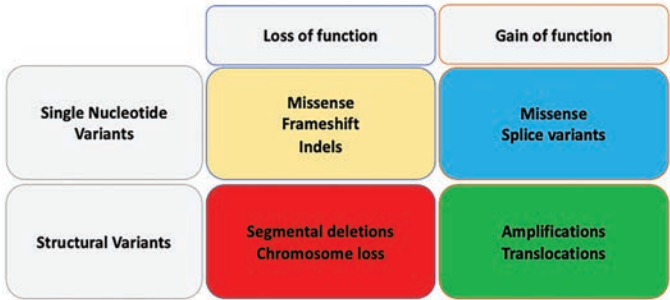


Figure 2: Gain-of-function (oncogenic) and loss-of-function (tumour suppressor) drivers in cancer

also co-deletion of other genes in the same genomic region, such that these genes may also have effects on cell growth and survival to establish synthetic lethality (where perturbation is synergistic, rather than additive). One gene that is co-deleted is called *FOCAD* and is thought to modify 3'RNA translation quality control and, through this mechanism, may generate a co-dependency. Following the generation of isogenic pairs, we are investigating the synthetic lethality interactions across this region and the impacts on translational ribosomal stalling and processing.

Amplifications and translocations

Sarcomas are characterised by several structural gain of function events, such as the amplification of chromosomal regions and the development of driver fusion genes following chromosomal translocations. One such amplification region is 17p11, which has increased copy number and extra chromosomal DNA (ecDNA) generation in osteosarcoma and leiomyosarcoma. By selecting cell lines with different degrees of regional amplification of this region, we are performing initial enCas12a IN4MER screens to evaluate the survival dependency of coding and non-coding regions of the amplified region. Moreover, co-regulatory non-coding regions may also be selected, both on chromosome 17p11 and elsewhere, requiring a multi-OMIC evaluation. Defining multi-gene interactions, potentially in additional contexts, may define selective dependencies that interact with this region.

The specific selection for drivers based on translocation-generated fusion genes is also relatively commonplace in sarcoma. Here, single driver gain-of function events appear to re-programme sarcoma cells to generate highly aggressive tumours with absolute driver dependency, e.g. EWS-FLI1 in Ewing Sarcoma. There are two main lethality strategies that we are pursuing in this context. The first concerns the specific regulation of the fusion protein, with the aim of inducing selective lethality by altering the 'Goldilocks' optimum for fusion gene function, as either low or high expression can lead to lethality. We are generating fluorescence reporter constructs that will allow us

to perform CRISPR screens to select for specific disrupters of EWS-FLI1 and mechanistically define the subsequent selective lethality.

A further lethality strategy involves the evaluation of the hypothesis that the peptide sequences at the translocation based fusion region can be recognised as non-self by the immune system. We have determined the full range of potential breakpoint long peptides for Ewing sarcoma (EWS-FLI1, EWS-ERG) and Alveolar Rhabdomyosarcoma (PAX3/7-FOXO1) and have used these to select TCRs on T-Cells that recognise breakpoint peptides with specific MHCs. Here, naïve donor Peripheral Blood Mononuclear Cells (PBMCs), provided by the Anthony Nolan charity, have been used to cross-present and select naïve T-Cells with binding to personalised breakpoint peptides pMHC Class I and Class II. We have validated TCRs in Jurkat reporter cells that display high affinity and selectivity. This work is the basis for the development of TCR-based therapies that are personalised to both the patient's HLA and fusion breakpoint. Moreover, these *in vitro* immunogenicity experiments also support the rationale for a long peptide vaccine personalised to the fusion breakpoint and tested in a Phase I/IIa clinical trial that we are developing.

Conclusion

The above general discourse covers the newer experimental questions that are currently being explored in my lab and where we as a team are aiming to try and make progress. It is important to state that my views are directly shaped by my personal and ever deeper understanding and appreciation of cancer science and its clinical relevance for the epidemic of patients (us) who carry the burden of cancer suffering in our world. I would also like to take this opportunity to acknowledge my formative experiences gained from early DPhil days with Peter Cook (Dunn School), post-doctoral fellowship with the late Chris Graham (Zoology) and all the great mentors and fruitful collaborations I have had the pleasure to engage with over several decades, including in the real-world clinical setting as a sarcoma medical oncologist.



99 years of women at the Dunn School

Alice Lomas

In March this year the Dunn School marked two important dates: our 99th birthday, and International Women's Day, in partnership with Suffrage Science (see the news section for more details). Here, Alice Lomas (Freeman group) reflects on only a few of the remarkable women that, over the years, have studied and worked in the Dunn School, and have gone to make outstanding contributions within and outside academia.

Women have contributed to the Dunn School throughout its 99-year history at every level; serving as technicians, secretaries, students, and academics. Yet, many of their contributions, within the Dunn School and more widely, have often gone under-recognised. The upcoming Dunn School Centenary provides an opportunity to reflect on some of the remarkable women who have helped shape the Dunn School.

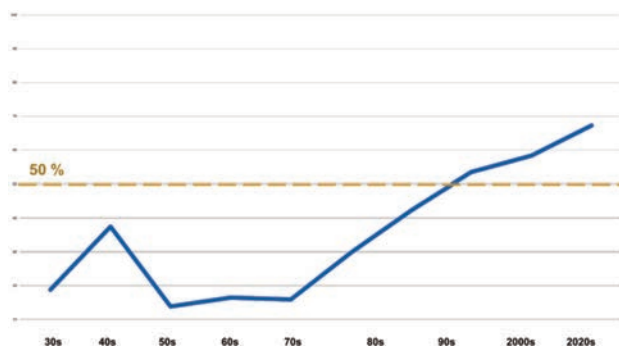


Edith F. Stubbington

An always, a valuable reference point when exploring the department's history is our portrait collection.

Unlike traditional science portraiture, women are represented from the early days of the Dunn School. Indeed, the first woman in the collection pre-dates the Dunn School's foundation. Born in London in 1888, we know very little about

Edith F. Stubbington. Her photo tells us that she joined the then Department of Pathology in 1918. She was a supervisor in the Standards Laboratory, under A. D. Gardner, which supplied the military and naval forces with reagents for the diagnosis of typhoid and paratyphoid fevers during WWI. She had an Oxford degree, which would have been rare in those days, and retired in 1946.



The % of women across the decades in our portrait collection. Perhaps unsurprisingly, the number of women peaked during the war years. Our intake of students is now more than 50% women in most years.

Arguably the Dunn School's most notable achievement (so far!) is the development of penicillin as a therapeutic. The core penicillin team included several women that were instrumental in the work. The most notable contributors were Ethel Florey, Margaret Jennings and Jean Orr-Ewing, authors in several of the major papers, and recognised in the penicillin rose garden outside the Botanical gardens. Ethel Florey was instrumental in the clinical trials in the Radcliffe



Ethel Florey

Infirmery, having abandoned her medical training earlier in life to start a family. Margaret Jennings had initially studied English and then Philosophy, Politics and Economics at Lady Margaret Hall (LMH), before switching to Medicine and later working as part of Florey's team. Jean Orr-Ewing was a bacteriologist.



Margaret Jennings

Jean also studied at LMH, passing her pathology exam in 1920 before receiving a Bachelor of Medicine from St Mary's Hospital in London. She later returned to Oxford to join the Dunn School, where she worked with George Dreyer (our first head of department), with whom she co-authored several papers, before joining Howard Florey's penicillin team, where she focused on the effect of penicillin on bacteria.

Alongside her research, she lectured in Natural Sciences at LMH and later became a tutorial fellow for the female medical students (as well as keeping busy with many other activities, such as tennis, hockey and organising the 1934 University Women's Iceland Expedition!). Tragically, her scientific career was cut short when she died at the age of 47 from heart complications likely caused by a diphtheria infection she acquired from her work.



Jean Orr-Ewing

But there are also women that played a crucial role in the penicillin work but were never named in the papers. Huge quantities of mould were required to produce the precious

few milligrams of penicillin needed for research and clinical trials. To meet this challenge, six local young women were recruited, later known as the 'Penicillin Girls'. Ruth Callow, Claire Inayat, Betty Cooke, Peggy Gardner, Megan Lancaster,



and **Patricia McKegney** performed the labour-intensive work required for the early research into penicillin. Importantly, their photographs are not in our portrait collection, an important reminder that, although our collection is uniquely diverse and representative, it often forgot individuals in support roles that were crucial for the research to happen. This is something that the department is hoping to correct as part of our centenary celebrations, so watch this space.



Peggy Turner

The success of the Dunn School has depended not only on scientists and technicians, but also dedicated administrative staff. **Peggy Turner** joined the Dunn school in 1936 as a junior secretary and eventually became departmental administrator, working under both Howard Florey and Henry Harris. Her contributions to the Dunn School, across 40 years, were so significant that in recognition of her service she received an honorary MA from Oxford upon her retirement.

Not all women associated with the Dunn School spent their entire careers within its walls. For some, their time in the department formed part of a much broader journey. One such example is **Shirley Sherwood**. A trip to Pakistan in her teenage years sparked a lifelong interest in plants, and she went on to earn a BA in Botany from Oxford. She then studied at the Dunn School in the 1950s



Shirley Sherwood

before working for SmithKline where she completed her PhD in the Nobel-prize winning team that developed Tagamet, one of the world's first blockbuster drugs. Despite her success in industry, she later returned to her passion for plants as a collector of botanical art. Her collection of over 1,000 paintings has been displayed all over the world and there is a gallery in Kew Gardens named after her. Pieces from her collection were included in the Ashmolean Museum's '*In Bloom*' exhibition earlier this year.

The Dunn School's alumnae also include two Directors of the Kennedy Institute of Rheumatology: **Helen Muir** and **Fiona Powrie**. Helen Muir worked with Dorothy Hodgkins on the



Helen Muir

structure of penicillin, as part of her DPhil on the chemical synthesis of penicillin. She then worked as a researcher at the Dunn School before moving to London and becoming interested in collagen and connective tissues. This research eventually led to her becoming Director of the Kennedy Institute in 1977. Potentially our first female FRS, she held several positions of distinction: she was the first woman to serve on the Medical Research Council and was later a trustee of the Wellcome trust. One of her more interesting honours was being cautioned by police for speeding in Richmond Park – whilst she was riding her horse!

Fiona Powrie completed her DPhil at the Dunn School under Don Mason in the 1980s, investigating the immunology of the gut. After a period in California, she returned to Oxford where her work on regulatory T cells led to her appointment as the Sidney Truelove Professor of Gastroenterology and Head of the Translational Gastroenterology Unit from 2009-2014. She was then made director of the Kennedy Institute. She was awarded a DBE by Queen Elizabeth II for her services to medical science.



Fiona Powrie

These women represent just a small selection of those who have studied and worked at the Dunn School over the past 99 years. One striking feature of the history of women at the Dunn School, however, is the limited ethnic diversity represented in the portrait collection for much of the twentieth century. Although significant progress has been made in increasing the visibility of women in science and supporting their careers, in the Dunn School and elsewhere, further work remains necessary, particularly in addressing the intersections of gender and ethnicity, alongside other intersectional identities.

From the 'Penicillin Girls' and early researchers to institute directors and internationally recognised scientists, women have helped shape the Dunn School at every level. As the Dunn School prepares to celebrate 100 years in 2027, the future will continue to be shaped by talented women pushing the boundaries of science, medicine, and discovery.



Supporting the Brightest Students: join our Centenary Campaign

The Centenary Scholarship Endowment will enable us to support graduate students at the Dunn School for generations to come



Prof Matthew Freeman, Head of Department, said on the launch of the campaign:

"In thinking about the potential legacy of our centenary, we realised that supporting our brilliant students, allowing as many as possible to benefit from the Dunn School's research and training opportunities, would have the biggest impact – both on individuals and the Department as a whole. We turn away fantastic students every year simply because we do not have the funding to make it financially possible for them to accept our offer of a place. Supporting graduate studentships is investing in a future of the most valuable kind."

I am particularly grateful to the trustees of the EPA Research Fund for their offer to match all donations. Their generosity will dramatically accelerate the success of our campaign.

I do hope that friends and alumni of the Dunn School will recognise the huge value of this ambitious plan and feel able to make a donation of any size, ensuring that we can continue to support the best young talents from around the world."

Over our 100-year history, the Dunn school has supported and trained thousands of students, whose talent, enthusiasm and work have fuelled world-changing scientific discoveries, and who have gone on to extraordinary future achievements.

To celebrate our centenary, we are launching a campaign for donations to establish the **Centenary Scholarship Endowment**. This will fund one or more graduate student scholarships in perpetuity. By giving to this campaign, you will enable us to fund outstanding students for generations to come. Our scholarships are aimed at ensuring that we can take as many students as possible, regardless of their economic circumstances.

Thanks to the generosity of the Edward Penley Abraham (EPA) Research Fund, donations to this endowment will be matched 2:1: **every pound you give will be worth three to the campaign.**

Support the campaign:

More information on the campaign can be found on www.path.ox.ac.uk/campaign. If you would like to discuss the campaign with us, you can contact our Head of Scientific Strategy and Projects (catarina.vicente@path.ox.ac.uk)



Tabea Elsener (graduated in 2025)

"I am deeply grateful for the four years I spent pursuing my DPhil at the Sir William Dunn School of Pathology. The Dunn School offered a supportive environment that encouraged curiosity, learning and scientific excellence. Thanks to a studentship, I could fully dedicate myself to my research without the burden of financial stress, allowing me to thrive both as a researcher and as a person."

"The diversity of research interests within the Dunn School made my DPhil training a life-changing experience, one that continued to influence my subsequent career."

Malik Peiris (virologist, notable for being the first person to isolate the SARS virus, graduated 1980)



A personal memoir of the cloning of the gene encoding blood coagulation factor IX

Keith Gould

Keith Gould reflects on his time in the Dunn School, his contributions to the cloning of factor IX (an essential step in the subsequent development of new treatments for haemophilia B) and his instrumental role running the oligonucleotide synthesis facility, which supported countless Dunn School and Oxford researchers.

I arrived at the Dunn School for my first day of work on 1st December 1980 with almost no idea of what I would be doing. George Brownlee and Francisco Baralle (known as Tito) had moved from the Laboratory of Molecular Biology in Cambridge to the Dunn School earlier the same year and had advertised in *New Scientist* two 3-year technician positions in the section of Chemical Pathology, headed by George. I applied, had a rather brief interview in George's office with only George and Tito present, and was appointed. This turned out to be an amazing piece of good luck, and I only left the Dunn School 16 years later.

I had a degree in biochemistry and had been doing a PhD in enzymology elsewhere in an environment I found difficult and had become rather disillusioned. I knew that George and Tito had been doing exciting work in the relatively new field of molecular biology, publishing papers in top journals including *Nature*, and I desperately wanted to learn the techniques involved. I had seen images of DNA sequencing autoradiographs, and I thought they were amazing. Little did I know that in a few months' time George would be introducing me to the person who made large scale DNA sequencing possible, Fred Sanger. The University of Oxford was obviously a desirable place to work, but at that time I was completely ignorant of the history of the Dunn School, and what a special place it was.

It had been decided that my initial role would be to set up DNA oligonucleotide synthesis under George's direction. The other technician appointed worked with Tito. At that time, it was not possible to buy custom-made oligonucleotides of defined sequence, or indeed the precursor nucleotide derivatives required to chemically synthesise DNA. It soon became clear to me that months of serious organic chemistry lay ahead. However, George knew how important it was to have available specific oligonucleotides as primers and probes, and very few laboratories at the time could make them. The Laboratory of Molecular Biology in Cambridge was one of those places, where Mike Gait was the expert in oligonucleotide synthesis, and we followed their methodology: a solid phase phosphotriester method based on the chemistry developed by H. G. Khorana. This required several visits to Cambridge, and it was during one of these visits I was fortunate enough to meet Sanger, even if only very briefly.

Because the joining together of nucleotides to make oligonucleotides involves hydroxyl groups, everything must be free of water as much as possible during the synthesis. The main solvent used for the phosphotriester method was pyridine, which has a rather strong characteristic smell I became very familiar with, and my first practical task was to learn how to prepare anhydrous pyridine. This required reflux over sodium hydroxide pellets, followed by distillation. Chemical Pathology was located on the top floor of the New

Sign-up to our Alumni and Friends Network!

We are very proud of the achievements of our alumni. We established the Dunn School Alumni and Friends Network to keep in touch with former staff, students, and their family and friends.

If you haven't yet joined, please sign up to -

- Receive regular updates on what is happening in the Dunn School.
- Keep up to date with our centenary celebration plans in 2027.
- Have access to exclusive events and opportunities.

And please spread the word! If you are still in touch with anyone from the department who you think would also be interested in signing-up, please send them the link.



Building (officially named the Leslie Martin building, but nobody called it that). There were drawers and cupboards full of quickfit glassware of every description, and all the equipment required for organic chemistry. I soon realised how well equipped the Dunn School was. I noticed that a few pieces of the glassware had the initials NGH neatly painted on them in white. It was only later that I realised these were the initials of Norman Heatley, the man who had done so much to work out the methods of producing and purifying penicillin. A few pieces of specialist custom glassware were acquired via the excellent Dunn School workshop, and they also built the reciprocal shaker that was used to agitate the solid phase resin during the nucleotide coupling reactions.

The first DNA oligonucleotide to be made was designed by George to try and isolate the gene for bovine blood coagulation factor IX. With the move from Cambridge, George was keen to explore a new area of research, as well as continuing his work on influenza virus. The full amino acid sequence of the bovine factor IX protein was published in 1979 by Earl Davie and his colleagues in Seattle. This information could be used to deduce possible sequences of the coding region of the mRNA, and therefore also oligonucleotide sequences complementary to the mRNA. The design is illustrated in Figure 1. The amino acid sequence of the human protein was not known, but the eventual aim was to isolate the human gene and to investigate the mutations that caused disease in patients who were deficient in factor IX: the disease haemophilia B, also known as Christmas disease, named after Stephen Christmas the first patient described.

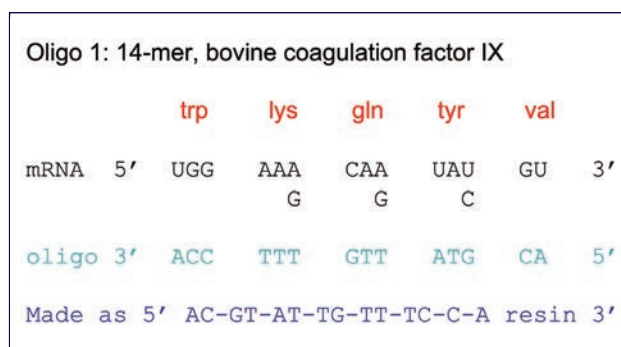


Figure 1. Design of the first DNA oligonucleotide synthesised in Oxford (April 1981).

The approach was to find a short region of amino acid sequence which was encoded by the fewest possible mRNAs and so methionine and tryptophan, each with only a single codon, were ideal to be included. The oligonucleotide needed to be long enough to give a good chance that it would only bind to the desired mRNA sequence and not to irrelevant sequences. However, as the oligonucleotide length increases so does the number of possible coding sequences. As indicated in Figure 1 the oligonucleotide was made mostly using pre-formed dimers. This was both to speed up the overall time of synthesis because the coupling reaction was slow (each cycle of addition took 2 – 3 hours), and to increase the overall yield and purity. At that time the entire process of producing a 14-mer oligonucleotide ready to use in

experiments typically took 4 days; after synthesis the side chain protecting groups had to be removed, and the oligonucleotide crudely purified on a desalting column. For the first oligonucleotide we wanted to keep things simple and not make a mixture of sequences. This would allow full characterisation of the oligonucleotide to ensure everything was working correctly.

During the time I was busy learning the chemistry of oligonucleotide synthesis and preparing the reagents required to make the factor IX oligo, a post-doctoral fellow K. H. Choo (known simply as Choo at that time) arrived from Australia and set to work on purifying mRNA suitable for making a cDNA library for the attempted isolation of a factor IX clone. Choo was hard-working and meticulous in everything he did, including playing table tennis in the staff hut, which was at the rear of the Dunn School near the old animal house. Factor IX mRNA was expected to be low in abundance, and Choo set about enriching specific mRNA from total mRNA derived from bovine liver. To be able to do this an assay for factor IX mRNA was required, and Choo set up a rather demanding assay that used *in vitro* translation in the presence of radiolabelled cysteine followed by immunoprecipitation, two-dimensional gel electrophoresis, and autoradiography. The assay and its validation were made possible by the generous gift of some purified bovine factor IX and specific antiserum from Peter Esnouf based at the Radcliffe Infirmary site on Woodstock Road. Sucrose density gradient fractionation of mRNA was used, and the fractions assayed for factor IX mRNA as described. Choo was able to enrich factor IX mRNA about 10-fold using this approach.

After almost five months of hard work, I was ready to make the oligonucleotide shown in Figure 1. The scale of the synthesis was such that the oligonucleotide could be purified by HPLC. After labelling the 5' end of the oligonucleotide with phosphorus-32, the chemical method of Maxam and Gilbert was used to confirm the sequence. The oligonucleotide was used as a primer in reverse transcription reactions using factor IX enriched mRNA as template, but unfortunately no evidence of any specific priming could be found. I want to emphasise at this point that George was very much involved directly with the practical work for this project; I believe that doing hands on experiments in the laboratory was the activity George enjoyed the most at that time.

After repeated negative results, two further different sets of oligonucleotides were designed and made. Now that we were confident about the synthesis, all possible nucleotide sequences corresponding to different regions of the amino acid sequence of bovine factor IX were synthesised as mixtures. The first set was a mixture of 8 different 14-mers. The second set was a mixture of 16 different 17-mers (full details are in reference 1), but this was synthesised as two separate sets of mixtures of eight; we still had some concerns about making complex mixtures of oligonucleotides. As it turned out later, we probably needn't have worried; subsequently mixtures of up to 64 different oligonucleotides

were made in a single synthesis and used successfully to isolate different genes. There was some delay before the new sets of factor IX oligonucleotides could be made because additional pre-formed dimers had to be synthesised and purified.

The first set of 14-mer oligonucleotides was used as a primer to synthesise cDNA using factor IX enriched mRNA as template, the cDNA converted into double-stranded DNA, ligated into cut plasmid pBR322 and a library of approximately 7,000 colonies prepared. The library was screened with the second mixture of 17-mers, and a single colony identified that gave a positive hybridisation signal above background. DNA sequencing of the insert confirmed that it contained sequence corresponding to amino acid residues 52-139 of bovine factor IX, including the sequence of the probe used to screen the library. This was a truly momentous result which led on to all the further work on human factor IX in George's group by many people over many years. The bovine sequence was used to screen a cloned human gene library and the human gene isolated. In the initial work Choo and George were helped greatly by an excellent undergraduate biochemistry project student Jasper Rees. My personal involvement was solely the synthesis of the DNA oligonucleotides, but when the time came to publish George included both myself (a technician) and Jasper (an undergraduate project student) as authors. A letter to *Nature* was submitted in May 1982 and accepted for publication six weeks later¹.

Jasper went on to do a DPhil with George continuing his work on factor IX and then did a post-doc with Richard Hynes at MIT during which he cloned and sequenced the murine gene for the large cytoskeletal protein talin. He returned to the Dunn School as a Wellcome Trust Senior Research Fellow and was instrumental in setting up and running computing and bioinformatics in the Dunn School. Jasper left in 1995 to take up the Chair in Biochemistry at the University of the Western Cape, South Africa. He later became the first Vice-Chancellor of the Botswana University of Agriculture and Natural Resources. Choo, who later preferred to be known as Andy Choo, returned to Australia after his postdoctoral fellowship and had a distinguished research career in human genetics and chromosome structure at the Royal Children's Hospital in Melbourne.

Once DNA oligonucleotide synthesis had been set up and was working, George was keen that others should have access to oligonucleotides for their research. The idea was that people would make their own oligos after instruction from me, and I would ensure that all the chemicals necessary for syntheses were available, including all 16 possible dinucleotides. Because of this system and the time required to make an oligonucleotide, I was able to get to know many interesting people and learn something about what they were working on. Initially Tito's group in our section were the other main users, and they made oligonucleotides which were used to clone the genes for the apolipoproteins AI, AII, CII, CIII and in addition fibronectin. Fibronectin was particularly interesting because it was one of the first genes in which the importance of alternative splicing became apparent.



Figure 2. Some of the members of the factor IX team reunited at George Brownlee's retirement symposium in Oxford on 26th September 2008. From left to right: Don Anson, Andy Choo, George Brownlee, Ian Jones, Keith Gould and Francesco Giannelli.

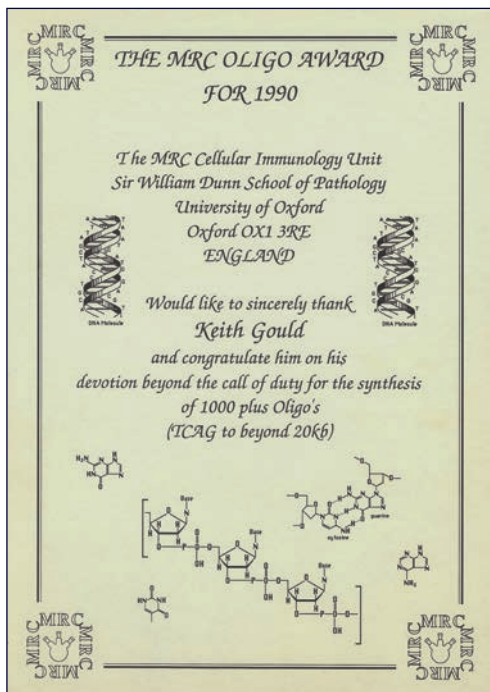
Photo courtesy of Susan Brownlee.

The other two main early users of our oligonucleotide synthesis facility were two MRC Units in Oxford: Immunochemistry headed by Rodney Porter based in the Department of Biochemistry, and Cellular Immunology headed by Alan Williams located on the ground floor of the New Building in the Dunn School. Scientists from the MRC Immunochemistry Unit were able to clone genes encoding complement components C1q, C2, C4 and factor B. Scientists from the MRC Cellular Immunology Unit were able to clone genes encoding OX2, CD2, CD4, CD43 and CD45. There were also many other users too numerous to mention, both within the Dunn School, other Departments in Oxford including at the John Radcliffe site, and occasional visitors from abroad.

During the 1980s automated machines for oligonucleotide synthesis became available, and laborious manual synthesis was no longer necessary. The chemistry used also changed, and the phosphotriester method we had copied from Cambridge was superseded by the phosphoramidite method developed by Marvin Caruthers in Colorado. The increased reactivity of phosphoramidites meant very short cycle times and increased coupling efficiencies. Long DNA oligonucleotides could be made using only 4 mononucleotide blocks. All the reagents necessary for syntheses became commercially available, and we set up a service: people no longer had to make their own oligonucleotides and paid per nucleotide at cost price. In the late 1980s the new technique of PCR ensured that demand for oligonucleotides boomed, and at one time we had three Applied Biosystems automated synthesisers with a total of 11 columns, so we had the capacity to make 22 oligonucleotides per day.

Commercial companies also began selling custom made oligonucleotides, but for quite a long period most scientists within the Dunn School continued to prefer to order from our in-house service. I know someone who made a direct comparison between the same commercial and in-house sequence in their experiments and found the in-house

oligonucleotide to be of higher quality! Eventually competition between different companies and scale of operation meant that the in-house service became uneconomic, and it was closed in 1997. But I think it had served its purpose well.



I would like to conclude this memoir with an anecdote which I think illustrates perfectly the friendly and collaborative environment in the Dunn School during my time there. From the first DNA oligonucleotide synthesised in the laboratory onwards, each one was given a consecutive number. In 1990 we reached number 1,000 and one day I received a message

to go downstairs to the MRC Unit of Cellular Immunology tearoom at 5pm. Many members of the Unit were there, including Alan Williams and Neil Barclay, and on the table were four bottles of wine. One was labelled A, the next T, another G and the last one C, representing the four nucleotides found in DNA! In addition, someone in the Unit had gone to a lot of trouble to produce an 'MRC Oligo award' certificate which had been signed on the back by oligo users within the Unit, and it was presented to me by Alan. The bottles of wine didn't last very long!

I left the Dunn School in 1996 to become a lecturer in the Department of Immunology at St Mary's Hospital Medical School in London. Rodney Porter had been the first Professor of Immunology in that Department, and of course Alexander Fleming had discovered penicillin at St Mary's, so there was a strong link to my time at the Dunn School. In 1996 St Mary's Medical School was in the process of becoming part of Imperial College London, and I remained at Imperial until my retirement in 2020. I was able to continue my association with the Dunn School via a fruitful collaboration with Anton van der Merwe, which gave me much pleasure.

Acknowledgement

I would like to record my grateful thanks to George Brownlee for all his support and guidance throughout my time in the Dunn School, and indeed after I left. It was only because of George that I was able to do a DPhil and embark on an independent career in science.

Reference

- ¹ Choo K. H., Gould K. G., Rees D. J. G., Brownlee G.G. (1982) Molecular cloning of the gene for human anti-haemophilic factor IX. *Nature* 299, 178-180.

Leaving a legacy

If you are considering leaving a gift to the Dunn School in your will, the University's legacy team will be very happy to provide any guidance you may need regarding area of support, or to help you with the wording to share with your solicitor or family members. If you would like to let the team know about a gift in your will to the Dunn School, they would love to be able to offer you the opportunity to join a wonderful programme of events around all parts of the University, including next year's Centenary celebrations at the Dunn School.

A will is very personal, and the legacy team quite understand if you prefer to keep your intentions private. However, if you do wish to let them know about a gift in your will to the Dunn School, they would be delighted to be able to thank you personally.

Please contact the legacy team at: legacies@dae.ox.ac.uk / (+44) 01865 611538



Radcliffe Science Library 1996-2026: a transformed space for a 21st century library

Karine Barker

Karine Barker has worked in a variety of roles throughout her career in the Oxford University libraries that support the medical division and is currently Lead Librarian for Non-Clinical Medicine at the Radcliffe Science Library. The Radcliffe Science Library first opened in 1901 and has recently undergone significant change. In this article, Karine explains how the Radcliffe Science Library has changed over the past 20 years.

In the 1990s, the Radcliffe Science Library (RSL) was primarily a reference library, built around printed scholarly materials and traditional library practices. Users located books and journals using print catalogues and early computer terminals. To request items from the book stack, readers completed paper slips and waited for scheduled fetching rounds every hour, unless the materials were already available on the reading room shelves or on return trolleys.

Photocopiers were an essential part of library life. Students and researchers made several trips to the machines so they could copy journal articles or book chapters to take back to their departments or colleges. When materials were not available in Oxford, users completed another paper form through the Interlibrary Loans service and waited several days for delivery.

The reading rooms reflected the formal atmosphere of a traditional academic library. Portraits of celebrated male scientists lined the walls, while the environment itself could feel uncomfortable: too cold in winter, too warm in summer, and noisy whenever the windows had to be opened. The reading room in the basement was officially known as the Lankester but room became unofficially renamed by readers with a variety of names including bunker and dungeon. The furniture was functional rather than comfortable, and there was little flexibility for different styles of study. There

were no spaces for group work, informal discussion, or private meetings. Silence was expected throughout most of the building.

Food was prohibited, and even bottles of water were not allowed in the reading rooms. There were no refreshment areas inside the library and few opportunities nearby to buy drinks or snacks. Despite these limitations, the library remained a vital centre for scientific study and research, supporting generations of Oxford students and academics.

In 2020, plans to establish a new college created an opportunity to rethink the future of the Radcliffe Science Library. The redevelopment project brought together the library, Reuben College, and museum storage facilities in a major transformation of the historic building.

This redevelopment marked the beginning of a new chapter for the RSL: one that would balance the heritage of the building with the changing needs of modern research, teaching, and student life.

After a three-year closure for major refurbishment, the RSL reopened to readers in October 2023, transformed into a modern lending library at the heart of Oxford's science community. Today, the library is both a modern and welcoming study environment and a carefully preserved





historic building. It supports individual study as well as collaborative and social learning, while promoting accessibility, inclusivity, and wellbeing.

While high-demand books and key research texts remain available in print, users now access thousands of electronic journals and digital resources both on and off campus through secure online access.

The refurbished library offers a wide variety of welcoming and flexible study spaces designed to support different ways of working and learning:

- Two large traditional reading rooms, staffed and adapted for modern study, where drinks in secure containers are permitted.
- Two large social spaces where students can take breaks, eat snacks or cold food, and meet friends while studying.
- Four group study rooms, available for online booking and equipped with audio-visual technology for hybrid meetings.
- Individual study carrels with priority booking for readers registered with the Disability Advisory Service.
- A seminar room available to all members of the University.
- A vending area with machines providing hot and cold drinks and snacks.

One of the most distinctive additions is the dedicated Wellbeing Room. Furnished with flexible seating and stocked with activities including origami, jigsaws, knitting, and Lego, the room forms part of a wider wellbeing programme designed to support both students and staff.

Across the library, study areas are equipped with comfortable desks and chairs, height-adjustable tables, laptop stands, plentiful power sockets, and reliable Wi-Fi.

The library's lending collection has also evolved. In addition to books, users can now borrow keyboards, mice, monitor

risers, laptop stands, cables, adapters, portable chargers, headphones, and other equipment for use within the library.

Alongside scholarly collections, the library now includes a loanable wellbeing collection and a Curiosity Collection featuring accessible and topical scientific writing and science journalism.

The refurbishment has also improved the environmental performance of the historic building. Secondary glazing enhances thermal and acoustic comfort, while intelligent LED lighting systems reduce energy consumption.

The library's portraiture has been reconsidered to reflect a broader and more inclusive scientific history. Displays now highlight scientists connected to Oxford whose contributions have not always received the recognition they deserve. Among them is the Dunn School's own Norman Heatley, displayed alongside the portrait of Dr John Radcliffe, the library's benefactor and several women scientists.

Whiteboards placed throughout the library encourage readers to share ideas and feedback, reinforcing the sense that the RSL is an evolving and collaborative space.

The role of librarians has evolved alongside the building itself. Librarians now support researchers and students in areas such as open access publishing, institutional repositories, research data management, copyright guidance, and specialist literature searching. They also provide training on critical thinking, referencing, and the responsible use of AI in an age of misinformation through workshops and one-to-one consultations.

As subject specialists and academic partners, librarians maintain strong links with departments and faculties, supporting teaching, research, and outreach activities across the sciences.

Since reopening, the library has continued to evolve in response to student feedback. Improvements have included replacing casual furniture with additional study desks, creating more study spaces during examination periods, and providing print copies of popular science magazines.

Further developments are still to come. The future opening of the museum teaching and collections space within the same building will create exciting opportunities for shared teaching, training, and public engagement events for academics, students, and the wider community.

Further information

Website: www.bodleian.ox.ac.uk/libraries/rsl/ with description of various library spaces.

RSL wellbeing programme:

ox-ac.libcal.com/calendar/rsl-wellbeing

This article has been written based on internal documents produced by Donald Mackay and the RSL team.

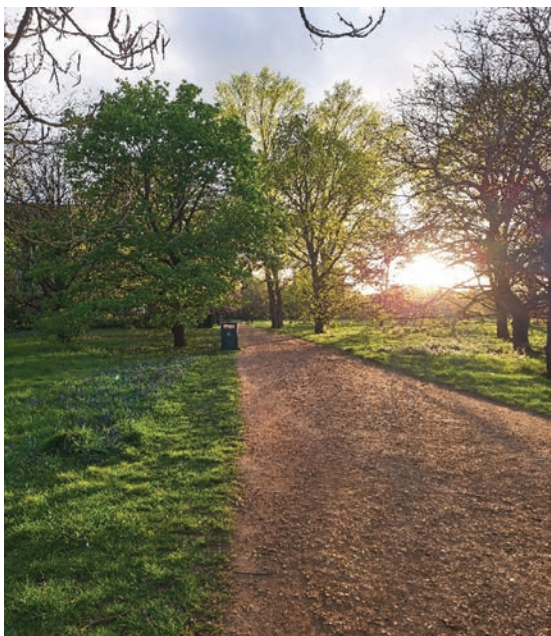
Calling all research staff: get associating with the Postdoc and Research Staff Association!

Charlotte Melia (Electron Microscopy Facility Manager)

Charlotte reflects on 10 years of the Dunn School Postdoc (and Research Staff) Association

What's in a name? Aside from the ability to engineer cool backronyms, a good name is vital for indicating a group's purpose and as a signpost to potential members. For this reason, the group formerly known as the Postdoc Association have recently widened their name to the Postdoc and Research Staff Association (PRSA).

The association – by one name or another – has a storied history in the Dunn School, with this year marking its 10-year anniversary. What began as a loose group of volunteers looking to represent the needs of postdocs in the department has changed significantly over the last decade, reflecting the evolving research culture, scientific focus and personalities of the department. It is now a formal part of our department, with an organising committee that meets regularly and 2 co-chairs (currently Emma Roberts, from the Raff lab; and Ines Diaz del Olmo, from the Thurston Lab) that attend Departmental Committee, the senior leadership committee of the department.



Special events, like wine and cheese evenings in the University Parks, are hosted by the PRSA and open to everyone at the Dunn School

The PRSA now arranges and hosts a wide variety of scientific and social activities throughout the year. These are open to all research staff at the Dunn School – be they postdocs, research assistants, lab managers, technicians – or anyone else who finds themselves holding a pipette or having a



BLAST on computational projects. Reflecting this, the topics and purposes of these events are selected for their appeal to a range of interests and backgrounds. Regularly held careers events recognise the diverse pathways and interests of research staff, with talks from researchers, scientific communicators, and those working in careers beyond academia. The mentoring scheme organised by the PRSA is dynamic, with mentor-matching to suit both academic and non-academic aspirations for mentees. Research staff of all kinds are also warmly invited to contribute to the PRSA's annual symposium, where they have an opportunity to showcase their work in talks and posters. On the social side the committee organises regular monthly coffee meetups for researchers to unwind, chat and (importantly) eat doughnuts together.

Many of the PRSA-led or co-led events are open and of interest to all members of the Dunn School. These include one-off evening gatherings for wine and cheese in the park, as well as the regular themed Dunn Drinks after-work socials, hosted by volunteer labs each month. The popular 'get to know...' series is also a calendar highlight; the informal interview-style approach taken by the hosts is a great way to learn more about key figures and group leaders in the department as well as, more recently alumni guests.

The PRSA also plays an important role in suggesting new departmental initiatives that can make a real difference to the career development of postdocs. For example, the PRSA has been instrumental in bringing the EMBO Postdoc Leadership Course to the Dunn School, which is now an annual occurrence. Another example was the suggestion that postdocs might be allowed to observe some of the

recruitment process for Dunn School PIs, a great experience for future job applications. The pilot was a success, and the opportunity will now be available to postdocs in the future.

The PRSA also had impact outside the Dunn School. Underpinned by strong support from the departmental leadership, the Dunn School PRSA became a flagship organisation for research staff in the division, serving as a template for researchers looking to organise and represent in their own departments.

With the new name the PRSA hopes research staff of all career stages, positions, and backgrounds will feel welcome to come along to these events and become part of the research staff community. We're always looking for ideas, feedback – and new members! – so if you'd like to contribute to ongoing events or bring in new ideas then do get in touch at pathology-pda@maillist.ox.ac.uk.



A view from the cheap seats: one of the early 'Get to know' events organised by the PRSA back in 2018, with HoD Matthew Freeman

The Dunn School Memories Collection Project, a year on...

Last year, we launched our **Memories Collection Project** – an initiative to gather and share the stories, people, and moments that have shaped the Dunn School over the past 100 years. Thank you to everyone who has taken the time to share their memories with us: it has been a real pleasure to receive your stories and unique documents and photographs.

The project is still open to all our alumni, friends and family of alumni, as well as our current staff. We are looking for any stories of time spent in (or outside) the lab, memorable discoveries, or simply the day-to-day experiences that made the Dunn School feel like more than just a place of work or study.

If you have anything you'd like to add to our growing collection, please get in touch with us at alumni@path.ox.ac.uk. For inspiration, here are two of the memories we've received so far:

Elaine Griffin was a DPhil student in Henry Harris' group in the early 1990s and also the captain of Oxford University's gymnastics team. Here she can be seen performing an impressive cartwheel in front of Professor Henry Harris's office.



Philip Thornton-Evison worked in the Dunn School from 1975 – 1988:

"I began working in the Dunn School on Monday Sept 1st. 1975, as a trainee technician. Having left school with A levels in Chemistry, Biology, and English Literature I was uniquely unsuited for any form of university education, but I had a vague idea that actually working in a laboratory might be quite fun. I was interviewed by the then administrator, Mrs Peggy Turner. I think she must have taken pity on me for I was offered a post there and then.

Initially I was put under the care and training of Mrs Mary Williams, who was in charge of the Cell Bank. It was a pretty steep learning curve I had to admit, but my colleagues were all friendly and welcoming, so I soon settled down. In those days tissue culture work was done standing in front of a blowout fume cabinet. Neither were there any rules about smoking in the workplace. My abiding memory is of Mary working at the hood, cigarette in mouth, with the ash and smoke being blown back into the lab. behind her.

Following my three years of training I moved into the Bacteriology and Teaching group, with Ken Mabbatt as my boss, an absolutely lovely man to work with.

I left the department in 1988, having worked in the Bramwell group for a couple of years."

Two new endowed PhD Studentships established at the Dunn School

The new studentships are part of our centenary fundraising efforts to secure long-term support for research students at the Dunn School.



The **Oxford-Stephen Cobbold Graduate Studentship**, named in honour of Professor Stephen Cobbold, Emeritus Professor of Cellular Immunology, and the **Waldmann Family Scholarship**, have both been established thanks to the generosity of former Head of Department Professor Herman Waldmann, further supported by the EPA Research Fund, the EPA Cephalosporin Trust and the CIU Trust.



The two scholarships will support PhD students in the Dunn School in perpetuity, with the first two students benefitting from these scholarships starting this academic year.

"We are so grateful for the generosity of Herman Waldmann and the trusts who made these two scholarships possible. It is hard to think of a greater possible impact than supporting future biomedical research students at the Dunn School." said Professor Matthew Freeman, Head of Department *"We are very proud of our past achievements but even more excited by the future. As we approach our Centenary, I am confident that our students will continue to be the lifeblood of the department and the catalysts of our future discoveries."*

Ensuring the future of graduate study at the Dunn School is one of our fundraising objectives for the department's Centenary in 2027. You can find out more about supporting our Centenary Campaign on page 41.

Diary of the development of penicillin

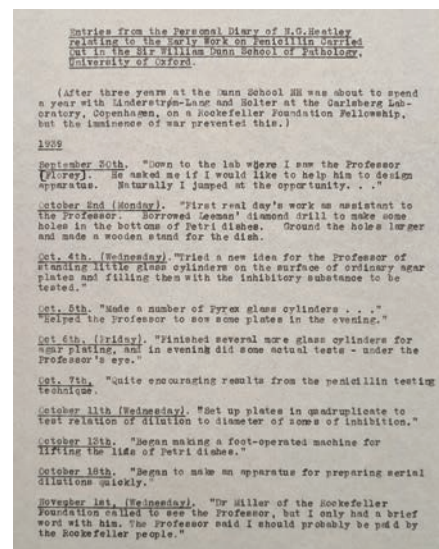
Catarina Vicente

One of the best first-hand accounts of the world-changing research that transformed penicillin from curiosity to a wonder drug are Norman Heatley's personal diaries. A scientist and amateur inventor, Norman's ingenuity was crucial to solve many of the problems that the Dunn School team encountered in resource-strapped Oxford during the Second World War. Our most prestigious annual lecture, the Heatley Lecture, celebrates his legacy.

As part of the preparations for our centenary, I am visiting the archives holding documentations related to the history of the Dunn School. The most obvious are of course the archives of the Bodleian library, which hold both the general research and administrative records of the Department, but also a special collection dedicated specifically to penicillin. But this is where things get complicated. For those that spent only a few years here, either as students or researchers, the relevant papers can be held in archives anywhere in the world. Even for individuals who worked here at the Dunn School for most of their careers, Oxford is not necessarily the place where their records and papers can be found.

The text below is an interesting example of the varied locations and connections awaiting discovery. I was recently at the Royal Society, and took this opportunity to visit the society's archives, which hold Howard Florey's papers. While Howard Florey was Head of the Dunn School for most of his career, he was also elected a Fellow of the Royal Society in 1941, and became its 50th president in 1960. It is perhaps not surprising therefore that his

papers are kept in the society's archives (catalogue reference: HF). Among Florey's papers related to the Dunn School were an interesting set of typed notes.





Norman Heatley

One of the best first-hand accounts of the development of penicillin are Norman Heatley's personal diaries. In them, he provides details of the progress of the research, the people who were involved, and his own experience of exciting and challenging research in the context of a world war. The Heatley diaries are kept in a different

archive in London, at the Wellcome Collection. The diaries are accessible, but only catalogued at a high level and have never been transcribed or published. The notes that I found in Florey's archive at the Royal Society seem to be an attempt to summarise, or highlight, the main events in the diary. Two archive documents talking to each other, 2 miles apart!

It is unclear who collated these notes, and when, but they are an interesting find. They provide not just an extremely useful reference for anyone wanting to explore the Heatley diaries in detail, but also a fascinating overview of the penicillin research and the fantastic detail of the Heatley diaries. Personal highlights for me are the references to the famous penicillin bedpans, and their various iterations, as well as the recruitment of the 'penicillin girls', the group of young women who worked closely with Heatley to produce penicillin in the vast quantities needed for experimental work and subsequent clinical trials. Closer to the end are references to the secretive and dangerous crossing of the Atlantic made by Heatley and Florey during the war. This was an important trip, during which Florey was able to persuade pharmaceutical companies in the US to take on the industrial production of penicillin.

This selection of the notes is republished here by kind permission of the Heatley family.

Entries from the Personal Diary of N.G. Heatley relating to the Early Work on Penicillin Carried Out in the Sir William Dunn School of Pathology, University of Oxford.

(After three years at the Dunn School NH was about to spend a year with Linderstrøm-Lang and Holter at the Carlsberg Laboratory, Copenhagen, on a Rockefeller Foundation Fellowship, but the imminence of war prevented this.)

1939

September 30th. "Down to the lab where I saw the Professor [Florey]. He asked me if I would like to help him to design apparatus. Naturally I jumped at the opportunity ..."

October 2nd (Monday). "First real day's work as assistant to the Professor. Borrowed Leeman's diamond drill to make some holes in the bottoms of Petri dishes. Ground the holes larger and made a wooden stand for the dish."

Oct. 4th. (Wednesday). "Tried a new idea for the Professor of standing little glass cylinders on the surface of ordinary agar plates and filling them with the inhibitory substance to be tested."

Nov. 27th. "Moved properly into Bob Ebert's old room (No 46)... "Had a conference with the Professor (and Chain) about the problem of finding the best growth conditions for Penicillium and what makes it produce penicillin."

December 9th. "... took first steps in trying to isolate a pure mould for the penicillin work."

December 28th. "The penicillin experiments are now going quite nicely."

1940

March 20th. "Yesterday's ether extraction experiments were encouraging: it looks possible to isolate P by ether extraction."

March 21st. "Did some more experiments with ether extraction. Chain thought he had some crystals of the sodium salt of penicillin."

March 28th. "Tried incubating P with rat blood and rat liver."

March 29th. "Was very glad to find that P was not destroyed by incubating with blood or liver."

April 4th. "Worked up a P solution which contained no pigment."

April 5th. "The Professor tried injecting two mice (intravenous) with strong Penicillin with not very marked success, but the mice were still alive and well an hour later."

April 6th. (Saturday). "The mice injected with penicillin yesterday were still alive, and the Professor and Chain and I had a long discussion in my room."

April 10th (Wednesday). "The Professor injected some strong penicillin into two mice. One was rather sick, but eventually recovered."

April 26th (Friday). "Was delighted to find that colloidal iron can be used to stop emulsion formation, but does not reduce penicillin activity." ... bought a number of enamel pans for growing the mould in."

April 30th. "Did some experiments on the assay of P in blood."

May 6th. "Spent the day preparing more trays for growing penicillium in, with Gordon's inspection hole idea."

May 7th. "George Glistler, a new technical assistant, who is eventually to take over the culture of the penicillium, arrived and spent all today with me in my room doing odd jobs."

May 20th. "A system has been started in which four people spend the night at the lab, to keep guard over it."

May 25th (Saturday). "We tested today for the first time the effect on P Streptococcus in vivo. This entailed working all afternoon and sitting up till 3.30 a.m. tomorrow... and met the Professor to give a final dose of P to two of the mice. The controls were looking very sick, but the treated mice seemed very well. I stayed at the lab till 3.45, by which time all four control animals were dead. It really looks as if P may be of practical importance. I discovered I had put on my pants back to front - a lucky omen?"

May 26th (Sunday). " ... went to the lab at 11.45 and found all four treated mice alive and well. Had a discussion till 1.15 with Professor and Chain, who wanted me immediately to produce 100 litres of Penicillium broth per week. Chain ordered £200-£300 worth of stuff straight off, including 500 litre flasks!"

May 27th. "Busy day at the lab getting ready to grow really large quantities of Penicillium. Gordon [Sanders] came to help and is going to work on this problem, and so are Prof. Gardner and Dr Vollum. Went to the lab at 9.30 [p.m.] and stayed till about 12.30 to help the Professor to inject some mice with Penicillin."

May 30th. "Plans afoot to move from room 46 to the suite, 47-48. The idea was that George G and I should... prepare Penicillin on a large scale. I had the idea of using

bedpans for growing the stuff in and the Professor rang up Professor Seddon. We later had the idea of using biscuit tins, varnished inside with Bakelite varnish. I constructed a special "bedpan-type culture vessel" out of a biscuit tin."



June 1st. "First tested the biscuit tin I had varnished, by autoclaving some 1% HCl in it. It seemed to be quite alright, so I set up it and some other vessels with medium and got George to autoclave them... helped the Professor inoculate some mice at 8 o'clock. Did the same at 11 o'clock and 2 o'clock and in between times was very busy setting up plates and inoculating batch XXIII. Spent a good deal of time drying off a preparation of Chain's, an eventually left the lab at about 3.40 am on Sunday morning..."

June 3rd. "Tried to collect biscuit tins from various grocers in the town."

June 4th. "Caught the 9.15 to Reading and went straight to Huntley and Palmers. Could not get any square tins, but they let me have 100 round ones. Then went to Huntley, Bourne & Stevens, the tin box manufacturers, and their Mr Jewell was most helpful."

June 5th. "Miss Smart came with me in her car to collect 6 bedpans from the Radcliffe for growing Penicillium in."

June 13th. "Letter came from home with Parashoot (sic) silk, so I made two filtration bags on Mrs Mitchell's sewing machine."

June 15th. "Collected a pass from the military authorities in the Old Clarendon, for our lab is to be guarded by the Army after 7.0 p.m."

June 21st. "Sowed a further 56 rectangular tins which had been autoclaved yesterday" [These were upright tins with screw caps, such as might hold a gallon or half a gallon of, say, motor oil.] Began to make a trial percolating machine for extracting P."

June 27th. "George and I collected about 40 litres of P solution and filtered it. In the afternoon tried the dustbin still I had designed and it worked perfectly, although the cooling condenser was not quite efficient enough."

July 17th. "Began to make a new P extracting apparatus. The Professor showed me how to inject mice ..."

July 25th. "Spent all day playing with P-extracting apparatus. Gained several useful experiences, and I think it will work quite well, eventually."

July 26th. "A letter from Dr Pope of Burroughs Wellcome, asking for further details about P assay method, which he cannot get to work." "The Professor put forward for the first time his serious suggestion that we ought to test as many other fungi as possible, in order to try to find an antagonist for the coli-typhosus group of organisms."

Sept 2nd, (Monday). "Professor Fleming and Dr Young came up to see how penicillin was produced and spent nearly two hours with us."

Sept. 4th. "Decided to make big modifications to the extraction apparatus ..."

October 3rd. "Chain was very worried because all the penicillin was used up and they were short of it for the chemical work. (Was demonstrating in Bacteriology this term, also helping blood-group donors at Bodleian and taking blood from donors at Wingfield, with J. M. Barnes.)"

Oct. 18th. "In evening drew up a rough specification for earthenware vessels for growing P in."

October 29th. "Ran some P through the extracting machine fitted with the vibrating jet; quite good results. Prof. had a wire from Dr Stock giving the name of a pottery firm who could make the culture vessels for us, and also offering to put me up for the night. Put through a trunk call to him and learned he could put me up tomorrow."

Oct. 30th. "Caught the 9.15 to Stoke, which arrived at 4.50 instead of 1.45. Rang McIntyre's, but they said better come tomorrow."

October 31st Thursday. "Took a bus to Burslem where I went to see McIntyre's pottery. Mr Watkins showed me all over the

works... and was most helpful about the culture vessels. The model-maker was a very able and obliging man too."

Nov 9th. "Began at last to get some concrete ideas of how to construct the large-scale P extraction apparatus."

November 11th. "Spent most of the rest of the time demolishing a bookcase and making a frame from it for the new P extraction apparatus. Had discussion in the evening with George and Chain about the assistance we shall need for preparing P on a large scale."

Nov 18th. "The first samples of the ceramic culture vessels arrived and were much admired."

December 2nd. "The M.R.C. had after all been unable to obtain any trained assistants for us, so we set about getting some girls. Engaged a Miss Geddes and also Donald's [Callow] sister..."

December 9th. "Donald's sister [Ruth] came to the lab today to start work with us ..."

December 11th. "Miss Inayat - recommended by Miss Mitchell - arrived, to learn more about the job."

December 18th. "Ran the extraction apparatus, with both 1° and 2° columns in action. With amyl acetate the 2° column is not usable as the emulsion breaks up too slowly to allow any but a very slow rate of passage of solvent through it. This throws the whole apparatus out of gear. We shall probably have to extract by hand from the solvent."

Dec. 22nd. "... got out the E.P.H.S. Ford 10 cwt. van and... set off North ... arrived [at Stoke-on-Trent] at 2.45"

Dec 23rd. "Rang up James McIntyre ... The culture vessels were packed in straw directly in the van. 174 of them good run back to Oxford ... 4.45."

Dec. 31st. "What a year! ... The latter part of the year I have left research entirely and have been concentrating on the production of P on a large scale. Now, with the help of George Glister, Ruth Callow and Claire Inayat we are beginning to grow P on nearly one thousand times the scale on which I was growing it a year ago."

1941

Jan 4th (Saturday). "Today we harvested the first big batch of P in rectangular culture vessels and the improved changing apparatus we had made worked very well. We can already empty and fill 25 vessels per hour (two operators)."

Feb. 2nd. "Penicillin is being tried on human patients now."

Feb. 14th. "Made the first rough bottle-separating-funnel idea, and it looks as if it will work nicely. Forgot to mention yesterday the dramatic effect of Penicillin on a policeman with staph. and strep. Septicaemia. He had been in a bad state for a month, oozing pus everywhere, but 24 hrs after P, he showed a dramatic improvement. He was about the same today, so they are going to increase the dose."

Feb. 25th. "Got the bell of the warning device rewound, so that it will ring in series with the lamps."

Feb. 26th (Wednesday). "Began to fix the cooling coil to the extracting apparatus. Professor Fleming drove up from London to see it, and brought E.J. King and Dr MacLean with him. The latter wanted to see the arrangement for spreading agar inside the Winchesters, but the other two seemed quite impressed with the apparatus. They took me to lunch at the King's Arms and then left at about 3.15."

Mar. 1st. "John Barnes drove me up to the Wingfield after lunch and showed me to see Arthur Jones, the 16-year old boy who had penicillin. He was looking much better, John said."

March 10th. "The Professor said that he was getting into touch with a large-scale firm for the production of large amounts of penicillin."

March 17th. "Decolourised a batch of strong P with charcoal and then extracted it into ether - both operations for the first time."

March 23rd. "Had some very good ideas for a really large scale extraction apparatus for Penicillin."

March 24th. "... the Professor, Chain, and I had a long discussion as to what we are going to tell Sir Henry Dale & Co when they come on Wednesday to discuss the large scale production of penicillin."

March 28th. "Posted a sample of dried penicillin to Prof Fleming."

April 12th. "The Zal spray arrived yesterday and we tried it then and also today. I hope and think it may mark a new era in the penicillin work." [Because there was rather a lot of infection of cultures lately.]

April 14th. "Sent off a sample of spray-dried penicillin to Dr Trevan. The Professor injected some penicillin into a rabbit and I assayed three samples of urine. He went to London during the day and I saw him when he came back. He had had a most stimulating interview with Mr Warren Weaver of the Rockefeller Foundation about P on a large scale."

April 25th. NGH was taken by Prof & Mrs Florey and Mrs Jennings to see a film "Foreign Correspondent". "The sinking of the "Clipper" in the film struck the Professor & me as rather a bad thing to see, in view of recent plans for large scale penicillin production" This must mean that NGH was aware of a possibility of going to America.

May 13th. "The case we had hoped to treat had got much better, so the Prof naturally decided not to do anything to it... The Professor told me a case had come in from Banbury of a 4-year old boy with infected ocular sinuses: Dr Macbeth, whose patient he was, said he would be in his grave in three days. M& B 693 had been tried without effect. Even the CSF was cloudy. I went across to the hospital with the Professor and Gordon - who went to take photographs - and he was certainly looking very ill."

May 14th. "The boy, John Cox, is about the same - no worse, anyway."

May 15th. "The boy is still no worse today, and the Professor actually thought he was looking better. His pulse temperature and respiration are all down, too."

May 16th. "The little boy, Johnny Cox, was certainly no worse and the Professor thought he was looking better ..."

May 17th. "Met the Professor at the Radcliffe at 10.00 and Johnny Cox certainly seemed much better than when I had seen him admitted to the hospital. The Professor was sent a cutting from the "New York Times" by Dr Warren Weaver, which described Dawson's work on Penicillin. (No mention of Oxford, and Dawson was one of the people to whom Chain sent a culture of our mould in Sept 1940.)

May 19th. "... the Professor did a big experiment requiring 12 assay plates. With George's help I dispensed a little more penicillin for Johnny Cox, who is still doing very well"

May 28th. "Yesterday the Professor returned from the Radcliffe with the sad news that John Cox, our case No 4, had had a stroke; blood in CSF. Temperature up to 106, paralysed down one side, etc. It is now four? Five? Days since he last has penicillin."

May 29th. "The Professor was away all today, but Fletcher decided to give John Cox another series of penicillin doses ..."

May 30th. Friday. "The Professor was away in London all today and he rang me up at 10.30 to say that he thought I might "begin to polish up the bags" (ready for our visit to A.)"

June 4th. "Practically all day was taken in showing Dr Hobday [of Boots] how penicillin was grown and worked up.. Took some penicillin to the Professor for his own inflamed eye."

June 5th. "Dr Hobday, of Boots, came along to the lab till 12.00, and saw a few more processes in the making of penicillin. He also had a talk with Abraham. The Professor had been in London and rang me up when he returned. We met at the lab and filled in exit permits, etc"

June 16th. "From Paddington went straight to 80 Pall Mall, where I had my notes examined by the censor and sealed."

June 20th. " ... was given my air ticket to Lisbon and told of the latest arrangements."

June 21st. "The Prof gave me the final copy of the paper to read through. [Must have been the second *Lancet* paper 1941 ii 177.]"

June 23rd. "Only 6 vessels had survived out of batch D, so the girls had slack day."

June 26th, Thursday. "After lunch today the Prof and his wife are taking me to Bristol by car. We stayed the night at the Grand Hotel, and leave at 7.0 a.m. for the airport, where we embark for Lisbon. On June 30th we are due to leave by Clipper for U.S.A."

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PATHOLOGY**

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From the *Fusion* Archives...

The following is a selection of excerpts, chosen by the Editor from past editions of *Fusion*, that give a flavour of events and topical issues within the Dunn School during years gone by...

Ten years ago...

In 2016, *Fusion* included an article written by Stephen Cobbold, where he gives a personal account of experiencing kidney failure, and the subsequent surgery and treatment. Steve was given a kidney transplant and found himself on the receiving end of CAMPATH - the very drug he had helped develop.

"The transplant: 5 days in hospital

Peter Friend (now the Director of the Oxford Transplant Centre) performed both Peppy and my surgeries. The first thing I remember as I awoke in the recovery room was a nurse saying "the CAMPATH is going in now"! After the operations both Peppy and I recovered well, with no pain (no need for the magic morphine button). I now had a 20cm half-moon wound sealed with superglue and 3 kidneys (they don't remove the old ones). The transplanted kidney started producing urine immediately but creatinine and potassium levels took longer to normalise. They got me up a day later but I was very tired. They wheel around noisy trolleys all night and surround you with machines designed only to provide a continuous beeping sound or alarms! The anaemia rapidly improved, so no more EPO. Peppy went home on day 3, but visited with my parents on day 4, when I was allowed out to the coffee shop (plus my "yellow handbag"). I was supposed to be pushed in a wheelchair, but I ended up pushing my mum instead. After being discharged I had to avoid infections and be monitored by the Churchill clinic 3 times a week."

Twenty years ago...

The fifth issue of *Fusion* (2006) included an article by Ruth Harvey, then a postdoctoral researcher at the Dunn School, looking at the research of George Brownlee and Ervin Fodor's groups on influenza, and their development of a reverse genetics system for the production of influenza vaccines, with a particular focus on bird flu due to the health concerns at the time. The technology has since been used to generate influenza vaccine strains for the production of influenza vaccines used worldwide, including the Fluenz formulation which has been given to more than 20 million children in the UK as part of the National Childhood Vaccination Programme.

"The current vaccine used worldwide is a trivalent vaccine. Each year, the World Health Organisation (WHO) predicts the influenza strains, (A – H1 and H3 subtype and B) likely to circulate the following year based on epidemiological data collected worldwide..."

Influenza research at the Dunn School by George Brownlee, Ervin Fodor and others led to the development of the reverse genetics system that allows the construction of 'designer' viruses from potentially any combination of the virus genome segments. This is a huge step forward for the manufacture of vaccine strains, allowing vaccine candidates to be made that are, for example, antigenically relevant in a high growth background. This new reverse genetics system has been used to create a nonpathogenic seed vaccine against the H5N1 bird flu virus. The UK government plan now includes the manufacture of H5N1 vaccine from such a seed stock if pandemic bird flu occurs in the UK."
