

CamPathology

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Retiring at Thirty:
Professor Nabeel Affara

Alumna Focus:
Dr Teresa Niccoli

Global Health News



**UNIVERSITY OF
CAMBRIDGE**
Department of Pathology

Contents

4 – 6	Retiring at Thirty: Professor Nabeel Affara
6	Get to Know - Louisa Bailey
7	The Vikings Have Landed: Professor Klaus Okkenhaug
8 – 9	Immunology Division News
10	Cambridge Science Festival & Student Spotlight
11	Blastoma from the Pastoma!
13 – 14	Cellular & Molecular Pathology News
14	Green Impact & Disease Detectives
15	Dr Naomi McGovern
16 – 17	Alumna Focus: Dr Teresa Niccoli
18 – 19	Global Health News

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Professor Geoffrey L Smith, Professor Nabeel Affara, Dr Naomi McGovern, Dr Louise Boyle

We welcome any contributions to future issues. Our next issue will be released in Michaelmas 2018, so we will be accepting submissions during the summer. Please email us at news@path.cam.ac.uk.



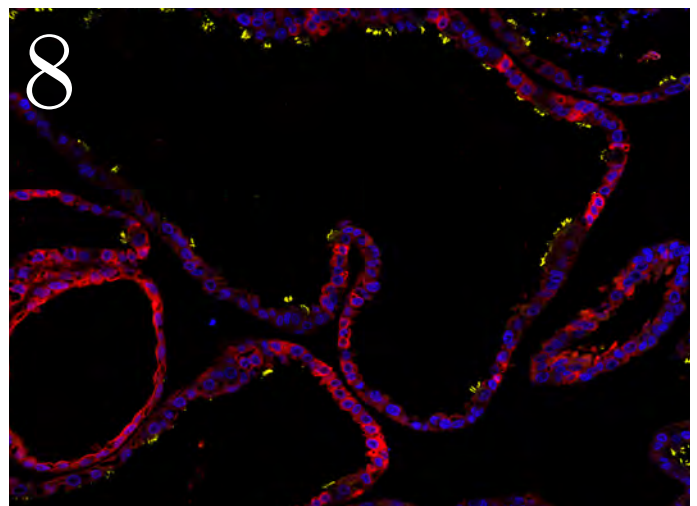
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Geoffrey L. Smith
Professor of Pathology
Head of Department
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A Note from our Head of Department

*The
Department
strives
continually
to make
this a better
place to
work*

In this new year the Department of Pathology looks forward with confidence to the rest of the academic year. In the last term we welcomed many new staff and students and said a fond farewell to those moving on, especially to those long serving and retiring members.

To all our new undergraduate students, welcome to Part 1B Pathology. I hope you will enjoy this course and be inspired by it to consider Part II Pathology in your third year. To our new Part II students, thank you for choosing Pathology and congratulations on being enrolled onto this heavily-oversubscribed course. I hope you enjoy your time here and some of you will feel inspired to consider a research career. To our PhD students, thank you for joining us. I wish you, together with the scores of postdocs working here, every success.

The Department was pleased that the quinquennial Teaching and Learning Review of the Department went so well during the last year and our teaching was widely applauded. So congratulations to all our dedicated teachers and special thanks to Colin Hughes, our Director of Teaching, and Alison Cook, our Academic Secretary, and many others for putting together the report. The Department now looks forward to a similar review of its research during Michaelmas Term 2018.

During the last year two senior, long serving, loyal members of the department have retired (partly!): Professors Nabeel Affara and David Dunne. To Nabeel and David we all say a warm thank you for your excellent service to the department

and best wishes for your future. To Nabeel, I add my own thanks for being acting head of department while I was on sabbatical and for keeping the department ship-shape. It was a pleasure to return to find that not all the money had been spent! To David, many thanks and congratulations on your inspirational efforts in promoting the Cambridge-Africa programme widely within in University and as Director of the Centre for Global Health within the Department. We are delighted that you are continuing to lead these enterprises while “in retirement”.

We welcome several new group leaders and congratulate others on achieving promotion. So to Suzanne Turner and Ian Brierley warm congratulations on your promotion to Reader and Professor, respectively, and to Kyriaki (Kiki) Ranellou, Naomi McGovern, Elizabeth Soilleux, Arend (AJ) te Velthuis, Anton Enright, Klaus Okkenhaug and Richard Hayward welcome to the department. Special congratulations to Naomi and AJ for winning Sir Henry Dale Fellowships.

Thank you to the ongoing excellent work from all our support staff who make such a positive impact and who keep the department running. In particular thanks to Alan Kirby, Alison Cook and Michelle Lucas without whom my job would be far more difficult and far less enjoyable.

Finally, the department strives continually to make this a better place to work and our Equality, Diversity and Wellbeing Committee is dedicated to this task and welcomes ideas from everyone on how to achieve this.

Professor Geoffrey L. Smith

Retiring at Thirty: Professor Nabeel Affara

A Summary of My Time in the Department

I came to the Department from the University of Glasgow in 1987 when Professor Malcolm Ferguson-Smith took up the Chair of Pathology. Unlike the West of Scotland, it was a sunny day on the 1st of October 1987 and really quite a strange experience. Our “mission” was to introduce human genetics, molecular genetics and genomics into the Department’s research and teaching and, Malcolm, to build the Department of Medical Genetics and associated regional NHS clinical, molecular and cytogenetics services based at Addenbrooke’s and the Clinical School.

The Department wasted no time in making me both overall and Cellular Pathology Part II organiser a year after my arrival! Over this time, the old Cellular Pathology Option underwent far reaching change reflecting the way in which research strategies for investigating disease mechanisms have evolved. The option first metamorphosed into the Cellular and Genetic Pathology Option and subsequently into the Cancer and Genetic Disease Option of the present day. The option has always been popular and I would like to think that it has had a positive influence on medical students in demonstrating the relevance of genetics, molecular genetics and genomics to medicine and understanding

disease processes. In this respect, I was intrigued to receive an e-mail flier from NHS Health Education England advertising a 3 week online course called “Step Inside the Sequencer”, described as a “course on whole genome sequencing covering the fundamentals of DNA sequencing and genomics in healthcare, and is ideal for non-experts”.

We established the Mammalian Molecular Genetics Group focussing on the genomics and molecular genetics of the sex chromosomes. Two of the original members of this group remain to this day; namely myself and Dr. Carole Sargent who joined me in 1988 after completing her Ph.D. in the Department of Biochemistry, in another place!. This group has remained well funded up to the present day and has trained over 35 Ph.D. students and annually some 2-3 Part II project students. Over the past 30 years, the research interests of the group have broadened to study a wider range of pathologies using mouse, human and pig models of disease. These include a more detailed focus on male infertility and spermatogenesis, pig models to study the molecular genetics and genomics of psychotic maternal behaviour and investigations into the role of epigenetic mechanisms in the aetiology of non-communicable diseases. It was from the activities of the group that the Department’s substantial genomics facility eventually emerged.

As I became more senior in the Department, I assumed more administrative and leadership responsibilities, becoming deputy head of department over the past 5 to 6 years.

Industrial Collaborations

The group has always been (and continues to be) open to engagement with industrial partners, through the various facilitating conduits; CASE studentships, LINK Grants, IPA Grants and direct funding from commercial partners. This has been extremely beneficial to our group and more widely to the Department. We established a long-term collaboration with The Pig Improvement Company (PIC) that formed the basis of using the





pig as a model for a number of studies with relevance to the genetics of disease resistance and maternal behaviour. This led to several CASE studentships, joint BBSRC grants and several million pounds of direct funding which brought in a hefty overhead for the Department! Importantly, such collaborations illustrate how very significant resources can be made available to researchers. In the case of PIC, a massive historical archive of DNA samples, pedigree relationships and careful phenotypic assessment that provides the basis for large genomic and genetic studies to uncover important genes for health and growth that are likely to have human relevance.

One of the striking features of Cambridge is the way in which the collegiate structure promotes unlikely collaborations across disciplines. I was fortunate enough to be involved in two initiatives, both driven by the needs for technology development demanded by the execution of the human genome project.

One of the striking features of Cambridge is the way the collegiate structure promotes unlikely collaborations across disciplines

The first was collaboration with Dr. Tom Bligh in the Manufacturing Engineering division of the Engineering Department and two former engineering graduates from Kings College, Dr. Martin Davies and Mr. Stuart Elmes. The need for automated bacterial colony picking and subsequently the printing of DNA microarrays required the production of sophisticated robotics. I supplied the biological specification and testing of the robots as they were developed and insight into the potential target market. Two very successful robots (colony picker and DNA microarray printer) emerged from this collaboration that formed the basis of a company called BioRobotics. The Department gained robots for free and these provided the basis for the establishment of a genomics facility.

The second project was again a collaboration with Engineering, in this case with Dr. Nick Hahn and Dr.

Graham Snudden linked to the Signal Processing Division. They had formed a company called BlueGnome based on the development of imaging software for quantification of DNA microarray signals and then eventually the design of diagnostic DNA arrays for use in NHS molecular genetics services. My group contributed expertise and advice on microarrays and the specification for image processing of microarray images. BlueGnome was eventually sold to Illumina Inc. but not before I had secured a 3% stake for the Department. This resulted in £1.3 million coming to the Department and the establishment of two endowment funds to support molecular genetics and genomics based research; the BlueGnome Molecular Genetic Pathology Fund and the Genomics and Bioinformatics Support Fund.

The Change in Research During My Time in Pathology

Since 1987 and throughout the 1990s towards the completion of the Human Genome Sequence, the greatest change in the nature of research has been the impact of the technologies that have evolved to permit what might be termed Genome Biology. There are two main components to this; first the tools of the trade - very powerful sequencing technologies and extremely sophisticated means of genome manipulation; second, the development of massive interconnected databases containing huge amounts of data and, bioinformatic tools to manipulate big datasets and to manage and interrogate online databases. These technological and bioinformatics developments were traditionally the preserve of elite groups with massive funding. However, the further advance of technologies and their capabilities have reduced the cost and in a sense democratised access. The result is that much more modest groups can take a systems and genome biology approach to their particular field of investigation. This permits the discovery of unsuspected interactions and hence the generation of new hypotheses that can go on to be tested.

Continued overleaf...

Exciting Advances and Opportunities for the Future of Research

The advance of research capabilities has always been a blend of technology development and creative imagination in the use of new technologies. In the world of genetic and genomic approaches to biology and disease the last decade has seen a huge increment in technical capability and, hence, the sophistication of the questions that can be addressed to unpick biological and disease processes. I think the technological sensitivities to study what is happening in single cells and to manipulate genomes in a very sophisticated way through

genome editing are very exciting prospects. To this, I would add the explosion in our technical ability to study epigenetic modifications of the genome in response to environmental cues and exposures. This really has opened a whole new perspective on understanding disease mechanisms induced by a variety of exposures beginning even in the womb and early stages of gestation. The public health implication of insights gained from such research are obvious.

What Next?

After retiring at the end of September 2017, I will remain in the Department for about another two years on a Voluntary Research Agreement

(VRA). This will allow me to complete three research grants two of which are involved with collaborative projects based in West Africa; one on the epigenetic correlates of stunting and, the second, on the environmental exposures, epigenetic and gene expression changes associated with NOMA, a disfiguring facial disease involving massive tissue destruction. I will retain a lifelong connection with the University through my College, Hughes Hall, where I have been made a Life Fellow.

Next Issue: Read about David Dunne's time in the Department and his plans for the future...

Get to know... Louisa Bailey

LOUISA BAILEY is the Chief Teaching Secretary in the Department of Pathology. Louisa runs the Teaching Office in the Department which provides administration and support for our Undergraduate and Graduate students.

How would your friends describe you? I think my friends would say I am an organiser - always planning our next get-together or trip, and that I am a positive and happy person.

The top 3 highlights of my life are... Childhood summers down on the family farm, going to University and becoming an Auntie.

What single thing would improve the quality of your life? The invention of teleportation, so I could travel wherever I wanted, and also so I wouldn't have to sit in Cambridge traffic every day.

Which 5 famous people, living or dead, would you want at your fantasy dinner party? J. K. Rowling, Stephen Fry, Peter Kay, Princess Diana, and Mickey Flanagan.

What are your pet peeves? People who leave their trolleys in the middle of the supermarket car park, badly made Subway sandwiches and terrible drivers.

If you could time travel, where would you go? The 1560s to meet Elizabeth I.

What would be the title of your autobiography? "Always On Time" (I hate being late for anything!)

If you were the Prime Minister, what is the first thing you would do? Find Larry, the Downing Street cat.

If you were on an island and could only bring 3 things, what would you bring? My Kindle, lots of snacks and a luxury yacht.

If you were a cartoon character, which one would you be, and why? Not so much a cartoon but a book character - I would be someone from Harry Potter. Not one of the main protagonists though as they get into too much danger, but just a background Hufflepuff so I can go to Hogwarts and do magic.

What is your favourite song, movie and book? Song: Mr Brightside by The Killers, as it reminds me of being at University. Movie: I'm a big fan of the Marvel movies. Book: The Harry Potter series (Harry Potter and the Prisoner of Azkaban if I had to choose one).

What is your motto or personal mantra? Safety First!

Tell us something about yourself that no one would ever guess. I have a twin sister, but we are not identical so you'd never tell.



The Vikings Have Landed: Welcome to Klaus Okkenhaug and his lab

Interviewed by Professor Ian Brierley

We are delighted to welcome Klaus Okkenhaug to Pathology as Professor of Immunology following the retirement of John Trowsdale. Klaus was born in Montreal, but educated at the Rudolf Steiner school in Oslo. He returned to Canada at the age of 16 to attend high school in Toronto, finding biology quite boring, but liking physics, chemistry and mathematics! Naturally, he became a biologist. I had the pleasure of meeting up with him on the eve of his departure from the Babraham Institute, where he has been a group leader since 2003, and asked him how he felt about the move.

“The Babraham Institute, of course, has many benefits, including fantastic facilities, core funding and wonderful colleagues, but I really look forward to meeting new colleagues in the University, within the Department of Pathology and also in other Departments. I am also excited about being more involved in teaching. In terms of research, I am delighted to be moving to a department where there is such a broad interest in immunology. I will bring with me expertise in cell signalling and tumour immunology. Much of our work involves genetically modified mice and hopefully some of the models we bring will be useful for others in the Department. I remain highly motivated by the thrill of discovery and I very much enjoy running a lab and seeing people develop their research projects and gain scientific insights.”

Klaus has an established international track record in molecular immunology, with seminal contributions to our understanding of cell signalling pathways in the immune system, with particular focus on the PI3K

family of enzymes. In recent years, he has contributed to the description of a new primary immunodeficiency syndrome caused by activated PI3K δ mutations (APDS) and his group demonstrated that inhibition of PI3K δ in regulatory T cells unleashes a potent anti-tumour response.

“One of my main goals is to better understand host-pathogen interactions and how these can be manipulated using inhibitors. In parallel we are very interested in tumour immunology and I think the two strands of research inform each other. My PhD focused on signalling through the T cell co-stimulatory receptor CD28. I tried to prove that PI3K was essential for CD28 co stimulation. It wasn't, but it made me wonder what PI3K does and I have been wondering ever since! PI3K δ was a relatively obscure newly discovered enzyme and I've seen it become a major drug target.

I did my postdoctoral work with Bart Vanhaesebroeck at the Ludwig Institute for Cancer Research at UCL and he has had a very big influence on how I approach scientific questions and lead my lab. We still talk regularly on the phone and meet from time to time. We know each other well enough that we can bounce ideas off each other and ask for genuine advice.”

Klaus lives in West Wrattling with his wife, two children and a lively border collie. I asked him what he did in his spare time.

“I spend my weekend mornings watching my boys play football. I like to go running and I used to be an avid rower and a cross country skier. I quite like listening to opera but growing up, I was a David Bowie fan. I like to listen to a variety of music. I also read modern literature. My favourite authors at the moment are Sebastian Faulks and Ian McEwan. I've also enjoyed books by Mordecai Richler and Rohinton Mistry. The Ancestor's Tale by Richard Dawkins is one of my favourite non-fiction books.”

On behalf of the Department, I welcomed Klaus to Pathology and we look forward to his company in the years to come.



Immunology Division News

There has been a lot of change in the Immunology Division in recent months. We have the good news of announcing Klaus Okkenhaug as the new Professor of Immunology. Klaus takes the reins as Head of Immunology, succeeding Jim Kaufman, who has been acting Head since John Trowsdale retired in 2016. Klaus joins us from the Babraham Institute bringing with him a wealth of expertise in molecular immunology. His research focus is on the role of PI3K signalling in the immune system with particular focus on T-cell activation, differentiation and regulation. You can read more about his research and interests on page 7.

We are also delighted to welcome Naomi McGovern to the Division as a Sir Henry Wellcome Fellow. Her lab will investigate the specific functionalities of human dendritic cells and macrophages in different tissue inflammatory and developmental states. Her work, published in Nature earlier this year[†], uncovered a previously unappreciated role of dendritic cells within the developing fetus and showed that that these cells may mediate homeostatic immune-suppressive responses during gestation.

Louise Boyle, a Wellcome Trust Senior Fellow in the Division, won

the position of University Lecturer in Immunology. Her research is on understanding the role of TAPBPR in the MHC presentation pathway. In recent work, published in the eLife journal, she has discovered that in addition to being a peptide editor, TAPBPR improves peptide optimisation in this pathway. She is now interested in discovering ways to manipulate antigen presentation to enhance the repertoire of antigens presented for immune recognition.

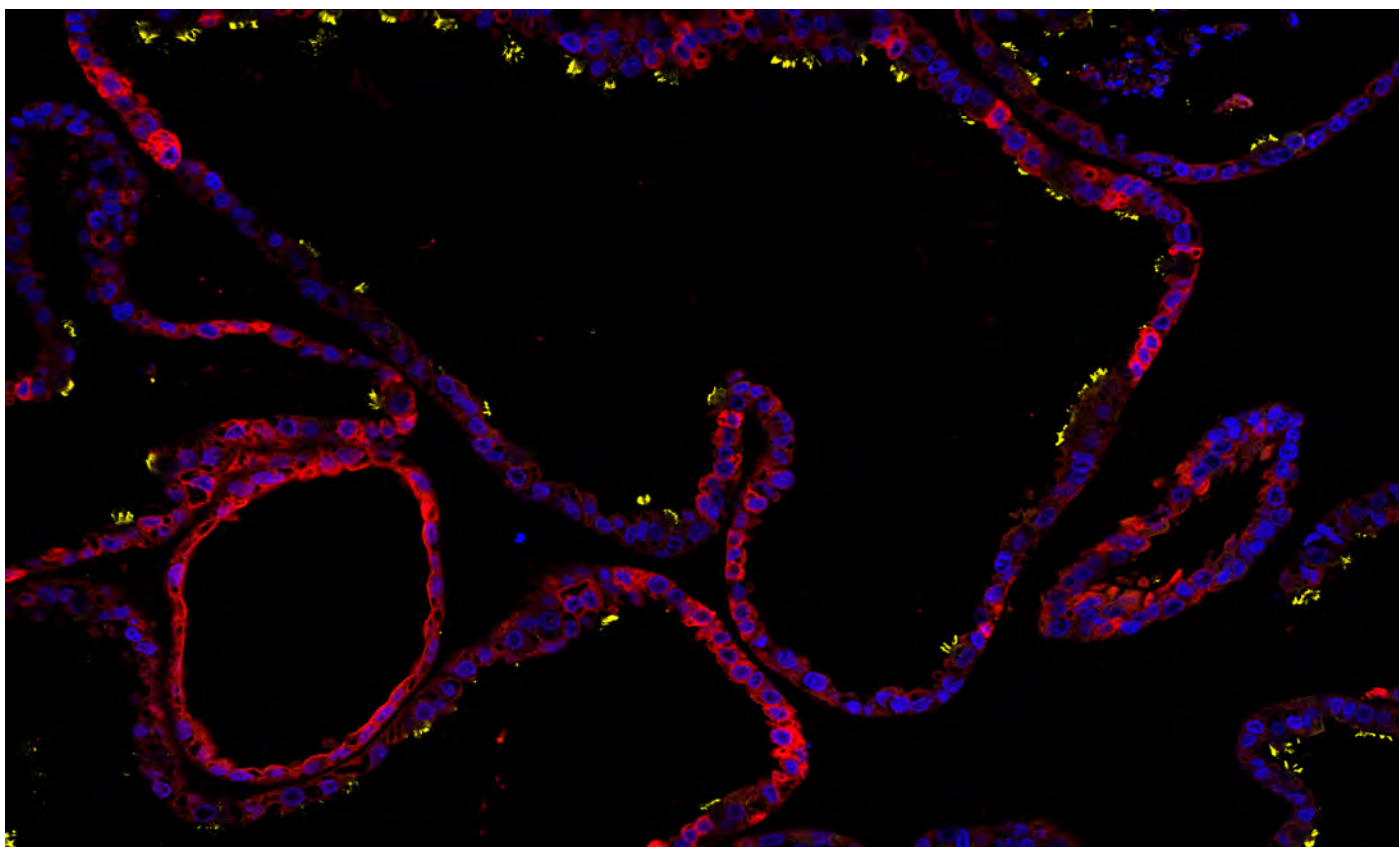
Naomi McGovern's work uncovered a previously unappreciated role of dendritic cells within the developing fetus

At the beginning of 2017, Kattia van der Ploeg and Shirin Ashraf, both from John Trowsdale's group, successfully defended their PhDs. Kattia has moved to Memorial Sloan Kettering Cancer Center in New York to start postdoctoral work with Katherine Hsu. She will be applying her expertise in NK cell research to try to harness their innate capacity for tumour recognition and eradication. Shirin has moved to the MRC-Centre for Virus Research in Glasgow to study emerging viral infections in Sub-Saharan Africa with particular attention to arboviruses. Jyothi Jayaraman is moving to Moffett-Colucci Group to start her CTR-funded PhD, and we also

welcome Dayana Hristova, Becky Martin and Helena Teague as PhD starters.

In funding news, Jim Kaufman was awarded a Wellcome Investigator Award to carry out studies to understand the role of class II molecules expressed in epithelial cells. An ERC Advanced Grant has been awarded to John Trowsdale for the purpose of investigating NK receptors in disease. Andrew Sharkey won an MRC project grant to study how expression of KIR on uterine NK cells regulates human pregnancy. Margherita Turco was awarded a Royal Society Dorothy Hodgkin Fellowship to study early placental development in humans (see image). Maja Wällberg was awarded Lollipop Foundation funding to develop gene therapy strategies to restore normoglycemia. Brian Ferguson was successful in winning a grant from the Cambridge Teaching and Learning Innovation Fund to update Part 1B Immunology practical classes.

A number of Divisional members have been busy helping to organise conferences, such as the 18th Cambridge Immunology Forum held at Queens College, the 10th KIR workshop held at St John's College and the Centre of Trophoblast Research 10th Anniversary Meeting. The Division also contributed to the



These organoids could be a useful tool to model the physiology and disease of human endometrium

Cambridge Science Festival (see p.10) and the Big Science Day at Bottisham Primary School organised by Louise Boyle.

Under the auspices of the Cambridge-Africa Programme, Ashley Moffett is hosting PhD student Stephen Tukwasibwe, who is visiting from Makerere University. This programme aims to strengthen Africa's own capacity for sustainable research. Stephen is investigating the role of KIR and HLA polymorphisms in transmission and severity of malaria in Uganda. Ashley leads the Maternal, Neonatal and Reproductive Health section of the Wellcome Trust—Cambridge Centre for Global Health Research. Through Cambridge-Africa, she has developed a broad collaborative research network with Makerere University and Mulago National Referral and Teaching Hospital in Kampala

over the last ten years. These collaborations involve researchers from across the University and the Wellcome Trust Sanger Institute. She has also established a clinical collaboration between Ugandan and Cambridge obstetricians (in partnership with Addenbrooke's Charitable Trust, Addenbrooke's Abroad). This clinical partnership has delivered workshops and skills drills (emergency response training) related to guideline development for sepsis, pre-eclampsia, haemorrhage and obstructed labour at Mulago Hospital. Ashley is currently compiling the first textbook dedicated to African obstetrics, which was recently approved for publication by Cambridge University Press. She and her laboratory technician, Lucy Gardiner, recently jointly celebrated their 30th anniversary of working in the Department.

With great sadness to everyone that knew her, Sue Hiby passed away in August. Sue took retirement from Ashley Moffett's group in February 2014 having worked for the University since September 1987.

Dr James Traherne

Image: Immunofluorescence of endometrial organoids differentiated to form the two main epithelial cell types of the human endometrium - ciliated (in yellow, stained with acetylated alpha-tubulin) and secretory (in red, stained with PAEP). Margherita Turco has succeeded in growing miniature functional models of the lining of the uterus in culture. These organoids could be a useful tool to model the physiology and disease of human endometrium.

†Turco, MY et al. Long-term, hormone-responsive organoid cultures of human endometrium in a chemically defined medium. Nature Cell Biology; 10 April 2017; DOI: 10.1038/ncb3516



STUDENT SPOTLIGHT

Dan Wise is a PhD student about to enter his fourth year. He previously attended the University of Exeter and gained a BSc and an MRes. He is a member of Jim Kaufman's group.

How did you decide on Pathology?

I was looking for a post as a Research Assistant and applied for a job I was interested in, working with Jim Kaufman. Unfortunately, I didn't get the original position but ended up working for Jim, first voluntarily and then as an RA. I moved to Addenbrooke's for another RA post but I had decided that I would love to undertake my PhD at the department.

Kaufman Lab's research focuses on chickens – do you have a favourite chicken?

I do actually! The silkie is suave and super fluffy. Can you replace the picture of me with that?

What is life like in the Department?

I enjoy PhD life here. There are many helpful people with a lot of expertise, if you are struggling with any aspect of your work there's always someone who can offer advice and support.

Animal, vegetable or mineral?

Animal because of the silkie.

What's coming next for you?

I would like to stay in academic research, and hopefully continue with some long term projects I've started.

If you weren't in science what would you do?

Interpretive dance.

And finally....any advice for students wishing to follow in your footsteps?

Work hard and study hard. Find an area of interest and follow it. Gain experience in the lab, as it's very different to studying. Make contact with the supervisor whose work you are interested in and have a chat!

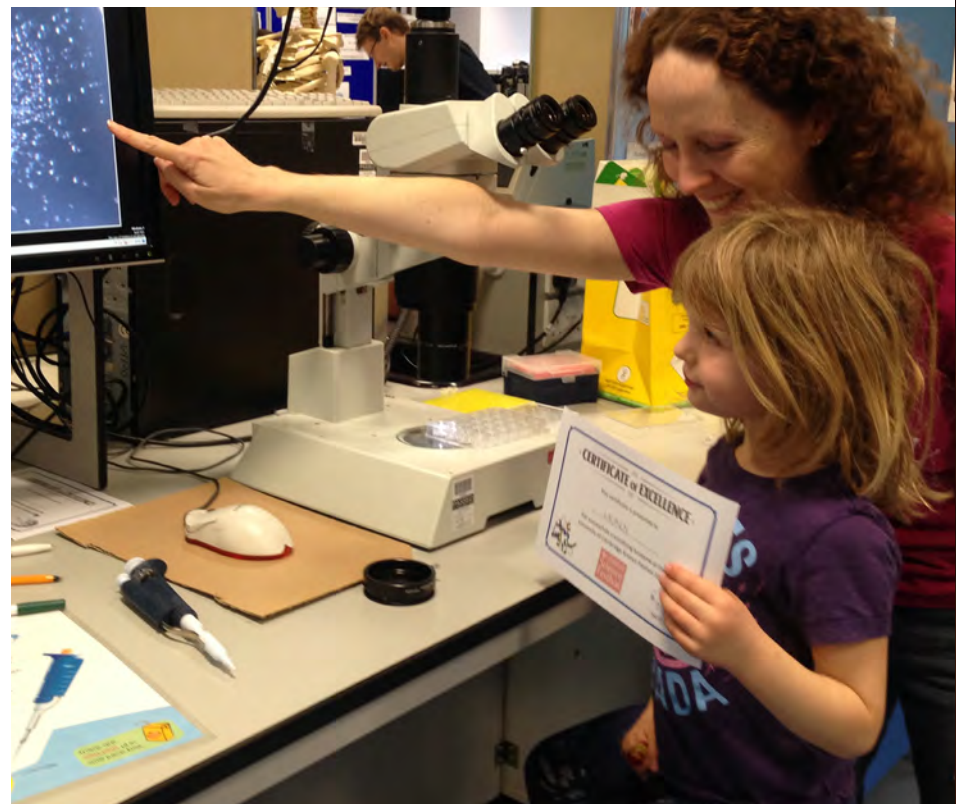
2017 CAMBRIDGE SCIENCE FESTIVAL

On Saturday 18th March 2017, the Department of Pathology opened its doors to the public as part of the 2017 Cambridge Science Festival. Enthusiastic students and staff from all over the Department turned out en masse to provide eight fun, hands-on activities for all ages. You could grow your own crystal with the Deane & Graham labs, be an antibody detective with researcher from the Goodfellow lab and learn how infection spreads using glitter bugs with members from the Doorbar lab.

Children enjoyed writing their name in genetic code with the Laman lab, building sweetie nucleosome with the Affara group and playing hide and seek games with members of the Boyle lab. The Kaufman lab highlighted the universal problem of pathogenic microorganisms with many fun

activities, including egg painting, and members of the Moffett lab eloquently explained what happens during pregnancy using a placenta made out of jelly!

The 2018 Cambridge Science Festival will run from 12-25 March 2018 and will provide another excellent opportunity for researchers and the public to explore, discuss and debate issues of scientific interest, to encourage young people to study STEM subjects and to consider careers in these areas. The departmental deadline for contributions is Friday 27th October 2017. If you would like to get involved or have any ideas for forthcoming Science Festival then please email Louise Boyle (lhb22@cam.ac.uk). We are also keen to hear about any other outreach or public engagement activities you are involved in.



BLASTOMA FROM THE PASTOMA!

Please had
forgive we had
typescript it by
hand writing

August 27, 1984

SCHUSTER
Mrs N. H. NICHOLLS
72 CLAREWOOD COURT
CRAWFORD STREET
LONDON W1H 5DF
TELEPHONE: 01-262 2979

Dear Professor Wildy

I am sorry that at 92 I feel far too old to take on any more commitments than I already have so I am enclosing a single gift (by cheque) to your Appeal. I do so especially as a thank offering to H.R.DEAN. who really gave me my first real introduction to pathology especially in relation to its clinical applications. This was in Manchester 1916 to 1918 when, as a student, I acted as clinical pathologist at the Royal Infirmary during the War.

When I took the Natural Science Tripos at Cambridge in 1915, pathology was not a separate subject although the names of Sims Woodhead, Nuttall and Strangeways were of course familiar to us, preparing for medicine.

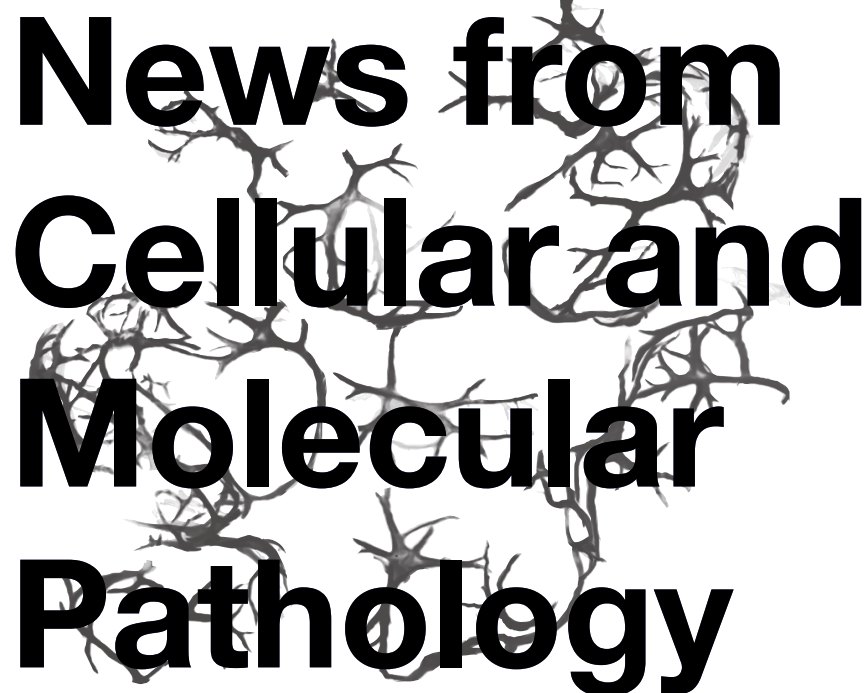
Your Appeal put me in mind of a galaxy of anatomists and physiologists with whom one became familiar in 1912 to 1915. Sir Clifford Allbutt sailing through the laboratories in majestic robes and on one occasion Dr Barcroft (I think it was), finding me idling one afternoon, took me with him to watch my first animal experimentation. Prof Gaskell walked in and held forth in a somewhat embarrassingly candid discussion. He was retired by then I think and Langley was our professor and once in a lecture, made the astonishing statement that acquired characteristics could not be inherited because, after cutting off the tails of 300 generations of rats, not a single one was born without a tail. He and his wife gave entertaining tea parties on Sundays and there was much personal hospitality then, even to the women students (if you had an academic father!)

Considering my sex, Cambridge was a happy and profitable period as an introduction to medicine though bi-passing the University rules made for some comic situations which I won't bother you with. I think I was the first woman allowed in the dissecting room (in 1912) when old Alexander Macalister was still, nominally, the professor of Anatomy, and very kind.

I missed the Long vacation course in Pathology under Dr Sims Woodhead but lots of the people described in Dr Rooks' collections of essays were very familiar figures and I was allowed to take the 2nd M.B. examination (in secret) and get exemption when I went to Manchester for the hospital work. I am glad to be able to give thanks for various concessions in Cambridge. I never knew Dame Honor Fell though I have been introduced to her once.

I am sending, under separate cover, a rather trivial Memoir because it has a good photograph of Prof. DEAN and a few words on page 2 and 3 if you can be bothered to look at it. I think I sent a copy to Dr Rook. I should like to attend the centenary meeting but ~~aaaax~~ but can't see myself getting there and anyhow would not know or be known by anyone. I much enjoyed Dr Rooks book and knew the people of that period better.

With all good wishes Yours sincerely Nora H. Schuster



News from Cellular and Molecular Pathology

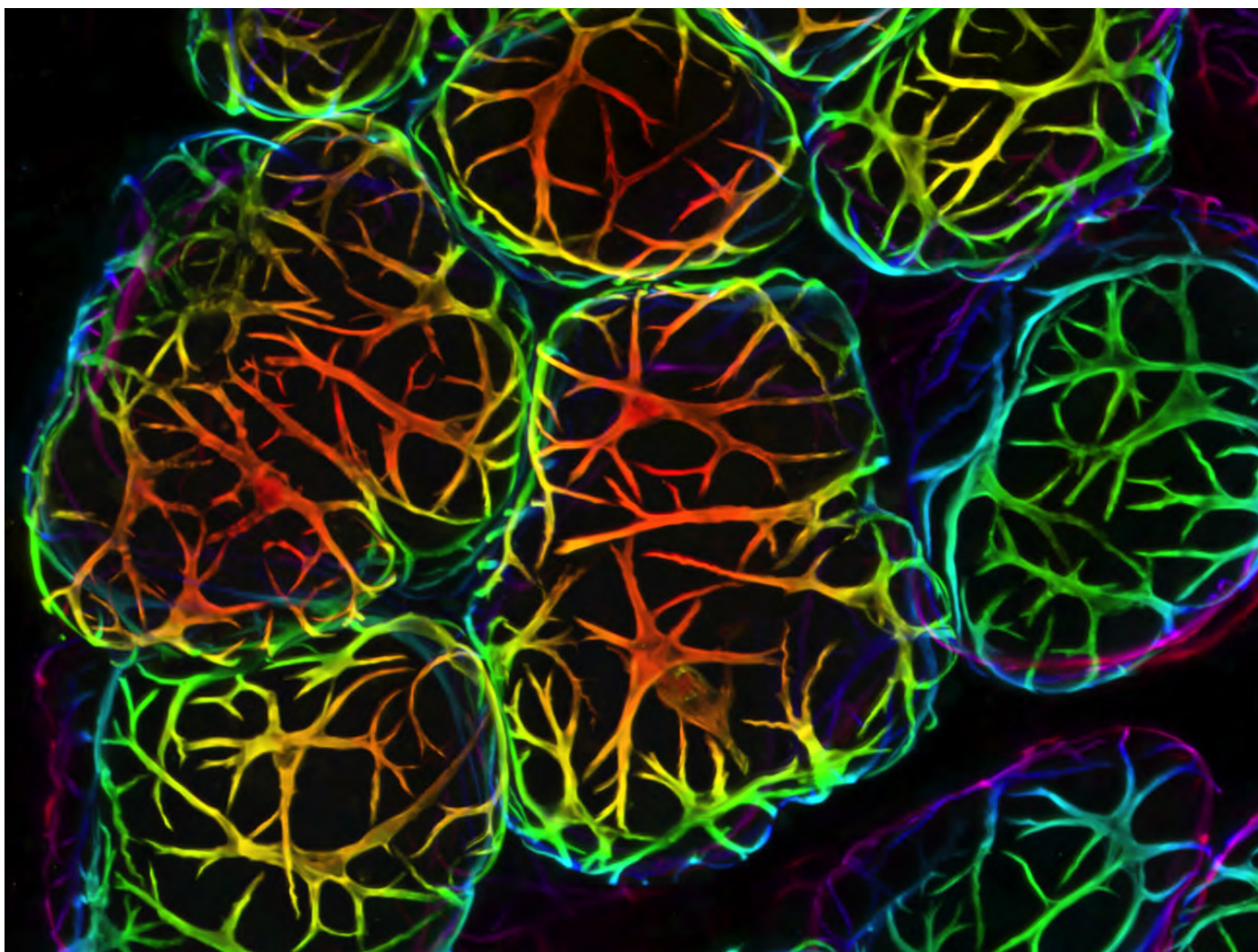
At first there were two divisions, Histopathology and Cellular and Molecular Pathology, but, in spite of their names, many of the research themes overlapped, with a focus on normal and abnormal cellular development in disease. In recent years, progress in genome-wide technologies means many of the labs are handling and interpreting large datasets alongside the more traditional methods for fine-detailed molecular, histopathological and cell-culture analysis. Cross-fertilization of ideas, and convergence of practices, meant that the existence of two separate divisions was more artificial than logical. Finally, the halves have merged, creating our 'new look' Cellular and Molecular Pathology Division, with Professor Nick Coleman at the helm.

Physically, the research labs remain split over two main sites: Tennis Court Road (TCR) and the ever-enlarging Biomedical Campus which has Addenbrookes Hospital as its nucleus. The TCR team includes the groups of professors Nick Coleman, Christine Watson and Nabeel Affara, Drs Heike Laman, Matt Murray and Paolo D'Avino. The Addie's team consists of Professor Ming Du, Drs Suzanne Turner, Janet Deane, Liz Hook, Olivier Giger and Elizabeth Soilleux. Nabeel retired this year, after almost 30 years with the Department (see p.4), whilst Janet, Liz, Olivier and Elizabeth are the most recent additions, with Janet hijacked from Immunology (sorry!). Of course, CMP also has associates embedded

elsewhere around the University, notably Emma Rawlins in the Gurdon Institute.

“Improved image capture techniques applied to model organisms and tissue samples have resulted in spectacular multi-colour models”

Research continues to concentrate on how cells mature and differentiate in normal tissues, and how aberrations in these processes are key to understanding the diseased state, particularly cancers. Progress in 3-D culture systems, plus improved image capture techniques applied to model organisms and tissue samples has resulted in spectacular multi-colour models generated by Christine Watson's group, enhancing the understanding of mammary gland origins and development. In contrast, the 'omics' revolution has increased the ability to interrogate multiple large datasets of cellular components, and has led to the discovery of how both coding and non-coding regions of the genome have a role in the control of gene expression. For Matt Murray and Nick Coleman, study of these non-coding



regions has identified a set of signatures which allows clinicians to provide better diagnosis, prognosis and treatment plans for subsets of childhood tumours arising from germ cells.

Of course, as with all of the divisions, CMP is involved with the design and delivery of University lectures and practical classes. Liz Hook has been instrumental in developing the Clinical Pathology courses for year 4, 5 and 6 medical students, 2017 being the last of the old style and first of the new style exam structures. Liz is now on a mission to revise and revamp the Part IB Histopathology course, much of which is still familiar from her time as a Cambridge undergraduate! Olivier Giger is engaging with professional development within the NHS, leading a new course in Molecular Pathology for Clinical Histopathologists.

In addition to the retirements of Paul Edwards in 2016 and Nabeel Affara in September 2017, this has been a year of promotions, prizes and new grants. Congratulations to Suzanne Turner on her Readership, Christine Watson on her election to the Academy of Medical Sciences, Matt Murray on his lectureship, Paolo D'Avino and Emma Rawlins on major funding awards, and 'Welcome' to Anton Enright, a new appointment who arrives in the Department with his group from the European Bioinformatics Institute (EBI) at Hinxton during the 2017-2018 academic year.

Dr Carole Sargent

“In recent years, progress in genome-wide technologies means many of the labs are handling and interpreting large datasets alongside the more traditional methods for fine-detailed molecular, histopathological and cell-culture analysis”

Image: Lactating mouse mammary gland, imaged using optical clearing combined with 3D confocal microscopy. Olivia Harris, Felicity Davis, Bethan Lloyd Lewis: Watson Lab.



THE CAMBRIDGE *green* CHALLENGE

The first meeting of the Department's Green Impact Team took place on Monday 23rd October 2017. The meeting was well attended by members of staff from across the Department.

Gráinne Kennedy, the University's Environmental Coordinator and Martin Howes, the Sustainable Labs Coordinator came along and gave a useful talk about what the Department can do to attain at least a Bronze Award. The good news is that we are already well on the way towards a Bronze Award! Martin was particularly excited by our energy monitoring project, which allows us to monitor energy usage on a floor by floor basis within the Department.

The University aims to be a world leader in sustainability and intends to be carbon neutral by 2050. Goals include utilising renewable energy, sending zero waste to landfill and sustainable transport policies. While great steps have been made towards this, particularly

in the area of waste, there is still much to do. There is also a determination to teach sustainability principles to students, so they can carry these ideals out into the world when they leave Cambridge.

There are currently around forty Green Impact teams in the University and more in the making. Lots of exciting developments are on the way, such as online learning modules with games and information to help teach people how they can make a difference. The team learned about the many ways in which we can go green; from using the funding offered by the Energy & Carbon Reduction Project to help purchase energy efficient freezers and drying cabinets to switching off personal heaters and air conditioning. The Green Impact Newsletter spotlights a different subject each month; including travel in April and the Christmas switch off in December. The plan for the Department's Green Impact Team will be to also highlight a different green issue each month.



If you'd like to join the Green Impact Team and help both the Department and the University make a difference, or if you just want further details, please get in contact with Anna Rudd (aks60@cam.ac.uk) for further details.

Disease Detectives Wanted! Volunteer at the 2018 Cambridge Science Festival



We are busy planning the departmental events for the 2018 Cambridge Science Festival, which takes place between 12th and 25th March 2018.

In addition to our usual hands-on drop-in session in the teaching lab on Saturday 17th March 2018, we have two new events planned. Firstly the departmental canteen will be transformed into "The Path Caf". In addition to serving as a relaxing space for families to take time out from the hands-on activities, the Path Caf will provide a place for the public, particularly teens and adults, to meet our scientists. We are looking for volunteers covering all levels of the career ladder, from students to Professors, to be part of this event.

Secondly, we will host an exciting event called "Disease Detectives: Outbreak ALERT!" in the Greaves and

Dixon rooms. This interactive group activity for school-aged children is based on diagnosis of a transmissible infectious disease. In this activity, participants become "Disease Detectives" assisting doctors during an outbreak. Detectives will receive mission packs with all the resources to help them evaluate how the infection is spreading, which infectious agent is responsible, treatment and how to prevent further spread.

We are looking for lots of enthusiastic volunteers to help facilitate these sessions on the day. If you would like to participate in any of these events or have any other ideas for public engagement or outreach activities then please get in touch with us using the below email.

Department of Pathology Public Engagement and Outreach Committee Email: engage@path.cam.ac.uk

Dr Naomi McGovern

My research involves understanding how different human tissues and their changing microenvironments (e.g. inflammation vs. steady state, fetus vs. adult) impacts on immune cell fate and function. My interest in this line of research first arose during my PhD under the supervision of Prof. Edwin Chilvers and Prof. Alison Condliffe at the Dept. of Medicine, Addenbrooke's hospital, Cambridge. There I studied the effects of hypoxia on neutrophil fate and function.

For my first postdoc (2010-2013), I moved to the laboratory of Prof. Matthew Collin at the Institute of Cellular Medicine, Newcastle University, UK. There I studied antigen presenting cell (APC) subsets within a number of human organs, including blood, lung and skin. The primary purpose of my research during my first postdoc was to characterize CD14+ cells located within the dermal layer of human skin. Through this project, I demonstrated that dermal CD14+ cells arise from circulating CD14+ monocytes and are distinct in their ontogeny, phenotype and function from tissue resident macrophages and classical dendritic cells (cDC). My second major project during this period involved the identification and characterization of cDC subsets within human lung. Through this project, I demonstrated that human lung CD1c+ DC trigger Th17 polarization in response to *Aspergillus hyphae*.

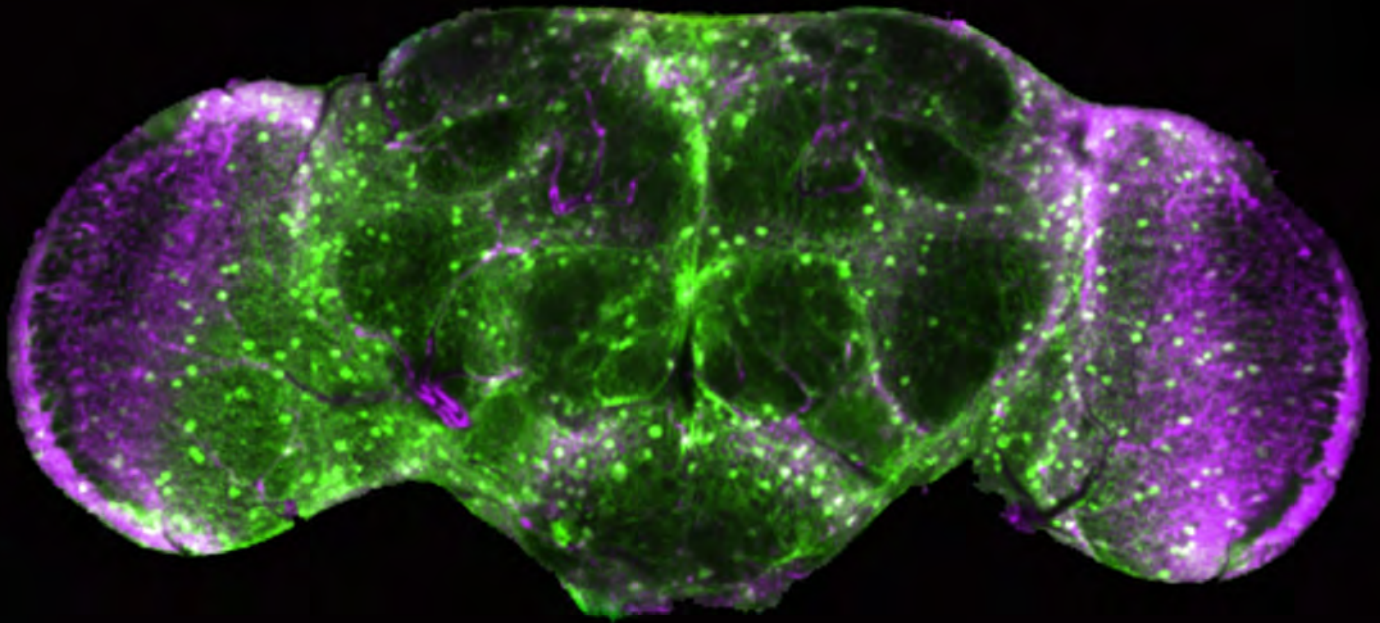
During my first postdoc, I had a strong collaboration with Dr. Florent Ginhoux at Singapore Immunology Network, Singapore. Hence, I moved there for my second postdoc (2013 – 2017). There I carried out the first in-depth analysis of the human fetal APC network. I identified the fetal APC subsets by advanced flow cytometry and showed that equivalent APC subsets can be identified across fetal and adult tissues by comparing subset specific gene signatures. I showed fetal APC can sense foreign protein (e.g. pathogens) via Toll-like Receptors (TLR) recognition and migrate to the lymph nodes like adult cells. However, fetal APC are very

different to adult APC in that they strongly suppress T cell pro-inflammatory cytokine production and promote regulatory T cell induction.

Through my current Sir Henry Dale fellowship (commenced in March 2017), I will continue to study tissue antigen presenting cells. My current focus is on characterising human placenta embryonic-macrophages, commonly termed Hofbauer cells (HBC). Embryonic macrophages such as HBC are the only immune cell present on fetal side of the placenta barrier. Through my fellowship I will study the properties of HBC using some of the most advanced tools available, including advanced multi-parameter flow cytometry and single-cell RNA sequencing. In particular I plan to develop our understanding of the role HBC play in preventing transplacental infection.



Figure: Fluorescence microscopy image of glial cells (green) and cell nuclei (purple) in the adult fruit fly brain.



Alumna Focus:

Dr Teresa Niccoli

Mini CV

2010-2017: Senior Post-doctoral Researcher at the Institute of Healthy Ageing (Partridge lab) and the Institute of Neurology (Isaacs lab), University College London.

Recipient of the UCL Neuroscience Early Career Prize (2015)

2006-2009: Masters in Medical Ethics and Law (passed with Merit)

2005-2010: Teresa took a career break to care for her two young sons.

2003-2005: Beit Memorial Trust Research Fellow in Daniel St Johnston's lab at the Gurdon Institute, University of Cambridge.

1998-2002: PhD student in Paul Nurse's cell cycle laboratory at Cancer Research UK.

1994-1997: B.A. Natural Sciences (Pathology, First Class Honours), Queens' College, University of Cambridge.

Why did you choose to study in the Department of Pathology?

I joined the Department in 1997 in my final year of studying for my undergraduate degree in Natural Sciences (Pathology). I had just come back from a summer working in a laboratory at Cold Spring Harbor, just outside New York City, and I was extremely keen to get back in the laboratory. I had studied Molecular and Cellular Biology the previous year and I wanted to learn how these basic mechanisms applied to a human disease contexts.

What was the most interesting thing you did as a student in the Department?

Dr Paul Edwards was offering a very interesting project looking into cloning an Epidermal Growth Factor Receptor (EGFR) into a viral vector and then transfecting cell lines to see if over-expression of EGFR had a phenotype. It all sounded very exciting, as mutations that cause overexpression of EGFR are associated with many cancers, and I was over the moon when Dr Edwards offered me the project. I had a great time in my year in the Department, working in a laboratory doing "proper science", where I could develop and move forward my

own project. Dr Edwards and the post-docs in the lab were very patient and helpful and I gradually gained confidence in running and performing my own experiments. The project went well, and I tried a range of techniques: I managed to clone the receptor, generate the virus and transfect cells. By the end of the year I realized that this is what I wanted to do as a career.

What are your best and worst memories of your time in the Department?

I only have good memories of my time in Pathology! In Paul Edward's lab, I was given a lot of freedom to organize my own experiments. Since I had worked all summer in a lab, I already knew my way round pipettes and restriction enzymes, and in the Edward's lab I was given all the help I needed but at the same time I could take the project forward myself.

The lectures were another major highlight, as they covered many different aspects of human disease mechanisms, which was (and still is) my main interest. We were taught the latest cutting edge research by leaders in the field, which was unimaginable to someone who had arrived in England from a small village in the Italian Alps only a couple of years before!

How did your time in Pathology influence what you do now?

The incredible support I got from the Department, especially from my project supervisor, Paul Edwards, gave me the confidence to apply for a PhD position at Cancer Research UK, where I worked under the supervision of Paul Nurse, who won a Nobel Prize while I was there. I never looked back. I am still actively working as a research scientist today, although I have changed my research to focus on different diseases.

We were taught the latest cutting edge research by leaders in the field, which was unimaginable to someone who had arrived in England from a small village in the Italian Alps only a couple of years before!

After working on cancer, I spent some time in developmental biology with Prof Daniel St. Johnston at the Gurdon Institute in Cambridge where I first worked with *Drosophila melanogaster*, the humble fruit fly and my favourite model organism. I now work at University College London across two departments: the Institute of Neurology, with Adrian Isaacs, and the Institute of Healthy Ageing, with Linda Partridge. I am interested in understanding diseases of ageing, in particular neurodegenerative diseases like Alzheimer's and fronto-temporal dementia, and I use fruit fly models of disease to understand pathogenic mechanisms.

What's next for you?

I have some very exciting results looking at the role of glucose in neurodegenerative disease development^{1,2} and I am in the process of getting funding to set up my own laboratory to continue my work.



What skills did you gain in the Department that have been particularly useful in your current position?

I learned some of the most important skills for a good scientist while I was in the Department of Pathology, skills I still use today: how to run a good experiment and the importance of craftsmanship (the ability to perform an experiment well). I also learned from my supervisor, Dr Edwards, how to look after students, and I now put these skills into practice with my own students, offering as much (or as little) supervision as they want, and letting them take ownership of their own project.

What advice would you give to someone starting out in the Department of Pathology today?

I would encourage any student in the Department to take full advantage of the excellent research facilities and learning opportunities. Once you start work in the "real world" it is rare to have time just to concentrate on learning something new and interesting. As an undergraduate, taking your first steps into the world of science, you are exposed to lots of interesting and novel research, and in the Department of Pathology you are taught by top leaders in the field. It's a very privileged position to be in, and I would encourage students to make the most of it.

¹Niccoli, T. et al. (2016) Increased glucose transport into neurons rescues A β toxicity in *Drosophila*. *Current Biology*, 26: 2291-2300.

²Duran-Anniotz, C. & Hetz, C. (2016) Glucose metabolism: a sweet relief of Alzheimer's Disease. *Current Biology*, 26: R806-R809.

Dr Teresa Niccoli was interviewed for this article by Dr Gillian Fraser, University Senior Lecturer and Head of the Division of Microbiology & Parasitology, Department of Pathology. Dr Fraser is the Niccoli Fellow in the Natural Sciences at Queens' College. The Niccoli Fellowship was endowed in 2015 by Dr Demis Hassabis and Dr Teresa Niccoli.

GLOBAL HEALTH RESEARCH

1 Dr Carole Sargent and her collaborators in Ghana, including previous CAPReX Fellow Dr Richard Osei-Amponsah, were awarded funding to genotype pigs in Ghana.

The long-term aim of the project is a targeted breeding programme to generate a climate-smart animal for local meat production that is larger but includes the beneficial robustness traits of the indigenous Ashanti Dwarf pig.

2 Goylette Chami's research in Uganda has shown how important social networks are for the reduction of the burden of infectious diseases in low income countries.

They suggest that social network-based approaches are more efficient than the traditional health interventions targeting established community members for reducing the spread of disease or uptake of preventative chemotherapies in rural Africa.

3 The Cambridge-Africa Alborada Research Fund, coordinated from Pathology, enables many diverse collaborative projects between Cambridge and African partners.

One such project is a collaboration between researchers from the Wellcome Trust Sanger Institute and researchers from the University of Malawi. This project aims to investigate how to preserve Lake Malawi's natural reserve of cichlid fish, a resource of high economic value for the country and the main protein source to the local population.

Using the cichlid genome variation data available in Cambridge, researchers in Malawi will investigate the impact of fishing methods on the selection of cichlid fish sizes in lakes Malombe and Malawi. The findings from this project will contribute to the preservation of this important natural food resource for future generations.

4 Dr Dora Pereira and her collaborators at the MRC Unit in The Gambia are running a large nutrition intervention study in one of the most rural and deprived areas of Sub-Saharan Africa. The IHAT-GUT trial starts screening this month and aims to determine safety and efficacy of iron supplements in young anaemic Gambian children.



1



2



3

“Our goal is to improve health for everyone by enabling researchers from resource-poor countries to reach their full potential”



4

Campod

CAMBRIDGE FUND FOR THE PREVENTION OF DISEASE

Campod, Cambridge Fund for the Prevention of Disease, is a charity that raises money to directly support medical research in the Department of Pathology at the University of Cambridge. It was formed in 1983 and is supported through individual donations and legacies, grants from Charitable Trusts and income derived from fundraising activities. Campod offers the opportunity for individuals to directly support world-leading research into major diseases affecting the world-wide population.

Campod aims to:

- ensure research scientists in the department have access to the best of innovative technologies
- provide critical 'seed corn' funding for young investigators at the outset of their career
- kickstart 'blue sky' research ideas that might not otherwise get off the ground
- provide funding where there is no alternative source.

Why are funds required?

Research grants from the Government funded Research Councils and from major charities (e.g. CRUK) support the employment costs of staff but usually do not provide for all the necessary equipment.

'Blue Sky' research provides high risks for funders - but this work is crucial for progressive ground breaking work.

Technological advances have sped up research processes but come at high cost. Campod can make the difference in securing major pieces of equipment or helping to start-up a lab.

Support Us!

We are grateful for any support for our work, however small. You can support us in any of the following ways:



Gifts & Donations



- Make an online donation at <http://www.campod.path.cam.ac.uk/supporting-campod.html>.
- Send a cheque (payable to the University of Cambridge) to CAMPOD, Department of Pathology, Tennis Court Road, Cambridge CB2 1QP. If you are a UK taxpayer we can increase the value of your gift.
- Remember us in your will - if you would like to make a will and include a gift to CAMPOD or amend an existing will we suggest that you contact a solicitor.

Organise your own fundraising event

We are very grateful to those who arrange events and activities to raise money on our behalf. We are happy to provide support and advice.

Get Involved!

There are opportunities for volunteering at fundraising events – see <http://www.campod.path.cam.ac.uk>

