fusion

THE NEWSLETTER OF THE SIR WILLIAM DUNN SCHOOL OF PATHOLOGY

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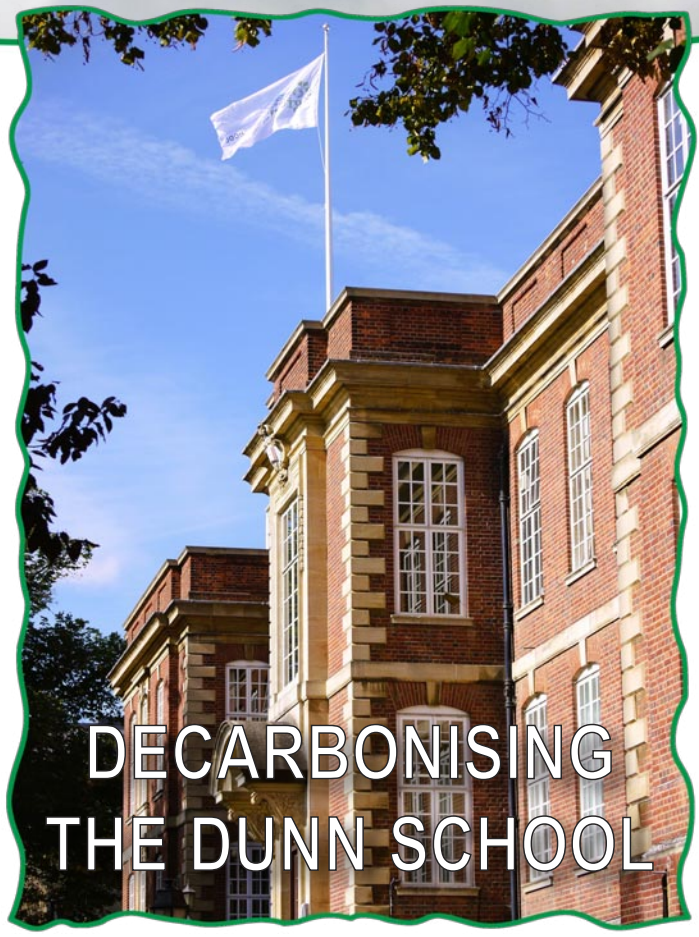
UNIVERSITY OF OXFORD

Interview with the University's Sustainability team

Bacterial persistence

Gordon Macpherson 1941-2021

Our immediate neighbours



100 years: 1000 faces

Glycans in immunosilencing

Rethinking academic travel

This issue is online at https://t2m.io/Fusion2023

SIR WILLIAM DUNN SCHOOL OF PATHOLOGY

Welcome…

…to the first post-pandemic edition of Fusion. Although Covid hasn't completely disappeared, I am pleased to report that the Dunn School is at last back to full energy and activity. As I wrote in Fusion19, the famous spirit of the department, combined with amazing efforts by everyone here, made the challenges of the last three years easier to manage. We pulled together through a hugely uncertain, disruptive and difficult period.

We set ourselves the goal of recovering full momentum as soon as the restrictions were relaxed, and I think we succeeded. Already the details and paraphernalia of the pandemic are blurring into a haze of black and yellow hazard tape, notices about social distancing, plastic screens and one-way systems. The Dunn School Summer Party in the University Parks returned [see *Parties!* in this issue], the café reopened, the Graduate Student Symposium restarted its annual rhythm, and in-person attendance at seminars is, once again, the norm.

Most importantly, Dunn School research and teaching are both thriving. We are continuing to welcome truly outstanding students and postdocs; and we are energetically recruiting spectacular new group leaders at all career stages. This issue of *Fusion* includes profiles of them [see *Arrivals and Departures*]. Recruitment of outstanding new people is at the heart of our continued focus on research and teaching excellence and, as head of department, I see it as my single most important job.

In the same period, we have also said goodbye to several PIs, as well as to many other colleagues, both academic and professional support. We miss them all of course, but will continue to bask in their past and ongoing successes. We also all know that once a member of the Dunn School family, you can check out, but can never really leave.

A theme of this issue of *Fusion* is sustainability, and specifically the Dunn School initiatives to pioneer a more thoughtful approach to environmental impact of our research. By its nature, experimental science is not very green: our activities are power and water hungry, and carbon-intensive travel to conferences and other meetings forces us to think hard about costs and benefits [see *Rethinking academic travel*]. Along with our huge consumption of single-use plastics, these are issues that we can no longer ignore. I am very pleased to report that, led by the Dunn School Green Group [see *Greening the Dunn School*], we're now acknowledged leaders in the University, responding to both the urgent global need and to our specific target of reaching net zero carbon and biodiversity net gain by 2035.

Now beginning to move to the centre of our attention is the Dunn School centenary, which we will celebrate in 2027. Although still at an early stage, let me give you a sneak preview of some of the plans. Most importantly, mark your diaries for a centenary symposium and summer party, to be held on 7th July 2027 (yes, really; celebrations on this scale need booking that far in advance). It will be a great event and we hope to meet as many Dunn School alumni, friends, and colleagues as possible.

The centenary is also motivating a focus on our history. In the spirit of trying to know more about the people responsible for our success, our project to digitise and catalogue our almost 1000 photographic portraits of Dunn School alumni is now in full swing [see *100 years; 1000 faces*]. If yours is amongst them and if you want a digital copy of it, please let us know. Many of you have been in touch already with stories, memories, and even objects associated with your time here. Please keep them coming: they provide lovely colour to the more famous black-and-white elements of our history. And don't forget that we welcome visits. Whether or not you can make it in July 2027, please let us know if you are in Oxford and would like to see your old haunts (even if they may have changed beyond all recognition!). To stay in touch, drop an email to alumni@path.ox.ac.uk, or message us via **X**/Twitter, or visit the Alumni webpage.

Tediously but importantly, data protection law requires your active consent for us to keep sending you *Fusion* and to contact you about our plans – parties as well as science! If you haven't received an email this year headed "Dunn School Alumni Newsletter" then you're not yet on our new mailing list. Please check now. If you want to register to keep in touch, simply email us at alumni@path.ox.ac.uk. It's just a one-time requirement. With the centenary approaching, I am sure you won't want to miss out.

The centenary is also a chance to look forward and work towards securing the next century for the Dunn School. Consistent with my earlier point about the importance of our people, our focus will be on raising funds to endow both new graduate studentships and academic posts. The recent very generous endowment of an associate professorship by the Berrow Foundation is a fabulous example of how a gift can directly support our long-term scientific future excellence. And by the next issue of *Fusion*, we hope to have good news – and a challenge! ¬– about graduate studentship endowments.

Finally, those of us who can make it to the Dunn School in 2027 will have the privilege of celebrating the Department's extraordinary first 100 years on our present site. Whether it's penicillin and antibiotics, the cellular basis of immunity, the technology for cell fusion and monoclonal antibodies, Factor IX, flu vaccines, antibody therapies, or the many other discoveries of which the Dunn School is so justifiably proud, we passionately believe that the best is yet to come. Perhaps the theme of the celebration should be: 'You ain't seen nothing yet'!

Matthew Freeman

Contents

Front cover images were taken on 24 September 2022 by Simon Hunt. Our flag was flying to celebrate Great Big Green Week

News in brief: round-up 2021 to 2023

Lady town crier, 1943

Oyez, Oyez! News-hungry reader, the Dunn School webpage www.path.ox.ac.uk/about-us/news/ is at your service to keep you always updated if you want. Or you can Follow our X/Twitter @DunnSchool or Linked-In feeds. Newsworthy stories about highlights from the Dunn School are written by our team of volunteer news reporters who change their pipette tips into quill pens from time to time. Here are some snappy snippets, mainly selected from their items between September 2021 and June 2023.

To easily click the links in this article online, go to https://t2m.io/NewsTo2023 or point your phone at the QR code.

Date	Headline	Snippet	Note
Oct 2021	Yet more Teaching Excellence Awards	Four senior academic staff have returned to the podium they're already very familiar with, to collect further University awards: Rachel Exley (Somerville College; Tang lab) and Chris Norbury (Queens College) as "Excellent Teachers"; Anton van der Merwe was given a Lifetime Achievement Award for outstanding work in graduate recruitment and teaching; and David Greaves (Hertford College) received a Major Educator Award	The citations for their richly-deserved awards are here

© Joana Veríssimo Ferreira

Excellence in Teaching: Chris Norbury, David Greaves, Anton van de Merwe, Rachel Exley

Date	Headline	Snippet	Note
Dec 2021	Dunn School academics recognised with Full Professor title	Omer Dushek is now Professor of Molecular Immunology. He researches the immunology of T cell receptor signal integration at the interface between mathematics, physics, and biology. See https://dusheklab.com/ Fumiko Esashi is now Professor of Molecular Biophysics. Her group investigates regulation of homologous recombination in DNA repair and genome stability. Centromeres as hot-spots for DNA breaks: the latest news. https://esashilab.wordpress.com/	Dushek lab ORCID Esashi lab ORCID[1]
Feb 2022	Prof Ulrike Grüneberg wins a CRUK Discovery Programme Award	This 5-year grant will enable Ulrike and her group to further study the spindle assembly checkpoint, a vital cellular surveillance system for ensuring faithful chromosome segregation at mitosis	Since 2021, Ulrike (Keble College) now holds the title of full Professor. ORCID[1]
Feb 2022	Ivan Ahel (Lincoln College) appointed as EP Abraham Professor of Chemical Pathology	His group focuses on ADP-ribosylation, which is a reversible post-translational modification underlying the DNA damage response. Studying different inhibitors will for instance illuminate: tuberculosis; certain neurological disorders; resistance of cancer cells to chemotherapy. Ivan introduced himself in 2013: Fusion 12, page 3. Ahel lab: https://ivanahellab.wixsite.com/ivan-ahel-lab	Received GSK Award of the Biochemical Society. Elected member of EMBO ORCID[1]
Spring 2022	In March, our Graduate Students Association, GSA enjoyed a get-together Dinner in Lincoln College. In June, the GSA held its first ever Graduate Student retreat, in sunny Wales.	Glad to say goodbye to pandemic restrictions! The GSA also celebrated the return of the Graduate Student Symposium, in-person at St Catz, where all students either gave a talk or a poster about their work. The GSA, together with the post-doc and research staff association PRSA jointly hosted an informal discussion with the Dunn School's Visiting Professor Maria Leptin, President of the European Research Council, about making good journeys in scientific research.	GSA Facebook page (unofficial) See too X/Twitter @Dunn_GSA and Instagram @dunnschoolgsa Maria Leptin ORCID[1]

Eight of the members of the 2022 Post-Doc Association

April 2022	Andrii Gorelik awarded Sir Henry Wellcome Fellowship	His four-year fellowship will enable Andrii, who originally hails from Kyiv, to study cysteine ADP-ribosylation independently within the Ahel Lab.	Andrii holds a Junior Research Fellowship at Lincoln College
May 2022	Prestigious BSCB prize for Iona Manley (Queens College)	The British Society for Cell Biology recognised Iona as "Young Cell Biologist of the Year." As a member of the Grüneberg lab she studied accuracy of chromosome segregation during mitosis: how kinases and opposing phosphatases regulate the spindle assembly checkpoint	Iona is now a post-doc at Kings College London/Crick
May 2022	Susan Lea and Jordan Raff elected Fellows of the Royal Society	Susan (Wadham College) was Professor of Microbiology until 2021. Jordan (Lincoln College) holds the César Milstein Chair of Molecular Cancer Biology in the Dunn School. He won the Biochemical Society's 'Excellence in Science' Award in 2022.	Raff lab ORCID[1] Susan Lea ORCID[1]
Aug 2022	Prof Monika Gullerova (Wadham College) becomes titular Full Professor	Her research aims to elucidate molecular mechanisms of RNA- dependent DNA-damage response, which might pave a new way for design of RNA-based cancer therapies. Gullerova lab: www.gullerova.com/	See Fusion16 page 11 ORCID[1]
Aug 2022	Audio file (83 minutes)	Podcast by Prof William James (Brasenose College), interviewed in the series Collecting COVID: Oral Histories. An autobiographical conversation about his background and his lab's role in the COVID emergency	Automated transcript

Date	Headline	Snippet	Note
Sep 2022	Lachlan Deimel (Sattentau lab; Brasenose College) was awarded £500 runner-up for the Beaconsfield Prize	Lachlan's essay is published in this issue of Fusion. See "overcoming the glycan blind-spot". We also belatedly note that Wearn-Xin (Edeline) Yee (Tang lab) won the similar award in 2020. Now a post-doc at UCSF, she held a Prize Scholarship at Merton College. Tabea Elsener (Jesus College; Tang lab again) has won the runner-up prize in 2023. *Fusion* offers sincere congratulations to them all.	The Peter Beaconsfield prize is open to graduates who recently transferred to DPhil.

© Simon Hunt

As a mark of respect at the news of the death of HM Queen Elizabeth II, the Union Flag flew at half-mast on 8th September 2022

Dec 2022	Prof Ervin Fodor, FMedSci, (Exeter College) wins MRC Programme Award	Ervin's 5-year grant is to further study RNA-dependent RNA polymerase. His lab researches transcription, genome replication, trafficking, in Influenza and other RNA viruses, specifically focusing on the cellular context of these processes.	Elected EMBO member, 2021 Fodor Lab ORCID[1]
Dec 2022	Wellcome Trust Early Career Fellowship awarded to Viktoriya Stancheva	Vicky will study the 'rewiring' of contact sites during flavivirus infection. Such viruses evade immune detection, replicating at the so-called replication organelle (RO) whose contact sites with other organelles regulate their homeo-stasis and immune signalling.	Sanyal Lab ORCID[1]
During all of 2022		The GSA hosted a series of alternative career events with external speakers and former Dunn School DPhils, sharing insights into a variety of career paths outside of academia. Alums: here is a chance to hand on your experience!	This series continues. Alum offers, please, to alumni@path.ox.ac.uk
Jan 2023	Catarina Vicente selected for Fellowship of UK Young Academy	Cat is in the first group of 67 members, selected from 400 applicants. She is the Dunn School's Science Strategy and Projects Manager. At Reuben College she is Official Fellow in Public Engagement with Research. Read Cat's article in this issue of *Fusion* on conserving the Dunn School portraits.	The UK Young Academy is one of 40 similar academies globally. Guide. Apply to join.
Jan 2023	Matthew Freeman to Chair EMBO Council	"EMBO *has been part of my scientific life ever since I was a graduate student. It's a force for good in European and world science.*" It is a major and prestigious appointment to be invited to lead EMBO as its principal custodian.	Matthew's reflections on his responsibilities as Chair
Feb 2023		GSA's inaugural joint social event with Weatherall Institute (WIMM GSA) and Kennedy Institute graduate students to foster inter-departmental links between students within the Medical Sciences Division.	
June 2023	Don Mason Flow Cytometry facility: celebratory opening at the Dunn School	Two first-rate ultramodern cell sorters and three analysers including an ImageStream were inaugurated in the fully refurbished suite housed on the top floor of the Old Building.	Don Mason: [see page 22] Obituary …Appreciation

[1] ORCID is short for Open Researcher and Contributor ID https://info.orcid.org/the-o-in-orcid/

Date	Headline	Snippet	Note
June 2023	Natalia Gromak secures prestigious MRC Senior Research Fellowship	Natalia and her group study R-loop biology in health and disease. She came to the Dunn School as a post-doc with Nick Proudfoot, established her own lab here in 2011. She is now newly-appointed Associate Professor and Fellow and Tutor in Medicine at Trinity College	ORCID[1]
June 2023	Emeritus Prof Herman Waldmann (Lincoln College) publishes updated Henry Stewart Talks on "The Immune System"	Video playlist of over 89 lectures; present and past Dunn School members give several of them. Free via SSO to current University students/staff: or via paywall Herman's seven Henry Stewart lectures ORCID[1]	
Aug 2023	Herman Waldmann is awarded one of this year's three Royal Medals of the Royal Society	Citation: "For pioneering monoclonal antibodies for human therapy" … "He successfully re-engineered the immune system to combat a variety of disorders, including leukaemia and multiple sclerosis, as well as to reduce the risk of rejection and graft versus host disease in organ transplants. Herman's work led to the first use of a humanised antibody as a clinical therapy." The medal's diameter is 73mm and it weighs 294 g	

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Arrivals and departures

As the Romans put it: *"Salvete et Valete"*. *Fusion* notes the following comings and goings of senior and of long-serving staff, updated to mid-2023

At the ARRIVALS platform, we welcome the following:

Emma Slack comes to us as the first Barclay-Williams Professor of Molecular Immunology[1], held in association with a professorial Fellowship at The Queens College. This new Chair honours the research of Neil Barclay and Alan Williams at the former MRC Cellular Immunology Unit in the Dunn School.

She will work jointly here and in her present Laboratory for Mucosal Immunology at ETH Zurich. Her own research has focussed on adaptive immunity in controlling bacterial replication and clearance kinetics in the intestine. In broad terms, she seeks to understand how diet, microbiota, metabolism and immunity interact in health and disease. She intends to pioneer oral vaccines, for instance by developing a pipeline for so-called "evolutionary trap vaccines" that weaponize rapid bacterial evolution in the intestine. ORCID SlackLab

Mathew Stracy will further strengthen bacterial research in the Dunn School. Read his article on Bacterial Persisters in this issue of *Fusion*.

He has arrived from postdoctoral work at the Oxford Biochemistry Department and the Technion Israel Institute of Technology. His multidisciplinary approach has an amazing span, from single molecule imaging to epidemiology. His work is aimed at treating bacterial infections: preventing the spread of antimicrobial resistance and understanding bacterial 'persistence'. Mathew was awarded a Sir Henry Dale Fellowship by the Wellcome Trust. Publications StracyLab

Anthony Roberts is a leader in the structural and molecular biology of cellular motor proteins and their roles in motility, intracellular organisation and human disease.

His group studies dynein and kinesin protein families, ATPase motors which co-operate to form bidirectional transport systems with the ability to selectively attach to intracellular cargoes. View an animation of dynein's mechanochemical cycle: https://vimeo.com/75401151. In April 2023 he moved his group from Birkbeck College in London to take up a newly endowed associate professorship here at the Dunn School, coupled with the Berrow Foundation Lord Florey Fellowship in Biochemistry at Lincoln College. He currently holds an ongoing Wellcome Senior Research Fellowship. Publications RobertsLab

[1] *Fusion* 15 (2016), page 2 and *Fusion* 06 (2007), pages 3-6

Natalia Gromak researches "R-loops", the RNA:DNA hybrid structures which are emerging with important functions in both normal cell physiology and also in disease, especially neurodegeneration.
Already a familiar member of the Dunn School since 2002, she first held an externally funded early career fellowship. Her interview in *Fusion*10 (2011) describes her earlier research on "Raver" as an RNA-splicing factor. Her group studies R-loops from multiple viewpoints: as gene expression regulators; in their own regulation by a range of proteins identified by proteomics as R-loop binders; in expanded-repeat non-coding DNA sequences, such as those found in Friedrich ataxia and Fragile X syndrome where transcriptional silencing of FXN and FMR1 genes seem to play a role. She progressed to her present appointment as an associate professor in conjunction with a tutorial fellowship at Trinity College. This career milestone is underpinned by a prestigious MRC Senior Research Fellowship. ORCID GromakLab

Georgia Isom researches how the outer membrane of Gram-negative bacteria is built and maintained. Her work therefore complements that of the TangLab and RobertsLab in deepening understanding of bacterial pathogenicity and antibiotic resistance.
Her group focusses on the transport of lipids/phospholipids, hydrophobic proteins and lipopolysaccharides (LPS – the classic bacterial endotoxin) across the aqueous periplasm via shuttles or direct bridges between the inner and outer membranes. They approach this by a combination of structural biology, biochemistry and bacterial genetics.
Holding now an MRC Career Development Fellowship, she comes to us from the Langone Institute of New York University. Before that she gained her PhD at Birmingham University. She has immediately and nobly taken on organising our annual Departmental Symposium every January. She introduced the "Power Hour", for any or all scientists in our community this year to discuss 'Mentoring' and 'Networking'. ORCID IsomLab

Geoff Smith in about 1990

In January 2023 we welcomed back Prof Geoffrey L Smith, FRS who rejoins the Dunn School after just over 22 years away. He held chairs of Virology at Imperial College London (2000-11) and Pathology at Cambridge (2011-22). Recently, his group's research has included the worldwide monkeypox virus outbreak[2]; their work investigates poxvirus immune evasion strategies and novel host proteins that restrict viral replication or spread. One approach is to study cellular proteins that are degraded after infection, such as TRIM5α – see his group's 2023 *Nature* paper. ORCID.

STOP PRESS! Girish Ram Mali is an expert on cilia who has just joined the Dunn School from the University of Bristol. He holds an MRC Career Development Fellowship and is developing his lab group in OMPI to study how cells assemble large multi-subunit protein bio-motor machines. How do axonemal dyneins power the rhythmic beating motion of eukaryotic cilia and flagella? What general underlying principles govern the congregation of proteins into multi-macromolecular complexes? Will these insights help us better understand the dozens of diseases caused by failure of the development or the function of cilia – the 'ciliopathies'? ORCID MaliLab

Chris Bowler

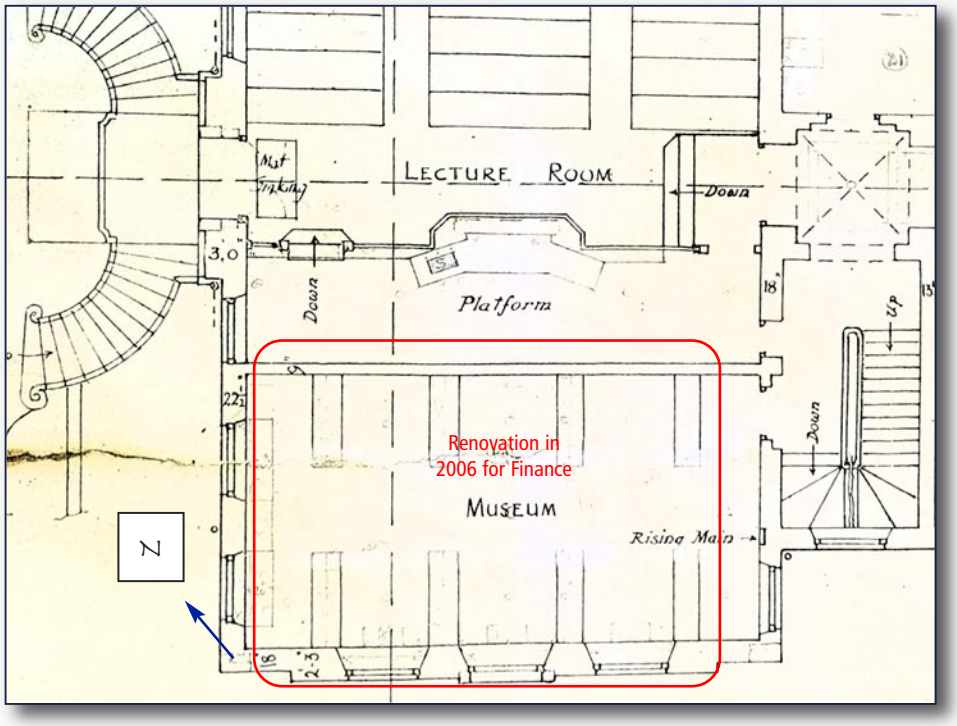
The Finance team has been refreshed by the arrivals of **Chris Bowler**, the new Finance Manager, along with **Sheji Bhaskaran**, purchasing Manager; **Frida Koslowski** / **Marlen Llanes**, Grants administrators; and **Haydee Thomas**, Research Grants Manager

[2] The disease monkeypox is abbreviated by some to *mpox*. The virus that causes it retains the name "monkeypox", unaltered.

At the DEPARTURES platform, we waved fond farewells to these stalwarts:

Martin Wilkins, in the early 1990s

Martin Wilkins, our Finance Manager, retired from the department in May 2021, having first arrived in 1980 as finance assistant. He worked under the then-Administrator, June Clark, and afterwards Denis McMiken. "I *had intended to give it six months to see what it was like… During the late 90's spreadsheets and computer systems took over from the old ledger books and then in 2004 along came Oracle and everything turned upside down...The Dunn School has always been a very pleasant place to work and this is entirely due to the people here especially my excellent colleagues in the finance team* [see "*Parties!*"] *Audra [Giles], Joanne [Collett], Rita [Richards] and Mark [Hawkes]*". It was not only Oracle that upended everything. Also at that time, Finance administration moved into the renovated space designed originally[3] as the department's Museum of pathology specimens. Martin and his team somehow always managed to rise above the ghosts of the past.



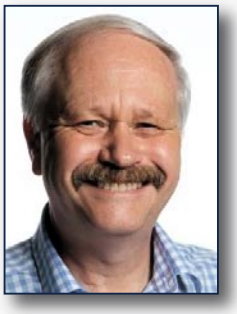
Susan Lea, FMedSci and elected FRS in 2022, first came to the Dunn School in 2000. She worked her way up through two Chairs here in succession, Chemical Pathology (Brasenose College) then Microbiology (Wadham College). She has now crossed the Atlantic to lead the Center for Structural Biology at the NIH National Cancer Institute at Bethesda. Her FRS citation says: "*…she is an internationally renowned structural biologist who has pioneered the use of mixed structural methods to study host-pathogen interactions and other medically important molecular pathways…*" See Fusion09, 2010, page 7. She helped to unravel mechanisms underlying the Type III secretion and Tat systems, for transporting folded proteins in bacteria, important contributors to virulence in some pathogens. Other work elucidated normal regulation and dysregulation of the alternative pathway of Complement activation. The Complement cascade of plasma proteins provides a first line of defence against invading pathogens. Those micro-organisms that find ways to evade it can become pathogenic, including for instance *Neisseria meningitidis*, a significant cause of serious meningitis. Susan ably led the Dunn School's qualification for a Bronze[4] Athena Award, 2015, certifying our commitment to supporting and developing women's careers in science. Her interview about this is in *Fusion*14, page 5.

Eva Gluenz (St Edmund Hall) was here for 16 years. She arrived in 2004 to work with Keith Gull, eventually starting her own lab in 2011: see *Fusion*10 (2011), page 6. She moved her group to University of Glasgow at the end of 2020. She now holds the post of Professor (Extraordinaria) in Molecular Parasitology at the University of Bern, Switzerland.

Tanmay Bharat started here in 2017. He and his group study biofilms: how molecules on the surface of bacterial cells mediate bacterial biofilm formation, using correlated light and electron microscopy with mass spectrometry: see *Fusion*17 (2018) page 8. He has been recruited back in 2022 to the MRC Laboratory of Molecular Biology in Cambridge as a senior group leader leading his electron tomography lab there. He departs with a very impressive truckload of medals and awards. ORCID

[3] The building was designed in 1922-3 by the architect Edward Warren (1856 – 1937), whose drawing is copied here.
[4] Thanks to further sustained effort, notably by Ivan Ahel, we now hold Athena Silver.

Additional farewells



Paul Fairchild FHEA has been a senior scientist and then group leader at the Dunn school for 27 years (1994-2021; latterly at Trinity College). He first came to Oxford in 1987, to study for his DPhil in the Nuffield Department of Surgery supervised by Jonathan Austyn[5]. His thesis title "The role of dendritic cells in selection of the T cell repertoire" presaged a career-long interest in the control by dendritic cells (DCs) of T cell activity, particularly in the prevention of autoimmunity but also as an adjuvant for anti-tumour vaccines. After a post-doc period in Cambridge, he joined Herman Waldmann's newly established Therapeutic Immunology Group in the Dunn School in 1994. Paul and his group developed techniques to differentiate stem cells into dendritic cells, and in 2008 he became the founding co-director of the Oxford Stem Cell Institute, funded by the Oxford Martin School. In recent work, he demonstrated the feasibility of reprogramming existing DCs to pluripotency, thereby exploiting the epigenetic memory of iPSCs for the cell type of origin. By capturing the epigenetic profile of existing DCs, the resulting iPSCs spawn populations of CD141+ DCs that are highly immunostimulatory and suitable for use in immunotherapy. These observations may provide a valuable route towards applications in immuno-oncology.

In addition to leading this research, Paul earned a thoroughly well-deserved reputation as an outstanding teacher, acknowledged by more than one Medical Sciences Divisional award. His professionalism in teaching was reflected in his successful study for a Diploma in Learning and Teaching in Higher Education, entitling him to become a Fellow of the Higher Education Academy.

His name appears in every single issue of *Fusion* since 2005, when he wrote about the Tithonian Dilemma[6]. In addition, his extraordinary dedication as co-editor of the fifteen excellent issues of *Fusion* between 2007 and 2020 is an unbeatable record. He deserves our immense gratitude for undertaking a sometimes thankless task so devotedly and well.

Following his retirement from academic life, Paul will be focussing on his psychotherapy practice, Nuance Counselling in Eynsham.

Tim Davies joined the Dunn School in 1983, initially as a research scientist under Richard Gardner (later, Sir Richard). The group became the ICRF Unit in Developmental Biology, and he moved with it in 1986 across the road to Zoology, co-authoring 13 research papers with him. In 2007 he returned to the Dunn School to bring his expertise with mammalian early embryonic stem cells, underpinning the Oxford Stem Cell Research Institute with Paul Fairchild. With the closure of the Fairchild lab he became Head of Lab Operations at OxVax Ltd. He is now working at the BioEscalator on Old Road Campus with the recent Oxford-based start-up, Infinitopes, researching targeted immunotherapies.

Steve Cobbold[7] (Christ Church) also arrived at the Dunn School with Herman Waldmann in 1994, having been his first PhD student in Cambridge. He worked as senior scientist with Herman's Therapeutic Immunology Group right through to his recent retirement, initially as Reader, then Professor in Cellular Immunology (2011). The mechanisms of immune tolerance induction and its maintenance were the central focus of his research, especially on the roles of regulatory T cells.

In *Fusion*15 page 16 (2016) he wrote a memorable account of how he had a "taste of his own medicine" when he received a kidney transplant[8]. He has frequently contributed other features to *Fusion*[9]

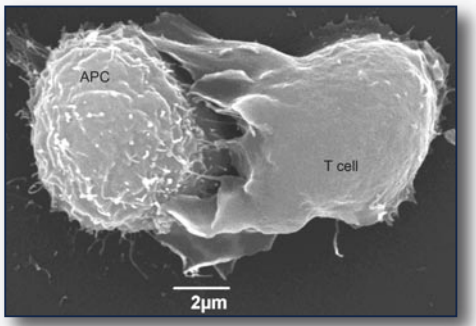
[3] Jonathan was himself Siamon Gordon's first DPhil student at the Dunn School

[6] Paul wrote: "…[the Greek god] Tithonus endured an eternity of the debilitation and dementia of old age… increased longevity provides no guarantee of greater quality of life… For Tithonus these developments [i.e. Paul's work on stem cells] may prove rather too late…" *Fusion* 04, page 8.

[7] https://orcid.org/0000-0003-1206-4880

[8] Read his interview published in Transplantation. "The Campath's going in now" http://doi.org/10.1097/TP.0000000000002633. Alemtuzumab is the current generic name for this and similar humanised anti-CD52 monoclonal antibodies.

[9] *Fusion* 18 (2019) about super-resolution imaging flow cytometry; *Fusion* 17 (2018) in the Science and Art competition; *Fusion* 06 (2007) on Reprogramming the Immune System; *Fusion* 02 (2003) about the Therapeutic Antibody Centre



Antigen-presenting cell (left) signalling to a T cell. SEM by Nika & Acuto, 2015

Oreste Acuto[10] joined the Dunn School in 2006, having previously held senior professorial posts in Immunology at the Pasteur Institute for nearly 20 years[11]. His T cell signalling group occupied a laboratory converted from the old Lecture Theatre at the West end of the original Dunn School building. From his group's work there, their most frequently-cited paper showed that catalytically active Lck, a key protein kinase belonging to the Src family, was readily detectable even in unstimulated naïve T cells and thymocytes. This finding, published in 2010, obliged a revision of models of T cell receptor-mediated signal transduction. Instead, they proposed a "standby" model for Src-family kinases in T cells in which preactivated Lck, kept under strict control by the phosphatase CD45, would be necessary and sufficient to ensure TCR-induced ITAM phosphorylation. The immune system must explode into action when a pathogen enters, absolutely immediately leaping out of bed from its normally dormant state. No time to rub its eyes! Oreste's work is an excellent example of a mechanism that may contribute to this.

Marion at the close-down of the MRC Cellular Immunology Unit, 1999

Marion Brown[12] (Dunn School since 1991; University Reader in Immunology from 2008). Her research examined several ligand-receptor interactions at immune cell surfaces important in signalling, latterly focussing on CD6, a protein containing scavenger-receptor cysteine-rich domains. The most highly-cited paper of which she was senior author was the 2002 review of CD200[13]. She initiated and ran the very valuable annual Research Techniques Days for graduate students within the Medical Sciences Division. On occasion she brought her interest in the mutual engagement of science and theatre to the Dunn School[14]. Very memorably she arranged for a performance of the drama by Siobhán Nicholas, "Hanging Hooke" (that's Robert Hooke FRS (1635-1793), first Curator of Experiments at the time of foundation of the Royal Society in 1660).

The departure through retirement of these last five scientists lowers the curtain at the Dunn School on the wide and very distinguished spectrum of cellular and therapeutic immunology, rooted in the work of Alan Williams, Neil Barclay, Siamon Gordon, Don Mason and Herman Waldmann, and even further back to Jim Gowans. The Arrivals noted above give plenty of hope that it could be simply an interval curtain and not the finale.

We shall miss every one of our leavers. Each of them made big contributions to the joie de vivre of working in the Dunn School [see "*Zest for Life*" in this issue], way beyond what the short snippets above can portray. They leave a yawning gap. Fusion wishes them all a fond farewell.

[10] Full scientific bibliography is at https://t2m.io/OAcuto
[11] See *Fusion* 06, page 14.
[12] Her full scientific bibliography is at https://t2m.io/MBrown here (Oxford University SSO required). Her oral history interview with Georgina Ferry in 2017 is catalogued at https://archives.bodleian.ox.ac.uk/repositories/2/archival_objects/357622 but access is Closed for the time being.
[13] "CD200 and membrane protein interactions in the control of myeloid cells" Trends in Immunology (2002) 23: 285–290. http://doi.org/10.1016/S1471-4906(02)02223-8.
[14] See *Fusion* 07, page 2

Our neighbours – what's happening nearby?

Our immediate neighbours are changing. Fusion brings you an update - and an old monochrome Aerofilms photo

To the South directly opposite us, huge excavators, pile borers and tower cranes have been dominating our view. The construction of the **Life and Mind** Building, affectionately known as LaMB, has already been noted by *Fusion*[1]. It is due for completion in 2024 and will house the Zoology and Cell Biology components of the new Department of Biology (see below), alongside Experimental Psychology.

*1. Built on rust? View North towards the Dunn School, almost one hundred years old, over the site of the demolished Tinbergen building which lasted fewer than fifty. Drone operated by **Hufton & Crow**, March 2022*

The Ineos Oxford Institute for Anti-Microbial Resistance Research[2] led by Prof Tim Walsh will also move there, having been accommodated within the Dunn School Old Building since 2021. (It currently occupies the former Acuto lab, on the site of the department's original lecture theatre). By March 2022 the LaMB site had been cleared and dug out. A drone's-eye view at that time revealed the Dunn School in all its pre-centenary glory (photo 1[3]). The Dunn School and LaMB share their underlying Gravel Terrace geology[4], which has somehow generated a rusty-looking orange subsoil.

2. View towards North West, showing the Dunn School in its Science Area context. We face the excavations for the new LaMB. The University Parks with its Cricket Pavilion are to the North. Linacre College is on the far right.

[1] www.path.ox.ac.uk/wp-content/uploads/2023/07/Fusion-19-Michaelmas_2021.pdf, page 4
[2] www.ineosoxford.ox.ac.uk/what-amr-final-version
[3] Copied from https://lifeandmind.web.ox.ac.uk/current-progress, with permission
[4] See www2.bgs.ac.uk/groundwater/flooding/oxford.html and references therein; also Newell, A.J (2007) "Morphology and Quaternary geology of the Thames floodplain around Oxford" https://core.ac.uk/reader/33452811

3. Life and Mind Building nearing completion, October 2023. View south-east from the Dunn School roof

4. Aerial view in June 1932 southwest over the River Cherwell and the Parks towards the centre of Oxford. Spot the Dunn School, built six years earlier: far left. ©Historic England CC-BY-NC-SA-4.0

Ninety years ago, things were much less crowded. Then, the Dunn School comprised simply our treasured "Old Building" opened in 1927, with its Animal House (can you see it in photo 4?). There were no other Science buildings nearby. The University authorities took no chances when they allocated that location. Keep those nasty germs at a safe social distance from anywhere else please!

Returning to the present day, to our immediate West the Department of **Plant Sciences** (photo 5) has merged in 2022 with Zoology to form the **Department of Biology**[5] within the University. The building itself, planned in the 1930s, dates from its opening in 1950 when it housed the former Forestry Institute as well as Botany and Agricultural Science. These coalesced in the 1980s to become Plant Sciences, containing valuable herbaria, a xylarium and other unique resources.

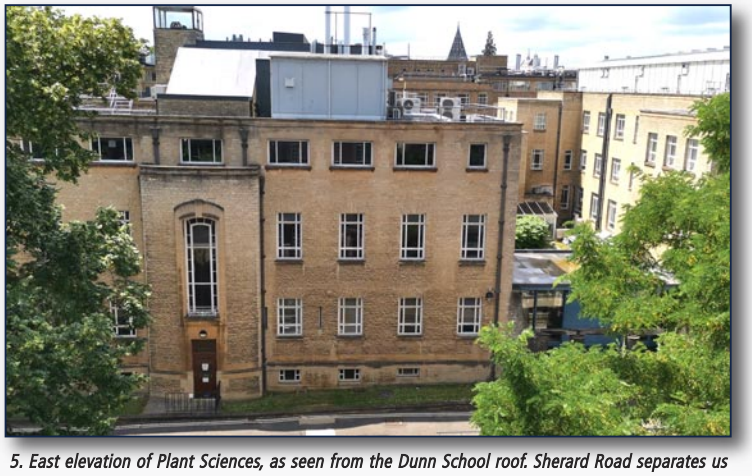
Significant research collaborations between the Dunn School and Plant Sciences took place during the 1980s (Peter Cook and others). Might it be time to renew the link? After all, *flora* and *funga* are eukaryotes which share plenty in common with the *fauna* in our own Cell Bank. Plants exhibit intriguingly quirky features, for instance: chromosome ploidies that are off-the-scale; susceptibilities to tumours and infections; extraordinary self- and allo-recognition systems; rates of ageing far slower than *fauna*; and so on. Collaborations with the Dunn School could once more ripen under the new Biology arrangements - perhaps via their MBiol fourth-year students?

The University Cricket Pavilion (Grade II-listed) is directly North of us, well-known to present members of the Dunn School as the venue for our Grade I-listed Summer Parties (see '*Parties!*' in this issue). In early 2023, eagle-eyed *Fusion* noticed an unusual planning application there[6]. The Curators of the Parks sought permission to make an alteration, not to the building but to the immediately adjacent land. The change will be invisible since it's entirely underground. Two 1.8m

[5] www.ox.ac.uk/news/2022-08-01-oxford-launches-new-department-further-bioscience-teaching-and-research

high fences are being buried into deep trenches at the rear of the pavilion. Then they're to be covered as though nothing has happened. Permission was granted. The work has lasted many months, has required very visible contractors' temporary fencing, and is not finished as we go to press.

Why all the bother? Badgers! Over the years, our fossorial friends *Meles meles*, with their long claws and stripy snouts, have been building their underground sett behind the pavilion – without planning permission! Like Dunn School researchers, their explorations are pushing the boundaries. The newer entrances to the sett (photo 7: pink spots on the aerial view) are threatening the hallowed turf of the adjacent football pitch. The Curators' cunning solution is to prevent badger expansion to the north and south, constraining their further exploration only to the east and west.



5. East elevation of Plant Sciences, as seen from the Dunn School roof. Sherard Road separates us from them. The two ***Sherard brothers*** *founded the Professorship of Botany in 1728*

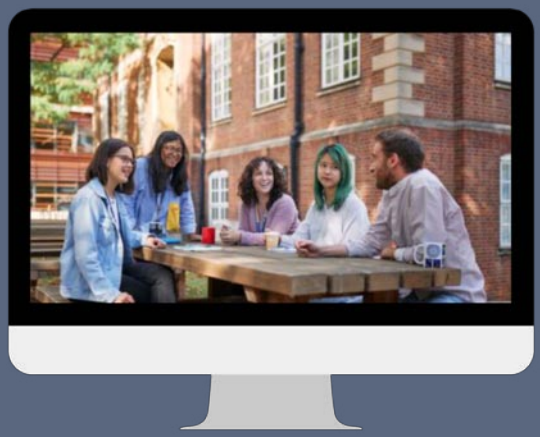
The real reason? *Fusion* guesses that the University's famed evolutionary biologists are setting (😔 – sorry!) off to make another world-beating claim. Employing nothing more than old-time Natural Selection they will develop a super-badger, capable of deep-digging at least 2 metres into the ground. Their studies of the genetics of FOR ("fence-obstacle resistance") in badgers will give them work for centuries to come.

6. Rolls of fencing ready for burial

7 Aerial view of the cricket pavilion, showing locations of the badger sett entrances. Blue - disused. Pink - active. Relocated path - yellow. Fence burial - grey. Image copied from the Heritage Statement in the planning application

If you, nostalgic reader, have memories of your Dunn School connections with any of our near neighbours, please email them to alumni@path.ox.ac.uk. We'd be very pleased to share them publicly in future issues of *Fusion*

[6] 23/00299/FUL: https://t2m.io/PavPlan23



SHARING DUNN SCHOOL STORIES ONLINE

We tweet about all things Dunn School: news, celebrations or just beautiful pictures of the department! /Twitter also allows us to reply to your questions and share your comments! If you also tweet, follow us on @Dunn_School

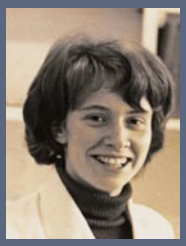
Use LinkedIn to connect with us and other former members of the department! You can follow us on: www.linkedin.com/company/dunn-School-oxford

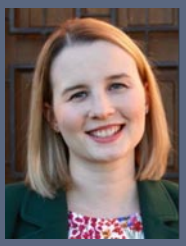
Our website relaunched after a makeover in 2023. Do you like it? Please tell us! The address is still www.path.ox.ac.uk

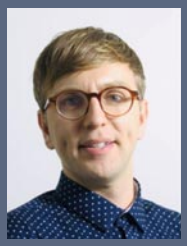
If you are a former Dunner, our alumni newsletter is the best way to contact you! Sign up on our website for a roundup of recent updates and also exclusive behind the scenes information regarding our centenary in 2027.

BEEN THERE, DUNN THAT

One of our ongoing social media campaigns aims to highlight, once a month, a former member of the Dunn School. Covering both recent and not so recent alumni, this is a way to celebrate our community and history in the build up to our centenary. Do get in touch if you would like to nominate yourself or someone else!







Follow the campaign on social media on the hashtag #BTDT1927 and on our website www.path.ox.ac.uk/content/alumni-network

(George) Gordon Macpherson, 1941-2021

Gordon's time in the Dunn school spanned his whole employed professional career, from 1973 to his retirement as Reader in Experimental Pathology in 2009. Some recollections of this much appreciated, very broad-shouldered all-rounder in the department are summarised by his contemporary, Simon Hunt.

It is the cold and dank first week of Michaelmas Term in October 1963. A 22 year old medical student ascends the steps of the Dunn School of Pathology to begin his fourth year course in Pathology and Bacteriology - universally nick-named "Path and Bac". That summer he'd obtained an upper Second in the Final Honour School of Animal Physiology. Previously, his education had been at Birkenhead School on the Wirral peninsula. In his family background were two uncles who were themselves practising doctors; his father was a sculptor and artist. He won an exhibition to Corpus Christi College, where his medical tutor was Dr David Jamieson, an anatomist with an interest in leprosy. He selected Medicine because he was keen to study the science of disease but not, as he put it, the "social side" of the practice of medicine. By the time of his retirement forty-five years later, he had co-pioneered important studies on the many regulatory roles of dendritic cells as antigen-presenting cells in specific adaptive immune responses. Let's identify some of his immunological steps which followed from those Dunn School steps.

Photo ©Simon Hunt 2005

The theatre, seen from the lecturer's podium

Gordon himself noted the variable teaching quality in Path and Bac. Some was frankly poor, notably the lectures starting at 4 p.m. But others were grippingly good. *"The one … who most stimulated me was this young guy called Jim Gowans… not like any of the straightforward science that you'd come across before"*. Gowans narrated the tale of his own very recent research which had co-founded the field of cellular immunology. Between 1957 and 1963 he had elucidated the induction of immune responses by recirculating small lymphocytes. Lectures were held in the theatre, which is now the Ineos lab on the ground floor; and practical classes were conducted in the classroom directly above it on the first floor. All the Lecturers and Readers would demonstrate in the practical classes. Gordon especially remembered Margaret Jennings[1] as a really superb teacher. *"She used to pull up a stool and sit down beside you to examine a microscope slide. She would say 'Now what can you see down there?' She would proceed to take you apart but actually teach you a great deal"*. Then again, the anecdotes told by W.E. "Kits" van Heyningen about bacterial toxins ingrained themselves deep in his memory.

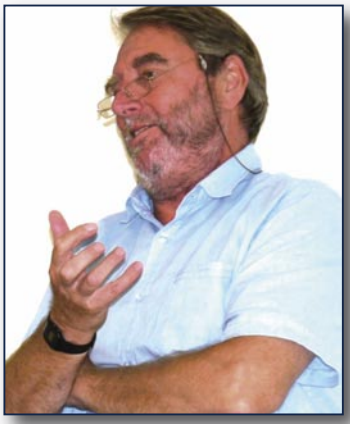
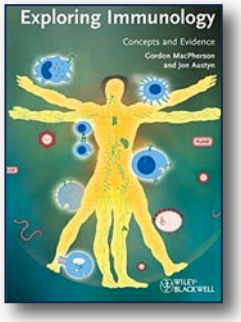


Photo © Simon Hunt

Gordon Mcpherson in 2011

The anecdotes contributed to the repertoire of his own storytelling for many years. Gordon was a great raconteur, full of half-credible but very entertaining episodes to enliven any discussion. From his first-hand experience in the Path and Bac course he learned not only the ropes of general pathology, but he acutely observed and absorbed what worked well and what worked poorly in teaching. Even bad lecturing can beget wisdom. All this must surely have sunk in as the foundation for his own later reputation as an excellent teacher. One term, he was voted by the students as the best lecturer in the medical undergraduate course. The tricks of the trade that he adopted included using a whiteboard or visualizer to hand-write the development of his story, thereby disciplining his pace to a steady rate that a student audience could easily digest. *"I enjoyed that a lot. I really got to like lecturing."* He converted his powers of clear explanation into print by authoring, with Jon Austyn[2], a well-received text book: "Exploring immunology: concepts and evidence[3]" (2012).



For Gordon the practical classes and the whole Path and Bac course overall were really enjoyable. They confirmed Pathology as his prime focus. To complete his medical education he moved to the London Hospital at Whitechapel, as did many clinical students in those days. Blood cells and their diseases captured his particular interest and after 2nd BM he returned in 1968 with a further scholarship to the Dunn School for a D Phil with Dr John French as supervisor, who was the departmental expert on haemostasis and platelets. Gordon's thesis was on "Megakaryocytes and blood platelets: an ultrastructural analysis". Under the tutelage of the superbly skilled Brian Shepherd and his wife Ute[4] he learned the use of the department's Philips EM200 electron microscope. An interest in, and the

Photo ©Simon Hunt 2005

TEM200; about 1960
No transistors – hot!

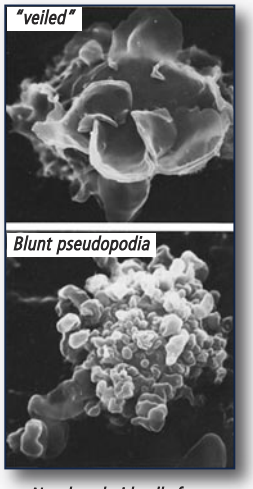
[2] Jon Austyn, Professor of Immunobiology with long expertise in dendritic cells, did his DPhil in the Dunn School (1977-80), supervised by Siamon Gordon. In 2004 he co-founded, and subsequently directed, Oxford's two-year MSc course in Integrated Immunology.

[3] Reviewed in European Journal of Immunology by Diogenes Ferreira https://doi.org/10.1002/eji.201270098

[4] They were ably assisted also by the seemingly indestructible Mary Bergin, who still pops into the Dunn School from time to time

limitations of, deductions solely from ultrastructural morphology resurfaced later in his work on dendritic cells. He had a large batch of postcards printed for free distribution to lab visitors. They displayed his scanning e-m photo of a very convoluted, tortured-looking dendritic cell tickling a T cell (or *vice-versa*?)

Professor Harris was keen to bolster the department's research and teaching in immunology, so he facilitated the award of a Florey Fellowship to Gordon to learn some at the John Curtin School in Canberra, Australia. Bede Morris, a larger-than-life veterinary scientist who studied lymph flow in sheep, took Gordon on as his postdoc. Morris himself was a Dunn School doctoral alumnus from Gowans' lab seven years earlier. Gordon researched ovine renal transplantation and learned the surgery for cannulating the afferent lymphatic ducts that drain kidneys to local lymph nodes. Some of the cells in the ducts were eye-catching, mysterious "veiled" cells: of which, more later. With Morris as oenological guide, he also enjoyed the fruits of the Australian grape harvest. Returning by ship with his family in 1973, he was appointed university Lecturer in Experimental Pathology at the Dunn School and a couple of years later also became Turnbull Medical Fellow and tutor at Oriel College, with all its consequent tutorial and administrative responsibilities: broad shoulders needed.



Pugh, Macpherson and Steer, 1983 Fig 2

Non-lymphoid cells from afferent lymph

Leading into every lymph node in the body from the organ it drains are very small vessels, similar to capillaries – "afferent lymphatics". Thus for example, lacteals drain the intestinal wall to the mesenteric lymph nodes nearby, carrying antigens as well as the molecular digestate of the gut contents. Each lymph node also has a rather bigger outlet leading away from it - the "efferent duct" - which joins with others from nearby nodes eventually into a major duct such as the thoracic vessel. In the Gowans lab in the late 1970s, Graham Mayrhofer and the surgeon Howard Steer were examining the leukocyte types in lacteals draining the gut of rats, particularly noticing some non-lymphoid cells there. These cells normally are naturally filtered out by the lymph node and don't reappear downstream of it. If lymph nodes are removed surgically, as Sanders and Florey in 1940 had shown, the nodes themselves do not regrow, but the afferent and efferent lymphatics heal and rejoin over a period of a few weeks. Alongside Gordon and his DPhil student Chris Pugh, all of them together devised a surgical model to freshly obtain the non-lymphoid cells *ex vivo*. Rather like the 1940 experiments, they extirpated the chain of mesenteric lymph nodes of an anaesthetised rat, then allowed healing and direct reconnection of afferent to efferent lymphatics when it recovered. With no lymph nodes there, the numbers of lymphocytes dropped below normal whereas the proportion of non-lymphoid cells, now no longer intercepted, correspondingly rose. They were not macrophages or lymphocytes. "Veiled" cells once more made their appearance, plus some other weirdly blebbed ones[5]. By collecting this pseudo-afferent lymph and the cells it contained, Gordon now could prepare abundant non lymphoid cells already in suspension, without having to disrupt a solid organ like a lymph node or spleen. This source of what came to be called "dendritic cells[6]" was ideal for characterising, enriching and studying them functionally. The "MLNX[7]" rat model formed the centrepiece of Gordon's research for all his subsequent scientific career.

The light-bulb moment came when Siamon Gordon introduced to the Macpherson lab his friend and colleague from the Rockefeller Institute, Ralph Steinman, who since 1972 had been working on "accessory cells" in mouse spleen. The similarities with Gordon's cells provoked a loud "Aha!". Their work converged conceptually with that of several other labgroups worldwide who from different perspectives realised they were all researching antigen-presentation to, and regulation of, T and B lymphocytes, during the induction of specific adaptive immune responses. Initially, they showed how dendritic cells serve as "nature's adjuvants[8]", magnifying the stimulus to antigen-specific T cells. Later, it became apparent that certain kinds of dendritic cells in certain circumstances can conversely be very effective inhibitors of immune responses via regulatory T cells, Tregs. Gordon said his group's most interesting piece of research was their demonstration that dendritic cells could capture apoptotic gut intraepithelial cells and transport them to local lymph nodes[9]. This finding could help to explain why otherwise highly immunogenic gut contents might be inhibited from triggering endless unwanted immune responses, including highly debilitating autoimmunity in the gut. His post-doc, Simon Milling, now professor of immunology at Glasgow University, continues with research in this area. Another highlight was Fang-Ping Huang's finding[10], in Gordon's group, that the scrapie agent PrP^{Sc} in the gut, the initial site where prions infect humans or farm animals, could be transported by dendritic cells to the draining lymph nodes where it begins replicating before causing catastrophic encephalomyelitis[11].

Gordon rather tended to pooh-pooh history. But we can see how his own contribution heavily leaned on antecedent and ongoing research in the Dunn School, support from its senior staff, and on its very high quality core facilities including the Workshop. He also fulsomely acknowledged the vital, loyal and long-lasting contribution of his lab technician, Chris Jenkins, who stayed in his group throughout.

[5] Pugh Macpherson, and Steer (1983) http://doi.org/10.1084/jem.157.6.1758

[6] See Steinman (2007) "Dendritic cells: understanding immunogenicity" https://doi.org/10.1002/eji.200737400. "Dendritic", from the Greek "dendron", means "tree-like". Steinman (1943-2011) won, with two others, the Nobel Prize in Medicine and Physiology in 2011. He was a great supporter and friend of the Dunn School.

[7] MLNX = Mesenteric lymphadenectomised rat. Cannulating its thoracic duct provided the dendritic cells that the Macpherson lab studied.

[8] The Latin word *adjuvare* means "to help"

[9] Huang, F-P *et al* (2000) J Exp Med 191: 435 https://doi.org/10.1084/jem.191.3.435; and Cerovic *et al* (2008) Int Rev Cell Mol Biol 272: 33 https://doi.org/10.1016/S1937-6448(08)01602-X

[10] Huang, F-P *et al* (2002) J Gen Virol 83: 267 https://doi.org/10.1099/0022-1317-83-1-267 J Exp Med 191

[11] Epidemic Bovine Spongiform Encephalopathy (BSE) broke out in the UK in the late 1980s and spread to humans as "variant Creutzfeldt-Jacob Disease" with 179 fatal cases since 1995 www.cjd.ed.ac.uk/sites/default/files/report30.pdf

A little known aspect of Gordon's commitment to all students - not just those he taught or supervised - was his chairing of the University's "Advisory Committee for the Student Counselling Service" in the mid-1990s. Elsa Bell, who was Head of the Counselling Service at that time, recounts how his gentle but authoritative guidance was so important in the service's University-wide growth and development. She says he was masterful in managing to be both challenging and supportively wise. It constantly amazed her that he generously found time among all his demanding research and teaching obligations, to put his experience and knowledge at the disposal of her and of the whole service. Another major academic role he undertook for a number of years was Senior Tutor at his College, Oriel, again benefitting all students there. For quite a long period, he was Biological Safety Officer at the Dunn School. Oxford depends on the broad shoulders of Good Citizens like Gordon.

"Broad shoulders" brings us to his love of playing cricket (and hockey; and angling; and photography; and cooking curries; and mentoring secondary school pupils to apply to Oxford; and volunteering for the National Coastwatch Institution in Dorset - to mention some of his other interests). He was a mainstay in the departmental cricket team[12], both as batter (formerly called " batsman") and as bowler – a true all-rounder. As a left-hander he bamboozled many cricket teams from the Oxfordshire villages which we used to visit for evening matches. At Great Tew, due to a quirk of their local genetics (or nurture?) eight out of the eleven in their team were left-handers. Gordon was their equal. Though we were still defeated, at least it was not abjectly shameful.

Gordon's shoulders also shared the upbringing of a family, first with Anne, the mother of their children: "young" Gordon and Caitlin; a third child sadly predeceased him. Following a divorce, his second wife Shelley survives him as his widow and continues to live in Dorset, where they retired to. Her question to him over the marmalade one breakfast-time in the mid-1990s "What have dendritic cells got to do with BSE?" stimulated his research foray into the scrapie agent referred to above. From innocent questions come significant advances.

Oxford University, the Dunn School, research and teaching styles, and immunology itself: all have moved on a long way since the second half of the 20th century. Nonetheless, many of our core values, aspirations, motivations, concerns, interdependencies, leadership qualities, relaxations still feature prominently now these days, just as they did then. Thank you, Gordon, for setting us a fine example of collegiality, friendship, effective concern for others, and broad-shouldered good citizenship.

Photo: 2015 © Judie Waldmann

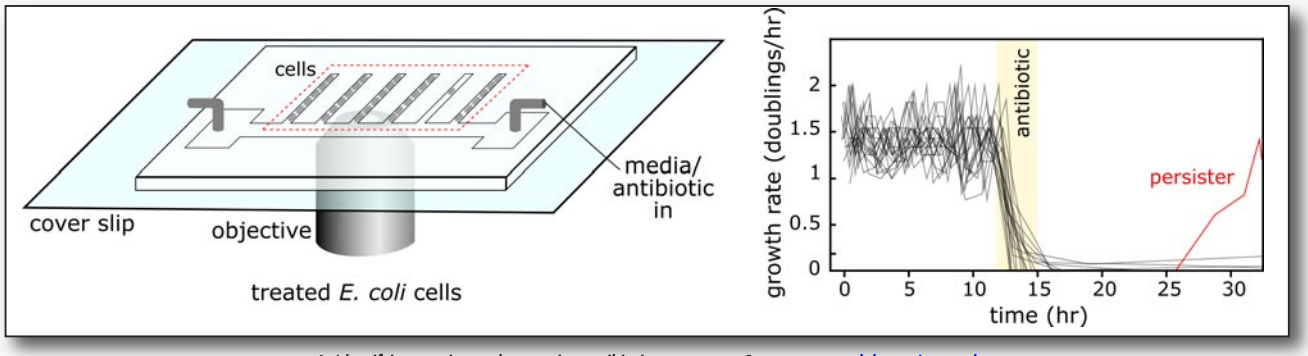
Further resources:
Gordon's own Retrospective: Fusion issue 7 (2008) page 5: https://www.path.ox.ac.uk/wp-content/uploads/2023/07/Fusion-7-Michaelmas-2008.pdf
His interview with Georgina Ferry in 2017: www.podcasts.ox.ac.uk/gordon-macpherson (audio) (transcript)
His full scientific bibliography: https://t2m.io/GMacpherson
An appreciation by Prof Chris Pugh: https://issuu.com/oxfordmedicalalumninewsletter/docs/oxford_medicine_summer_2022_final_print/s/16352346

[12] See *Fusion* issue 8 (2009) page 16

Persistence is the key to failure

'Persistence is the key to success', so the inspirational quotation goes. But when it comes to antibiotic treatment of bacterial infections, persistence may instead be the key to failure. Mathew Stracy has recently started a research group in the Dunn School[1] as a Wellcome Trust Sir Henry Dale Fellow. Here, he introduces their fascinating research insights into this phenomenon, which has very obvious translational applications.

The problem of bacterial persistence is not new. In 1944, just a few years after Howard Florey, Ernst Chain and colleagues isolated penicillin here in the Dunn School, an Irish physician named Joseph Bigger[2] was experimenting with the antibiotic. He was interested in why Staphylococci infections so frequently relapsed following penicillin treatment. "*Penicillin has undoubtedly saved lives and limbs of patients suffering from staphylococcal infections, but it has not usually cured the disease as it has cured gonorrhoea*" Bigger wrote[3]. "*During the first few days after the cessation of treatment it appears possible that the infection has been eliminated but then, in most cases, the disease again becomes active.*" The recalcitrance of some bacterial infections to antibiotic treatment despite the pathogen continuing to be penicillin-sensitive, remains a major problem to this day.

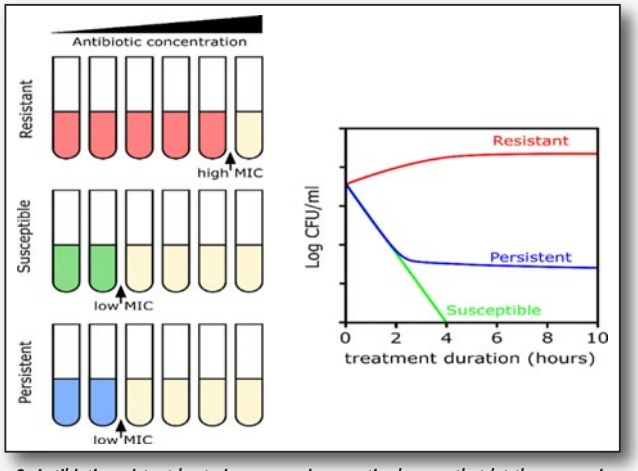


1. Identifying persisters that survive antibiotic treatment. See www.stracylab.com/research

Why do such treatments relapse? Bigger noted that, although adding penicillin caused very effective bactericidal lysis of staphylococci *in vitro*, a few colonies still grew when the apparently bacteria-free culture was then plated without antibiotic. These surviving bacteria were not resistant: penicillin still lysed them when regrown in fresh culture. Bigger termed this subpopulation of surviving bacteria 'persisters'. He hypothesised that treated infections can relapse primarily because of '*the survival in the focus of infection of persisters which, within a few days of the withdrawal of penicillin, begin to multiply.*'

Unfortunately, this first report identifying the problem of persisters remained largely forgotten for more than sixty years, superseded in importance by the emergence and spread of antibiotic resistance. Resistance and persistence are fundamentally different phenomena; resistance is conferred by mutations or acquisition of genes that allow bacteria to grow in the presence of higher concentrations of antibiotics. Persisters, on the other hand, tolerate antibiotics by a more general mechanism: they enter a slow-growing or non-growing state where bactericidal antibiotics like penicillin no longer cause cell death.

From an evolutionary perspective, persistence is a bet-hedging strategy. When conditions are prosperous, uniformity of phenotypic state is favoured. But in the face of fluctuating environmental conditions stochastic switching between phenotypic states to include some persisters can be a more optimal strategy. Since only a small



2. Antibiotic resistant bacteria can acquire genetic changes that let them grow in higher concentrations of antibiotics: the minimum inhibitory concentration (MIC) is raised. In contrast, persister bacteria are not resistant. Their MIC is unchanged. Therefore standard susceptibility testing in the clinic does not pick them up. Since persisters are typically a small subpopulation of phenotypic variants, the killing curve is bimodal. Most of the population is rapidly killed just like susceptible strains, but the small percentage of persisters exhibit a very slow rate of killing.

[1] https://www.stracylab.com/research
[2] https://heritage.rcpi.ie/Whats-On/Blog/adopted-treasure-portrait-of-joseph-warwick-bigger-by-sean-keating
[3] Bigger, J.W. Treatment of staphylococcal infections with penicillin by intermittent sterilisation. The *Lancet* 244: 497–500 (1944). https://doi.org/10.1016/S0140-6736(00)74210-3

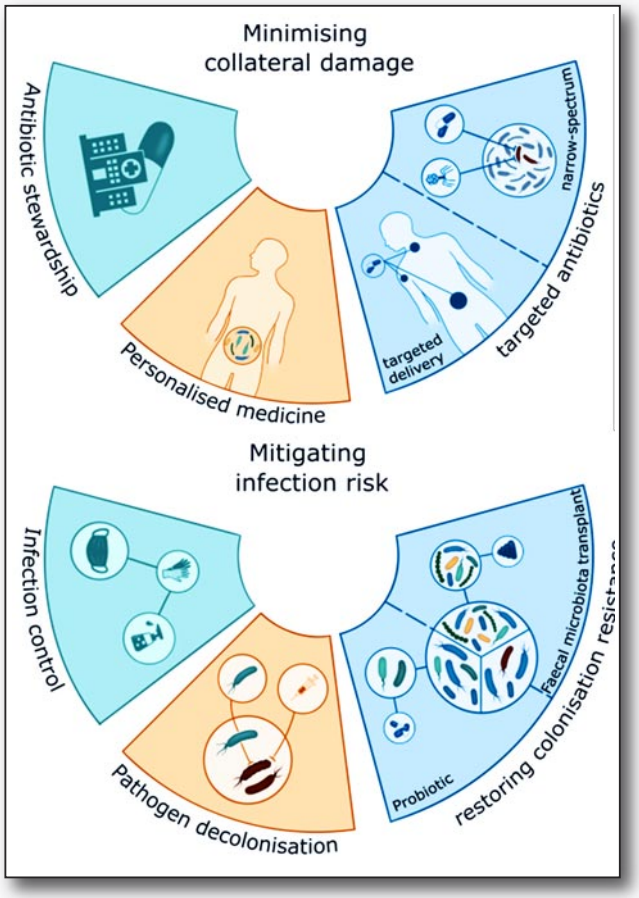
subpopulation of the initially genetically-identical bacteria enter a slow-growing state, the persister phenotype carries low fitness cost to the overall population in good growth conditions. Their persistence during transient stress such as antibiotic treatment benefits survival as a population.

Following newer research into persisters, some of the pathways that can trigger this phenotypic switch have been identified. For example, in *Escherichia coli*, the HipA protein phosphorylates Glu-tRNA-ligase leading to an increase in uncharged tRNA. This induces amino acid starvation and dormancy. *HipA* is part of a type II toxin-antitoxin (TA) system[4] and normally its action is suppressed by expression of the corresponding antitoxin. However, mutations to hipA have been identified that lead to more toxin than antitoxin being produced. So each cell is more likely to become dormant and hence exhibit a high-persistence phenotype.

There are multiple mechanisms of persistence. High tolerance to antibiotics via persistence can in fact evolve much faster than resistance. While evolution of resistance requires specific mutations in specific genes, typically genes that encode the target protein of the antibiotic, there is a larger mutational spectrum that can lead to cell dormancy. Broadly speaking, there are many more ways to break the carefully orchestrated pathways needed for rapid growth, leading to a slower-growth persister state, than there are to regain a fast growth in the presence of the external stress. When high concentrations of antibiotic are applied periodically, such as in typical once-daily treatments, evolution of resistance is suppressed but antibiotic tolerance can evolve rapidly. Importantly, this rapid evolution of antibiotic tolerance can in turn facilitate subsequent evolution of resistance.

Despite a revival of interest in persisters, many questions remain unanswered. Non-growing persisters often survive treatment to multiple classes of antibiotic. The exact molecular mechanisms that confer higher survival in a slow growing state remain poorly understood; they are key to developing new approaches to eradicate persisters.

Like Bigger's original work, much of the current research into persisters is performed *in vitro*. But how do persisters behave in real infections and what role do they play clinically? Antibiotic resistance is routinely measured in the clinic by highly-standardised susceptibility tests but these do not assess the presence of non-growing persisters. By adopting sequencing approaches, researchers can identify clinical isolates carrying some well-characterised high-persister mutations such as *hipA* mutants. Examples include recurrent and chronic infections like uropathogenic *E. coli*, or *Pseudomonas aeruginosa* from patients with cystic fibrosis. Recent work screening for persistence in *E. coli* sepsis cases has also shown that infection with a high-persister strain is associated with a higher risk of infection relapse. Nevertheless, we still don't know if persister phenotypes cause some antibiotic treatments to fail, because they are not routinely measured in the clinic.



3. Strategies to minimize antibiotic-associated infections. See explanatory text near Fig. 5 of De Nies et al (2023) https://doi.org/10.1038/s41579-023-00936-9

The many factors beyond bacterial persistence that play a role in the efficacy of antibiotic treatment include pathogen type, virulence, resistance levels, infection site, patient immune response and demographics. Determining the relative importance of bacterial persistence compared to these other factors will highlight where new treatment strategies are most needed. In our recent work[5] we have been sequencing bacterial isolates from patients before and after antibiotic treatment failure. We showed that in most patients' infections, resistance was not acquired by random mutations. Instead, resistance emerged due to reinfection by existing resistant bacteria from the patient's own microbiome. We found that the antibiotic susceptibility of the patient's past infections was strongly associated with their risk of returning with a resistant infection following antibiotic treatment. Based on these associations the best antibiotic for each patient to minimize this risk can therefore be recommended.

Lateral-thinking reader, what do you imagine? Might 'persistence' also apply to treatments of other microbial infections of humans or animals - by viruses or protozoa perhaps? Maybe cancers when they become treatment-resistant? Maybe in plants too? Please send your comments or suggestions to alumni@path.ox.ac.uk and we'll pass them on.

[5] Stracy, M. *et al.* (2022) Minimizing treatment-induced emergence of antibiotic resistance in bacterial infections. *Science* 375: 889-894. http://doi.org/10.1126/science.abg9868.
de Nies, L., Kobras, C.M. & Stracy, M. (2023) Antibiotic-induced collateral damage to the microbiota and associated infections. *Nat Rev Microbiol.* https://doi.org/10.1038/s41579-023-00936-9

Nomenclature corner: the best name please! Win a prize!

Over the years, names have come and gone to describe someone who currently works and/or studies in the Dunn School, or who did so in the past. It's high time for a rigorous social science survey. We sorely need an appealing, friendly, non-gendered word that's apt, pithy and not liable to ridicule. Obviously it must include the syllable "dun(n)" and it must be able to withstand the test of time for our bicentenary in 2127.

What do you think is the right name, inventive reader?

Here are some possibilities from the world's most authoritative dictionary

Name	OED (Oxford English Dictionary) definition	Editor's comment
Dunnart	*a small insectivorous marsupial of the genus Sminthopsis (family Dasyuridae), native to Australia and New Guinea, typically with a pointed snout and prominent eyes*	Quite a cute word, but too many of us lack the right kind of eyes and/or snout for this to be suitable.
Dunbird	*a dun-coloured duck, especially a (female) pochard, Aythya ferina.*	Too gender-sensitive these days ☹
Dunce	*A person who is slow at learning or of low intelligence; a stupid, dim-witted person*	We are definitely not Dunces here, or even Dunnces. That's self-evident.
Dunner (noun)	*"A creditor who makes insistent or repeated demands for repayment of a debt"*	Oops! Not what I'd like to be called!
Dunner (adjective)	*Means "more dun" - a deeper shade of a "dull or dingy brown colour"*	Dull or dingy is rather unattractive, surely?
Dunnekin	Sorry, but the dictionary definition indicates something too revolting to print here	What a shame! If it had no meaning already, the word itself is a nice friendly-sounding diminutive, rather endearingly Scottish – a "*wee dunnekin*"

None of these seems to work well. Might we be better with a beyond-dictionary word? Imaginative reader, now's your chance to suggest one! To get the ball rolling, here are some playful ideas as starters:

Dunnee.....a person who has joyfully been on the receiving end of some Dunning by being a member of the Dunn School. Compare "Payee" – someone who receives a payment. Rhymes with "Yippee".
Dunnonian.....derived from Dundonian, an inhabitant of Dundee, but lacking the second letter 'd'. It's therefore an epigenetic derivative of a mutant of "Dunnee" above.
Dunnite.....has explosive connotations, which may be a good or a bad thing
Dunnian.....the word has a nice lilt to it so it would be great in the next Dunn School hit song (any songwriters out there?). Rhyming possibilities with "onion", "bunion", "trunnion" and many others.
Dunno.....it's OK to admit ignorance occasionally but not all the time, please

We dearly need your suggestions. Send yours straightaway to alumni@path.ox.ac.uk: definitely before 1st March 2024.
Include "Dunnawesome" in the header. We'll then survey current Dunn School members for the name they prefer. The prize-winner will be the person who suggests the most popular name, judged by this survey.

The prize will be a brand new, cosily warm, gloriously handsome and pride-inducing sweatshirt with the Dunn School logo, delivered to the winner's door!

Editorial disclaimer: none of the names may turn out to be used in actual practice! Language is very fluid and no-one can ever predict which word will become popular.

100 years, 1000 faces: a conservation task

Loyal readers of Fusion who once did or still do, work or study at the Dunn School surely must know the portrait photographs displayed along its walls. Curious about them? Our Science Strategy and Projects Manager, Catarina Vicente, discusses the cataloguing and preservation of this unique collection

I have many memories of my time as a PhD[1] student, but one of the earliest is to sit for a photographer to take my Dunn School portrait. Unlike other places where I had studied before, the purpose was not to get a blurry shot for my access card. Rather, the resulting photograph was to be placed on the same walls as Dunn School greats, up alongside Florey, Heatley, Chain and more recent achievers. The underlying assumption is that you, also, will do great things, and are part of a continuum of scientists who have researched and taught at the Dunn School since 1927. It captures us at our most enthusiastic, and full of anticipation for the future… before the inevitable ups and downs of research life!

Every year our new cohorts of students continue to experience this quintessential Dunn School rite of passage. But whether you are student, staff or a visitor, everyone passes these portraits when they wander along the corridors of the department. Maybe they have a favourite: a subject with a particularly inquisitive look; an intriguing caption or a particularly glamourous pose with a pipe!
Although embedded in the life of the Dunn School, this collection has so far been only sketchily examined. There is no systematic list of who is on the walls and where. And what would happen if some were damaged or needed replacing? Back up copies of some of the photos exist in the Bodleian archives, but not in a complete way. As our centenary in 2027 approaches, the time is ripe to change this.

Getting started

I decided to start with the basics. How many portraits are there? Where are they located? Are any damaged? I have established that there are currently 946 portraits, but this is a growing collection. After the inevitable pause during COVID, the photos of the 2020, 2021 and 2022 student cohorts are now being added to the walls. We should reach a thousand photographs by 2027, the year of our centenary.
This first investigation also highlighted some issues. The photos most exposed to light are showing clear signs of irreversible damage, especially a set of photos from the 1960s located by the bridge walkway that links the Old Building to the EPA building. In addition, there were almost eighty photographs from the 1970s/80s obscured behind four -80˚C freezers, potentially damaged due to heat exposure. I decided to prioritise these two sets of photos.

I consulted the conservators of the Bodleian on how to approach such an old collection, which resulted in the protocol shown in Figure 1. With the financial support of the E.P.A. Research Fund I recruited Lizzie Bond, a masters student in History, over the summer of 2022 to help us with this project, starting with the most 'at risk' photos. Lizzie did a fantastic job, cataloguing, digitising and cleaning roughly three hundred photographs, almost a third of the collection! Most of the photographs were returned to their original location, but over one hundred photographs are stored temporarily, away from excessive light and heat, as we identify more suitable positions for them.

The stories behind the faces

Lizzie was also interested in piloting how we discover more about the personal stories of the people in the photos. She chose a handful to investigate further. She looked at the information publicly available on the internet but also explored what is available in archives and collections, including at Oxford. We were surprised to find that there isn't a single unified record of everyone who has ever worked and studied in the Dunn School, but there are several sources that can be used to piece this together. One interesting source is the University Administrative Archives, which are partially located under the Weston Library, and partially in one of the towers in the School's Quadrangle. This collection holds many artefacts about the history and life of the department. One of the most interesting (and relevant

Editor's note: QR code link to Bodleianholdings of Dunn School archives https://t2m.io/Bod_Dunn

[1] *Editor's note:* Oxford University still officially names its PhD degree "D Phil", the Anglicised abbreviation for the Latin term *Doctor Philosophiae*.

Figure 1. The process A) *Photos were carefully removed from the walls in batches.* ***B)*** *The Bodleian's Digitisation Services scanned each photo to professional standards.* ***C)*** *Lizzie then cleaned decades of dirt from the glass and frame.* ***D)*** *Photos were carefully dusted with a bamboo brush.* ***E)*** *Each photo was re-sealed and labelled with its own unique identifier.* ***F)*** *Back on the walls!*

for this project) is the collection of index cards that recorded the thesis, supervisor and graduation dates of all PhD students of the department (Fig.2). The Bodleian Special Collections also holds its own collection of Dunn School portraits and negatives, which were saved and archived by Eric Sidebottom and Lance Tomlinson when the department's own photography unit closed (more below). Some of these, but not all, correspond to the collection that we can find on our walls.

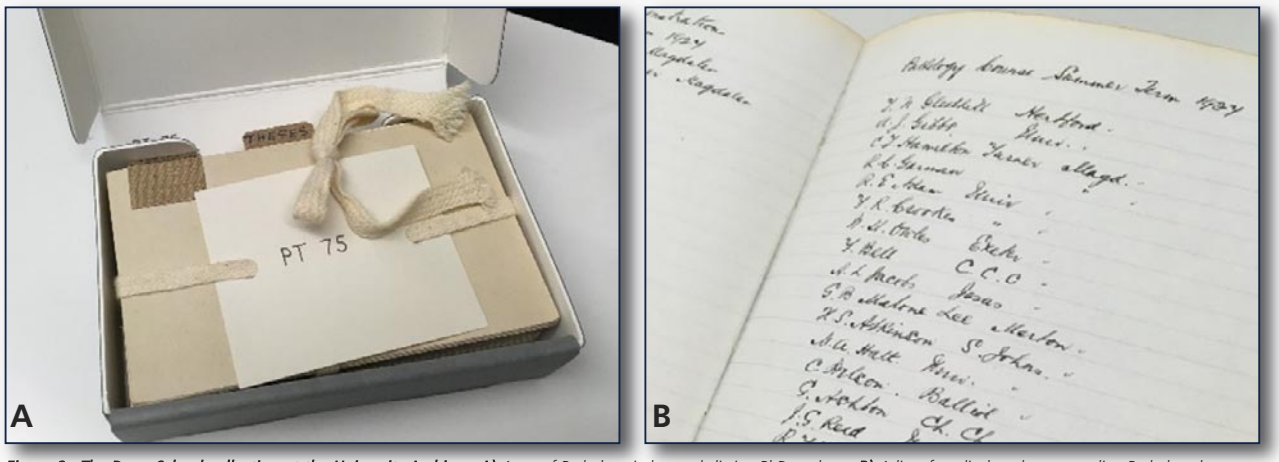


Figure 2. The Dunn School collection at the University Archives A) *A set of Pathology index cards listing PhD students.* ***B)*** *A list of medical students attending Pathology lectures in the Summer Term of 1927.*

Who isn't on our walls?

As we start creating a record of who is on our walls, it is as important to consider who was not included in the collection. Some of you may have noticed that there is a clear shift in the collection in the late 90s/early 2000s. Before this date, most staff and students (and even academic visitors) were included, as far as we can tell, on the date they left the department: after this date, only students. Our former Head of Department Prof Herman Waldmann was able to shed some light on this shift. The Dunn School used to have its own in-house photography team, first led by Stan Buckingham and then by Lance Tomlinson, which was located in the roof of the Old Building. With the shift of photography into digital and Lance's retirement, the photography team was no longer needed. At the same time, the number of researchers in the department increased significantly, so lack of wall space became an issue.

A closer look at the collection also showed that research support and administrative staff are conspicuously absent.[2] Photos of some of them do exist, but are not on display, such as the famous 'Penicillin Girls'. Another angle that particularly interests me is how our collection reflects, in a very visual way, the change in diversity in science over the last 100 years. The collection is surprisingly diverse from its inception. Female and east/south Asian researchers feature from the very beginning of the collection in the 1920s. Yet you have to go as recently as the 1980s to find the first black scientist. I am excited by the insights on diversity that the full cataloguing of the collection may provide, and investigating further the lives behind some of these 'firsts' of the department will provide fascinating insights into the history of diversity in science (and the Dunn School).

The next steps

This short summer project only scratched the surface. Almost 600 portraits remain to be catalogued and digitised, and we have only started exploring how and what we can find about the amazing people on our walls. The start of the project has generated more questions than answers about this unique collection, but we are keen to investigate them further in the years building up to the centenary.

We have just recently taken on a new student to help us move the project forward. We hope to continue sharing updates on this project both in Fusion and through our regular alumni newsletter.

We need your help!

One of the most rewarding aspects of starting this project has been the enthusiasm of current and former members of the Dunn School. I have received several emails and social media messages by former members as well as relatives, who want to find out more about specific portraits or share their memories of the collection. For example, a long-serving current member of staff seemed to recollect that on occasion retiring Dunners were allowed to take their photo with them as a memento. If true, this would have biassed the present display. Do you remember this happening? A few portraits seem to be located in the wrong decade and some photos have little secrets hiding behind them, such as other photos. Was this done deliberately? The frames are surprisingly consistent across the decades, suggesting that they were reframed at a particular point in time. Do you know when this might have been? We would be delighted to hear any of your stories or memories to help us fill these and other gaps. Just email us at alumni@path.ox.ac.uk.

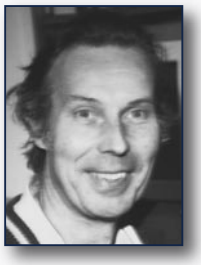
We would also like to ensure that our collection is compliant with GDPR and personal data legislation. This allows us to keep a digital copy of the portraits once we have digitised them (useful not just for future reference, but also to replace the original if it is damaged), as well as use the images as part of our centenary celebrations. We are only allowed to do so if we have your written consent.

If you are a current or former member of the department and you know that you are included in the collection, please do get in touch with us at alumni@path.ox.ac.uk. We would also be delighted to share the digital file of your photograph if you would like a copy.

Figure 3. The photo of Eric Sidebottom, former Fusion editor, awaits conservation treatment. His DPhil dates were 1966-1969.

[2] *Editor's note:* except for Mr Jim Kent, Florey's technician, and Mrs Peggy Turner, department Administrator. Both were granted Honorary M.A. degrees by the University in recognition of their very long and valuable service. Their photos are on the wall of the top corridor of the Old Building.

Donald W. Mason (1934 - 2021) - flow cytometry and cellular immunology



Many tributes and appreciations have been written about Professor Don Mason's scientific contributions[1], made during a 26-year period in the MRC Cellular Immunology Unit here at the Dunn School. His science endures. Additionally, he left a lasting legacy of several distinguished scientists whom he mentored and supervised at early stages of their careers[1]. Commemoration of his achievements came to a focus at the official opening of the Don Mason Flow Cytometry Facility on 12th June 2023 by his widow, Mahalla, with other family members also present[2]. This facility, open to scientists outside the department as well as internally, houses a suite of the most up-to-date flow cytometers[3] under the leadership of Dr Bobby Hedley[4], its manager and expert adviser. In this article Fusion's editor reflects on the dependence of research advances upon technical innovations, as exemplified by Don Mason's immunology research.

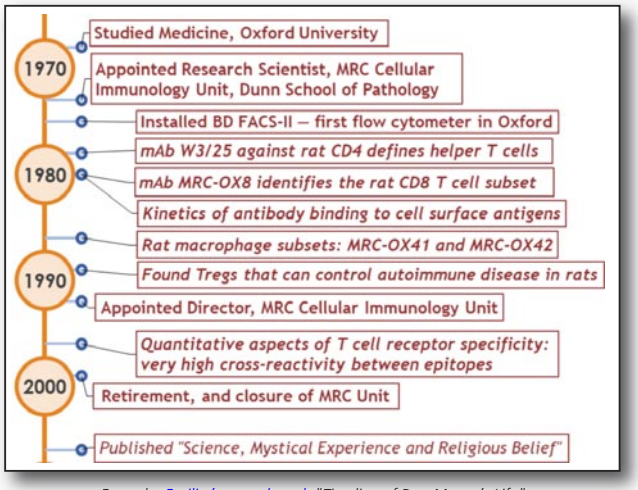
The MRC Cellular Immunology Unit was formed in 1963 to progress the science cracked open by Jim Gowans, its first Director. He had already definitively established during the preceding ten years that small lymphocytes physiologically recirculate between blood and lymph and that they initiate adaptive immune responses. In 1973 he appointed Don Mason to the scientific staff of the Unit. Don was freshly out of medical school at Oxford University as a mature student, with an earlier first career in nuclear physics research behind him. After Jim Gowans departed in 1977 to run the Medical Research Council, Don continued under the Unit's new young Director, Alan Williams.

Alan was a biochemist who developed the first monoclonal antibodies (mAbs) against lymphocyte membranes. Over the following fifteen years Alan and Don, with Neil Barclay, collaborated synergistically and very productively. Don concentrated mostly on subsets of ex vivo rat lymphocytes stained with fluorescence-labelled monoclonal antibodies and sorted by flow cytometry. He tested immunological functions of these subsets both in cell culture and in vivo by adoptive transfer into suitable host recipient rats. After cancer took Alan's life in 1992, Don became the Unit's third and last Director, until its closure in 1999 when he retired. During this final period Don broadened his research on the topic of T cell receptor specificity and cross-reactivity, particularly in relation to autoimmunity.

"*Technik ist alles* - Technique is everything", the quip goes. Amen to that, although it stretches a good point too far. The marriage of two technical advances was a main reason cellular immunology bloomed so flourishingly in the final quarter of the 20th century. mAbs were one of the wedding partners. Alan Williams, working with César Milstein and Giovanni Galfré in 1976, initiated making (mouse) mAbs for research purposes against epitopes on (rat) lymphocyte membrane macromolecules. These reliable, reproducible probes could now mark out one subset of lymphocytes differentially from another. (At international workshops the specificities of independently-derived mAbs were classified into "Clusters of Differentiation" antigens – CD antigens; the list of these today numbers over 370). It was partly luck and partly scientific nous, whether a new monoclonal might usefully identify an interesting subpopulation. The other wedding partner was flow cytometry. In Oxford, Don was its Best Man. Its powers of analysing and sorting cell populations labelled with fluorescence-tagged antibodies were unprecedented. As the union of these two technical approaches was consummated, light-bulb moments started flashing frequently. Don with his co-workers were the first to show that mAbs such as anti-CD4 against the cell surface could inhibit T lymphocyte function *in vitro*, paving the way in principle for the many present-day therapeutic applications of mAbs clinically. Luck-plus-nous observations followed on MRC OX22, which subdivided the CD4s. He and his labgroup spear-headed the renaissance of regulatory T cells in the 1980s, especially in animal models of autoimmune disease.

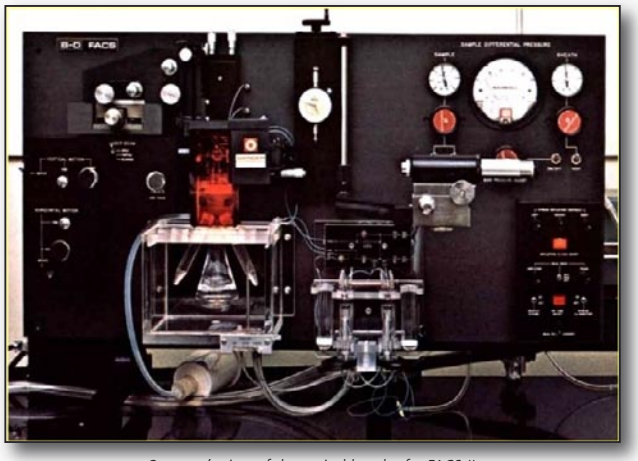
From the Facility's posterboard: " Research Publications "

[1] See a compilation at this Commemorative: https://t2m.io/DWMason
[2] www.path.ox.ac.uk/news-article/don-mason-flow-cytometry-facility-inaugurated/
[3] The cytometer suite in 2023 comprises: Analysis: BD LSRFortessa X20 (two instruments); Cytoflex LX; Amnis Imagestream MkII; plus an Analysis workstation running FlowJo/Cytobank/IDEAS. Sorting: BD FACSAria III; BD FACSAria Fusion
[4] @theDonMasonFlow Visit www.oxforddmflowcytometry.com



From the Facility's posterboard: "Timeline of Don Mason's Life"

A FACS-II flow cytometer like the one that Don Mason installed.



Operator's view of the optical bench of a FACS-II, with fluidics and the argon ion laser behind

Initial developments in the 1960s at Stanford University[5] had led to the commercial marketing by Becton-Dickinson of FACS-II flow cytometers in the early 1970s. The first FACS-II in the U.K. was installed at the ICRF[6] labs at Lincoln's Inn Fields in 1974-5. It wasn't long before Don's experiments would require him to rise exceptionally early in the morning to travel 13 miles from home in Witney to the Dunn School. He would label cells with fluorescent antibody, take the train to London, sort the cells for several hours, double back on the train to the lab to inject them into recipient rats, then finally return home exceptionally late at night. The responses of the rats over the next couple of weeks told him which subpopulations underwrote the immune reactions that he was interested in.

The Unit clearly needed its own FACS-II. The royalties from cephalosporins helped to pay for one for Oxford. Don applied his Physics expertise to oversee its installation, staffing and service provision. In those days the light to excite fluorescence was produced by large, power-hungry metre-long gas-filled ion lasers; first, argon (514 nm) then later, additionally, krypton (647 nm) for a second colour. They gobbled many tens of Kilowatts of electricity. The optical power output was less than one-thousandth of the electrical power the laser consumed. 99.9% of the electricity turned into useless heat, which had to be removed by pumping water through the lasers to a purpose-built cooling tower outside the building. From the Workshop, Peter Stroud's skills as nurse-engineer were frequently needed. These were vital to keep this complex set-up running.

FACS-II was unambiguously cutting-edge half a century ago. Previously unattainable analysis and sorting experiments became possible, even if still pretty heroic! They were limited to just two emission wavelengths: green and red. Look now at the new cutting-edge. It was beyond the imagination of even an ultra-fertile mind like Don's that in 2021 we'd be reading papers such as: "*High-throughput single-cell quantification of hundreds of proteins using conventional flow cytometry and machine learning*"[7]. Data scientists are providing us with the techniques to crunch and visualise phenomenal quantities of raw, high-dimensional data. Researchers who can conceptualise in n-dimensions have a distinct advantage over those who can't. (That means me!). Two-dimensional FACS dot-plots from the 1970s have given way to UMAP arrays of the 2020s. Just for fun, let's also add yet more UMAPs from single-cell RNAseq analyses to the fluorescence-based UMAPs. Rigour, quantitation, and a head for dizzying mathematical heights were all traits that Don exhibited in abundance. He would have loved to be at the current cutting-edge all over again.

Three posterboards on the walls of the Facility briefly summarise Don Mason's life: "Research publications"; "Timeline of his life"; and "Academic legacy…outstanding scientific heirs": https://t2m.io/DWMBoards or use this QR code. His full scientific bibliography is at https://lnnk.in/gccN. If you knew Don, please help us to collect an e-scrapbook of comments, anecdotes, reminiscences and photos. Send them to alumni@path.ox.ac.uk for sharing with his family, colleagues and the wider public.

[1] Herzenberg, Sweet and Herzenberg (1976) "Fluorescence-activated cell sorting" Scientific American 234: 108 www.jstor.org/stable/10.2307/24950310. The German physicist Wolfgang Göhde independently developed analytical flow cytometers at Muënster at the same time.

[6] Imperial Cancer Research Fund, a predecessor of Cancer Research UK.

[7] Becht, E *et al* (2021) Science Advances 7. http://doi.org/10.1126/sciadv.abg0505. The data science package *Infinity Flow* has already been improved computationally with the introduction of "*pyInfinityFlow*": Ferchen et al (2023) https://doi.org/10.1093/bioinformatics/btad287

Stars from the Dunn School

Stardust conferred on those who successfully graduate with a doctorate from the Dunn School can twinkle brightly for years and years to come. Some reach the brightness of supernovae, easily visible to the naked eye. *Fusion* celebrates distinctions achieved by four of our old members. Long may they inspire the current generation of pre-supernovae.

Credit: NASA and STScI

Pre-supernova Wolf-Reyet 124, imaged in 2022. See NASA's Webb Telescope Captures Rarely Seen Prelude to Supernova

Fiona Watt, DPhil (Oxon), FRS, FMedSci. Appointed Director of EMBO in January 2022

Between 1976 and 1979 Fiona studied for her DPhil on the top floor of the Old Building, supervised by Prof Henry Harris. She researched microtubule-organising centres in cell cultures. This developed into her career-long interest in how the differentiated state of adult tissues is maintained. Using mammalian epidermis as a model system she has investigated self-renewal and lineage selection by human and mouse epidermal stem cells, the role of stem cells in epidermal and oral tumour formation, and the assembly and function of the epidermal cornified envelope.[1] In her most recent paper, her group has identified Lunatic Fringe, Manic Fringe and Radical Fringe as three key N-acetyl-glycosyltransferases important in regulating *notch* signalling. See www.wattlab.org

She is a long-standing strong advocate for women in science. She also promotes Review Commons, a platform for journal-independent peer-review which provides authors with a Refereed Preprint[2].

(J.S.) Malik Peiris, DPhil (Oxon), FRS. Awarded Hon DSc by Oxford University at Encaenia 2023

From 1977 to 1980 Malik[3] studied for his DPhil, supervised by Dr James Porterfield, Reader in Bacteriology here until 1989. Examining yellow fever virus in vitro, they established the important phenomenon of infectivity enhancement by anti-virus antibody at titres lower than neutralising. He is Sri Lankan by birth and was educated at the University of Peradeniya there. The major part of his career has been at the University of Hong Kong, where in the early 2000s he and his lab discovered that the very infectious virus causing Severe Acute Respiratory Syndrome, SARS, was a then-novel coronavirus[4]. Malik has a preceding family connection with the Dunn School. His father-in-law is Prof S.N. Arseculeratne, distinguished emeritus professor at Peradeniya. "Ratne", as his supervisor Kits [W.E.] van Heyningen used to call him, was himself a DPhil student in the Dunn School (1962-5). Following a totally unproductive, torrid first year of research he successfully showed that Clostridial exotoxin has phospholipase activity, hence explaining its ability to disrupt cell membranes and cause disease[5]. It confirmed his own original idea that the mechanism might be like snake venom. He went on to have a stellar academic career in his own country.

On his way to the Sheldonian to accept his Hon DSc, Malik revisits Keble, his old College, flanked by the Warden, Sir Mike Jacobs, and Simon Hunt

Taole Mokoena, DPhil (Oxon), FRCS. Appointed Health Ombud for South Africa, June 2023

Taole, a medical graduate of the University of KwaZulu-Natal, came to the Dunn School between 1982 and 1985, following an introduction by Dr Graham Bird, clinical immunologist at the Churchill Hospital. He worked for his DPhil in Prof Siamon Gordon's lab group and successfully submitted a thesis titled "Modulation of human monocyte/macrophages *in vitro* by interferons and other agents"[6]. His research publications at that time reflect how DPhil students took part in interdepartmental projects, both clinical and non-clinical. After further training in Glasgow, he returned to South Africa, where he pursued a career in academic surgery. He rose to become professor and academic head of the department of surgery at the University of Pretoria, and chief surgeon at the Steve Biko Academic Hospital there. He has retired from these posts. His new appointment could be a "hot potato" if ever there were one. *Fusion* applauds his public service in taking it on. We wish him well.

[1] An overview of her research and its impact is at https://kclpure.kcl.ac.uk/portal/en/persons/fiona-watt. See https://orcid.org/0000-0001-9151-5154 for her scientific bibliography and career overview. Her DPhil thesis is in the departmental library and the Bodleian: https://solo.bodleian.ox.ac.uk/permalink/44OXF_INST/35n82s/alma990169292940107026

[2] On taking up the EMBO directorship, she reflected, partly autobiographically, on issues and attitudes and careers in scientific research: https://network.febs.org/posts/reflections-from-fiona-watt-embo-s-new-director. This page www.reviewcommons.org/about/ explains how Review Commons: - (i) allows peer-reviewers to focus on the science, not specific journal fit, of an article submitted for publication; (ii) enriches the value of preprints; (iii) reduces re-reviewing at multiple journals; and (iv) accelerates the publishing process by providing journals with high-quality referee reports. *Fusion* stands right behind her in these worthy aims.

[3] ORCID: https://orcid.org/0000-0001-8217-5995, and see his Hong Kong University webpage: https://hub.hku.hk/cris/rp/rp00410. Malik has featured in previous issues of *Fusion*: in 2021; in William James's overview of virology at the Dunn School, 20

[4] He came to the department in 2004 to give a seminar on this fundamental finding: see Fusion2004

[5] Recounted by him in https://t2m.io/Fusion2014, page 21. Copies of his thesis are in the Dunn School library and the Bodleian

[6] Deposited in the Bodleian: https://solo.bodleian.ox.ac.uk/permalink/44OXF_INST/35n82s/alma990161441320107026. His thesis advisor was Richard Wood, academic surgeon with the immunologists at the Nuffield Department of Surgery.

Bob Vonderheide (R) with Simon Hunt during a visit to Bob's office in Philadelphia in 2019

Bob Vonderheide, DPhil (Oxon), MD. Re-appointment in 2022 as Director of Abramson Cancer Center, University of Pennsylvania

Bob joined the Hunt lab as a Rhodes scholar, having majored with a first degree in chemical engineering at Notre Dame University. For his DPhil (1986-8) he researched lymph node germinal centre B cells and their precursors, in a rat model[7]. After Oxford, he qualified in medicine in Boston, at the Mass General with a fellowship at Dana-Farber, where his interest in immuno-oncology sprouted. As a leading clinician scientist he's been pushing forward Chimeric Antigen-Receptor (CAR) T cell therapies as mainstay treatment for certain types of cancer. With Susan Domchek, he is steering his Center strategically towards "cancer interception[8]", making use of the formidable power of modern indicative blood biomarkers and single-cell sequencing. Bob's reappointment as Director will let him drive this promising concept forward, connected very closely to clinical translation. Recall the outcome when in 1941 Florey's team in the Dunn School linked with the patients and doctors in the Radcliffe Infirmary for first-in-human trialling of penicillin.

Basic science on public display in the foyer of the clinical academic environs of the Basser Center, part of the Abramson. This overhead mobile sculpture is based on ribbon representation of BRCA2: "Homologous Hope" by Mara G. Haseltine. It's seen by every patient, researcher and visitor to the Center

[7] Online at https://solo.bodleian.ox.ac.uk/permalink/44OXF_INST/35n82s/alma9910252231476070 26

[8] www.pennmedicine.org/news/news-blog/2023/february/can-we-intercept-cancer-a-new-frontier-in-cancer-research

Zest for Life - joie de vivre!

A place of work, study, teaching and mentoring such as the Dunn School is no use at all if there's no enjoyment of life. Bucketloads of zestiness need to flow continuously through everyone's bloodstream, pulsing as the vital backdrop to everything we do. We are a very international bunch in our department and everyone chips in communally. Each of us expresses our bubbliness and ebullience in our own particular zesty way. *Fusion* thinks it's time to publish translations of the phrase "*Zest for Life*" in 30 different languages. Thank you, Wiktionary[1], for providing this list.

Arabic: تلذذ بالحياة
Basque: bizipoz
Chinese: Mandarin: 生活情趣 (shēnghuó qíngqù)
　生活樂趣 / 生活乐趣 (shēnghuó lèqù)
Danish: livsglæde *c*, livslyst *c*
Dutch: levensvreugde *f*, levenslust *m*
Esperanto: vivĝojo
Faroese: lívsgleði
Finnish: elämänilo, elämänhalu
French: joie de vivre *f*
Galician: delicia de vivir *f*
German: Lebensfreude *f*, Lebenslust *f*
Hindi: जीने की ख़ुशी *f* (jīne kī xuśī)
Hungarian: életöröm
Icelandic: lífsgleði *f*
Italian: gioia di vivere *f*
Japanese: 生きる歓び (いきるよろこび, ikiru yorokobi)
Kannada: ಬಾಳಸವಿ (bāḷasavi),
　ಜೀವನ ಮಾಧುರ್ಯ (jīvana mādhurya),
　ಜೀವನದ ಸುಖೋತ್ಕರ್ಷ (jīvanada sukhōtkarṣa)
Korean: 삶에 대한 열정
Latvian: dzīvesprieks *m*, dzīves prieks *m*
Limburgish: laeveslös *m*
Luxembourgish: liewensfreed
Norwegian: Bokmål: livsglede *m* or *f*, livslyst *m* or *f*.
Nynorsk: livsglede *f*, livslyst *f*
Polish: radość życia *f*
Portuguese: alegria de viver *f*
Romanian: bucurie de a trăi *f*
Russian: жизнерáдостность *f* (žiznerádostnost´)
Spanish: alegría de vivir *f*
Swedish: livsglädje *c*, livslust *c*
Ukrainian: життєрáдісність *f* (žyttjerádisnist´)
Uzbek: xushchaqchaqlik
Vietnamese: niềm vui sống

Pins on our wallmap in the Bridge Café show the countries that current members of the Dunn School come from. This photo shows just the Eurasian portion of the world! Variety is the spice of life! 丰富多彩的经历会令生活充满乐趣

Fusion loves 'Bizipoz', the Basque version. No wonder there's so much zesty basking in Basque country. Esperanto 'vivĝojo' is not bad, either. Polyglot reader, is your phrase for "Zest for Life" properly translated above? Or is your language perhaps missing? Can you help with Arabic or Korean? Please send your suggestions and your photos of Dunn School zestiness to alumni@path.ox.ac.uk. Also maybe you could edit Wiktionary to put it right if it's wrong.

[1] https://en.wiktionary.org/wiki/joie_de_vivre

Parties!

The quality of Dunn School research is indisputably up there in the highest rank. Equally, the standard of its parties cannot be bettered. Fusion finds it quite hard to keep track of them. Fortunately, Jo Peel, Executive Assistant to the Head of Department, has come to the rescue by providing highlights of the following VIPs, Very Important Parties.

© Jo Peel

Farewells to Administrative staff

A retirement party took place for Finance Manager Martin Wilkins in September 2021 at Balliol College. See 'Arrivals and Departures' in this issue for a note about his long service. To have been counting the beans for over forty years, in all their varying shapes and sizes, was a daunting task that only Martin's Stern Stuff could have handled so successfully. Does *Fusion* detect smiles of relief on his face at his party, like an exuberant ultramarathon runner at the finish?

Photo Jo Peel

113 years of service between them, still with irrepressible gales of laughter left. L to R: Jo Collett; Martin Wilkins; Rita Richards; Audra Giles. With their combined total of 113 years of Dunn School service, these four certainly earned their well-deserved party.

Due to the pandemic Rita Richards unfortunately missed a party when she left in December 2021. Virtual parties are feeble by comparison to real ones! Nevertheless, she received well-wisher messages, heartfelt thanks, and gifts from colleagues as she headed into early retirement. Rita worked in the purchasing department at the Dunn School since May 2005.

Joanne Collett, Research Grants Administrator, left in October 2022 and had a leaving dinner at Cote Brasserie with finance team and other colleagues. She worked for our University for 30 years, 27 of them at the Dunn School. She wrote in her farewell message "*…an absolute pleasure working with you all. The Dunn School is a very special place. You do not stay for 27 years if it isn't! This is mainly down to the people….*" We thank her for everything, especially for her tireless help in administering the departmental Library and all those "Bull sessions" for Professor Brownlee.

The unfailingly friendly and dependable Audra Giles enjoyed a leaving lunch with professional services staff at Browns Restaurant in March 2023. Audra worked at the Dunn School for 29 years, step by step up to the post of deputy finance manager. It was always very reassuring to know that her ever-capable hands were on the Finance tiller when Martin had to be absent.

Dunn School family fun in high-summer party mood, outside the cricket pavilion in the University Parks

©Simon Hunt

In July 2022, a 350-strong throng proved that their party-going skills had not withered because of COVID. Festivities were held outside the Grade-II listed Cricket Pavilion in the University Parks, a cricket ball's throw from the Dunn School. With Crazy Golf, giant Football Darts, Beat the Buzzer, the throb of the open-air disco, the scorching summer heat, fantastic food and drink for kids and grown-ups..... this come-back party was a stunner! Philip Cobden and his team hit for six the organisation of this joyful event. Howzat!

The 2023 version of the Summer Party was held at the same location. It was just as good, with help-yourself ice-creams and ice-lollies an uber-popular feature. Young and old alike particularly loved the apparatus for making giant bubbles that wafted in the breeze across the cricket pitch towards the river. As social glue between everyone who works in or is associated with the department, these relaxing family-friendly summertime events hit the bullseye.

At the other solstice, every Christmas party in the department generates abundant warmth, conviviality, and good cheer. The popular party raffle fundraises for charity. In 2023 it gave over £1200 to Razom for Ukraine, and for the Helen and Douglas House Hospice. The workshop continues the time-honoured tradition of the decorated tree that reaches the ceiling in the front hall. On this occasion, the organisers were the Murphy and Gromak (photo) lab groups.

Organising these events is a non-trivial task. It is a tribute to the Dunn School's spirit and cohesion that there is always someone or some labgroup who steps up to the plate each time. Fusion is sure we speak on behalf of all the party-cipants 😤 when we say 'thank-you very much' to all these good people.

Philanthropy past and present: please make a donation

Prize competition - it's a BLAST!

Our School owes its existence to Sir William Dunn's original philanthropic gift more than a century ago[1], worth well over £5mn in today's money. Through the years we have been the beneficiary of many generous acts of bounteousness, not least from those who have worked here. Donations to the Dunn School directly help to further research here: either to support specific initiatives such as those described in this newsletter, or at the discretion of the Head of Department.

The best way to give

Online at www.development.ox.ac.uk/pathology. You can use the QR code; or type this short URL into your browser: https://t2m.io/DonateDunn
Kindly consider tax-efficient giving. For details of UK Gift Aid and similar schemes for other countries visit www.development.ox.ac.uk/contribute/worldwide_giving/index.html
If you have any difficulty with this, or if you want to ask any questions about a donation, please contact alumni@path.ox.ac.uk entirely confidentially.

Please donate:
https://t2m.io/DonateDunn

Hoc aedificium
A.S. MCMXXVI completum
suppeditavit
Gulielmi Dunn Baronetti
munificentia
pecuniis ingentibus
ad levandos humani
corporis dolores
testamento devotis

Prize competition!

Does this 142-letter sequence, or a part of it, match anything in the protein database of Homo sapiens?

HOCAEDIFICIUMASMCMXXVICOMPLETUMSUPPEDITAVITGULIELMIDUNN
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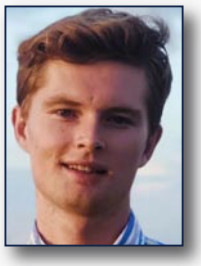
Answers please, showing your top alignments (maximum: six) to alumni@path.ox.ac.uk. The best match will receive a Dunn School jersey/T-shirt

Roughly translated, the inscription on the familiar marble and slate plaque which adorns the main oak staircase states: "This building, completed in 1926, was bestowed by Sir William Dunn, Baronet, a generous benefactor of large sums of money, to relieve the sufferings of the human body". "A.S." is an acronym for Anno Salutis, meaning "The year of Salvation." It represents a Western Christian calendaring system, identical with the more common "A.D." - Anno Domini – "The year of our Lord."

[1] The opening of the "finest scientific building in Oxford" was reported in Nature on 19th March 1927: www.nature.com/articles/119433a0.pdf

Overcoming the Glycan Blindspot:
raising antibodies against immunosilent cancer antigens



Lachlan Deimel (Brasenose College: Oxford<>Australia Clarendon Scholar) submitted this essay[1] for the 2022 Peter Beaconsfield prize. It won him won a £500 joint runner-up award. He worked in the Sattentau lab since 2020. The prize rewards young researchers who are "capable of escaping from the stereotype of narrow specialisation to engage with translational medicine, to display a wider grasp of the significance and potential applicability of their research". Lachlan recently successfully defended his DPhil thesis. His next stop is the Nussenzweig lab at New York University for his post-doc. Congratulations all round, Lachlan!

Prize details
https://t2m.io/Bcnsfield

This essay is based on work published in the following manuscript: Deimel LP..... Sattentau QJ *et al* (2023). "Engineered display of ganglioside-sugars on protein elicits a clonally and structurally constrained B cell response". BioRxiv, https://doi.org/10.1101/2023.06.03.543556

Abstract

Glycans are carbohydrate structures essential for life, are endogenously conjugated to proteins and lipids, and are tolerated by the immune system. Their weak immunogenicity is exploited by cancers and viruses to shield sensitive protein surfaces from B cell recognition. My aim is to selectively break immune tolerance and raise glycan-specific antibodies. I have chemically installed a cancer-associated glycan onto model proteins using a glycoconjugation strategy absent from the mammalian glycome. These semi-synthetic glycoconjugates are highly immunogenic in mice, and I have characterised antibody responses using B cell cloning. My results encourage translation of this approach towards novel anti-cancer vaccination strategies.

Antigen glycosylation as an immune evasion tactic

Self-glycans are classically regarded as immunosilent, presumably to avoid widespread autoimmunity[1,2,3]. Tolerance is imparted by both immunogenic constraints and elimination via negative selection of B cell precursors displaying self-glycan reactivity. However, there are circumstances where selectively breaking glycan immune tolerance may be favourable[4], since the apparent "glycan blind spot" is readily exploited by cancer and viruses (including HIV-1, HCV and IAV), which use glycans to shield otherwise antibody-sensitive functional epitopes from B cell recognition[5,6]. The elicitation of antibodies that recognise disease-associated glycans remains a central and unmet goal for vaccine development[7,8,9].

I envisage a way forward to initiate vaccine-induced, glycan-engaging antibody responses. The emergence of modern synthetic chemistry offers a platform to install artificial 'near-self' glycans to specific protein sites. For instance, while glycans are naturally conjugated to proteins via asparagine (N)- or serine/threonine (O)-linked motifs, imidate (2-imino-2-methoxythyl-1-thiol glycosides, IME)-mediated coupling allows for the unnatural conjugation of carbohydrates to primary amines, such as those of lysine sidechains[10]. I hypothesise that these approaches may improve glycan immunogenicity by modifying glycan presentation from that of natural self-glycans, thereby breaking immune tolerance to these structures.

Here, I outline preliminary data exploiting IME chemistry to conjugate SiaLac (2,3-sialyllactose) – a model sugar upregulated on several cancers including melanoma, lung cancer and brain cancer[11,12] – to overcome immune tolerance. This multidisciplinary approach combining chemistry, molecular immunology and structural biology may yield promising translational potential and reveal structural and biochemical information about the nature of carbohydrate-binding antibodies.

Characterising the immunogenicity of a SiaLac-based glycoconjugate

IME-activated SiaLac was chemically conjugated to lysine residues of Hen Egg Lysozyme (HEL) (Fig 1a, b). Mass spectrometry revealed highly efficient conjugation of the glycoconjugate to the carrier protein, with >95% of the product displaying full (6) lysine occupancy (Fig 1c). Mice were immunised twice with HEL-SiaLac or an unmodified HEL control with or without the TLR-4-agonising adjuvant monophosphoryl lipid A (MPLA) (Fig 1d)[13].

Antibody titres were subsequently measured, evaluating IgG binding against a SiaLac-modified unrelated carrier protein, gp120-SiaLac, to determine the glycoconjugate-specific response (Fig 1e). Data revealed high-titre, isotype-switched IgG antibodies that recognised the glycoconjugate in a protein backbone-independent manner. The median IgG endpoint in the absence of adjuvant was > $10^{3.5}$, which was bolstered to ~105 with adjuvant. To dissect the specificities of these antibodies, pooled SiaLac-reactive antiserum was screened against a large glycan library (Fig 1f). Data revealed binding to SiaLac and its close cousins, including SiaLacNAc. These indicate narrow glycan cross-reactivity, which may be favourable to avoid autoreactive outcomes.

This whole article, including full-size images, is available online at https://t2m.io/Bcnsfld_LD

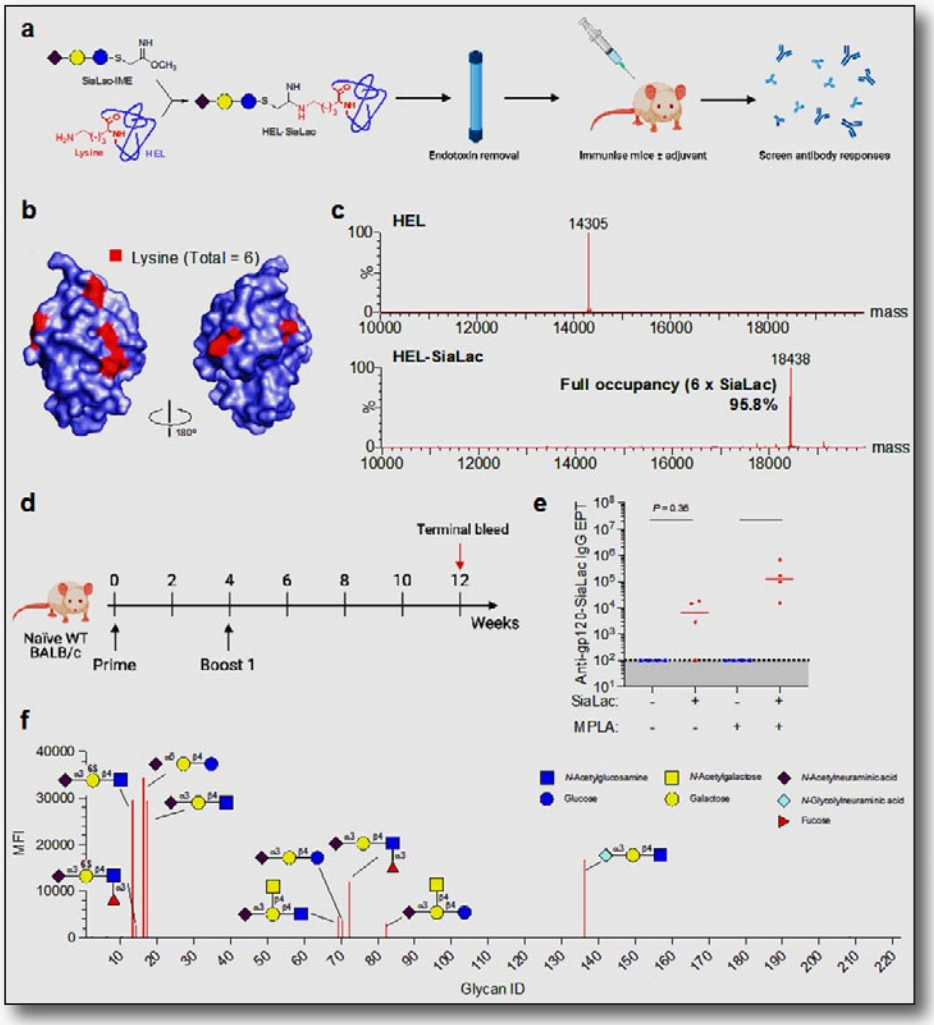


Figure 1: Semi-synthetic SiaLac glycoconjugate immunogenicity in mice.
(a) Protein-sugar coupling and immunogenicity evaluation strategy. Sugars are artificially activated to react with primary amines, allowing for selective conjugation to lysine sidechains.
(b) HEL (PDB: 193L) with the lysine residues shown in red.
(c) Mass spectra of unmodified (top) and SiaLac-modified (bottom) HEL.
(d) 6-week-old female BALB/c mice were twice immunised with 10 μg of HEL or HEL-SiaLac ± MPLA adjuvant.
*(e) Direct ELISA was used to evaluate serum IgG endpoint titres against gpl 20-SiaLac. Data are represented as median, with dots representing biological replicates. Statistical significance was determined via Kruskal-Wallis test. P-value denotations: * P <0.05 and ** P <0.01.*
(f) Pooled SiaLac-reactive antisera was screened against a glycan library (developed by Jim Paulson, Scripps).

Interrogating the clonality and structural features of anti-SiaLac antibodies

I designed a probe-based approach to sort single glycoconjugate-specific IgG+ B cells from a HEL-SiaLac-immunised mouse (Fig 2a–c). Heavy and kappa chain variable regions (VH, VK) were recovered from 33 events and their germline-encoded V(D)J regions were inferred. 5 families of shared V regions were identified (Fig 2d). A subset of monoclonal antibodies (mAbs) was recombinantly synthesised and screened against gp120-IME-SiaLac to validate glycoconjugate-specific binding (Fig 2e). The inferred germline (iGL)-encoded heavy chain (HC) regions reveal narrow V-gene use but diverse D- and J-gene use (Fig 2f–h). Kappa chain (KC) V- and J-genes show significant diversity (data not shown). Sequence alignment of utilised V-genes demonstrate high sequence identity between the IGHV2-3*01, IGHV2-6-5*01 and IGHV2-9*02 genes (Fig 2i). This indicates that the clones isolated rely on specific motifs encoded in these segments to bind the glycoconjugate, likely in CDRH1/2. Interestingly, the antibody sequences display very high similarity with the iGL, with a median change frequency in both chains of 4 nucleotides, representing ~1% of the V region, suggesting limited germinal centre experience (Fig 2j). Consistent with the gene usage frequencies, alignment of the CDRH1/2 amino acid sequences of isolated clones show significant homology not observed in CDRH3 (Fig 2k).

I synthesised the prototypical BAR-1 clone as a Fab. Its binding against SiaLac was measured by surface plasmon resonance and isothermal titration calorimetry, yielding a Kd in the mid-μM range (data not shown). We co-crystallised the Fab with synthetic SiaLac-amidine-lysine, a soluble ligand identical to that found on the HEL-SiaLac immunogen. The structure of the complex was successfully resolved at 2.1Å (in collaboration with Dr Lucile Moynie, Rosalind Franklin Institute) (Fig 3a). The structure indicated that the dominant glycoconjugate contacts were between antibody CDRH1 and CDRH2 interacting with the sialyl-galactose component of the ligand, with the kappa chain accommodating the amidine linker. Interestingly, CDRH3 was minimally used in ligand engagement, which may explain the diverse D-genes among these clones (Fig 2f). Informed by this structure, I synthesised single-residue substitution mutants to determine the contribution of specific residues in recognising the glycoconjugate. Select residues in the heavy chain, including F37 and W57, played a critical role in antibody binding, with their substitution to alanine ablating ligand recognition (Fig 3b–d), consistent with the conservation of these residues amongst the clones. Interestingly, mutations in the kappa chain were generally better tolerated compared to the heavy chain, except for the KCY99A mutant (Fig 3e–g). Of importance, strong reliance on antibody binding by the amidine-recognising kappa chain may present a challenge, implying that B cells may need to be 'weaned-off' linker recognition via affinity maturation to enhance antibody recognition of the sugar in native contexts where a synthetic linker is absent.

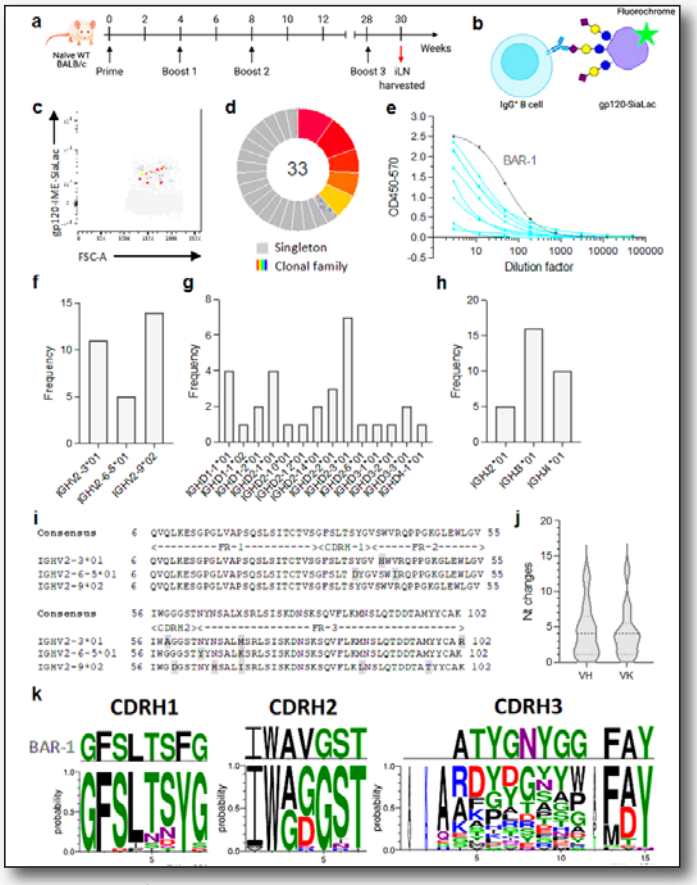


Figure 2: Clonality of antibodies mounted against the SiaLac glycoconjugate.
(a) Immunisation regimen. Mice were immunized subcutaneously with 10 μg HEL-SiaLac + 20 μg MPLA.
(b) Single IgG+ B cells that bound a gp120-SiaLac antigen probe were sorted.
(c) Sorted events, where colours are as per (d).
(d) Variable region sequences were recovered, and their clonal similarity was inferred according to their V(D)J identities determined using the NIH IgBLAST database. The number inside represents the clones isolated. Grey segments denote singleton clones and coloured segment sizes are proportional to the number of clonal family members (same V(D)J regions).
(e) Direct ELISA data of a subset of recombinant SiaLac-specific mAbS. Raw supernatant was screened against gP120-IME-SiaLac. The prototypical isolated mAb, BAR-1, is marked.
(f—h) Inferred HC VDJ region frequencies.
(i) Sequence alignment of utilised germline IGHV regions.
(j) Violin plots denoting mutation frequencies of isolated antibody clones compared with the iGL.
(k) CDRH amino acid sequences of isolated antibody clones.

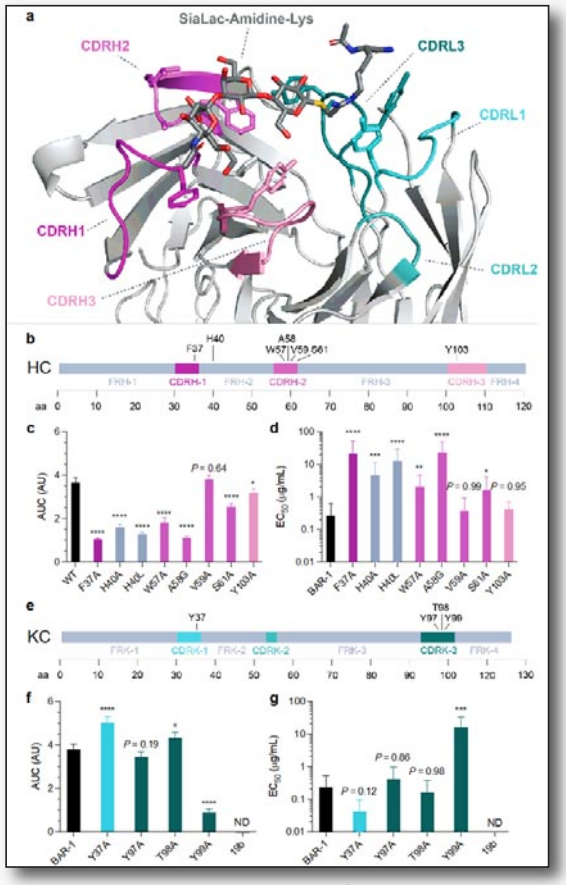


Fig 3. Structural and biochemical characteristics of the prototypical BAR-mAb
(a) Crystal structure of BAR-I Fab (ribbon) engaging its SiaLac-amidine-Lys ligand (sticks) (1.78Å). Complementarity determining regions of the heavy (pink) and light chains (teal) are marked
(b—d) Select residues of the heavy chain were selected and mutated Their bindng against HEL-IME-SlaLac were determined via ELISA. (e—g) Ljght chain BAR-I mutant scan
*(c, d; f,g) Data are represented as mean of three technical replicates + standard deviation. 19b is an unrelated HIV-specific mAb used as a negative control; ND = not detected. Groups were compared via one-way ANOVA and post-hoc Dunnetts multiple comparison test P-value denotations ****P<0.0001; *** P<0.001; and *P<0.05*

Conclusions and translational potential

These data provide proof-of-principle that synthetic glycoconjugation is an effective way of bolstering the immunogenicity of otherwise immunorecessive carbohydrate-based antigens. I now wish to investigate whether the induction of such antibodies is protective against, for example, a SiaLac-overexpressing cancer using an animal challenge model. However, regardless of the translational outcome of this approach, the evaluation of the clonal antibody response is instructive in revealing specific B cell germline-encoded motifs capable of engaging these sugars. Moving forward, we will use this information to improve the chemistry of glycan-linker designs to optimally target cancer and pathogen-associated carbohydrates.

Edeline Yee

The annual Beaconsfield prize, worth £1000 to the winner, is open to any bioscience graduate in the South Parks Road campus who has applied to transfer into their DPhil in the previous 12 months*. The Dunn School's track record is impressive. In 2014, 2016 (Philipp Kruger, Exeter College) and in 2018 (Scarlett Harris; Magdalen College) we had winners. More recently in 2020, Wearn Xin (Edeline) Yee (Tang Lab; Merton College Scholar) was a runner-up. Her essay is here https://canvas.ox.ac.uk/courses/22105/files/1434606/download. In 2023 Tabea Elsener (Tang lab again!: Jesus College) was a runner up. Hers is here (https://canvas.ox.ac.uk/courses/22105/files/6252297).

Tabea Elsener

*That means approximately 75 are eligible each year. Recently, the number of actual entries has been roughly one-fifth of those eligible.

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Net Zero by 2035
The Dunn School's fit within the University's target

In March 2021 following wide consultation, Oxford University's Council formally approved the new Environmental Sustainability Strategy[1], committing to achieve net zero carbon[2] and biodiversity net gain by 2035. Our University's Green credentials had already been significantly improving for several years. Now the new Strategy provides firm targets; methods for accounting and auditing; annual reporting[3] and publishing of outcomes. It also contains enabling policies including how to raise very roughly £200mn to pay for the capital costs. It offers all University members the opportunity to study environmental sustainability, either within or outside the examined curriculum. It stresses how everyone in the University must connect and engage with the Strategy.

1. Harriet Waters assessing suitability of University cycle racks

The Head of the University's Sustainability Team, **Harriet Waters** (HW), and its Deputy Head, **Tom Yearley**[4] (TY), kindly agreed to discuss with *Fusion* both the Strategy and the interface between the Dunn School and the University. In July 2022, **Saroj Saurya** (SS) and **Simon Hunt** (SH) met them in their office at the Malthouse in Tidmarsh Lane. Here's an abbreviated, edited digest of that discussion[5].

SH: In the [pre-Covid] year 2018/9 the University emitted 49,000 tonnes C_{eq} (excluding Scope 3[6]). The Dunn School's [share was] 5.2 percent, which is: 2,556 tonnes. That's not trivial. Approximately how much of the emissions can be eliminated? And how much is expected to be merely offset by the end of the Strategy?

TY: The Strategy has four priorities:

1. **"Spend to Save".** For a decade we've been finding energy saving and carbon reduction opportunities that will return the initial spend through energy savings…

> To date, we've averaged about 3½ years [rate of] return… on investment…There's still a huge amount of further potential to deliver more like that. We've estimated [we'll be] spending £40 million on our existing [asset] register across the whole University estate…. That will get us far in reducing overall emissions.SH: a

[1] https://sustainability.admin.ox.ac.uk/environmental-sustainability-strategy
[2] Definition of "Net zero carbon". *The University will account for carbon emissions associated with its Scope 1, 2 and 3 activities, reduce them as much as possible and then balance residual emissions through carbon offsetting to reach net zero carbon by 2035. The University will use its peak energy consumption of 2009/10 as its carbon baseline*". Oxford University in this context excludes Oxford University Press and all Colleges except Kellogg, Reuben and St Cross.
[3] The reports are at https://sustainability.admin.ox.ac.uk/annual-reports. Common questions about the Strategy are answered here: https://sustainability.admin.ox.ac.uk/strategy-q-and-a
[4] Tom Yearley wrote https://staff.admin.ox.ac.uk/article/how-to-decarbonise-a-university (March 2023). He has now moved on from his University post.
[5] The full transcript, 11500 words, is at https://t2m.io/Net0Interview
[6] Scopes 1 and 2 combined. Scope 3 is not included in these figures, nor are offsets and removals. The three Scopes are discussed later in this article. Ceq means all gases with "global warming potential" GWP, expressed as equivalents to CO_2. In this University, CO_2 itself is by far the predominant gas with GWP. One tonne is one Megagram = 0.984

particular example might be up-to-date "minus 80˚C"[7] ULT freezers?

TY: that's a really good example: [financial] returns in about 7 years. Another one might be lighting, or reducing thermal loss/gain through windows, walls, doors; installing LED lighting; better controls for lighting and heating/cooling; better insulation: all have a return on investment …the [recent] leaps in energy [prices mean] that the return on project investment is [now] a lot quicker and provides more significant savings than previously.

2. standards and "philosophy" documents. {For instance] our refreshed design guide[8] outlines sustainability requirements for new-build and refurbishment projects over £1mn value. The guide really provides our benchmark/reference point for sustainability in capital projects.

- it references energy efficiency standards such as Passivhaus
- it specifies some supply chain requirements …
- it examines biodiversity

SH: [Are…] design teams of major renovations or new-builds expected to implement these?

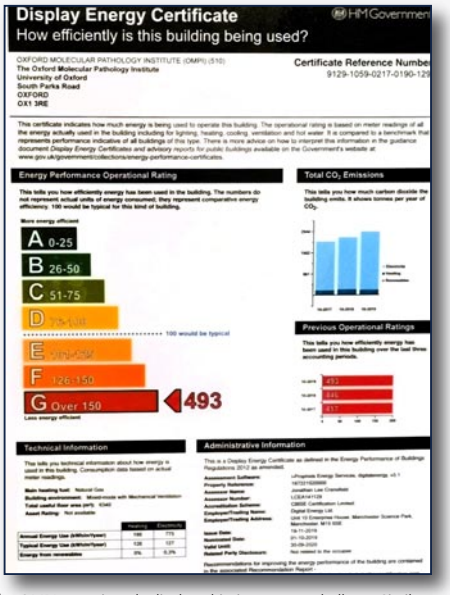
HW: …. It's a contractual obligation [to obey the standards]. Any derogations[9] … need to be flagged and managed.

TY: Over the last five years, physics of buildings, energy efficiency, biodiversity, embodied carbon … [are being] incorporated in the new design guide so that we're building even better buildings.

3. heat decarbonization: removing natural gas from the university's energy portfolio. It is a priority because burning natural gas on our estate is - apart from perhaps refrigerant release – our only direct release of CO2 to the atmosphere….

SH: [What about] dry ice [and liquid] CO2[10]?

TY: That'll be an interesting one!
Throughout the supply chain, someone else is […emitting Ceq] on our behalf. But natural gas is the one that we directly control. We can choose to remove it from our supply. We have recently completed an initial survey of [those University] buildings that use about 70% of our total natural gas…
In … the Dunn School, heat decarbonization has a big potential for reducing overall carbon emissions. [It depends on] an underlying assumption about the electrification of heat because of the ongoing decarbonization of the electricity grid in the UK. ….



2. DEC for OMPI, prominently displayed in its entrance hallway. Similar certificates are on display in each of the four Dunn School buildings. It's a game of hide-and-seek to find them. A small prize of Dunn School merch will go to the first person who emails correct photos of all four taken on their own camera to alumni@path.ox.ac.uk

As we progress to 2035, we expect more significant reductions in the carbon associated with the electricity we use[11].

4. everything else

- measurement verification: data quality, integrity and reporting. We really must get a firm grasp on our data.
- carbon offsetting. We agreed … not to discuss [this] in any detail until 2025. …What's the right way? … Is there an acceptable way to undertake offsetting[12]?

HW: We also want to see the market [for offsetting] mature… Our initial modeling suggested something like a 77% reduction in our carbon emissions by 2035. That [estimate] is likely to change very rapidly…We … will have to offset [everything else]. Not every university has [made that explicit decision] …
…Actually, our old buildings are not a big problem. They perform better than our newer buildings. If they're running quite well with gas …and if there's lots of issues in taking gas out, then we're going to leave them alone.

TY: That heat emissions map [of major University buildings in 2018] clearly demonstrates that. The hundred lowest-emitting buildings [put together] still [are] only the second largest emitters[13].

[7] We must stop calling them "minus 80". The default setting for Ultra-Low Temperature freezers in the Dunn School is now minus 70˚C. The amount of energy saved varies, depending mostly on the way they are used (Kammueller Pont (2023)). The higher temperature can reduce electricity use by up to 30%: Jain (2022) https://doi.org/10.1038/s43586-022-00126-6

[8] The previous Design Guide for Oxford University operated since 2014: https://estates.web.ox.ac.uk/files/buildingdesignphilosophydocument-lmupdate171114.pdf. It did not mention biodiversity and it relied on "energy efficiency", unspecified, to enhance sustainability.

[9] The lowering or partial breach of a required standard, due to a counterbalancing reason

[10] See "It's just a gas!..." article in this issue of *Fusion*

[11] The university buys more expensive "100% renewable" electricity but calculates carbon impact using an average national figure for the carbon intensity of electricity generation which includes fossil fuel.

[12] See https://www.smithschool.ox.ac.uk/sites/default/files/2022-01/Oxford-Offsetting-Principles-2020.pdf

[13] Available to University members via Single-Sign-On or from simon.hunt@path.ox.ac.uk on request. The University as defined in footnote 2 operates an estate of 235 buildings of which 44 are in the Science area and Keble Road triangle. The Dunn School occupies all or part of four of them: the Old Building (opened 1927; internal floor area 2779 sq m; C_{eq} emission intensity 0.09 tonnes/sq m/year); PSB (1997; 2202 sq m; 0.25 t C_{eq} /sq m/yr); EPA (2001; 2544 sq m; 0.11 t C_{eq} /sq m/yr); OMPI (2011; 6340 sq m; 0.23 t C_{eq} /sq m/yr). Data available publicly from DECs.

SH: [Let's turn to] Display Energy Certificates, DEC. Anyone who enters our newest building, OMPI, can't help noticing the one there. It has a big red arrow at the bottom pointing to "G", for the energy rating (Fig. 2). Most people know that houses, even old ones, are generally rated "D"s or "C". Why on earth does our nearly new building get the poorest rating, "G"?
HW: Let's go into the story of ... DECs.
TY: There are two very similar-looking documents: a display energy certificate (DEC), and an energy performance certificate (EPC). What's the difference[14]? EPC is generally associated with domestic [buildings, although] they're also relevant to commercial properties. They outline the specification of the building [relating to energy efficiency]: things like:- solar panels, insulation, [thermostat and lighting controls] etc.

[Unlike EPCs] DEC is based on actual [metered] energy consumption. We fill in annually [the data from the meters to] a national online tool. It pumps out this score. [The grade number and the letter are grade-scores relative to comparable types of buildings nationally]. It's very difficult …for any of our laboratory buildings to ever be much more than a G. [For us] it's much more useful to see which of those lab buildings are more relatively more efficient on the estate. As you say, it's really disheartening to see the DEC with a score of 493, relative to a group of other buildings.

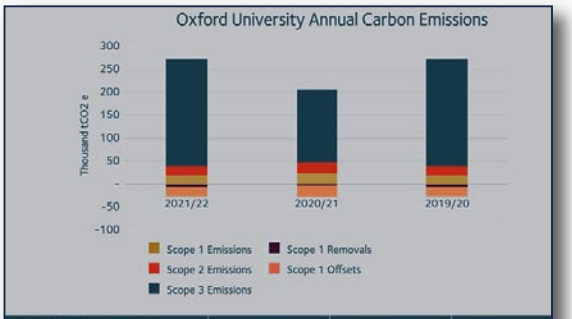
HW: …We like the fact that it raises awareness, but we don't like …that it worries people that they're a G…

TY: We've toyed with … [some kind of] "league table" … normalized [to] carbon per square meter or per person, but …it's more important to understand your carbon emissions at Divisional, Department or Building level, then choose the areas that you can specifically focus on. If behavioural change and your people are the biggest impact, let's [contact] the people and find out what they can do. If you've got an old heating system that needs replacing, focus on that. Even within your department it's difficult to compare one building to another…

SH: This [the annual DEC data] is all public information. You can look it up online on Government webpages[15].

HW: … [The University is] not public-sector, but we've [decided to count ourselves] as public-sector, which [also] helps us with some of our legislative requirements.

SH: [Let's move to] Scopes One, Two, Three[16]. …



University of Oxford Carbon Emissions (tCO2e)	2021/22	2020/21	2019/20
Scope 1 Emissions	19,854	25,009	18,097
Scope 1 Removals	- 4,534	- 4,534	- 4,534
Scope 2 Emissions	20,737	21,487	22,883
Scope 2 Offsets	- 20,737	- 21,487	- 22,883
Scope 3 Emissions	230,823	158,406	229,356
Total Gross	271,414	204,901	270,336
Total Net	246,143	178,881	242,919

3. Annual Oxford University Ceq emissions, removals and offsets, by Scope. Scope 2 emissions are from electricity consumed, accounted for as fully offset because the University buys 100% renewable. Graphic from https://sustainability.admin.ox.ac.uk/files/environmentalsustainabilityreport21-22pdf.

HW: Simplifying a bit, Scope One is where we are emitting on-site. [Most] of that is our [University-wide] gas consumption [mainly to warm our buildings], but also dry ice or refrigerant emissions or fleet emissions from vehicles. People always say: but what about [such and such]? When we…measure them, they are all tiny in comparison to our gas consumption - *de minimis*[17]!
Scope Two is electricity consumption. We control how much electricity we use, and we've got control over the source of that electricity, but it's not us [the University] emitting the carbon. We buy 100% renewable electricity at the moment. [For] the most recent work on our accounting for carbon, we now treat that as zero carbon because we pay extra for that electricity [to be] zero carbon. We …still want to encourage people to reduce the amount of electricity they use. Heat [however] is more of a focus for us.

Scope Three is absolutely everything else. … [It is hard to quantify] 'cause we [mostly] don't have good data. We [do have] great data from Merck[18] and Dell. We talk very regularly with colleagues in the sector about how they're [accounting for] Scope Three. We are in the forefront [compared] with other universities. A new sector methodology [is coming on] for calculating carbon emissions, which very heavily draws from what we've already published….

SH: [Scope 3] could be the biggest of the three components.

[14] In a nutshell, see http://compliance365.co.uk/what-are-the-differences-between-epcs-and-decs/. The UK Government is considering a modified "performance-based" rating system for commercial buildings but it's not yet in effect.
[15] www.gov.uk/find-energy-certificate Search by postcode. Old Building and OMPI: *OX1 3RE*. EPA: *OX1 3PL*. PSB: *OX1 3RJ*.
[16] Definitions of the three Scopes and how they affect carbon accounting within the University are in this 55-page methodology report published in 2019/20: https://sustainability.admin.ox.ac.uk/files/emissionsaccountingreport.pdf. See pages 6-7 there. The University's Environmental Annual Report, a very readable 20-pages, explains Scope 3 simply: "*Scope 3 emissions include all indirect emissions, which come from sources owned or controlled by other entities in the value chain and third-party payments. These include materials suppliers, third-party logistics providers, waste management, travel, etc*". https://sustainability.admin.ox.ac.uk/files/environmentalsustainabilityreport21-22pdf
[17] Latin, meaning: *too trivial or minor to merit consideration*
[18] Merck owns and controls Sigma-Aldrich, the major UK lab chemicals supplier. Searches of its catalogue can now be filtered for "Greener Alternative Products". "MyGreenLab" is a database run by ACT, a US-based not-for-profit, with an extensive classification system for eco-friendly lab supplies of instruments and reagents. https://actdatabase.mygreenlab.org/

HW: We definitely know that already (Fig. 3) – potentially around ten times as much as Scope One….in the university as a whole.

TY: …[in] the laboratory supply chain. And the amount of travel…

HW: Construction … is one of the biggest.

SS: The supply chain, they need to do more. … I talk to the [sales] reps all the time … "What's your sustainability goal and what are you doing about it?" ….
TY: That's really important. The more questions we ask of our supply chain, then we'll answer those questions [about accounting for Scope 3].

SS: About the gas: I don't know how you're going to [account for] that…

TY: EPA [building has] a direct gas supply to the building. [Many] Science Area [buildings] won't have a direct gas supply, but they'll be linked to one of the boiler houses [which] receive the gas. They [provide] hot water [which] is circulated around loops to the buildings.

HW: It [decarbonizing heat] will be a very long project with a lot of potential disruption. It'll involve digging up [and] shutting roads. But we are not even at the design stage yet and as this technology changes all the time we don't have a clear picture of what to expect.

SS: [Is the] heat source in discussion with the Dunn School?...

TY: … heat decarbonization certainly. Possible installation of air-source heat pumps in the EPA pathology building is being looked at…

SS: … Is it possible to include more solar panels around[19]?

TY: This week, we've sent a surveyor to, 5 or 6 buildings to explore … additional solar panels. Before my time we did a huge survey on solar panel opportunities around the University. Harriet [Waters] oversaw the roll-out of all the best opportunities. Many weren't viable because they wouldn't return on investment. With energy prices almost trebling over the last year, almost any solar PV installation will pay back.

HW: It's not just the finances, [but also] shading and what the local [electricity] network can accept….

TY: The condition of the roof [matters too]. If the roof [will have to be replaced] within 20 years, it's generally not viable for PV [photovoltaic] panels.

SH: [How] will [heat, light and power to] the Dunn School be reduced and how it's going to happen within 13 years [from now]? …

TY: The heat decarbonization plan [proposes options for] heat networks or … heat pumps; how we can share waste heat and waste cooling, across the Science Area. [Over the next… two to three years] we're hoping to develop that into a strategic delivery plan [via] considered steps towards …large … infrastructure projects. There's … efficiency work; … lighting, heating, insulation - to be … getting on with … learning from other institutions who have [already] undertaken this work…. Then over the next … four or five years, perhaps start implementing those infrastructure projects….

The value of engaged departments shouldn't be underestimated. We wouldn't be able to do this without the support of departments…. Heat decarbonization is about reducing the reliance on or removing natural gas by:
(i) sharing the waste energy from buildings, by [liquid] - not necessarily water, but some sort of wet medium network
(ii) installing renewable heat sources.

SH: ... [What is the] progress towards meeting the [2035] targets? … how far you are going and how fast...?

HW: [We report annually, and we definitely will continue]. It is on our website[20] [and] through our comms [communication] streams[21]. ..Comms in general in the university is … a very noisy place and our stuff doesn't necessarily get picked up. Quite often information … from Central University [appears] less interesting to people in departments [who are] much more interested in what their departments are saying.

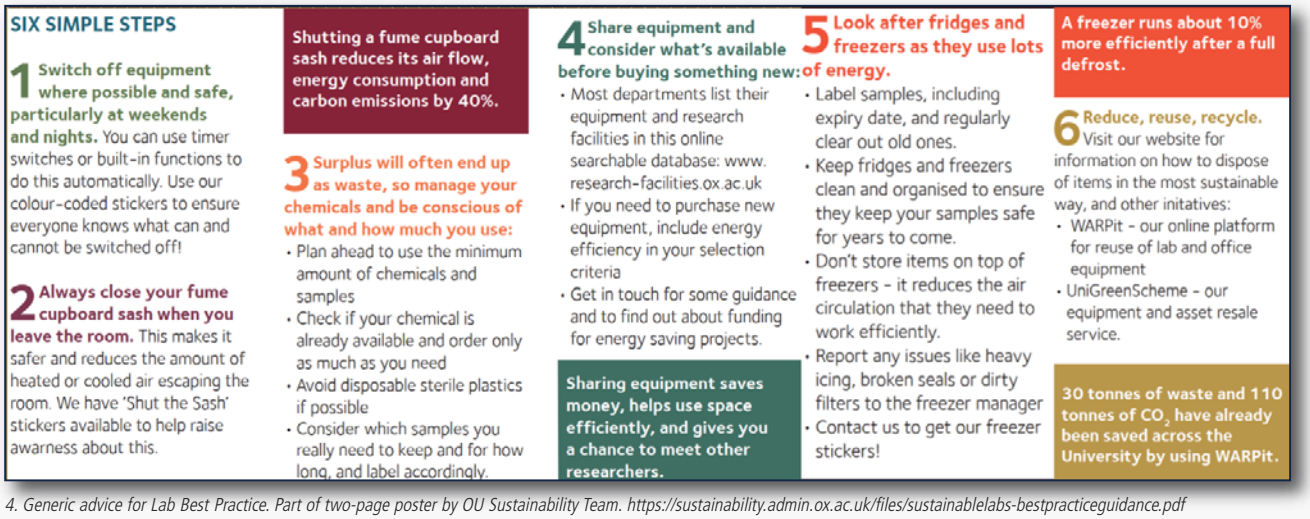
Departments can [usefully] amplify what we say. We tend to try to use our comms networks to say: "*This is some content that you can use*". Medical Sciences [Division] [have] a very active comms department who proactively come to us.
…We're a tiny team[22]. [What we produce] is as generic as it can be, to reach as many people as possible.

SH: What could we do to help make it [communications] effective?

SS: Whenever I write something, I say: "*with the help of Sustainability Team*". We're not alone. We get help from them, and they help us. … That's my plan: just get everybody involved; that's how we can do it.

HW: That's why we put the funding into LEAF[21] and Green Impact[23]. It empowers people on a departmental basis to make improvements….

[19] The present installation on OMPI is rated at 26 KW (peak)
[20] https://sustainability.admin.ox.ac.uk/annual-reports
[21] https://sustainability.admin.ox.ac.uk/leaf
[22] https://sustainability.admin.ox.ac.uk/about-us
[23] See https://sustainability.web.ox.ac.uk/labs and https://sustainability.admin.ox.ac.uk/sites/default/files/sustainability/documents/media/green_impact_-_programme_user_guide_sept_2023.pdf and the article by Saroj Saurya in this issue of *Fusion*.



4. Generic advice for Lab Best Practice. Part of two-page poster by OU Sustainability Team. https://sustainability.admin.ox.ac.uk/files/sustainablelabs-bestpracticeguidance.pdf

SS: That's really good. These things motivate people… We work as a group. I think that is the key. It's important to do [it] every year, rather than leave them for three years. [People] might come up with [new] ideas. …We have a lab meeting every week. I talk about Sustainability because people do forget. All these VC awards definitely motivate.

HW: But it will turn some people off! We have to be careful about [that too]!
The new Environmental Sustainability Subcommittee[24] has Divisional representatives. [Anyone in your department] could approach your divisional rep [with suggestions or queries]: he's Prof Peter Scarborough

> […Brief discussion about financial accounting of our solar PV panels…]

SH: …Is there anything that you would like [us] to publicize? ….

TY: More LEAF teams. More Green Impact[23] teams. Engagement is really key…. Highlighting opportunities. Building users know their buildings a lot better than we do…such as: rooms that are always hot or always cold when they shouldn't be. Areas that are always lit. … At 1 o'clock in the morning is there a building lit up like a Christmas tree? These sorts of things are obvious and are … often the quick wins …

SS: Involve students more … because they have to be the future. …Advertise more [at] induction…

TY: I agree, and … it's [particularly] postgraduate …students. … That's when … lifetime habits are formed, [to ingrain and embed sustainability] in the beginning of their post-graduate career…It's often completely omitted from doctoral candidate inductions….

HW: … 'Curriculum' is in the [Sustainability] Strategy… a subgroup [is reviewing] curriculum content…We need [our] 'product' [students] to be sustainable when they go out into the world…. It's down to departments to encourage their students to be more sustainable. We…work with departments to think of good ways. Induction is one that gets mentioned a lot.

SH: Reducing air travel is an obvious low hanging fruit… that message is pretty high profile….no more flights to Brussels and Paris! [see 'Rethinking Academic Travel' in this Fusion issue]

SS: …Some of the PIs say "…we have to fly; …. even though we have to pay [air travel] levy charges[25] [to the University] …."

HW: …When they're writing research bids, [PIs] need to budget to travel [by a mode] that's non-air travel….That's real leadership that we've taken. … Other universities [also] have a flight reduction target, but then [nothing] under it. By attaching a levy to it, [our] data [will] get much better

SH: It's also bottom-up. …a fifth-year medical student [recently raised the question]: should we really be going on electives to Hawaii and so on for five weeks[26]?

HW: Absolutely. That's happened in Earth Sciences as well, [and in] an academic group called Flying Less[27], [who have produced] a whole podcast series. [Our] levy is quite low… That's the best thing about Oxford, isn't it? You do something [worthwhile]; everyone [repeats it]; and it has some impact.

SS: Definitely incentivize people [to take] the train rather than [fly]. [If possible] they should not travel anyways [in the] first place.

SH: So now [when PIs prepare their grant applications, they've]

[24] https://governance.admin.ox.ac.uk/environmental-sustainability-subcommittee oversees the implementation of the Sustainability Strategy. It has representatives of both students and academic staff and meets twice each term.
[25] The University's income from the flight levy, currently £30 per tonne Ceq, is wholly hypothecated towards funding all its Sustainability projects, including, for instance, decarbonisation.
[26] Sarah Peters in *Oxford Medicine* page 45 https://issuu.com/oxfordmedicalalumninewsletter/docs/oxford_medicine_summer_2022_final_print
[27] https://sites.tufts.edu/flyingless/ #flyingless.

©Katherine Ansbro INEOS lab

Fig. 6 Dunn School awards at Vice-Chancellor's ceremony, June 2023. L to R: Aashna Saini, Saroj Saurya (both Raff lab), V-C Prof. Irene Tracey, Wayne Swan (Dunn School Facilities Manager), Martin Smith (Workshop)

got something to [justify] it: …it's obligatory university policy: 'we've got to go by train'.

HW: Exactly. We are talking to funders [to make this] acceptable….

SH: [Regarding] feedback mechanisms to the Sustainability Team from the Dunn School: What you would like to know? From active groups like the Green Group?
HW: Keeping on talking. That is also the point of LEAF and Green Impact, 'cause we then get everything back.

TY: We have one of the most fluent dialogues with the Dunn School, out of all the departments … [along with some others] where we have good operational conversations….

SH: Finally, down to the individual level. [What can] each person do[28]? … How much notice are people actually taking? … [For instance] those little stickers showing how far you [should] leave the sash open [on ventilated work cabinets] … Many people tend to ignore them… "1, 2, 3…. these are things you can do!"

HW: People love these, don't they? … The central University [considered] new ways of working because of the pandemic. We [offer] sustainability tips … it's a changing time. …What are top three tips?[29]

- Just **turn off energy when it's not being used**. Turn off the electricity. Turn things off at the plug. Turn things off when you go moving away from your desk. Standard boring advice, but it's the thing that will help.

5. Dunn School wins GOLD! ©Wayne Swan

TY: It is the single most important thing. **If it's not being used: Turn it off. If it is being used: Turn it down**.
- consider **[your] commute and its impact**. …We understand that's … a difficult message …
- **get involved in Green Impacts and LEAF**….

SH: you've been very good with your time. Thank you ever so much.

Planet-sharing reader, our University is a large institution with centralising tendencies. What do you think of its policies and achievements on Sustainability? What has it got right or wrong? Maybe missing something important? Would you like to influence decisions, or help create opportunities to study and learn, about Sustainability? Stay informed about the Sustainability Team https://sustainability.admin.ox.ac.uk/news. Browse https://linktr.ee/oxfordenvsust. Follow @oxfordenvsust on X/Twitter or Instagram; or Facebook. As usual, comments or suggestions to alumni@path.ox.ac.uk. We'll pass them on.

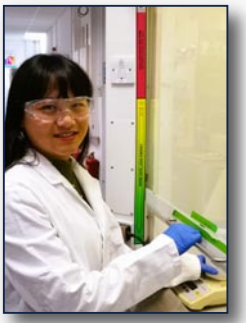
To use the links in this article visit https://t2m.io/DunnNet0 or use the QR code

[28] See https://sustainability.admin.ox.ac.uk/your-first-five-steps-for-environmental-sustainability
[29] See the summaries at https://sustainability.admin.ox.ac.uk/take-action for plenty of suggestions that each of the 24000 students and 16000 members of staff of the University can pursue.

Greening the Dunn School: who has the LEAFiest labs?

Well-informed reader, you'll know that the Dunn School has a vigorous Green Group. It is energetically led by **Saroj Saurya**[1], scientific manager of the Raff Lab. She urges us to cut down on single-use plastic and to (re- re- re- re-) recycle as much as we possibly can. Here she explains how the Group communicates the Green message and how LEAF awards help this.

The Dunn School's Green Group germinated from seeds sown in January 2020 by Anton van der Merwe, with enthusiastic and committed backing from our Head Landscaper, Matthew Freeman. Wayne Swan and Philip Cobden, who have day-jobs as senior service managers in the department, play vital roles as joint Head Gardeners alongside myself, Saroj. Enthusiastic Under-Gardeners from several lab groups swell the group's numbers. They push for collective action to save our world from extinction due to anthropogenic climate change. How does the Group synergise in the Dunn School Garden?



Yuqing Zhou from the INEOS lab shows the safe, eco-friendly use of the cabinet

Each of its members promotes overlapping Green special interests that they particularly want to nurture. As keen volunteers, their hard work and passion inspire others within and beyond the Group. Regarding practical matters, they practise what they preach, namely: adopt the path to Net Zero. For instance, some commend washing and re-using lab plasticware – don't discard it as "single-use"; some promote recycling of packaging (examples: Styrofoam boxes and racks for pipette tips); some are keen on lowering Ceq footprints of travel – both the daily commute and long-distance, to conferences etc.; some push to minimise energy usage in day-to-day lab activities – for example, be safe and frugal with lab cabinets by lowering that sash; and for ULT freezers, minus 70 is the new minus 80; some focus on minimising the Ceq footprint of the department's menus and refreshment facilities; some highlight re-use of research lab instrumentation, furniture and IT equipment[2]; some promote sharing ordering lab supplies and saving delivery costs when possible. We urge every labgroup meeting to regularly include a 5- minute Green issue on its agenda. The suggestions go on and on. Actions by each individual accomplish a great deal when added together.

The messages of the Group can be seen everywhere in the department: by e-newsletters; by X/Twitter; via our brand new website; by Instagram; by rolling screen projection in the Bridge Café; by fostering climate awareness weeks; by co-ordinating surveys of members of the Dunn School about attitudes and suggestions on environmental issues. Flying the Dunn School Green Group flag tells the outside world that we mean business [see front cover]. Theming this issue of *Fusion* on the Net Zero objective also sends the message.

Some Green Group members, in GoGreen T-shirts, Summer 2022

Climate action "hero's award" ©Dunn School

The Group's many initiatives accelerate the Dunn School as the leading environmentally sustainable department in the University. The dedicated work of the Green Group has been recognised publicly. They received the Oxfordshire High Sheriff's climate action "hero's award" in February 2022[3]. They won Vice-Chancellor's leadership awards for environmental sustainability, presented in the Sheldonian Theatre in June 2022[4]. The Green Group works closely with the University's Environmental Sustainability team, helping to formulate and implement the University's

Celebrating the LEAF Champions Award in the Sheldonian, 2022

[1] Read the blogpost by Saroj: *Sustainable science: Tips from the Raff Lab*" at www.babraham.ac.uk/blog/doing-sustainable-science

[2] WARP-IT (90-second explainer video: https://youtu.be/OTHmESRmCmE) and the Unigreen schemes facilitate the exchange and handing-on of unwanted fully functional lab items of all kinds: https://sustainability.admin.ox.ac.uk/warpit/reuse. To use them, you need to register (just once) via your ox.ac.uk account.

[3] See www.path.ox.ac.uk/news-article/green-group-celebrates-high-sheriff

[4] https://sustainability.admin.ox.ac.uk/article/vice-chancellors-environmental-sustainability-awards. The Awards Brochures for 2022 and 2023 display the very wide range of activities across the whole University. Have a look at them and count the number of times that the Dunn School is mentioned. https://sustainability.admin.ox.ac.uk/files/vcawardsbrochure2022.pdf and https://sustainability.admin.ox.ac.uk/sitefiles/vc-awards-brochure-2023.pdf

Dunn School LEAF award-winners with University Sustainability Team, July 2022

sustainability strategy [see *Net zero by 2035* in this issue]. Together with them, the department piloted the nationally-recognised Laboratory Efficiency Assessment Framework (LEAF)[5] awards, an expanding scheme that provides a standard for auditing and accrediting research labs around the world to improve sustainability and reduce their carbon footprint. In 2020 four labs at the Dunn School were accredited. Then in 2021 an impressive 13 labs gained their LEAFs (LEAVES?] – which was more than the rest of the University put together. (Surely it's time for them to take a LEAF out of our book 🙂). In 2022, all but one of the 41 labs and areas of the Dunn School achieved LEAFs. Awardees proudly post their sustainability credentials on social media, in email signatures, in CVs and grant applications and so on.

Saroj Saurya with the Vice-Chancellor June 2023 ©Aashna Saini

Fusion's editor adds: Saroj herself is an extraordinarily energetic dynamo, leading by her very committed example. She urges everyone in the department to join in schemes like LEAF and Green Impact. Because of her efforts in leading the Green Group, participation levels within the Dunn School stand out among the University's departments. The collaborative efforts have been publicly recognised in the Vice-Chancellor's Awards. They culminated in 2023 with superlative distinction of Saroj as this year's Winner of the Environment Sustainability Staff Award. Here's the photo of her receiving it from Prof. Irene Tracey in the Divinity School. Small steps by each of us all add up. A compelling Scottish motto says: "Many a little makes a mickle"[6]. How true! Every country has a saying like this. If you're an international reader, please tell us yours. Send it to alumni@path.ox.ac.uk, along with your own tips for greening labs and spreading the message. We'd love to publicise them!

Text: © Dunn School

[5] www.sustainabilityexchange.ac.uk/leaf_a_new_approach_to_achieving_laboratory_sustainability. Germinated at UCL www.ucl.ac.uk/sustainable/leaf-laboratory-efficiency-assessment-framework

[6] Memorably but crudely translated by the UK supermarket Tesco as "Every little helps!" Often misquoted as "*Mony a mickle maks a muckle*"

Rethinking academic travel

Joséphine Groslambert is a DPhil student in the Ahel lab, studying ADP-ribosylation. She's been a member of Green Group since 2020. In this article she examines scientists' selections of modes of travel for work purposes. This is the area of the professional activity of a typical scientist's that generates the biggest Carbon footprint over which they have direct choice. Following consultation then enactment by Council, the Travel Policy[13] of Oxford University came into force from August 2022. It applies to all travel that it pays for or reimburses. How might this be influencing scientists' choices, and will it work?

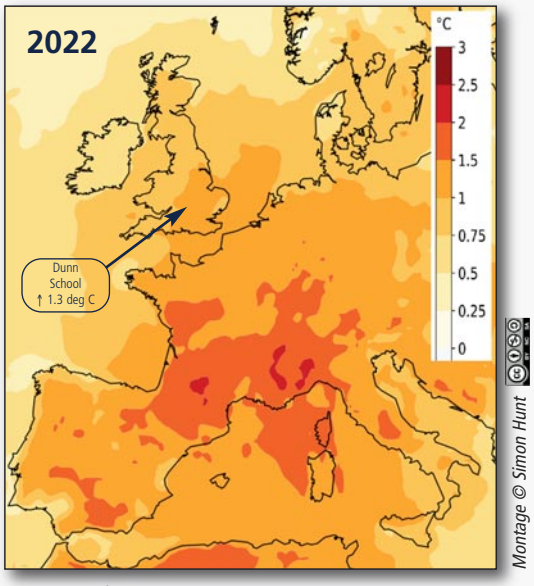
Connecting with fellow researchers across the globe, presenting one's work and engaging with an international scientific community can be among the most rewarding experiences of a career in academia. Before the COVID-19 pandemic, many researchers became frequent flyers when they attended conferences, gave seminars or met collaborators. The interruption of in-person conferences during the pandemic highlighted the uncomfortable drawback that air travel contributes significantly to the carbon footprint of academia[1]. For example, one return flight from London to New York releases around 2 tonnes of CO_2 per passenger[2] which is, on average, roughly equivalent to the annual amount produced by a fossil-fuelled car in the European Union. In hosting thousands of researchers from across the world, academic conferences have an

Global Temperature ↑ **1.2** °C (more) above pre-industrial level	**European Temperature** ↑ **2.2 °C** (more) above pre-industrial level	**Arctic Temperature** ↑ **3.0 °C** (more) above pre-industrial level
Carbon Dioxide (CO_2) **417 ppm** (more) annual average level	**CO_2 increase** ↑ **2.4 ppm per year** (more) since 2010	**Methane (CH4)** **1894 ppb** (more) annual average level
Global Glaciers ↓ **8600 km³** (more) ice loss since 1997	**European Glaciers** ↓ **960 km3** (more) ice loss since 1997	**Greenland Ice Sheet** ↓ **5850 km3** (more) ice loss 1992 - 2020
Global Sea Level ↑ **9.7 cm** (more) increase since 1993	**Global Sea Surface Temp** ↑ **0.5 °C** (more) increase since 1980	**Arctic Sea Ice Extent** ↓ **2600000 km²** (more) Sept loss, 1980s-2010s

Montage © Simon Hunt CC-BY-NC-SA 4.0. Data from: https://climate.copernicus.eu/climate-indicators Image: by EU_Copernicus

especially high carbon footprint. Air travel by University-paid staff for work-related purposes created about 30,000 tCO_2e[3] annually, according to the University's Sustainability Team. This corresponds to around half of the yearly carbon emissions of all the buildings on the University estate. Air temperatures in 2022 rose to unprecedented highs in the UK, Europe and globally[4]. These days, our own senses experience the climate emergency directly. What each of us sees and feels agrees fully with detailed global systematic quantitative surveys. Locally in Oxford, the Radcliffe Meteorological Station[5] next to the Tower of the Four Winds in the grounds of Green-Templeton College has a continuous daily record back to 1813, with some observations extending to 1772. Modern instrumentation, satellite-based with supercomputer number-crunching, is nowadays providing a much more accurate, time-resolved and thorough picture over the whole planet. The app at the EU's Copernicus site tells us hard truths – it's an excellent resource[6].

In this context reducing air-travel should be seen as a low-hanging fruit that can decrease considerably a researcher's carbon footprint. It's a choice that each individual can mainly make for themselves and thereby make a significant difference.



Montage © Simon Hunt

Overheating of Western Europe in year 2022, relative to the last thirty years. Colours indicate the mean air temperature anomaly in 2022 above the average for 1991-2020. Add about 0.8°C to compare with pre-industrial levels, the "global warming" baseline. Data source: ERA5. Credit: C3S/ECMWF. Copernicus Climate Change Service

1 "*During the pandemic, flights bought through the University's preferred supplier dropped by over 95% compared to 2018-19, the last full year before the pandemic. This represents carbon savings of an estimated 28,500 tonnes.*" (O.U. Sustainability report 2020-21)

2 Calculated just as the CO_2 produced by the combustion of the conventional jet fuel (kerosene) burned. This excludes upstream or downstream emissions (for instance in the production and transport of the fuel to the plane's tanks). It excludes the embedded carbon in the plane's manufacture and testing, or the operation of the airport terminals etc etc. It excludes the climate-warming potential of other products released (nitrogen oxides; water vapour; particulates) as fuel is burned for taxi-ing and flight. A typical modern commercial jet plane emits about 90 g CO_2 per passenger-kilometer. A fully tanked-up Airbus A320neo holds about 30000 litres of fuel which weigh 24 tonnes. When completely burned, this generates around 75 tonnes of CO_2. (Data from Airbus and International Council on Clean Transportation Report 2019 and ICCT Factsheet)

3 tCO_2e means "tonnes of carbon dioxide equivalent", that is, emissions that over 100 years have the same global warming potential as one metric ton (one Megagram = 106 grams) of CO_2. Definitions are at https://sdgdata.gov.uk/13-2-2/

4 "*There is a 66% likelihood that the annual average near-surface global temperature between 2023 and 2027 will be more than 1.5°C above pre-industrial levels for at least one year. There is a 98% likelihood that at least one of the next five years, and the five-year period as a whole, will be the warmest on record.*" World meteorological organisation, May 2023.

5 www.geog.ox.ac.uk/research/climate/rms/intro.html

6 https://climate.copernicus.eu/ The colours in the heat map refer warming above the 1991-2020 average, not to the warming above pre-industrial, which would require adding a further 0.8° C approximately.

What the COVID-19 pandemic changed

When the COVID-19 pandemic put a halt to in-person meetings, scientists at the Dunn School and across the globe adapted to the use of virtual format for conferences, seminars and workshops[7]. Shifting to a virtual setting highlighted some disadvantages of face-to-face conferences beyond their contribution to climate change. Many scientists are unable to attend in-person conferences for financial, visa or caring-responsibility reasons, thereby creating inequalities within academic communities. By removing the need to travel, virtual conferences are inherently more inclusive. Virtual conferences can also allow for unprecedented level of scientific discussion by enabling a multi-fold increase in attendance and promote a wider audience participation, through online forums for example[8]. The pandemic also led to the development of many interactive streaming platforms such as Gather.town, Remo and Sparkle, that greatly enhanced the virtual conference experience.

Transitioning into a post-pandemic world

More than two years after the pandemic, air-travel is picking up again, including by researchers. While everyone is relieved that restrictions affecting our research work ended, the transition into a post-pandemic world is an unprecedented opportunity to reimagine academic travel and conferences to make them more sustainable. The Dunn School Green Group has been thinking about potential solutions to reduce departmental air-travel and started discussing flight reduction with several Dunn School group leaders. Many of them said that they would not fly as often as they had before the pandemic. At least six PIs took the lead and publicly committed to reduce their flying. In their pledges, they propose to reduce air-travel by measures such as giving priority to online meetings when possible, travelling by train for destinations within 6 hours, assessing the pros and cons of long-distance travel and, if flying, combining several activities into one trip[9].

The Oxford University Travel Policy

Each individual's choice to change is important. The fact that several Dunn School PIs have chosen to fly less deserves praise as it should inspire more researchers across the department to follow their lead. In the face of climate change urgency, we also need long-lasting significant changes to be driven by institutions themselves. Some funding agencies now incorporate sustainable travel in their policies. For example, the Wellcome Trust requires grant-holders to reduce the environmental impact of their travel[10]. Recipients of their funding must minimize their travel by using virtual alternatives and choose travel with a lower carbon impact. The Trust commits to pay for low-carbon travel options and/or for carbon-offsetting even if these are more expensive: researchers should include an allowance for this in their grant applications.

In 2021, the University of Oxford approved its Environmental Sustainability Strategy[11] which sets a goal of achieving net zero carbon by 2035, along with a net gain in biodiversity. Reducing aviation emissions[12] caused by

University staff and student travel is one of the ten priority areas of the strategy. A new travel policy[13] came into effect for all travel on University business since August 2022. Virtual alternatives to air travel, and/or rail travel, are strongly encouraged. Rail should be used for all domestic journeys under 7 hours as well as for journeys to Paris and Brussels. The policy also sets a target of reducing CO_2 emissions from flights by 20% by 2024/2025 and 35% by 2035. The University Environmental Sustainability team urges all departments to follow the policy guidelines9 in order to meet this target. Staff and students need to determine which of their travel plans to prioritize in order to decrease the number of trips, to reduce long-haul flights which contribute the most to CO_2 emissions, and if flying, to choose economy class flights, which have the lowest emission profile per passenger. A flight levy of £30 per tCO_2e for all flights paid for or reimbursed by the University will be recharged to departments. The levy income will be allotted to the Oxford Sustainability Fund to implement the Environmental Sustainability Strategy, which over he next 12 years will need well over £100mn investment.

While imposing a flight levy is definitely an important strategy to lower the CO_2 emissions associated with flying, the Green Group has concerns that the current policy might not sufficiently incentivize reduction in air-travel. As presently designed, it will only impact departmental finances, and not frequent conference flyers. The departmental committee, inclusive of all

[7] Sarvenaz Sarabipour (2020) "Research Culture: Virtual conferences raise standards for accessibility and interactions%. eLife. https://doi.org/10.7554/eLife.62668; Milan Klöwer *et al.* (2020) "An analysis of ways to decarbonize conference travel after COVID-19". Nature. 10.1038/d41586-020-02057-2

[8] Sally Lowell *et al.* (2022) "The future of conferences". Development. https://doi.org/10.1242/dev.200438; "Academic Flying and the Means of Communication" Book edited by Bjørkdahl, K et al: https://doi.org/10.1007/978-981-16-4911-0

[9] Summarised in the University Sustainability Team's Travel Hierarchy

[10] https://wellcome.org/grant-funding/guidance/carbon-offset-policy-travel

[11] www.ox.ac.uk/news/2021-03-23-oxford-s-ambitious-environmental-sustainability-strategy-approved; See "*Net Zero by 2035*", article in this issue of *Fusion*

[12] Bergero, C. *et al.* (2023) "Pathways to net-zero emissions from aviation" Nature Sustainability 6: 404 https://doi.org/10.1038/s41893-022-01046-9

[13] Summary: https://travel.admin.ox.ac.uk/travelling-for-work/travel-policy. Detail: https://travel.admin.ox.ac.uk/files/travelpolicylatestpdf The policy's scope includes: meetings, conferences, working elsewhere, student field trips, research fieldwork, placements, interviews. It does not cover: international students travelling to/from the University. domestic students travelling between home/the University, staff travelling between home/normal place of work, staff relocation flights.

stakeholders, needs to determine the best balance to administer flight levies in order to foster sustainable changes.

In-person interactions remain important, especially for early career researchers to engage with their scientific communities. However, the overarching approach to academic travel needs to become more sustainable and the determination of funding agencies and the University of Oxford to reduce air travel is a strong sign that institutions are committed to reduce the environmental impact of academic research. These travel policies together with changes in individual behaviours should hopefully create a research environment that moves away from the idea that academic success has to be tightly associated with frequent academic air travel. Fostering the exchange of scientific ideas and reducing aviation is definitely possible. In addressing this issue, the Dunn School and the University of Oxford have taken important steps in pushing for more sustainability in academia.

Water vapour flight trails (artificial cirrus "con-trails" from burning jet fuel) above the roof of the Dunn School Old building (Sept 2018). Oxford lies under several flight paths, E<->W across the Atlantic and N<->S to Europe. The water can add to global warming via radiative forcing, over and above simply the CO_2 emitted. The non-CO_2 effects (water, NO_x, soot, etc) of airplane emissions need better climate-change modelling but are certainly significant[12]

Planet-improving reader, has global heating altered your travel choices for work purposes? Have you had experience of online platforms for virtual scientific conferences and meetings? Did they work well enough? To what extent did they facilitate personal networking? We'd be really interested in your comments about internet-based scientific interactions that you can recommend. Please send your views or suggestions to alumni@path.ox.ac.uk and we'll pass them on.

Designing and building the Next-Gen decarbonised labs of the future

A story of successes and lessons learnt from the construction of the EPA and OMPI buildings

Some of us glance at notices on a wall; many don't. But surely the poster in the entrance lobby to OMPI, prominently decorating its wall with no other distractions nearby, must catch everyone's eye. Its giant red arrow pointing at the bottom step of a coloured staircase screams at the retina "look at me: I'm so ugly!" **Anne Hedegaard** is a post-doc in the James Group, with neuroscience inclinations. She much prefers Green rather than Red and is an enthusiastic member of the Green Group in the department. In this article she explores the specification of modern lab architectural design and construction.

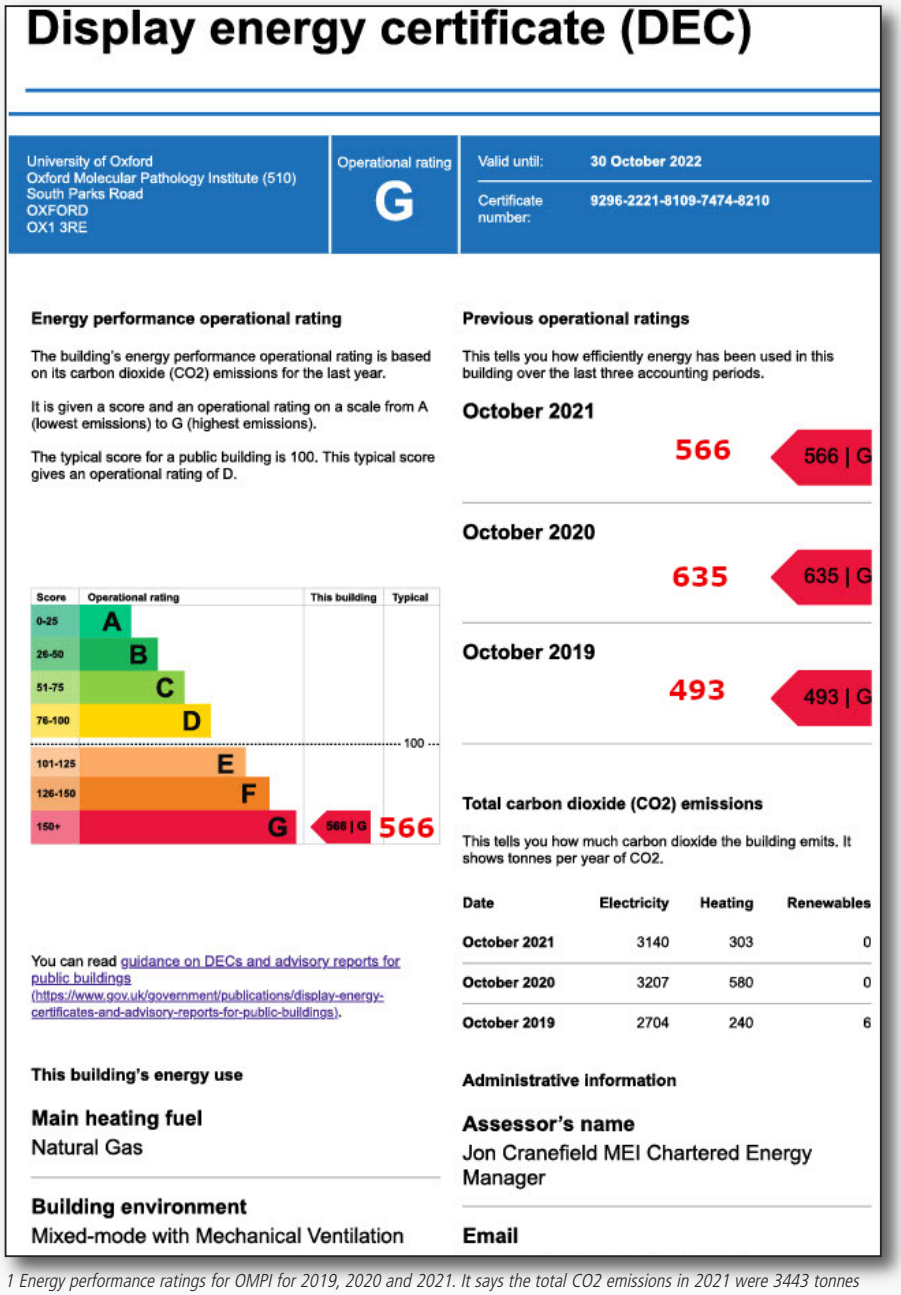
When entering our Oxford Molecular Pathology Institute (OMPI) at the ground floor by the bike sheds, you might have noticed the big "Display Energy Certificate" (DEC)[1] poster on the wall. It is mandatory in the UK for all public buildings to be certified for their CO_2 emissions, and to display a poster like this one. Have you ever found it a little strange that the relatively newly constructed (2010) OMPI building scores so abysmally? On a scale where a score of 100 is typical performance for this type of building, OMPI is currently at 566 and a rating of 'G'. '566' tells us that the CO_2 emissions per square metre of useful floor area are 5.66 times worse than the average of comparable buildings nationally[2]. But hang on, the design and construction of OMPI and, before it, of the EPA (Edward Penley

[1] See also the article "Net Zero by 2035" in this issue of *Fusion*.

[2] *Editor*. Page 9 of the official definition states: "The carbon dioxide emissions for the certificate are based on the adjusted energy consumption and adjusted total useful floor area and building type to give a measured CO_2 emission per square metre." It's an operational rating; a numeric indicator of the amount of energy consumed during the occupation of the building over a period of 12 months, based on meter readings. DECs are therefore different from domestic Energy Performance Certificates (EPCs), which are based on the way a house has been built (insulation levels; draught-proofing; heating systems, etc). Some people argue that the 'comparator' numerical score is unfair to research labs, because the comparison with ordinary office space, where there is no energy-hungry benchwork, is inappropriate.

Abraham) building completed in 2001, were specified to be "Excellent" according to the official BREEAM[3] design guide that was in force then. So how did it end up getting a 'G'?

Similar DECs are on display for EPA and for the Old Building designed a century ago. They too show 'G' ratings, with comparator scores respectively of 191 and 171 – poor, but not quite so bad.



Display energy certificate (DEC)

University of Oxford
Oxford Molecular Pathology Institute (510)
South Parks Road
OXFORD
OX1 3RE

Operational rating: G

Valid until: 30 October 2022
Certificate number: 9296-2221-8109-7474-8210

Energy performance operational rating

The building's energy performance operational rating is based on its carbon dioxide (CO2) emissions for the last year.

It is given a score and an operational rating on a scale from A (lowest emissions) to G (highest emissions).

The typical score for a public building is 100. This typical score gives an operational rating of D.

Score	Operational rating	This building	Typical
0-25	A		
26-50	B		
51-75	C		
76-100	D		100
101-125	E		
126-150	F		
150+	G	566 | G	566

You can read guidance on DECs and advisory reports for public buildings (https://www.gov.uk/government/publications/display-energy-certificates-and-advisory-reports-for-public-buildings).

This building's energy use

Main heating fuel
Natural Gas

Building environment
Mixed-mode with Mechanical Ventilation

Previous operational ratings

This tells you how efficiently energy has been used in this building over the last three accounting periods.

October 2021 566 — 566 | G

October 2020 635 — 635 | G

October 2019 493 — 493 | G

Total carbon dioxide (CO2) emissions

This tells you how much carbon dioxide the building emits. It shows tonnes per year of CO2.

Date	Electricity	Heating	Renewables
October 2021	3140	303	0
October 2020	3207	580	0
October 2019	2704	240	6

Administrative information

Assessor's name
Jon Cranefield MEI Chartered Energy Manager

Email

1 Energy performance ratings for OMPI for 2019, 2020 and 2021. It says the total CO2 emissions in 2021 were 3443 tonnes

Interview

It is a hot June day, and I am interviewing Prof William James in his lab office on the North side of the EPA building. He's friendly and energetic, emanating hundreds of Watts in all directions. He was the University's Pro-Vice-Chancellor for Planning and Resource Allocation between 2011 and 2017. During that period Estates Services, including the Sustainability Team, were his responsibility. I'll be calling him William since he is my lab-chief and we're on first-name terms. Through his close involvement as sponsor on three departmental building projects he might shed light on what plans for sustainability and decarbonisation got implemented, which ideas failed and what was learned.

What was your role in the EPA and OMPI building designs?

William had been involved in the planning for the Pathology Support Building (PSB, completed 1994). So, when Head of Department Herman Waldmann developed his ambitions to add first the EPA building and less than a decade later the OMPI building, William volunteered his expertise to the committees. One of his major contributions was to insist on adopting the BREEAM guidelines for both these proposed new buildings. BREEAM subsequently became adopted across the whole University.

What concrete measures to enhance sustainability and to contribute to decarbonisation of the department were implemented?

Many ideas were on the table, most of them conveniently covered by the BREEAM framework. For example, the carbon footprint of the building materials was considered. The manufacture of concrete accounts for about 8% of carbon emissions globally, due to the inherent chemical production of masses of CO_2 when calcium carbonate is heated and to the intensive energy this requires[4]. Reducing the amount of concrete was achieved by replacing it with steel wherever feasible.

In addition, creating the EPA building allowed for the centralisation of departmental services. Example: Stores, who buy in bulk, save on transport emissions. Example: centralised glassware washing and

[3] *Editor*: BREEAM, Building Research Establishment Environmental Assessment Method, is a widely-used methodology in the UK that is meant to ensure sustainable design and construction. See https://bregroup.com/products/breeam. The sustainability standard for Oxford University building design was tightened even further in 2017 to 'Passivhaus' standards. These now apply to all its buildings that cost more than £1mn. Very stringent 'Passivhaus' methodology heads the list of design principles and must be applied to proposed designs right from the start, at the pre-project stage. https://sustainability.admin.ox.ac.uk/files/estatesservicessustainabilitydesignguidepdf

[4] *Editor*: Nature editorial (2021) "Concrete needs to lose its colossal carbon footprint" www.nature.com/articles/d41586-021-02612-5. Fennell *et al* (2021) "Decarbonising cement production" https://doi.org/10.1016/j.joule.2021.04.011

autoclaving replaced the multitude of smaller dishwashers and autoclaves scattered around individual labs. Running big machines only when they're full saves water and energy.

Yet the biggest energy-drain in buildings like those in our Department is air-circulation: heating and cooling. The following measures provided solutions:

- The café and common room and seminar/meeting room areas have natural air circulation. Fresh air is drawn in from the bottom of the rooms through vents, controlled by sensors which determine when it is needed. The lab areas are kept separate from this system and 80% of their air gets passed through HEPA filters and re-circulated.
- Heating/cooling solutions: the brown wooden solar-shading slats on the South-facing elevations of both OMPI and EPA are not just decoration resembling DNA ladders to inspire our Dunn School logo. They are carefully designed and positioned. In the Summer they provide maximal shade when the sun is high, which reduces the amount of cooling needed. In Winter they allow sunshine in, generating passive heating of rooms.

Were there any decarbonisation aspects that proved to be impossible or impractical to implement?

As mentioned above, heating and cooling are where the big carbon savings can be made. When the OMPI building was inaugurated, it proudly sported a Combined Heat and Power (CHP) system on the roof. The CHP on the OMPI building was meant to capture heat both from its diesel engine driving the electricity generator and from the server room in the basement. Over 20% of that building's heat requirements on a cold winter's day should have derived from the CHP unit. However, problems became apparent within the first weeks of its operation. Initially, the server room[5] was only one-third full, insufficient to provide enough energy to run the heating system[6]. As soon as the diesel engine was turned on, labs on the top floors experienced both excessive noise and vibrations. In the end, the CHP was in operation for only a couple of weeks. The failure of this project is the major reason why OMPI's energy efficiency score is so appalling. To replace what the CHP system cannot provide, more of OMPI's heat and electricity energy passes through the import meters and so contributes to the 'G' and 556 scores.

As the name suggests, a CHP system can generate power AND heat at the same time. CHP can achieve 80% fuel efficiency, compared to 50% from conventional separate power and heat production imported from the grid. CHP technology ingeniously captures waste heat, for instance from an electricity-generating turbine. In principle it provides hot water and space heating (which can also be converted to cooling in the Summer) in addition to electricity. For more info on CHPs, and on air-source heat pumps, see footnote 11 on next page

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2. November sunshine streams through the louvres to warm the South face of OMPI

As William and I were enjoying the unfortunately non-CHP-generated air-conditioning in his office, we discussed other initiatives which at the time had not been feasible to implement, including solar panels and green roofs. Both suffer from the same fundamental issue of "where to put them", as space on roofs is actually pretty limited due to a clutter of exhausts, filtering and cooling machines. Furthermore, the solar panel solutions investigated at the time were not compatible with the main grid outside the Department, so could frustratingly not be linked up and had to be scrapped[7].

Drone Photo: HuftonCrow ©OU Developments CC-BY-NC-ND 4.0

3. Dunn School roofscape across its four main buildings in 2021. Note the solar photovoltaic panels and the air-conditioning units

If you were designing a laboratory building today, what would you like to see implemented from a decarbonisation/sustainability point of view?

In the future, William highlights that centralised heating and cooling systems need to be properly planned on a University-wide scale. To his knowledge, a shared water-heating system was successfully implemented at the Radcliffe Observatory Quarter. Such a system was intended for the science area too, but each building ended up equipped with individual boiler-rooms to control their own heating. For electricity, its sourcing needs to be worked out on a national[8] grid level, so that we can be confident that our supply comes from renewable energy sources[9]. In early 2022 the University received a 733-page expert detailed report[10] on a "Heat decarbonisation Plan for the so-called "Science City Campus" (i.e. mostly the Science Area).

[5] Downstairs in the basement of OMPI is a large-scale private cloud facility, housing servers that provide digital data storage for many parts of the collegiate University. It consumes a lot of electricity, which is included in calculation of the DEC rating of OMPI.

[6] Now, the server room is full, but all that hot air is expelled directly to the outside and not recycled.

[7] *Editor.* This has now been solved. Use the safety cabinets while the sun is shining!

[8] *Editor.* Or perhaps at regional or more local grid level. Project LEO (Local Energy Oxfordshire, 2019-22) has led the exploration of possibilities of local sharing of electricity generation and distribution. https://project-leo.co.uk/

[9] *Editor.* For at least the last ten years, the University has only purchased electricity that is certified 'renewable'

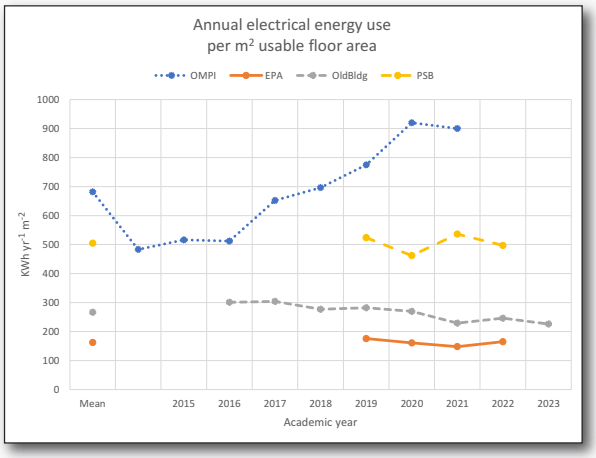
[10] Available to current members of the University at 2022_02nn_OxfordUniversity_21430 Science Area Heat Decarbonisation Plan-174D-DE005603.pdf . It includes building-by-building details of proposals.

The Sustainability Team in the University Estates Office have won an £800K UK Government grant[11], match-funded 50:50 by the University, to update the EPA building to make it less carbon-intensive. Although there is no timeline, the project aims eventually to install air-source heat pumps for EPA - a simpler system than the CHP. The Team regard this "big-building retrofit" as a pilot that might apply, if successful, to several other large University buildings. The Dunn School may be in the lead, once more! The changeover should cause less disruption, and it should expand the solar power capacity. Decarbonisation of the Department is therefore an ongoing project that started with the ambitious designs for the EPA and OMPI buildings and continues as new technology and funding become available.

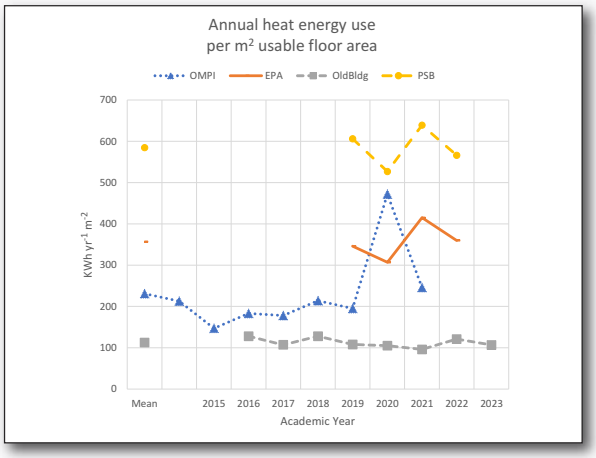
Editor's postscript: data on energy use by the Dunn School buildings

Current and historical annual data from professionally-audited DECs for the four Dunn School buildings (PSB; EPA; OMPI; Old Building) are available publicly online[12]. They show the energy in KWh used in each building, separately for electricity and for heat energy. Currently, 'Heat' is almost entirely by natural gas for space heating, via the Science Area's central boilers. The charts below show the progress since monitoring started. To allow for the differences in floor areas of the buildings, the energy usages have been normalised per square metre of usable space. For comparison, the mean total metered energy consumption per year (electricity plus heat) of a domestic property newly built in 2015 is roughly 125 KWh per square metre[13].

The total energy use[14] recorded on their published DECs was as follows. Academic year 2021 is the most recent for which data for all four buildings are available. For comparison, an ordinary UK home (EPC Band 'D') with a typical grid-based dual fuel supply uses very roughly 3 to 4 MWh electricity and 10 to 18 MWh gas annually. The Dunn School's meters therefore clock up very approximately the same as about 600 average homes.



4. Chart of annual electrical energy consumption of the four Dunn School buildings, normalised for useful floor area. (Some data points missing)



5. Chart of annual heat energy used by the four Dunn School buildings, normalised for useful floor area

Total energy usage MegaWatt-Hours per year					
Building	Electricity		Heat		[Floor area, sq. m.]
	Mean 2014-22	Academic year 2021	Mean 2014-22	Academic year 2021	
OMPI	4322	5706	1465	1560	[6340]
EPA	413	377	908	1056	[2544]
Old Building	742	636	313	267	[2779]
PSB	1111	1180	1287	1407	[2202]
All Buildings	6589	7899	3972	4289	[13865]

Energy-conscious reader, what is your view about the right balance for the Dunn School? Should we accept the leadership risks in being an "early adopter" of new technologies like CHP and heat-pumps? Should we tolerate the present enormous carbon footprint and the energy costs until more reliable advances come through? Please send your comments or suggestions to alumni@path.ox.ac.uk. If you'd like to collaborate with the editor to keep track of the data about energy used by the Dunn School for its heat, light and power needs, please email simon.hunt@path.ox.ac.uk direct. He is especially interested in comments on the above data and how it might be usefully interpreted to guide our way to the future.

[11] Here is the description of the BEIS scheme, administered for the UK Government by the Carbon Trust: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/376175/ECA761_Heat_pump_equipment.pdf. It describes the principles of air-source heat-pumps.

[12] Search https://find-energy-certificate.service.gov.uk/find-a-non-domestic-certificate/search-by-postcode. For OMPI and the Old Building, use OX1 3RE. For EPA use OX1 3PL. For PSB use OX1 3RJ.

[13] www.gov.uk/government/statistics/energy-consumption-in-new-domestic-buildings-2015-to-2017-england-and-wales See also https://assets.publishing.service.gov.uk/media/62334e14d3bf7f047bfa92b0/Energy_Consumption_in_the_UK_2021.pdf

[14] Scopes 1 and 2, not 3. See "Net Zero by 2035" for an explanation of the different Scopes.

Catering to a changing world

Lockdowns; social-distancing rules; apprehension that we might unwittingly cause someone else to catch COVID - all these conspired to inevitably close the Bridge café in March 2020. "Beyond ordinary" took on a new meaning and we lost our Compass (the caterers at that time). Habits changed. Here, **Charlotte Melia**, who works in the Electron Microscopy suite and is an active member of the Green Group, ponders our everyday choices about what we eat. How can we collectively influence the carbon footprint of our food and drink, particularly of the operation of the café, now that it has revived?

The close of spring evokes all kinds of lovely notions – long days, sun and shade, the sea breeze, serenity. Even better, in 2022 it also brought sandwiches! The Bridge café has long been an important foody focal point for people to come together, take breaks or chat over coffee, and its re-opening in the department was warmly welcomed. It also marked an important moment to reflect on how our diets adapted over the COVID-19 years, whether there are good habits we can keep, less healthy ones to shed – and new ones to foster.

Why invite even more changes to the way we eat? The idea that diet affects more than our health is far from new, but now there's another association for us to grapple with. Year by year, food has been nudging its way to the frontlines in the battle to save our planet. In fact, the latest analyses suggest our global food systems could account for a third of all anthropogenic greenhouse gas emissions[1, 2]. Trying to take on that challenge is enough to give anyone indigestion. Where do we even start? Instead of scrabbling for the antacids, let's look at the fundamentals.

Our agricultural systems are designed with a primary purpose in mind – keeping organisms alive and growing until they're ready for the plate. What matters from an environmental perspective are the required inputs and the unfortunate climate-altering by-products. All livestock production (even 'grazing-based') requires transporting-in crops, which requires producing said crops, which in turn requires the fertile soil needed to grow them. Facilitating each part is energetically demanding, and energy is naturally lost in the transfers (lambs have to frolic, seeds must be sown, entropy has to entropy). Even at this basic level it seems intuitive that eating plants ourselves, rather than enjoying them through a mooing middleman, will be more efficient. In fact, that most heinous of culinary climate culprits, beef, generates 25-50 times more C_{eq} per 100g protein than grains, pulses, tofu, peas, and nuts[3].

However, the complicating factors aren't trivial. Not all plants are equal when it comes to complete life-cycle emissions or land and water use, and we need to deliver the right macro- and micro-nutrients where they're needed. In many parts of the world economic and ecological constraints mean that cutting out or even cutting back on animal products simply isn't practicable. While the global future of meat[4] is uncertain, healthy and conscientious plant-oriented eating is already affordable and achievable – and increasingly popular – in the UK. As awareness of the benefits grows and the movement gains further traction it will only become easier to reduce our intake of meat, fish, dairy, and eggs or even eliminate them from our diets.

Throwing our lofty aims into the ring against a heavyweight champion steak might seem daunting, but not every meal has to be a showdown. Take the time to measure the environmental pros and cons, substitute in healthy alternatives gradually, and together we can set the example for a more sustainable way of eating. Try out the options available at the café today and let the department know what you'd like to see more (or less) of! What do we want? More seasonal, plant-based, efficiently grown ingredients transformed into nutritious flavour-punch-packing and all-round delicious meals at a reasonable price! When do we want it? Lunchtime!

Hungry reader, thirsty reader - what do you think? Does reducing your carbon footprint on the journey to Net Zero influence what you choose to eat and drink? If you'd like to suggest something constructive about the catering arrangements in the Dunn School, or if you have comments or suggestions about hitting the Net Zero target via menu choices, contact either alumni@path.ox.ac.uk or Charlotte directly.

1 Xu, X.M. *et al* (2021). Global greenhouse gas emissions from animal-based foods are twice those of plant-based foods. Nat Food 2: 724-732 http://doi.org/10.1038/s43016-021-00358-x

2 Crippa, M. *et al* (2021). Food systems are responsible for a third of global anthropogenic GHG emissions. Nat Food 2: 198-209 https://doi.org/10.1038/s43016-021-00225-9

3 Poore, J., and Nemecek, T. (2018). Reducing food's environmental impacts through producers and consumers. Science 360: 987-992 http://doi.org/10.1126/science.aaq0216

4 https://tabledebates.org/meat

It's just a gas[1]! No, not always!

Your Editor's route home from the Dunn School takes him past other departments in the Science Area. He has often wondered what one tonne of CO_2 looks like. One day he noticed a pile of ten frosty-looking, puffed-up plastic bags in the roadway near the service entrance to one of the Science buildings. It set him thinking…

Ten bags of dry ice, about 0.1 tonne, sublimating into CO_2 gas

Each bag, when delivered, originally held 10Kg of that very familiar and fun compound, solid carbon dioxide. "Dry ice" is a material beloved by theatrical stage managers, performing magicians, night-club DJs, and of course bench scientists who need a handy way to deep-cool their samples to -78°C. At the end of an experiment, don't we all like to pop a little pellet - with proper precautions - into a bit of water? We watch the mist gently waft across and down from the bench to the floor in a small dense cloud. It's such an intriguing, wondrous sight…but (a tiny bit) NOT good for our planet!

I wanted to visualise my own personal carbon footprint in terms of bags of solid CO_2. I entered my data to the World Wild Life Fund's Personal Carbon Calculator[2]. It estimated my footprint to be 9.1 tonnes Ceq[3] per year, which is 25 Kg daily. That covers my individual personal share of consumption within the categories: Home (mostly energy); Food; Travel; and other Stuff that I buy. Therefore my footprint corresponds to dissipating two and a half bags every day for 365 days: year in, year out. Put another way, the amount of CO_2 I see sublimating into the atmosphere from that pile of ten bags in the photo roughly equates to the carbon cost of what I consume every four days, due to the way I live. Actually that's a substantial underestimate of the footprint that should properly be attributed to me. The calculator explicitly excludes work-related activities (costs associated with employment and study are counted separately) and it also excludes the carbon costs of the services provided by local and national authorities to me.

There were 10 x 10Kg = 0.1 tonnes of CO_2 in that pile as delivered to the nameless department. How often do they arrive, I wondered? I don't know. But I could find out the consumption rate of dry ice bags in the Dunn School. Philip Cobden, our Services Manager and a vital Green Group member, orders our department's dry ice. He told me that we typically use 16-18 bags weekly, which is 8-9 tonnes per year for the whole of the Dunn School – about the same as my own annual personal carbon footprint. When the fresh bags arrive each week, he ensures that they are immediately stored in the very well insulated bespoke chest in the EPA foyer. Any lab member can then collect some when they need it, without charge to their labgroup. Philip would of course never ever allow dry ice to disappear uselessly into open air as in the photo.

Philip Cobden, 2023
©Dunn School

The Dunn School also uses significant quantities of liquid CO_2[4], whose ordering is again Philip's responsibility. This is mainly used for gassing our many cell and tissue culture incubators and flasks. Most of it is piped from the outside storage tank behind the EPA building. Some more arrives in the familiar black cylinders we see within some labs, which are directly connected to lab apparatus that uses CO_2. Annual deliveries to the tank total about 10 tonnes. Together with the 8-9 tonnes of solid CO_2 described above, researchers in the Dunn School therefore consume and then annually dissipate into the air at least 19 tonnes of CO_2 from the solid plus liquid we buy. When that quantity becomes a gas, what volume does it occupy? Let's imagine it goes into a vertical column over an area directly over our Dunn School site. 19 tonnes would occupy well over 2.3 Km (7500 feet) above ground level[5]. Actually the total carbon impact of the department's CO_2 usage is a lot more than this since, like all our other lab supplies, we should additionally include the carbon cost of its manufacture, storage and delivery[6].

Liquid CO_2 storage tank behind EPA. It contains about 1 tonne CO_2 when full. We use about 10 tankfuls yearly

I am not happy that my personal annual carbon footprint, which is about half of 19 tonnes, corresponds roughly to the CO_2 present in a column of ordinary air way over one kilometre high, across an area the size of the Dunn School site. Decarbonisation of me and my activities is needed – and soon!

Imaginative reader, in what ways do you concretely visualise the scale of your carbon footprint? Please share your ideas by emailing alumni@path.ox.ac.uk.

[1] See https://idiomation.wordpress.com/2010/04/28/its-a-gas/ for an explanation of this English idiom.
[2] https://footprint.wwf.org.uk/ The WWF Calculator is available as a mobile app: Apple. Android.
[3] My 9.1 tCeq for 2023 is very close to what every UK person needs to attain, according to the Climate Change Committee Balanced Net Zero Pathway www.theccc.org.uk. At present, each resident of Oxford currently averages about 12 tCeq, i.e. an overshoot 40% higher than what's required for Net Zero. The current world average carbon consumption-footprint per person per year is around 6.3 tCeq, though this indicative figure masks huge variation between different peoples of the world. www.iea.org/commentaries/the-world-s-top-1-of-emitters-produce-over-1000-times-more-co2-than-the-bottom-1
[4] CO_2 can be transported, stored and handled in liquid form: https://co2gas.co.uk/liquid-co2-can-uses/. The Dunn School's vacuum-insulated 950-Litre cryogenic storage tank at a pressure of around 10-20 bar can contain up to about one tonne of CO_2 when full.
[5] The Dunn School occupies a site, excluding MSTC, of 10600 square metres (2.6 acres) https://t2m.io/DunnArea. 19 tonnes of pure gaseous CO_2 at 20°C and 1 bar, undiluted by any other gas, fills 10370 m^3 (https://microsites.airproducts.com/gasfacts/carbon-dioxide.html), making it one metre deep. So we'd be up to our waists in 100% CO_2 gas generated from the quantity of solid and liquid CO_2 that the Dunn School uses in one year. Thinking of it evenly distributed at 0.042% (420 ppm) as in ordinary normal air, this would rise 2.3 Km above ground level if it didn't mix with adjacent air. This is a gross underestimate since the pressure at that height is only about 0.75 bar, so the air column with its CO_2 would be actually a lot higher.
[6] "Scope 3" – see the article on Net Zero in this issue of *Fusion*.

...continued from back cover

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Many thanks to Robin Roberts-Gant from Medical Informatics for his help over many years, and expertise in the layout of *Fusion*.

Also to all the authors who willingly contributed material to this issue.

Watchful reader, you'll see that this issue is full of footnotes and other citations, enough to make the heart of a History don beat faster in sympathy and admiration. This editor makes no apology for them. He believes: (1) you should be able to pursue your curiosity further (2) hyperlinks enable Supplementary Information to be added to some articles, just like research journals (3) crucially, no publication is credible or trustworthy unless it cites its sources. Accurate documentation of the ultimate provenance of information - its traceability - is the only defence against unsupportable claims, "Chinese Whispers" or, worst of all, Fake News. Every reader must be able easily to track a claim, a factoid or a data item back to its original source.

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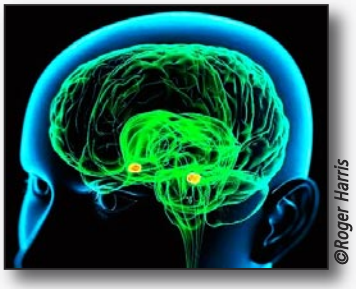
Credit: https://wallpapercrafter.com/desktop3/897021-Earth-globes-miniatures-hands-fingers-symbols.jpg

From the Editor's amygdalae

Your editor, proudly displaying his LEAF award



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This issue of ***Fusion*** is built on the shoulders of the two previous editorial giants, Eric Sidebottom and Paul Fairchild. As ***Issue*** 19 told us, their dedicated and experienced guardianship of the editorial role is now over. Thanks, both! When the invitation to produce ***Issue*** 20 drifted into the present editor's ears, it provoked the whole gamut of emotions and neural responses: excitement, apprehension, satisfaction, regret , appetitive learning, extinction, reward, attention, memory formation, decision-making, disgust[1]; and so on. Tell alumni@path.ox.ac.uk what you think of the job that the present editor, Simon Hunt, has done.

THE SIR WILLIAM DUNN SCHOOL OF PATHOLOGY
We are a department of the University of Oxford within its Medical Sciences Division

HEAD OF DEPARTMENT
Prof Matthew Freeman FRS,
Sir William Dunn School of Pathology,
South Parks Road
Oxford OX1 3RE, U.K.
matthew.freeman@path.ox.ac.uk

EDITOR
Simon Hunt
simon.hunt@path.ox.ac.uk

Sustainability — decarbonisation

The Decarbonisation theme of this issue was inspired, first, by COP26 in Glasgow in autumn 2021; and second, by progress in our University's overall policies and targets about Sustainability, particularly about downsizing its greenhouse gas emissions. Phrases like "Net Zero", "Modal Shift", "Biodiversity Net Gain", "Carbon Removal Obligations" buzz about in my brain, all the more insistently because I've been Chair of Cyclox, the advocacy group for cycling. But in truth I'm woefully illiterate and innumerate about climate change within the professional and personal space I inhabit. Everything I do as a biomedical scientist imposes a burden on the planet that contributes to seriously harming all life that occupies it, notably human life. But what are the major and what are the less substantial tolls? How big are they? To lessen those impacts, what is within my reasonable agency as an individual to change things, and are there opportunities to support others to change? Can I influence the governance of the frameworks I live and work within? Can I hold relevant authorities to account? I know I need to learn much more about sustainability: specifically about decarbonisation as a key aspect of it. *Fusion* 20's aim is to share with you how the Dunn School's Green Group, with me as part of it, answers these questions, at least partially.

People in the Dunn School operate in a microniche within a global context that is grossly behind the schedule needed to counteract anthropogenic climate change. The carbon budgets of the nations of the world are hugely in debt. For years past the alarm sirens have been screaming. Right now, the decibels are yet louder still. It feels overwhelming: what's the point of trying to do anything about it? We should not react, however, by running away from the terrible din. Feeling anaesthetised because we (wrongly) seem powerless won't ever stop the noise. Each of us can take action. Just as with research itself, collectively we can influence and achieve much more than the plain sum of the efforts of each individual. Our new vice-chancellor, herself a biomedical scientist, put it this way in her inaugural address[2]: "*if you fire together, you wire together*". In our University context, sustainability issues have notably progressed, fostered in part by our own William James[3] when he was pro-Vice-Chancellor (2011-17). The funders are also acting. UKRI is halfway through its five year Environmental Sustainability Strategy[4]. Alongside other major funders like Wellcome, it will soon publish a detailed Concordat[5] for Environmental Sustainability of Research and Innovation Practice. These frameworks matter a lot, for the success of everyone's research and of daily living, not to mention for our planet. *Fusion* 20 aims to nourish your ideas and to stimulate points for action. C'mon everyone!

...continued on inside back cover

[1] with himself because of the elephantine duration of gestation of this baby
[2] www.ox.ac.uk/news/2023-01-10-new-vice-chancellor-ready-fire-and-wire-university-oxford-and-world. Prof Irene Tracey was referring to Hebb, D.O. (1949) "The Organization of Behavior" https://ebookcentral.proquest.com/lib/oxford/detail.action?docID=227504
[3] https://orcid.org/0000-0002-2506-1198
[4] https://www.ukri.org/wp-content/uploads/2020/10/UKRI-050920-SustainabilityStrategy.pdf
[5] https://t2m.io/UKRISustain
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