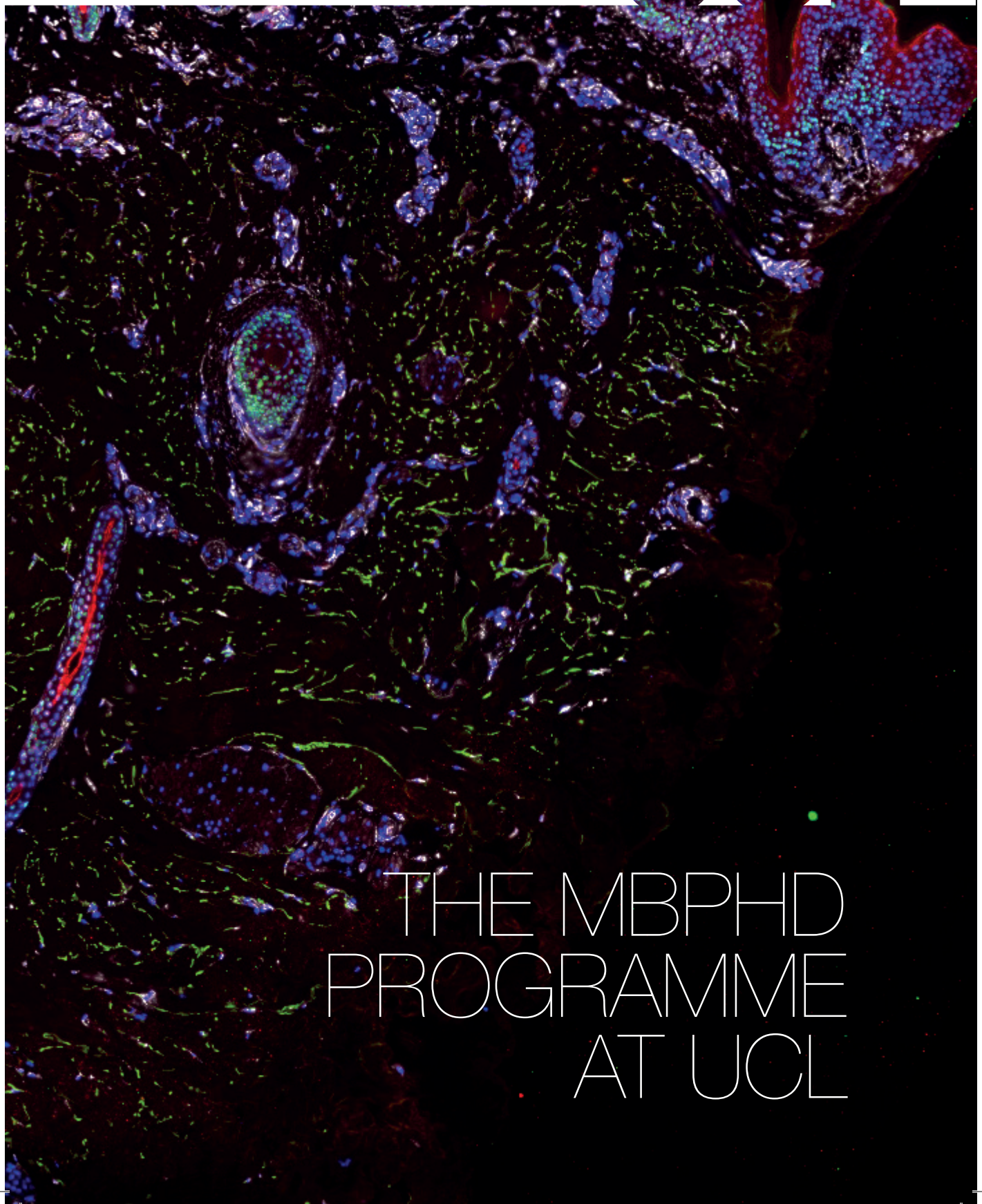
UCL FACULTY OF MEDICAL SCIENCES

UCL



THE MBPHD PROGRAMME AT UCL

Established in 1994, the UCL MBPhD programme offers bright, motivated and enthusiastic medical students the highest quality clinical and research training. The graduate emerges with both excellent bedside skills of diagnosis, investigation and patient management, along with a repertoire of practical scientific skills, including an understanding of the rigor and discipline necessary for translational science and with a track record of publication of high quality translational research. The programme equips its graduates with the skills required to become the academic clinical leaders of the future

The course

In the course, the PhD is integrated between the first and final two years of clinical training. An introduction to clinical medicine is essential, because it focuses thinking on potential translational benefits. Students enter the clinical part of the MBBS programme (Year 4: Integrated Clinical Care) with their contemporaries following their iBSc. After completion of MBBS Year 4, MBPhD students divert to research studies for a period of three years. During the PhD, a regular clinical teaching programme maintains the clinical skills and up-to-date knowledge of each student. Re-entry into the MBBS for the two remaining years is contingent on submission of the PhD.

The PhD research is undertaken within UCL, which includes many world-class institutes such as the Institute of Child Health, the Institute of Neurology at Queen Square, the Institute of Ophthalmology at Moorfields, and the Francis Crick Institute (headed by Nobel Prize winner, Sir Professor Paul Nurse). This new institute provides world-class scientific training that is second to none.

Year	Stage
1	**MBBS Year 1**: Fundamentals of Clinical Sciences
2	**MBBS Year 2**: Fundamentals of Clinical Sciences
3	**MBBS Year 3**: Scientific Method in Depth – iBSc
4	➜ Entry Point: UCL **MBBS Year 4**: Integrated Clinical Care
5	**PhD Year 1**
6	**PhD Year 2**
7	**PhD Year 3**
** At this point students have the option of adopting Continuing Research Student status (CRS) for an additional year if needed to write up their thesis.*	
8	**UCL MBBS Year 5**: Life Cycle
9	**UCL MBBS Year 6**: Preparation for Practice

The Benefits

The UCL MBPhD programme is ideal for students wanting to combine clinical and research training. The Programme helps identify funding for the PhD and offers layers of mentorship for the student during one of the most challenging and exciting courses at UCL. There are formal and informal contacts with multiple clinical and non-clinical academics during teaching sessions, on the wards, at Programme meetings and at the regular social events. Numerous collaborations and friendships have arisen from the Programme and will undoubtedly continue from what has become its own community.

The MBPhD serves as an excellent start to a clinical academic career. Establishing an early track record is key and such a programme can serve to catapult the individual into research fellowships later on in their careers, once his or her postgraduate clinical training is advanced. The combination of science and clinical medicine is a core feature of this Programme. The UCL MBPhD programme seeks to train doctors in the rigors of scientific analysis and discipline, so that they can continue to apply the art and science of clinical medicine in order to alleviate human disease and suffering.

Eligibility

The programme is only available to students who are currently undertaking a Primary Medical Qualification (MBBS, MBChB or equivalent) at a UK Medical School. At the point of entry, successful applicants will have completed the first two years of a full 5-years primary medical qualification and have achieved an upper second or first class honours degree (or iBSc). The candidate must satisfy the general regulations for transfer to Year 4 of the UCL MBBS clinical course. (**www.ucl.ac.uk/medicalschool/mbbs-admissions/ entry-requirements/**).

Applicants who entered a 5- or 6-year MBBS course as a graduate may request exemption from UCL's iBSc requirement if their degree is in a relevant field.

Students who are following an accelerated graduate medical programme are not eligible to transfer to UCL's MBPhD programme.

Entry to the MBPhD programme is conditional on achieving an upper second or first class honours degree.

Applicants from outside UCL are required to secure the offer of a clinical place at UCL, under the clinical transfer scheme, before applying to the MBPhD programme. Details of the clinical transfer application process may be found at: **www.ucl.ac.uk/medical-school/study/undergraduate/transfer**

At present, College regulations preclude transfers from institutions outside the United Kingdom.

Funding

Funding for Year 4 of the MBBS programme, taken prior to the PhD, is through the Student Loan Company (SLC). Funding for Years 5 and 6 of the MBBS programme is via the Government funding mechanisms in place at the point at which students return to the MBBS. The PhDs are funded from different sources.

We are very grateful for charitable donations from different bodies including the Astor Foundation, the Rosetrees Trust, The Sackler Fund, the International Journal of Experimental Medicine, AstraZeneca and the Royal Free Charitable Trust and the Middlesex Hospital Medical School General Charitable Tust. Other PhDs are supported by grants directly made to the supervisors.

PhD studentships are for 3 years, and include a £16,000 stipend, UCL home level fees, plus a contribution to laboratory costs. Students do not pay fees during CRS registration.

Students

We enrol approximately 6–10 per year. Most students have previously studied for their BScs at UCL, but we have welcomed students from other medical schools including the other London Schools, Nottingham, Brighton and Sussex, Cambridge, Oxford and Edinburgh. We have representatives from all continents.

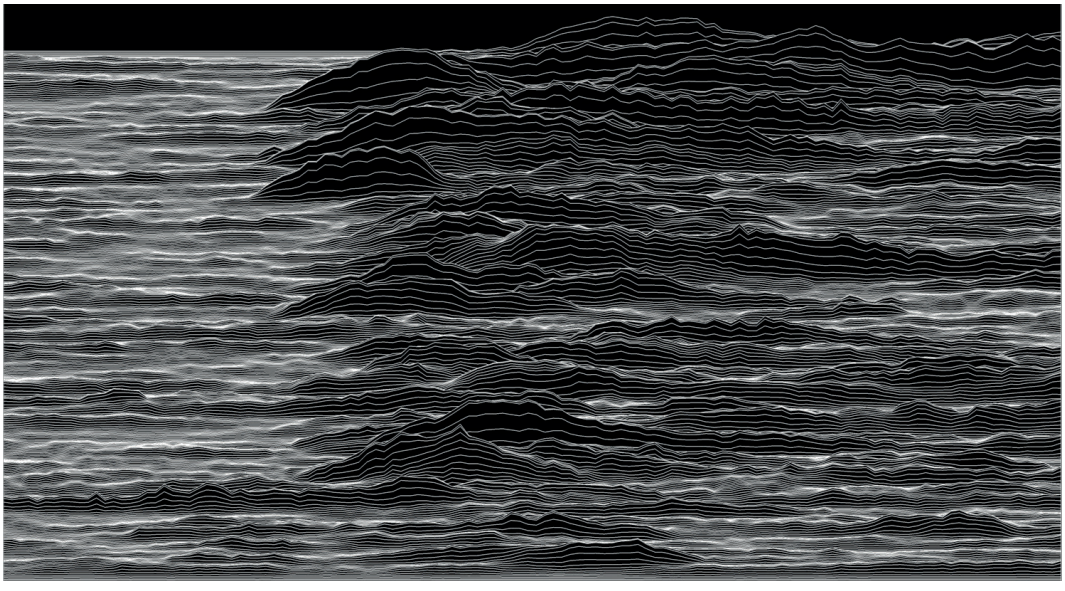
Subject Areas Studied

PhD topics have varied very widely, reflecting the major strengths of UCL. However, we are very open and encourage applicants to explore the whole range of subjects on offer at UCL.

Outcomes

The most senior students (who graduated in 1999 or 2000) are now consultant grade Professorial level. The more junior graduates regularly appointed to Academic Foundation Posts and Academic Clinical Fellowships. Many are physicians, but several have entered surgical specialties and other disciplines such as paediatrics and psychiatry.

Image below:
Mr Sean Cavanagh (current UCL MBPhD student), Institute of Neurology. Image shows the variability of responses of single neurons in Prefrontal Cortex to stimuli predicting rewards, whilst animals are making simple decisions. The image was featured on the cover of the journal eLife in October 2016 (https://elifesciences.org/content/5/e18937).



The Cordwainers' Prize

Each year the Worshipful Society of Cordwainers donates a generous sum awarded to the student submitting **the best MBPhD thesis**. These are judged by a panel of internal and external senior academics, and the award is made at the annual Marsden Lecture at the Royal Free Hospital.

Cordwainers' Prize former winners:

2016 Rafael Di Marco Barros
Tissue-Specific Butyrophilin-like Molecules are Master Regulators of Intraepithelial γδ T cell Composition.
Supervisor: Prof Adrian Hayday

2015 Fergus O'Farrell
Pericyte-mediated Regulation of Cerebral and Coronary Blood Flow in Health and Disease
Supervisor: Prof David Attwell

2014 Adam P Levine
The genetics of inflammatory bowel disease in extended multiplex Ashkenazi Jewish kindreds
Supervisor: Prof Tony Segal

2013 Christopher A McKinnon
The role of the ubiquitin-proteasome system in prion disease pathogenesis
Supervisor: Prof Sarah Tabrizi

2012 Anna M Rose
Transcriptional regulation of PRPF31: the role of variable gene expression in determining phenotype in retinitis pigmentosa
Supervisor: Prof Shomi Bhattacharya

2011 Sean B Knight
Lentiviral Vectors for Gene Therapy
Supervisor: Prof Mary Collins

Alvin J X Lee
An Investigation of Chromosomal Instability Survival Mechanisms in Cancer
Supervisor: Prof Charles Swanton

2010 Alex Rossdeutsch
The Role of Thymosin B4 in Vascular Development
Supervisor: Prof Paul Riley

2009 Catherine Hyams
The role of the Streptococcus pneumoniae capsule in interactions with Coaplement and Phagocytes
Supervisor: Prof Jeremy Brown

Panagiotis Kyrtatos
Cell Targeting and Imaging using Magnetic Nanoparticles
Supervisor: Prof Mark Lythgoe

2008 Abhishek Das
Constraints on T Cell responsiveness in Chronic Hepatitis B Virus infection
Supervisor: Prof Mala Maini

Mentoring, Supervision, Follow up

The intensive nature of this course demands that supervision be close. We have constant staff-student interactions, both formal and informal. These interactions can continue long after graduation.

Management & Administration

There is a management committee with representation from academics, administrators and students, which meets once a term. The day-to-day running of the programme is shared between Robert Unwin, Daniel Marks and Susan Beesley.

Achievements

A number of major scientific discoveries have arisen from research undertaken by UCL MBPhD students. Some very productive collaborations between bright ambitious young doctors and excellent supervisors have grown up, many of which have developed into enduring post-doctoral partnerships, which can be immensely valuable to both parties.

Image right: Dorsal Root Ganglia – neurons from the interface between the spinal cord and peripheral nervous system.
Mr Richard Bartlett (current UCL MBPhD student)

Extracurricular Activities

Many of our students maintain an active social life and excel in a number of outside areas including music, photography, rowing and ceilidh dancing.

Recruitment Open Day

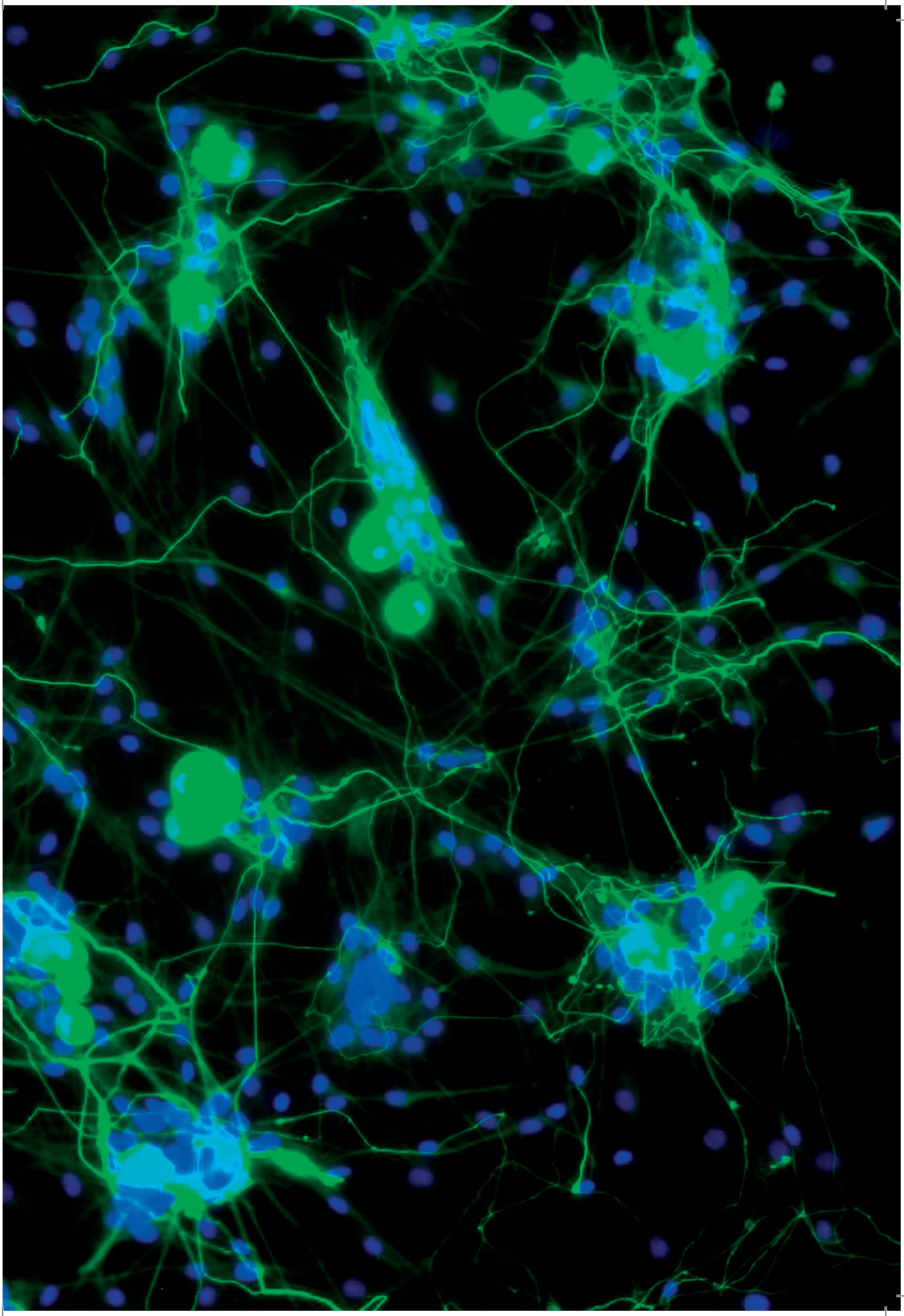
Interested candidates are invited to the MBPhD Recruitment Open Event which takes place annually. The Open Event provides an opportunity for prospective students to interact with not only members of faculty staff but also present and past students to find out more about the programme and to understand more about life as an MBPhD student. Please contact the Programme Administrator for further details and to register attendance.

MBPhD Annual Symposium

In January each year, the programme hosts its annual Symposium, where present MBPhD students give a series of scientific talks with short talks by senior UCL academics and MBPhD Alumni. Attendees include current and former students, prospective students, supervisors, senior UCL academics, and representatives of funding bodies. Please contact the Programme Administrator for further details and to register attendance.

Publication

There is a published report on the progress of the programme. Stewart GW, *An MBPhD Programme in the UK: the UCL Experience*. Clinical Medicine 2012, 12, 1–4.



Publications

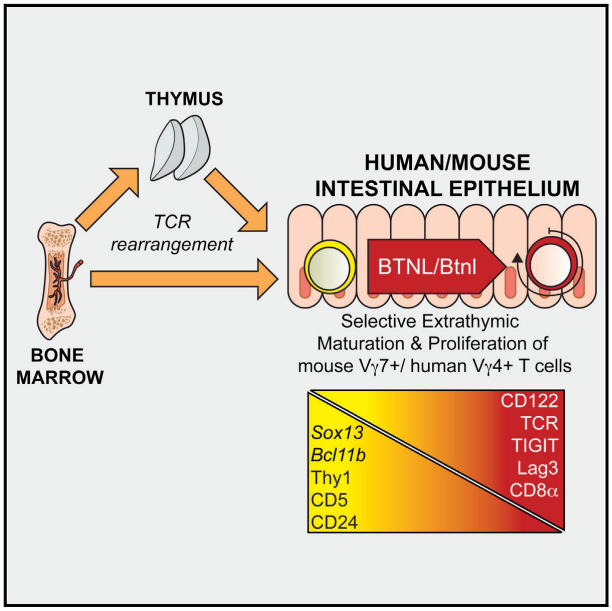
Examples of publications by past and present students:

Article

Cell

Epithelia Use Butyrophilin-like Molecules to Shape Organ-Specific γδ T Cell Compartments

Graphical Abstract



Authors

Rafael Di Marco Barros, Natalie A. Roberts, Robin J. Dart, ..., Pablo Pereira, Ulrich Steinhoff, Adrian Hayday

Correspondence

adrian.hayday@kcl.ac.uk

In Brief

Epithelial cells provide signals that instruct the development and function of their local γδ T cell compartments so that these immune cells can support the non-immune functions of the different barrier tissues.

Highlights

- Gut epithelial butyrophilin-like 1 (*Btnl1*) shapes the local γδ T cell compartment
- Other organ-specific epithelial *Btnl* genes select cognate γδ cells in other sites
- Btnl heteromers can specifically activate γδ T cells with cognate T cell receptors
- Human *BTNL* genes reveal a conserved biology of epithelial T cell regulation

Data Resources

GSE85422

Di Marco Barros et al., 2016, Cell *167*, 203–218
September 22, 2016
http://dx.doi.org/10.1016/j.cell.2016.08.030

CellPress

eLIFE elifesciences.org

RESEARCH ADVANCE

Autocorrelation structure at rest predicts value correlates of single neurons during reward-guided choice

Sean E Cavanagh[1], Joni D Wallis[2,3], Steven W Kennerley[1,2,3*†], Laurence T Hunt[1,4*†]

[1]Sobell Department of Motor Neuroscience, University College London, London, United Kingdom; [2]Department of Psychology, University of California, Berkeley, Berkeley, United States; [3]Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, United States; [4]Wellcome Trust Centre for Neuroimaging, University College London, London, United Kingdom

Abstract Correlates of value are routinely observed in the prefrontal cortex (PFC) during reward-guided decision making. In previous work (Hunt et al., 2015), we argued that PFC correlates of chosen value are a consequence of varying rates of a dynamical evidence accumulation process. Yet within PFC, there is substantial variability in chosen value correlates across individual neurons. Here we show that this variability is explained by neurons having different temporal receptive fields of integration, indexed by examining neuronal spike rate autocorrelation structure whilst at rest. We find that neurons with protracted resting temporal receptive fields exhibit stronger chosen value correlates during choice. Within orbitofrontal cortex, these neurons also sustain coding of chosen value from choice through the delivery of reward, providing a potential neural mechanism for maintaining predictions and updating stored values during learning. These findings reveal that within PFC, variability in temporal specialisation across neurons predicts involvement in specific decision-making computations.
DOI: 10.7554/eLife.18937.001

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†These authors contributed equally to this work

Competing interests: The authors declare that no competing interests exist.

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Introduction

Theoretical models of decision making emphasise the importance of evidence accumulation across time until a categorical choice is reached (***Bogacz et al., 2006***; ***Gold and Shadlen, 2007***). One widely studied class of evidence accumulation models are cortical attractor networks, originally derived from studies of working memory (***Amit and Brunel, 1997***; ***Wang, 1999***, ***2002***). These rely upon strong recurrent connections between similarly tuned neurons to integrate evidence across time, and exhibit temporally extended persistent activity that stores the outcome of the decision process in memory (***Wang, 2002***; ***Wong and Wang, 2006***). In value-guided decision making tasks, attractor network models predict the emergence of correlates of chosen value during choice (***Hunt et al., 2012***; ***Rustichini and Padoa-Schioppa, 2015***). These value correlates result from varying speeds of decision formation across different trials, an issue we explored closely in our previous paper (***Hunt et al., 2015***). However, in contrast to the relative homogeneity of chosen value correlates within such models, it is known that decision correlates are highly *heterogeneous* across different cells within a given region (***Kennerley et al., 2009***; ***Wallis and Kennerley, 2010***; ***Meister et al., 2013***). The source and functional significance of this neuronal heterogeneity remains unclear.

Neurons also exhibit heterogeneity in their *temporal receptive fields of integration* (***Chen et al., 2015***). The temporal receptive field of a neuron can be established by examining its spike-count autocorrelation function (ACF) at rest (***Ogawa and Komatsu, 2010***). A slowly decaying ACF whilst

Publications (cont'd)

Examples of publications by past and present students:

ARTICLE

Received 24 Jun 2016 | Accepted 28 Feb 2017 | Published 18 May 2017

DOI: 10.1038/ncomms15097 OPEN

Vagal determinants of exercise capacity

Asif Machhada[1,2], Stefan Trapp[1], Nephtali Marina[1], Robert C.M. Stephens[3], John Whittle[4], Mark F. Lythgoe[2], Sergey Kasparov[5], Gareth L. Ackland[1,6] & Alexander V. Gourine[1]

Indirect measures of cardiac vagal activity are strongly associated with exercise capacity, yet a causal relationship has not been established. Here we show that in rats, genetic silencing of the largest population of brainstem vagal preganglionic neurons residing in the brainstem's dorsal vagal motor nucleus dramatically impairs exercise capacity, while optogenetic recruitment of the same neuronal population enhances cardiac contractility and prolongs exercise endurance. These data provide direct experimental evidence that parasympathetic vagal drive generated by a defined CNS circuit determines the ability to exercise. Decreased activity and/or gradual loss of the identified neuronal cell group provides a neurophysiological basis for the progressive decline of exercise capacity with aging and in diverse disease states.

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Tracking the Evolution of Non–Small-Cell Lung Cancer

M. Jamal-Hanjani, G.A. Wilson, N. McGranahan, N.J. Birkbak, T.B.K. Watkins, S. Veeriah, S. Shafi, D.H. Johnson, R. Mitter, R. Rosenthal, M. Salm, S. Horswell, M. Escudero, N. Matthews, A. Rowan, T. Chambers, D.A. Moore, S. Turajlic, H. Xu, S.-M. Lee, M.D. Forster, T. Ahmad, C.T. Hiley, C. Abbosh, M. Falzon, E. Borg, T. Marafioti, D. Lawrence, M. Hayward, S. Kolvekar, N. Panagiotopoulos, S.M. Janes, R. Thakrar, A. Ahmed, F. Blackhall, Y. Summers, R. Shah, L. Joseph, A.M. Quinn, P.A. Crosbie, B. Naidu, G. Middleton, G. Langman, S. Trotter, M. Nicolson, H. Remmen, K. Kerr, M. Chetty, L. Gomersall, D.A. Fennell, A. Nakas, S. Rathinam, G. Anand, S. Khan, P. Russell, V. Ezhil, B. Ismail, M. Irvin-Sellers, V. Prakash, J.F. Lester, M. Kornaszewska, R. Attanoos, H. Adams, H. Davies, S. Dentro, P. Taniere, B. O'Sullivan, H.L. Lowe, J.A. Hartley, N. Iles, H. Bell, Y. Ngai, J.A. Shaw, J. Herrero, Z. Szallasi, R.F. Schwarz, A. Stewart, S.A. Quezada, J. Le Quesne, P. Van Loo, C. Dive, A. Hackshaw, and C. Swanton, for the TRACERx Consortium*

ABSTRACT

BACKGROUND

Among patients with non–small-cell lung cancer (NSCLC), data on intratumor heterogeneity and cancer genome evolution have been limited to small retrospective cohorts. We wanted to prospectively investigate intratumor heterogeneity in relation to clinical outcome and to determine the clonal nature of driver events and evolutionary processes in early-stage NSCLC.

METHODS

In this prospective cohort study, we performed multiregion whole-exome sequencing on 100 early-stage NSCLC tumors that had been resected before systemic therapy. We sequenced and analyzed 327 tumor regions to define evolutionary histories, obtain a census of clonal and subclonal events, and assess the relationship between intratumor heterogeneity and recurrence-free survival.

RESULTS

We observed widespread intratumor heterogeneity for both somatic copy-number alterations and mutations. Driver mutations in *EGFR*, *MET*, *BRAF*, and *TP53* were almost always clonal. However, heterogeneous driver alterations that occurred later in evolution were found in more than 75% of the tumors and were common in *PIK3CA* and *NF1* and in genes that are involved in chromatin modification and DNA damage response and repair. Genome doubling and ongoing dynamic chromosomal instability were associated with intratumor heterogeneity and resulted in parallel evolution of driver somatic copy-number alterations, including amplifications in *CDK4*, *FOXA1*, and *BCL11A*. Elevated copy-number heterogeneity was associated with an increased risk of recurrence or death (hazard ratio, 4.9; $P=4.4\times10^{-4}$), which remained significant in multivariate analysis.

CONCLUSIONS

Intratumor heterogeneity mediated through chromosome instability was associated with an increased risk of recurrence or death, a finding that supports the potential value of chromosome instability as a prognostic predictor. (Funded by Cancer Research UK and others; TRACERx ClinicalTrials.gov number, NCT01888601.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Swanton at the Translational Cancer Therapeutics Laboratory, Francis Crick Institute, 3rd Fl. SW, 1 Midland Rd., London NW1 1AT, United Kingdom, or at charles.swanton@crick.ac.uk.

*A complete list of investigators in the Tracking Non–Small-Cell Lung Cancer Evolution through Therapy (TRACERx) Consortium is provided in Supplementary Appendix 1, available at NEJM.org.

Drs. Jamal-Hanjani, Wilson, McGranahan, Birkbak, and Veeriah and Mr. Watkins contributed equally to this article.

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DOI: 10.1056/NEJMoa1616288

Further Information

Information on areas of research can be found on the UCL School of Life & Medical Sciences website: **www.ucl.ac.uk/research/domains**

Or via the MBPhD Programme website: **www.ucl.ac.uk/mbphd/supervisors/primary-supervisors**

For further information regarding the programme and application forms, please contact the programme administrator, or alternatively download the application pack from: **www.ucl.ac.uk/mbphd**

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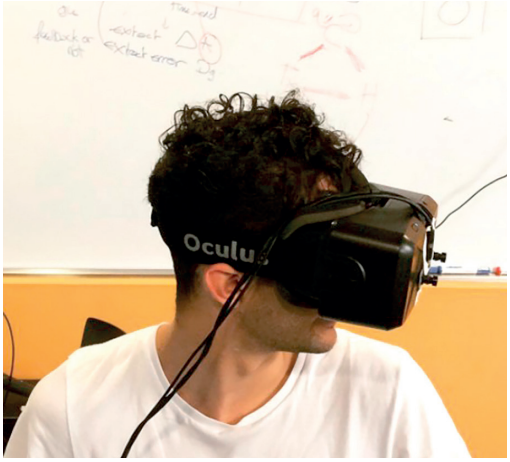
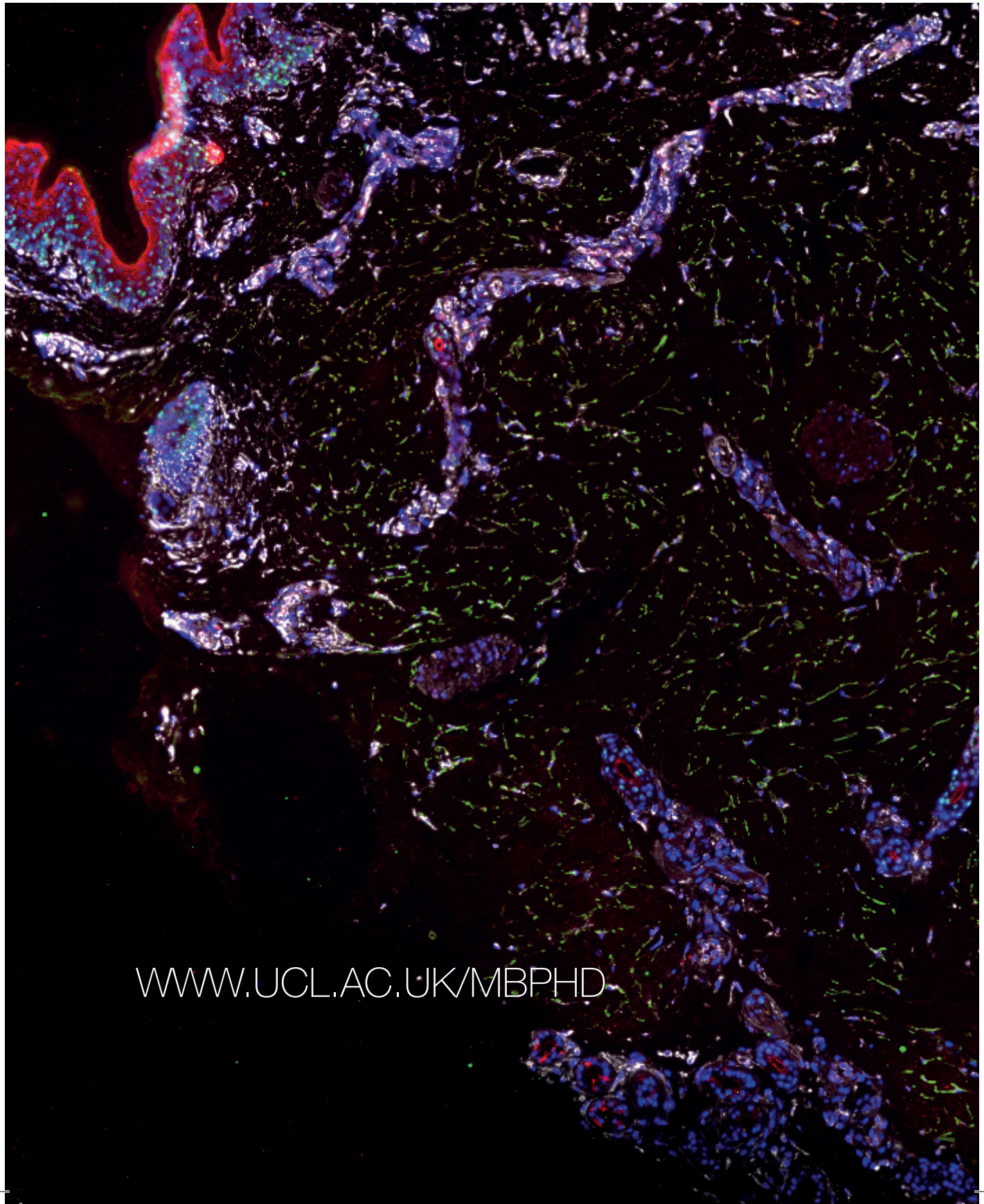
Cover image: DNA damage in human skin biopsies
Mr Oliver Devine (current UCL MBPhD student)




WWW.UCL.AC.UK/MBPHD