Dr Stephen Smith BSc, MB BChir, MPhil, MRCP (UK), PhD.

MRC Post-doctoral Clinical Research Fellow
University of Cambridge and EMBL-European Bioinformatics Institute
Honorary Speciality Registrar in Dermatology and Clinical Pharmacology
Addenbrookes Hospital, Cambridge

I am a clinician scientist based in Cambridge. My research is focused on using cutting edge computational and mathematical tools to understand the pathogenesis and aetiology of cancer, in particular squamous cell carcinoma. As a dermatologist and clinical pharmacologist I am ultimately driven by the need to translate the findings of fundamental scientific research into clinically relevant outcomes. I am available for consultancy via the contact details below.

Contents

Contact details

Email: sps41 "at" cam.ac.uk
Twitter: @stevesmithcam
Address: Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge CB21PQ, UK.

Education

Post-graduate formal qualifications

MPhil (Computational Biology)
2013 - 2014
University of Cambridge, UK

PhD (Molecular Immunology)
2001 - 2004
University of Edinburgh, UK

Post-graduate professional qualifications

MRCP (UK)
2012
Royal College of Physicians (London)

Cert. CompMath (Certificate in Computer Science and Mathematics)
2009 - 2010
Open University, UK

Undergraduate degrees

MB BChir (Medicine and Surgery)
2004 - 2009
University of Cambridge, UK

BSc (Hons) Virology (2:1)
1997 - 2001
University of Edinburgh, UK

Schooling

Tonbridge School, Tonbridge, Kent
1992-1997
5 A levels (AABCD)
Additional level French (A)
10 GCSE (4 A*, 5 A, 1 C)

Employment and Work History

2018 – Present
MRC Post-doctoral Clinical Research Training Fellow
University of Cambridge Joint Fellowship with EMBL-European Bioinformatics Institute (Hinxton)

2018 – Present
Honorary SpR, Dermatology and Clinical Pharmacology,
Addenbrookes Hospital, Cambridge

2017 - Present
NICE Health Technology Appraisals Guidance Committee
National Institute for Health and Care Excellence, Committee B

2013 – 2018
Academic Clinical Fellow (ST3+) Dermatology and Clinical Pharmacology
Cambridge University Hospitals NHS Trust, Cambridge
Training number: EAN/010/00108/A
Educational Supervisors: Prof. I. Wilkinson, Dr. T. Krieg & Dr. N. Burrows

2011 – 2013
Core Medical Training
CMT2: Oncology, Infectious Diseases Educational Supervisors: Dr. E. Gkrania-Klotsas & Dr. C. Parkinson
CMT1: Hepatology, Endocrinology Educational Supervisors: Dr. M. Allison & Dr. E. Gurnell
Cambridge University Hospitals NHS Trust/West Suffolk Hospital

2009 – 2011
Academic Foundation Training
AFY2: ITU, Hepatology
AFY1: Hepatology, Respiratory Medicine, Urology
Educational Supervisors: Dr. P. Bradley & Dr. W. Griffiths
Cambridge University Hospitals NHS Trust/Bedford Hospital

Research Work and Interests

Current Research

Computational analysis of next-generation sequencing data in squamous cell oncogenesis.
Sponsor: Professor Nicholas Coleman
Collaborators: Professor Eugene Healy (Univ. Southampton), Prof. Chris Smith (Cambridge, Biochemistry) & Dr. Anton Enright (Univ. Cambridge/EMBL-EBI)

Squamous cell carcinogenesis is a complex, highly integrated systems-based process. In order to more fully understand the nature of genomic processes underlying the transformation from epithelium to SCC I am interrogating large scale NGS datasets (both RNA-seq and DNA-seq). This MRC funded post-doctoral fellowship is focused on the analysis and integration of expression profiling and genomic sequencing data, including network analysis and comparative analysis of publically available data (such as from TCGA) with our experimental work. The project is particularly trageted at understanding the role of alternative RNA splicing in the pathogenesis of squamous cell carcinoma. We will use patient-derived samples from skin and cervix and aim to translate the findings across squamous-type carcinomas in other organ systems.

Understanding transcriptional events in melanoma carcinogenesis for early diagnosis, prognosis and novel therapeutic approaches.

Leveraging extensive and detailed publically available data collections of next-generation sequencing and microarray analyses of melanoma samples I have applied machine learning and network biology analyses to understand the early events that transition primary melanoma to metastatic disease. In order to further understand how molecular events drive melanoma initiation and progression I am leading a project targeting co-dependent pathways in order to identify genes showing genetic dosage lethality in melanoma. The project aims to translate these findings into potential avenues for therapy using repositioned existing drug treatments.

Drug design and repositionaing

The development of new theraies is costly and time-consuming. There exists an enormous library of therapeutic compunds whose activity can be predicted to extend across multiple diseases, but which are not used in such a way. By analysing transcriptomic and genetic data from diseases of interest (atopic drmatitis, skin cancer, cervical cancer etc) we aim to identify promising compunds with established pharmacological profiles to test in novel therapeutic areas, shortening the time from discovery to prescription.

Non-invasive Diagnostics in Skin Disease

The gold standard non-invasive diagnostic tool for skin cancer by dermatologists is the dermatoscope. Presently dermatoscopes are expensive and affordable models lack digital capabilities. These factors make their use outside specilist centres in wealthy countries infeasible. I am directing a project aiming to produce and refine a low-cost, simple digital dermatoscope for widespread use in clinical contexts where cost sensitivity curently limits their deployment. Additional imaging capabilities will also be integrated to the device to enable it to perform as a cutting-edge research tool in the optical investigation of skin biology. Future work will be focused on leveraging this tool as a platformm for computationally aided diagnostics with important potential applications in resource-limited settings. This work has been supported by a grant from the University of Cambridge Biomaker Challenge and will be published as an open-source hardware project.

Collaborations

Prof. Jacquline Boultwood *(University of Oxford).* RNA-seq and splicing analysis in myelodysplastic syndrome (Pellagetti et al, Blood 2018)
Narita lab *(University of Cambridge Cancer Institute).* Molecular basis of sensescence and its role in carcinogenesis (Parry et al, Nature Communications 2018).
Coleman Lab *(University of Cambridge).* Ongoing collaboration with Coleman group members on bioinformatics aspects of work in squamous cell carcinoma, HPV biology and paediatric tumours. (Kucia-Tran et al, British Journal of Cancer 2016, Journal of Pathology 2018)
Raffan/O'Rahilly group *(University of Cambridge, IMS).* Collaboration on data analysis of genetic effects on obesity in dogs. (Raffan et al, Cell Metabolism 2016, PeerJ 2015).

Previous Research

Masters Thesis

Functional genomics analysis of papillomavirus oncogenesis in W12 cell lines
Supervisor: Professor Nicholas Coleman
This research explored the functional genomic aspects of HPV carcinogenesis applying network models to high-quality gene expression data in a cell model of HPV16 mediated oncogenesis (Smith et al, Scientific Reports 2016).

PhD Thesis

Evidence for a remote lung response in endotoxin-mediated direct lung injury: a strategic application of microarray technology.
Supervisors: Dr David Collie & Dr Varrie Ogilvie
Construction and assay of a suppression-subtraction-hybridisation ovine lung sequence library followed by molecular genomic probing of sheep lung tissue from in vivo models of acute lung injury via novel microarray and qRT-PCR to characterise inflammatory responses in lung segments.

BSc Honours Thesis

Design and evaluation of mouse housekeeping genes for oligonucleotide microarrays.
Supervisor: Dr D Roy
Analysis of housekeeping genes in mice for the purposes of validating and assuring quality of internally normalised microarray data for mouse models.

Research skills

Computational Biology: RNA-seq, DNA-seq and microarray analysis, R programming, Python scripting, Bioinformatics skills, Machine learning, Image analysis
Molecular Biology: PCR (including qPCR and RT-PCR), molecular cloning, Western blotting, library construction, microarray design, construction and hybridization
Cell Biology: Cell and tissue culture (primary, mammalian and tumour), FACS, siRNA Clinical Research Trial design and statistical analysis training

Professional Service, Leadership & Management

Committee Positions (Present)

2017-present: NICE Health Technology appraisals committee B (Member)
2017–present: British Assn Dermatologists Research Sub-Commitee Trainee Representative
2017–present: UK TREND Steering Commitee member
2014–present: Local Negotiating Commitee, Cambridge University Hospitals NHS Trust Junior Doctors' Representative

Commitee Positions (Previous)

2017–2018: Cambridge University Hospitals Trust Junior Doctors' Forum Co-Chair
2014–2017: Joint Drugs and Therapeutics Committee, Cambridge University Hospitals NHS Trust Clinical Pharmacology Trainee Observer
2012–2013: Junior Doctors' Mess President, Cambridge University Hospitals NHS Trust

Memberships

British Association of Dermatologists (BAD)
European Society for Dermatological Research (ESDR)
British Society for Investigative Dermatology (BSID)
British Pharmacological society (BPS)

Leadership & Management Training

2018: International Investigative Dermatology Residents Retreat (Orlando, Florida)

Publications

ORCID #0000-0001-7744-3238
Google Scholar

Journal Articles (Peer-reviewed)

Pellagatti A, Steeples V, Armstrong RN, Sharma E, Repapi E, Singh S, Sanchi A, Radujkovic A, Horn P, Dolatshad H, Roy S, Lockstone H, Taylor S, Giagounidis A, Vyas P, Schuh A, Hamblin A, Papaemmanuil E, Killick S, Malcovati L, Gavin A-C, Ho AD, Luft T, Hellström-Lindberg E, Cazzola M, Smith CWJ, **Smith SP**, and Boultwood J
Impact of spliceosome mutations on RNA splicing in myelodysplasia: dysregulated genes/pathways and clinical associations.
Blood 2018 Jun 21. pii: blood-2018-04-843771. doi: 10.1182/blood-2018-04-843771.

Parry AJ, Hoare M, Bihary D, Hänsel-Hertsch R, **Smith SP**, Tomimatsu K, Mannion E, Smith A, D'Santos P, Russell IA, Balasubramanian S, Kimura H, Samarajiwa SA & Narita M
NOTCH-mediated non-cell autonomous regulation of chromatin structure during senescence.
Nature Communications May 2018 volume 9, Article number: 1840 (2018) doi:10.1038/s41467-018-04283-9

Kucia-Tran, J. A., Tulkki, V. , Scarpini, C. G., **Smith, S.P.** , Wallberg, M. , Paez-Ribes, M. , Araujo, A. M., Botthoff, J. , Feeney, M. , Hughes, K. , Caffarel, M. M. and Coleman, N.
Anti-oncostatin M antibody inhibits the pro-malignant effects of oncostatin M receptor overexpression in squamous cell carcinoma.
Journal of Pathology, Jan. 2018 244: 283-295. doi:10.1002/path.5010

Smith SP, Baxendale HE, Sterling JC.
Therapeutic use of the quadrivalent Human Papillomavirus vaccine for recalcitrant warts in idiopathic immune deficiency.
Clinical and Experimental Dermatology Jan 2017 42: 306-308. doi:10.1111/ced.13038

Smith SP, Scarpini CG, Groves IJ, Odle RI, Coleman N
Identification of host transcriptional networks showing concentration-dependent regulation by HPV16 E6 and E7 proteins in basal cervical squamous epithelial cells.
Scientific Reports Jul 2016; 6:29832. doi:10.1038/srep29832

Kucia J, Tulkki V, **Smith SP**, Scarpini C, Hughes K, Araujo AM, Yan KYM, Botthof J, Prez-Gmez E, Sanchez C, Quintanilla M, Cuschieri K, Caffarel MM, Coleman N
Overexpression of the oncostatin M receptor in cervical squamous cell carcinoma is associated with epithelialmesenchymal transition and increased metastasis.
British Journal of Cancer Jul 2016; 115(2):212–22. doi:10.1038/bjc.2016.199

Raffan E, Dennis R, O'Donovan C, Becker J, Scott R, **Smith SP**, Withers D, Wood C, Conci E, Clements D, Summers K, German A, Mellerch C, Arendt M, Iyemere V, Withers E, Soder J, Wernersson S, Andersson G, Lindlad-Toh K, Yeo G, O'Rahilly SO
A deletion in the canine POMC gene and its relationship to the obesity-proneness of Labrador retriever dogs.
Cell Metabolism 2016 May; 23(5): 893–900. doi: dx.doi.org/10.1016/j.cmet.2016.04.012

Raffan E, **Smith SP**, O'Rahilly SO, Wardle J.
Development, factor structure and application of the Dog Obesity Risk and Appetite (DORA) questionnaire.
PeerJ 2015; 3:e1278; doi.org/10.7717/peerj.1278

Smith SP, Crawley C, See TC, Screaton N and Preller J.
A case of BK virus causing bilateral ureteric obstruction in an allogeneic stem cell transplant recipient.
Journal of Clinical Virology 2013 Jan; 56(1): 1-4. doi:10.1016/j.jcv.2012.07.003

Published Abstracts

Smith SP, Mehta SG, Burrows N.
A Rare Form of Classical Ehlers-Danlos Syndrome with Arterial Rupture.
British Journal of Dermatology 2016; Online Supplement (Accepted)

Raffan E, **Smith SP**, Wardle J, O'Rahilly S,
Variation in appetitive behaviour between pet dogs; association with obesity and relationship to owner management factors.
Journal of Veterinary Behavior: Clinical Applications and Research 2015; 10 (5), 447, https://doi.org/10.1016/j.jveb.2015.

Raffan E, Diss S, **Smith SP**, Wardle J
Development and validation of the Dog Obesity Risk and Appetite (DORA) questionnaire
Acta Veterinaria Scandinavica 2015, 57(Suppl 1):O18

Smith SP.
Network analysis identifies master regulators of metastasis in cutaneous melanoma.
British Journal of Dermatology 2015 July; 173 (S1): 2176. doi:10.1111/bjd.13761

Smith SP
Bioinformatics Identification of Personalised Medicine Repositioning Candidates in Atopic Dermatitis.
Clinical and Experimental Dermatology 2015; Online Supplement

Smith SP, Tate S, Collie DD.
Interleukin 10 is upregulated in Contralateral Lung Segments Following Local LPS Challenge.
Proceedings of the 42nd IDSA Congress 2004

Books

Co-editor: BMA New Guide to Medicines and Drugs. (2015)

Awards, Prizes & Grants

Awards

2018: European Society for Dermatological Research Travel Award
2018: British Association of Dermatologists Travel Award
2018: Selected for International Investigative Dermatology Trainee Retreat
2017: Emirates Dermatology Society Fellowship
2016: Cambridge Biomedical Research Centre Bursary
2016: British Society for Investigative Dermatology Specialist Registrar Bursary
2015: THESIS BSID Fellowship

Prizes

2017: Emirates Dermatology Society Conference 2017, Best Abstract Prize

Grants

2018–2021: Medical Research Council Post-Doctoral Clinical Research Training Fellowship: "Computational Analysis of Transcription and Alternative Splicing Events in Squamous Cell Cancer." (Principal Investigator; £351,712)
2017: Cambridge Biomaker Challenge Grant: "Building DeepSkin a low-cost state-of-the-art digital dermatoscope" (Principal Investigator; £1,000)
2002: Normal Salvesen Trust: "Development of an Ovine Lung Specific gene array through Interspecies hybridisation." (Co-Investigator; £27,270)
2001–2003: MRC doctoral training Award

Presentations, Lectures & Invited Talks

Oral Presentations International/National Meetings

2018: Smith SP, Fascin and Cdk2 are synthetic lethal partners with exceptional potential as joint therapeutic targets in malignant melanoma. International Investigative Dermatology Conference 2018. (Orlando, USA).
2017: Invited Lecture: Epigenetics for Dummies. British Association of Dermatologists Annual Congress (Liverpool, UK)
2016: Plenary Lecture: The Next Revolution: Computational Biology and the Skin. British Association of Dermatologists Annual Congress (Birmingham, UK)
2016: Invited Workshop: Bioinformatics in HPV Research. HPV UK 2016 (Lake District, UK)
2014: Invited Research Talk: Functional genomics analysis of HPV oncogenesis in W12 cell lines. HPV UK 2014 (Lake District, UK)
2003: A novel Ovine immune/inflammatory microarray. Faculty of Medicine Research Emphasis Day (Edinburgh, UK)

Invited oral presentations

2018: Host Transcriptional Control by Human Papillomavirus. Univesrity of Cambridge Pathology Department Annual Symposium (Cambridge, UK)
2017: Big Data, Machine Learning and Dermatology: Rise of the Machines. Newcastle Medical School Research in Progress Lecture (Newcastle, UK)
2017: Invited Lecture: Computational Biology in Dermatology. British Association of Dermatologists THESIS course (London, UK)
2015: It's melanoma, is it serious? Addenbrookes Staff Grand Rounds (Cambridge, UK)
2010: A complicated transplant. Addenbrookes Staff Grand Rounds (Cambridge, UK)
2005: Medicine and the Media. Inter-faculty off-topic seminars (Cambridge, UK)

Conference Presentations

2018: Smith SP, Fascin and Cdk2 are synthetic lethal partners with exceptional potential as joint therapeutic targets in malignant melanoma. International Investigative Dermatology Conference 2018. (Orlando, USA). Poster
2017: Smith SP GATAD2A, a chromatin remodelling gene, is a powerful prognostic marker in malignant melanoma. British Society for Investigative Dermatology (Manchester, UK)
2016: Smith SP, Mehta SG, Burrows N. A Rare Form of Classical Ehlers-Danlos Syndrome with Arterial Rupture. British Society for Medical Dermatology (London, UK)
2015: Smith SP Network Analysis of Melanoma Metastasis. British Association of Dermatologists Annual Congress (Manchester, UK)
2015: Smith SP Bioinformatics Identification of Personalised Medicine Repositioning Candidates in Atopic Dermatitis. British Society of Investigative Dermatology (Southampton, UK)
2004: Smith SP, Tate S, Collie DD. IL-10 is upregulated in contralateral lung segments following local LPS challenge. Infectious Diseases Society of America Congress (Boston, USA)

Teaching, Training & Supervision

Research supervision

2018: Andrew Farr, research placement (Bioinformatics of drug repositioning).

Clinical supervision

2009–2016: Clinical Supervisor, University of Cambridge Clinical School Undergraduate clinical skills and mentoring, 4 to 10 students

Undergradate Lecturing

2014–present: Clinical Lecturing, University of Cambridge Clinical School Undergraduate Dermatology Lectures, 50 to 100 students
2011: Course Organiser, University of Cambridge Clinical School Medical Statistics, Ethics and Law - 2 day lecture course, final year undergraduates (30 students)

Courses & Qualifications

Current Certificates

2013– Good Clinical Practice Current, valid Certification
2011– Advanced Life Support Current, valid Certification

Courses Attended

2018: BPS Experimental Medicine Training Day (Early phase trial design)
2018: NIHR Statistics Group Early Phase Trials workshop
2017: NICE Technology appraisals Away Day
2017: BPS Clinical Pharmacology Training Day
2017: BAD Dermatology Registrars' Training Day
2016: BPS Clinical Pharmacology Training Day
2016: BAD Dermatology Registrars' Training Day
2016: Wellcome Advanced Course in Genomics for Dermatology
2015: BAD Dermatology Registrars' Training Day
2013: Introduction to Biology of the Skin
2013: An Introduction to Solving Biological Problems with R
2013: An Introduction to Solving Biological Problems with Python
2013: Bioinformatics: Microarray Analysis with Bioconductor
2012: THESIS/BAD/BSID Research Course (London, UK)
2010: BSMD DermDoc Course (London, UK)
2009: Immediate Life Support
2009: ALERT course

Personal Activities

I am a keen waterpolo player, having competed at all levels up to national. I have also been a referee at National standard and am a level 3 waterpolo coach. I have previoulsy held positions on the national governing board for UK national waterpolo. I still play, though less than I would like, and love the experience of being part of a competetive team. My current club is the City of Cambridge Waterpolo Club, and I have previously played for the Universities of

Cambridge and Edinburgh, Scottish Universities, Warrender Waterpolo Club, royal Tunbridge Wells Monsoon and Beckenham Swimming club.
I am an ex-competetive national-standard swimmer, having competed at middle and long distance front crawl. I still like swimming, but only for pleasure these days. I play squash, though not as well as I'd like and am a keen if not elegant skier.
With my family I enjoy cooking, perticularly what we can grow ourselves, skiing and supporting my wife on the hockey pitch.