

*Curriculum Vitae*

Professor Mark John Pallen

MA (Hons) Cantab, MBBS, MD, PhD

January 2014

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## Personal Details

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<b>Name</b>	Mark John Pallen
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## Education and Qualifications

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<b>PhD</b>	<b>1998</b>
<b>Imperial College, London</b> <i>An investigation into the links between stationary phase and virulence in Salmonella enterica enterica serovar Typhimurium</i>	
<b>MD</b>	<b>1993</b>
<b>St Bartholomew's Hospital Medical College</b> <i>Detection and characterisation of diphtheria toxin genes and insertion sequences</i>	
<b>MRCPath by examination in Medical Microbiology</b> (upgraded to FRCPath 2005)	<b>1991</b>
<b>MB BS</b>	<b>1981-84</b>
<b>London Hospital Medical College</b> Undergraduate Prizes: LEPR National Essay Prize, 1982 Turnbull Prize in Pathology, 1983, 1984 Sutton Prize in Pathology, 1983	
<b>BA (Hons) in Medical Sciences</b>	<b>1978-81</b>
<b>University of Cambridge</b> Fitzwilliam College (Lower Second, converted to MA, 1985)	

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## Employment

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<p><b>Professor of Microbial Genomics</b>  <b>Head of Division of Microbiology and Infection</b>                  Warwick Medical School, University of Warwick</p>	<p><b>Apr 2013-now</b></p>
<p><b>Professor of Microbial Genomics</b>                  University of Birmingham</p>	<p><b>2001-2013</b></p>
<p><b>Professor and Head of Department</b>                  Department of Microbiology and Immunobiology                  Queen's University, Belfast</p>	<p><b>1999-2001</b></p>
<p><b>Senior Lecturer (Honorary Consultant)</b>                  Department of Medical Microbiology                  St Bartholomew's and the Royal London School                  of Medicine and Dentistry (Queen Mary Westfield College)</p>	<p><b>1992-99</b></p>
<p><b>Visiting Research Fellow</b>                  Department of Biochemistry                  Imperial College of Science, Technology and Medicine                  (on a Wellcome Trust Research Leave Fellowship,                  working at Imperial, while still employed by Barts)</p>	<p><b>1994-97</b></p>
<p><b>Lecturer (Hon. Senior Registrar)</b>                  Department of Medical Microbiology                  St Bartholomew's Hospital Medical College</p>	<p><b>1988-92</b></p>
<p><b>SHO, then Registrar</b>                  Department of Medical Microbiology                  Royal Free Hospital</p>	<p><b>1986-88</b></p>
<p><b>Temporary Lecturer</b>                  Department of Medical Microbiology                  London Hospital Medical College</p>	<p><b>1986</b></p>
<p><b>Research Assistant</b>                  Department of Medical Microbiology                  London Hospital Medical College</p>	<p><b>1985-86</b></p>
<p><b>House Officer</b>                  London Hospital, Mile End                  Rush Green Hospital, Romford</p>	<p><b>1984-85</b></p>

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## Research Funding

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### Applications Under Review

**BBSRC project grant** **£557,004**

2014–2017 *Metagenomics of the Pig Caecal Microbiome: Methods and Applications*  
 PI, with Muna Anjum, AHVLA as collaborator

**BBSRC Bioinformatics and Biological Resources Fund grant** **£1.4m**

2014–2019 *Enterobase: An Online Resource for Analyzing and Visualizing Genomic Variation within E. coli and Salmonella enterica* Co-investigator with Mark Achtman

**NERC grant** **£971,611**

2015–2018 *Towards non-invasive monitoring: analysis of infectious disease and transmission dynamics in a vaccinated wild mammalian population.* Co-investigator with Liz Wellington

### Present and Past Funding

**MRC Infrastructure grant** **£9.2m**

Apr 2014–Mar 2019 *The MRC Consortium for Medical Microbial Bioinformatics*  
 PI, with co-investigators in Warwick, Birmingham, Swansea, Cardiff

**BBSRC project grant** **£609,112**

Sept 2012–Aug 2015  
*Bacterial chromosome structure and transcription* (co-investigator with Busby/Grainger)

**MRC grant (as PI)** **£681,842**

2010–2013, *Acinetobacter baumannii*: genomic profiling of an emerging pathogen

**BBSRC grant (as PI)** **£499,131**

2010–2013, *The chicken caecal microbiome: from baselines to biological impact*

**BBSRC CASE studentship (for Nick Duggett)** **~£75,000**

Oct 2011–Sep 2014, in collaboration with AB Vista

**NIHR centre grant** **~£10m**

2011–2016 *Surgical Reconstruction and Microbiology Research Centre*  
 I co-wrote the proposal and, as Microbiology Theme Lead, was responsible for ~£1.3m of the budget, until I was required to relinquish this role on leaving Birmingham

**NIHR CPHR grant** **~£200K**

2012–2015 *The contributions of virulent clones vs. highly transmissible plasmids to the changing epidemiology of carbapenemases in the UK* Co-applicant with Neil Woodford, PHE

**Visionary Winner of the Ion Torrent PGM Grants Program in Europe** **£100,000**

(<http://ir.lifetechnologies.com/releasedetail.cfm?ReleaseID=551131>)

Feb 2011 *Ion Torrent PGM Sequencer and server*  
 One of two successful entries out of ~150 applications

**BBSRC grant** **£909,978**

2007–2012 (PI with co-applicant Charles Penn)  
*xBASE: a bioinformatics resource for the AgriFood Bacteriology Community, BBSRC*

<b>BBSRC grant</b>	<b>£434,778</b>
Jul 2009–Jul 2012 (co-investigator with Mark Webber) <i>Evolution of multidrug resistance in S. Typhimurium as a result of biocide exposure</i>	
<b>Cancer Research UK Centre Development Fund</b>	
Sept 2010–Aug 2011 (co-investigator with Nick James; I wrote the proposal)	<b>£12,000</b>
<i>Detection of gene fusions suitable as biomarkers for invasive and non-invasive bladder cancer using transcriptome sequencing on two high-throughput platforms</i>	
<b>BBSRC grant</b>	<b>£254,971</b>
Jul 2007–2010 (PI with co-applicant Steve Busby) <i>Ler, a versatile global regulator from E. coli O157 and related strains.</i>	
<b>BBSRC grant</b>	<b>£147,467</b>
2007–2010 (Co-applicant with Jon Hobman and Charles Penn) <i>Environmentally relevant responses in different Escherichia coli pathotypes: a functional genomics study of motility and associated regulons</i>	
<b>BBSRC grant</b>	<b>£327,414</b>
Feb 2006–Jan 2009 (PI with co-applicant Laura Machesky) <i>The scatterlings of virulence: towards a complete type-III secretion effector repertoire in Escherichia coli</i>	
<b>DSTL grant</b>	<b>£327,414</b>
Jul 2006–Jun 2007 <i>One year grant to study Francisella tularensis</i>	
<b>MRC PhD studentship</b>	<b>~£60,000</b>
Sep 2005–Sep 2008 (for Sophie Matthews) <i>Towards a complete type-III secretion effector repertoire in EHEC</i>	
<b>BBSRC grant</b>	<b>£229,313</b>
Feb 2005–Jan 2008 (PI with co-applicant Steve Busby) <i>Regulation of gene expression within the locus for enterocyte effacement</i>	
<b>BBSRC grant</b>	<b>£124,013</b>
Jan 2005– Dec 2006 (Co-applicant with Ian Henderson, Charles Penn and Julian Parkhill) <i>Genomics of enterotoxigenic E. coli.</i>	
<b>MRC Special Research Training Fellowship in Bioinformatics</b>	<b>£117,000</b>
Oct 2003–Feb 2006 (for Scott Beatson ) <i>Bioinformatics and Bacterial Virulence</i>	
<b>BBSRC grant</b>	<b>£77,676</b>
Sep 2003–Feb 2005 (Co-PI with Brendan Wren and Julian Ketley) <i>Exploiting Campylobacter jejuni genomics</i>	
<b>BBSRC PhD studentship</b>	<b>~£60,000</b>
Sep 2002–Oct 2005 (for Helen Betts) <i>Unraveling protein-protein interactions in Salmonella enterica type-III secretion</i>	
<b>Health Protection Agency PhD studentship</b>	<b>£45,000</b>
Feb 2004–Jan 2006 (for Sally Ren) <i>Genomics and virulence of Francisella tularensis</i>	

<b>BBSRC grant</b>	<b>£1,320,820</b>
Feb 2002–Apr 2007 (Co-applicant: Charles Penn was PI; my component ~£300K) <i>Global gene expression in E. coli: exploitation of genomic data to dissect a model pathogen</i>	
<b>BBSRC grant</b>	<b>£152,014</b>
Dec 2000–Sep 2003 (PI with co-applicant Ian Day) <i>High-throughput whole-genome PCR with MADGE and SP-PCR for the analysis of genomic diversity in the enteric bacteria</i>	
<b>Research Project Grant from N. Ireland Health &amp; Social Services</b>	<b>£113,956</b>
Oct 2000–Sep 2003 (joint PI with Tim Foster) <i>Exploiting the genome sequences of Staphylococcus aureus</i>	
<b>BBSRC grant</b>	<b>£213,746</b>
May 2000–Apr 2003 <i>Starvation-stress response of S. typhimurium studied using mud-lac fusions and a microarray</i>	
<b>BBSRC grant</b>	<b>£209,520</b>
Apr 2000–Mar 2003 <i>ViruloGenome: An online resource for exploiting bacterial genome sequence data</i>	
<b>Joint Research Board Project Grant, St Bartholomew's Hospital</b>	<b>£68,671</b>
Aug 1999–Jul 2001 <i>Coiled-coil interactions in Salmonella type III secretion systems</i>	
<b>The Leverhulme Trust Project Grant</b>	<b>£106,398</b>
Feb 1998–Jan 2001 (Co-applicant with Gad Frankel and Stuart Knutton) <i>The EPEC adhesosome: the importance of coiled-coil interactions</i>	
<b>Wellcome Trust, Research Leave Fellowship</b>	<b>£228,554</b>
Nov 1994–Oct 1997 (Under supervision of Gordon Dougan) <i>An investigation into the role of stationary phase genes in salmonella virulence</i>	
<b>Joint Research Board, St Bartholomew's Hospital</b>	<b>£57,972</b>
Aug 1993–Jul 1996 <i>Typing of nosocomial pathogens using the polymerase chain reaction</i>	
<b>BSSI and Bayer, Gerhard Domagk Research Grant</b>	<b>£10,000</b>
Jan 1991–Dec 1991 <i>Rapid detection and identification of toxigenic C. diphtheriae using PCR</i>	
<b>MRC Short Project Grant</b>	<b>£15,238</b>
Apr 1990–Mar 1991 <i>The study of mycobacterial sigma-factor and heat-shock genes using the polymerase chain reaction with mixed oligonucleotide primers</i>	

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## Research Experience and Interests

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Microbial pathogens have exerted a decisive influence on the course of human history and still represent a **major existential threat to humanity**. Infectious diseases are seldom out of the news—media and scientific attention has focused on a range of problems, including microbial contamination of the food chain; emerging and re-emerging infections triggered by social and ecological changes, the spectre of bioterrorism and the alarming spread of hospital infection and multi-drug resistance. However, microbiology is about more than infection—the **complex microbial communities** associated with our bodies harbour many more genes than the human genome and play a role in determining the **balance between health and disease** in humans and other animals, even in conditions not usually considered as microbial in origin (e.g. obesity).

As a **medical microbiologist with an interest in bioinformatics and genomics**, my goal is to characterize and understand individual bacterial pathogens and microbial communities, with a view to translating research into outcomes favourable to human health and wealth. I am well equipped for this task, with

- an education that spans twin peaks of the “golden triangle” (**MA from Cambridge, PhD from Imperial**)
- **dual qualification as a physician/scientist** (MBBS/PhD)
- a multidisciplinary research programme that spans
  - **bioinformatics** and laboratory-based research.
  - genomics and hypothesis-driven research.
  - basic and translational research, from model organisms to pathogens.

Despite devoting over a decade of my professional life to medical training, I have had no difficulty competing on equal terms with non-clinical scientists, with a solid international reputation, as evidenced by

- **an exceptional publication track record**, with research publications in high-impact journals including *JAMA*, *Nature*, *Nature Biotechnology*, *NEJM*, *PNAS*, *EMBO J*, *Lancet* and *Nucleic Acids Research* and invited reviews in *Nature*, *Nature Biotechnology*, *Nature Reviews Microbiology*, *Genome Medicine* and *Current Opinion in Microbiology*. I have over 150 publications listed in PubMed, 48 of them in the REF2014 period. According to Google Scholar, I have an **H-index of 49**, with over 8000 citations to my work.
- **a strong funding portfolio**, with an unbroken record of research council funding stretching back nearly fifteen years; the total value of all grants in which I have been applicant or co-applicant is over £18m
- numerous invitations to contribute to **international meetings** (e.g. in recent years in Harrogate, Hinxton, Göttingen, San Francisco Uppsala, Warwick, Washington DC,)
- **research collaborations** with partners in the UK (UHB, Imperial, Oxford, Nottingham, QMUL, WTSI, PHE, DSTL/MOD, Illumina), Europe (Hamburg, Naples), America (WashU, JCVI, Maryland), Africa (MRC Gambia) and China (BGI and Hong Kong University).

## Bioinformatics: Domains And Proteins

My interest in the use of computers for the analysis of macromolecular sequence data began early in my career, at Barts, where I was soon recognised as the local expert on sequence analysis. These early efforts led to several research papers: in particular, I played a key role in **the first research groups**:

- to report the **sequence of the urease of *Helicobacter pylori*** and to show its unexpected similarity to plant ureases [160–163].\*
- to describe a group II intron and reverse transcriptase in a Gram-positive [141].

I further developed my sequence analysis skills during my Research Leave Fellowship at Imperial College, using such analyses to formulate hypotheses that could be tested in the laboratory. A key theme that informed this research was the identification within bacterial sequences of **protein domains** that had been chiefly the concern of eukaryotic cell biologists:

- coiled-coil domains [113, 118, 136]
- PDZ domains [106, 121, 134]
- FHA domains [105]
- beta-propellers [121, 122]
- tetratricopeptide repeats [77, 101]
- glucoamylase domains in the “regulatory subunits” of the iconic enzyme phosphorylase kinase (the first protein kinase to be isolated and characterized) [100]
- TIR domains [46]

After my research leave fellowship, my attention also focused on the analysis of proteins from type III secretion systems (see below).

## Bioinformatics: Databases

On my return to Barts in the late 1990s, I developed an interest in bacterial genomics:

- setting up a *Microbial Genomics* electronic mailing list.
- writing a regular column, *Microbial Genomics*, in *Trends in Microbiology* [173–216].
- hiring a talented school-leaver, **Nick Loman**, to build a series of web-based **genome browsers** that made it easier for bench-based collaborators to analyse genomic sequences from a variety of pathogens (*Campylobacter jejuni*, *Bordetella pertussis*, *Yersinia pestis*, *Clostridium difficile*, *Francisella tularensis*, *Staphylococcus aureus*).

The creation of these genome browsers primed a **successful application to the BBSRC** to create an online resource, **ViruloGenome**, to help bacteriologists data-mine bacterial genome sequences.

In 2000, shortly before moving to Birmingham, I joined two large successful research programmes running under the BBSRC's Exploiting Genomics (**ExGen**) **Initiative**, developing comparative genomics databases initially for *E. coli* (**coliBASE**) and *Campylobacter* (**CampyDB**) and subsequently for other bacterial genera (*Bordetella*, *Mycobacterium*, *Pseudomonas*, *Staphylococcus*). These databases were described in *Nucleic Acids Research* [59, 72] and saw extensive use from bacteriologists around the world during their five-year lifespan.

Under the auspices of the Birmingham ExGen project on *E. coli*, I was part of a team of eight investigators that met monthly for five years, working with the university's genomics facility to **establish an *E. coli* microarray facility**. My group was the first to publish a paper from this facility [91].

From 2003 to 2006, I sponsored and supervised a **MRC special research fellowship** in bioinformatics for **Scott Beatson** (now Senior Lecturer at the University of Queensland), which culminated in a *PNAS* paper on type III secretion ([69]; see below).



From 2006, my office and bioinformatics group were located in the **Centre for Systems Biology** at the University of Birmingham. Interactions with others within the centre broadened my understanding of computational and systems biology.

Building on our success with genome databases, in 2006 I submitted a **successful programme grant application to the BBSRC** to extend the coliBASE approach to create a new more ambitious facility, **xBASE**.

Funded by the BBSRC for five years (2007–2012) the xBASE facility

- provided coverage of >3000 bacterial genomes.
- incorporated an updated modularized backend, including a modified BioSQL schema.
- featured an improved user interface, incorporating attractive graphics, multi-genome comparisons, a taxonomy browser and a powerful full-text search facility.
- included a set of user-friendly pipelines for bacterial genome sequence assembly, annotation and comparison, under the umbrella of **XBase-NG**. These pipelines were used for >5000 jobs during the funded lifetime of the project
- led to 14 research publications, including a paper on open-source genomics in the NEJM ([26]; see below), a paper describing a new method for analyzing orthologs [25] and a report on **EntrezAjax**, a resource that enabled direct web browser access to the Entrez Programming Utilities [42]



The sustained and wide user base for xBASE is evidenced by statistics from Google Analytics, which documented nearly **2 million page views, over 250,000 visits from over 80,000 visitors** during the funded lifetime of the project.

Staff on the xBASE project built on the experience they gained to good effect:

- **Lori Snyder** obtained a Senior Lectureship at the University of Kingston
- **Nick Loman** gained an MRC Special Training Fellowship in Bioinformatics
- **Mike Halachev** gained a post-doc position in Edinburgh.

Since funding was discontinued for the xBASE project, Nick Loman, has, as a favour, maintained the facility in Birmingham. I have an application under review at the BBSRC to update and incorporate xBASE into a new facility, **EnteroBASE**, that will be supervised by Mark Achtman and myself.

## Bacterial Pathogenomics

In the mid-1990s, the advent of bacterial genome sequencing revolutionised academic bacteriology. From the late 1990s onwards, in collaboration with the Sanger Institute, I contributed to bacterial genome projects that culminated in high-impact publications in

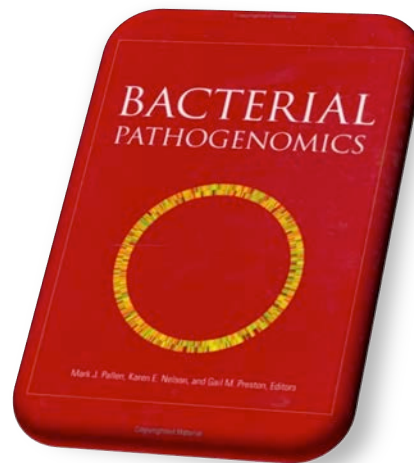
- **Nature**: the *Campylobacter jejuni* genome project [115; **cited >1200 times**]
- **The Lancet**: the *Tropheryma whipplei* genome project [103; **cited >180 times**]
- **Nucleic Acids Research**: the *Corynebacterium diphtheriae* genome project [98; **cited >220 times**]

Around the same time, with Ian Henderson, Julian Parkhill and others, I initiated an *E. coli* **genomics programme** and a BBSRC-sponsored **ETEC genomics project**, which led to papers describing genomes of several prototypical genomes [40, 44, 68].

In 2007, with the HPA at Porton Down, I was responsible for the **first bacterial genome sequence to be completed in the UK** outside of the Sanger Institute [63]. My group contributed to the annotation of the *Laribacter hongkongensis* genome, working with Professor KY Yuen and Hong Kong University [53].

As evidence of my standing in this field, in 2008 I was invited to:

- act as Editor-in-Chief of **Bacterial Pathogenomics** [66]. This 450–page book from ASM press took stock of a decade of progress in bacterial pathogenomics prior to the arrival of high-throughput sequencing. I enlisted the support of forty scientists from around the world to complete this volume.
- write a **review article for the journal Nature** [60], which appeared in late 2008 and has been **cited around 200 times**.



My expertise in bioinformatics/genomics led to several **collaborations with biotechnology companies** working on vaccine development (Microscience), anti-microbial drug development (Arrow Therapeutics), novel diagnostics (Oxford Immunotec) and animal nutrition (AB Vista).

## High-Throughput Sequencing

In the last five or six years, high-throughput (sometimes called "next-generation") sequencing technologies have come to market with the promise of genome sequencing at least a hundred times cheaper and faster than conventional approaches.

My research group has been at the forefront of efforts to harness high-throughput sequencing to the service of clinical and academic microbiology, as evidenced by a string of **invited reviews** in high-impact journals, including

- *Nature Biotechnology* (**Impact Factor 31**) [15]
- *Nature Reviews Microbiology* (**Impact Factor 22.5**) [18]
- *Genome Medicine* [8, 28]
- *Current Opinion in Microbiology* [38]

In 2009, with Charles Penn and Chrystala Constantinidou, I **established a 454 high-throughput sequencing facility** at the University of Birmingham. My contributions to the sequencing facility included:

- choice of platform and requisitioning of the instrument
- helping formulate and maintain a business plan
- supervising a **service bioinformatician**, Tony Haines, to provide bioinformatics support to users
- **championing the use of high-throughput sequencing** across the campus
- organising a **cancer genomics workshop** and launching a pilot study to sequence **bladder cancer transcriptomes** in the hope of discovering gene fusions that can act as personalized **tumour-specific biomarkers**.
- building a **substantial external user base**, with users from the Health Protection Agency, Nottingham, Southampton, Glasgow, Canada, Australia.

During its roughly two-year lifetime, applications of the 454 service included:

- bacterial whole-genome sequencing for epidemiology; drug and biocide resistance; pathogen biology (e.g. for Laura Piddock, Mark Webber, Pete Lund, Del Besra)
- viral sequencing (hepatitis C for Jane McKeating; a novel macaque herpes virus)
- fungal mitochondrial genome sequencing (for Robin May)
- amplicon sequencing for phylogenetic profiling (e.g. for Jeff Cole, Waltham Pet foods).

## Genomic Epidemiology

High-throughput sequencing brings the promise of genomics as a **standard diagnostic and epidemiological tool** in clinical bacteriology. I led the way here with the first published study in which **high-throughput whole-genome sequencing was applied to a small-scale hospital outbreak** [41], caused by a multi-drug resistant hospital pathogen *Acinetobacter baumannii*. This pioneering study primed a successful project **grant application to the MRC** to work on the genomic epidemiology of *Acinetobacter*. This in turn has led to several fruitful research projects on *Acinetobacter*:

- genome-sequencing of *A. baumannii* isolates from Italy [32]
- characterization of resistance associated with mutations and mobile elements [22, 30]
- using genomics to define species within the genus *Acinetobacter* [16].
- genomic epidemiology of a **protracted outbreak** of *Acinetobacter baumannii* pulsotype 27 in the Queen Elizabeth Hospital Birmingham (in collaboration with Beryl Oppenheim and the NIHR CSRM; manuscript under review at *Euro Surveillance*).
- Investigation of *Acinetobacter* clusters in the US and Germany.

Other ongoing or recent genomic epidemiology studies from my group include:

- Genome sequencing of serotype 6C strains of *Streptococcus pneumoniae*, in association with collaborators in Southampton [6].
- Genome analysis of a highly virulent serotype 1 strain of *Streptococcus pneumoniae* from Africa, with collaborators in the US (Weinstock) and Gambia (Antonio) [17]
- *Pseudomonas aeruginosa* strains from a hospital outbreak (with Del Ala'aldeen) [9]
- Genome sequence of an *Mycobacterium abscessus* strain (with Grace Smith) [23]
- Genome sequence of *Helicobacter canadensis* (with Brendan Wren) [44, 45]
- Genome sequencing of a cluster of vancomycin-resistant enterococci from Germany
- Genome sequencing of antibiotic-resistant *H. pylori* strains (with Lars Westblade)
- Genome-sequencing of carbapenemase-resistant strains of *E. coli*, with Neil Woodford, Public Health England (NIHR-funded study).

In early 2011 I was asked by a colleague, Richard Lilford, to draft the microbiology component of an application to the NIHR to establish a **£10m Centre for Surgical Reconstruction and Microbiology** (CSRM), a three-way collaboration between the University of Birmingham, a local NHS trust and military. I completed this within a tight 48-hour deadline and helped Richard complete the full proposal. The proposal was successful and the NIHR CSRM was launched in September 2011.

I served as Microbiology Theme Lead from the Centre's inception to my leaving Birmingham in March 2013. In this role, I recruited **talented staff** to the Centre (Beryl Oppenheim, Joshua Quick, Nicola Cumley, Robin May), oversaw the requisitioning of an **Illumina MiSeq** and initiated an exciting research programme, which encompasses:

- the genomic epidemiology of ***Pseudomonas aeruginosa* in burns patients**, linking clinical samples to environmental sources
- culture-independent approaches to the diagnosis of **osteomyelitis**.

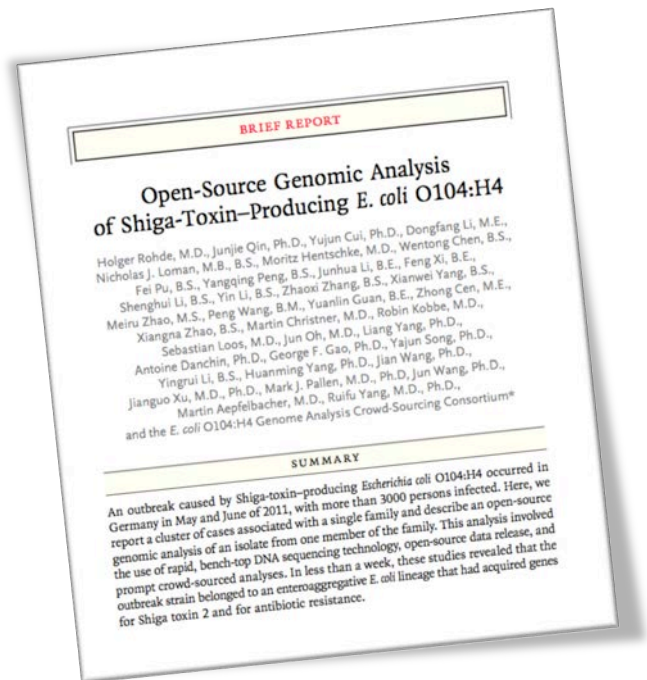
I presented a progress report on this work at the CSRM's first anniversary meeting in late 2012, which coincided with a visit to the Centre that I organized by **Captain Benjamin Kirkup** from the US Army.

Around the same time, I also initiated studies on culture-independent approaches to the **microbiology of cystic fibrosis** and on the genomic epidemiology of *Pseudomonas aeruginosa* in these patients. This line of work formed the basis of Nick Loman's successful application for an **MRC fellowship in bioinformatics**. The studies I initiated for the CSRM and for Loman's fellowship are on going and are certain to lead to high-impact publications.

## Open-Source Genomics of German STEC

In February 2011, I won a new benchtop sequencing instrument, the Ion Torrent PGM (worth ~£100K), in a Europe-wide competition (one of two winners out of ~150 applicants). As a result, my group quickly had to work out how to analyze sequences from this platform. In May-June 2011, a **lethal outbreak of Shiga-toxigenic *E. coli*** (STEC) infection struck Germany, resulting in >5000 cases and >50 deaths, mostly in previously healthy individuals.

During the outbreak, the Chinese research institute, **BGI-Shenzhen**, sequenced the German STEC genome using the Ion Torrent PGM, and released the data into the public domain. Equipped with know-how primed by receipt of our own PGM, Nick Loman in my group performed an initial analysis of the data and then set in motion a burst of “crowd-sourced” analyses carried out by bioinformaticians on four continents **communicating via Twitter, blogs and a wiki**. This culminated in a pioneering “**open-source genome analysis**” of the outbreak, drawing on **rapid DNA sequencing, speedy data release and crowd-sourced analyses**, powered by **social networking tools**—an approach which augmented, and even challenged, traditional approaches to public health microbiology and academic scholarship.



This community effort led to the rapid design of new strain-specific diagnostic reagents and revealed that the outbreak strain had emerged from an enteroaggregative lineage of *E. coli* that had acquired genes to make a toxin and become resistant to antibiotics. We replicated all the crowd-sourced analyses in house and I wrote them up in a paper that was published in the *New England Journal of Medicine* [26] (**Impact Factor 53**, the highest of any journal). I was credited as joint last author and corresponding author. This paper has been **cited over 180 times** in less than 30 months, i.e. an average of over **six times per month**.

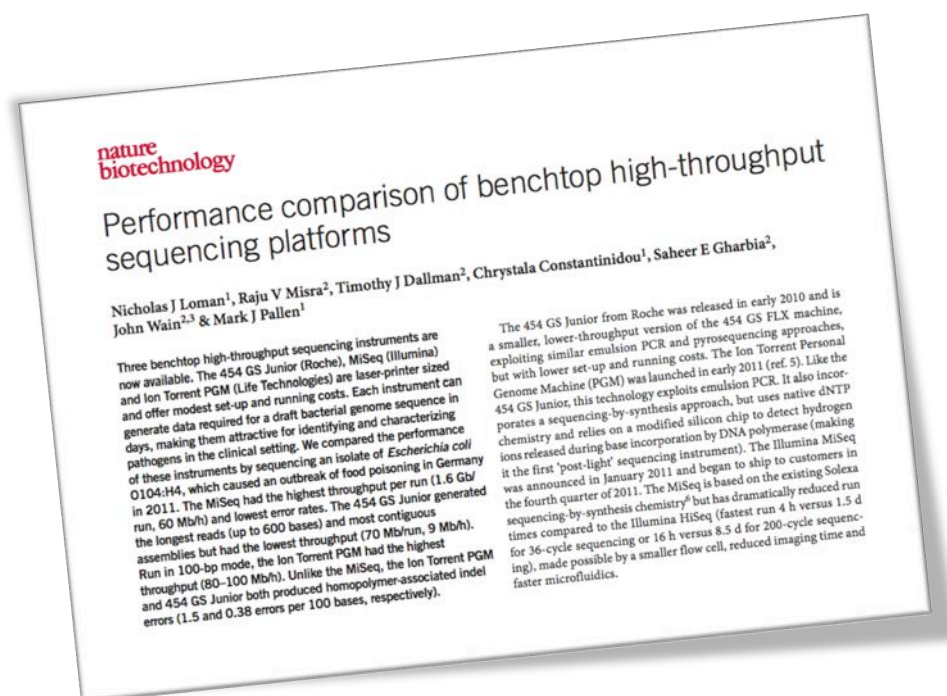
## Benchmarking Benchtop Sequencers

In 2011, two other “benchtop” sequencing platforms, the **454 Jr** and the **Illumina Miseq** arrived on the market, alongside the **Ion Torrent PGM**. All three instruments were roughly the same size as a laser printer and offered modest set-up and running costs. Crucially, each of these instruments was able to generate data required for a draft bacterial genome sequence in days, making them attractive for identifying and characterizing pathogens in the clinical setting. However, on arrival at market, it remained unclear which instrument performed best under realistic circumstances.

I therefore assembled a team—which included collaborators at the Health Protection Agency and Illumina—to carry out a **performance comparison** of the three platforms. Drawing on our experience with the German STEC outbreak, we used all three instruments to genome-sequence a UK isolate from this outbreak.

In our evaluation, all three benchtop sequencing platforms generated useful draft genome sequences of the outbreak strain. Although there was a trade-off between advantages and disadvantages for each technology, our investigations led us to abandon the Ion Torrent for the MiSeq as our own preferred benchtop sequencing platform.

This work was published in *Nature Biotechnology* (**Impact Factor 31**) [20] in April 2012 and has already received >200 citations: **an average of >10 citations a month**.



## Microbiome studies

High-throughput sequencing provides a powerful new **culture-independent approach to the study of complex microbial communities**, whether through deep sequencing of molecular barcodes (e.g 16S rRNA gene sequences) or through wholesale shotgun sequencing of DNA extracted from the community (“metagenomics”). Although the chicken is the most abundant bird and most abundant food animal on the planet and despite the fact that the health and wealth of nations depends on this animal, we know little about the microbial inhabitants of the chicken gut. To address this deficit, I have been funded by the BBSRC to study the **chicken caecal microbiome** (<http://chickenmicrobiome.xbase.ac.uk>), using high-throughput sequencing approaches. In pursuit of this goal, we have established a collaboration with an industrial partner, AB Vista, who has arranged the supply of caecal samples. A CASE studentship has run alongside this project since October 2011. This work has been highlighted by the BBSRC online, in a magazine article and in YouTube videos (<http://www.bbsrc.ac.uk/news/food-security/2013/130404-f-what-lives-inside-a-chicken.aspx>).

We have already published a scoping study on the technical and informatics pipelines used for these analyses [19]. We have a manuscript in revision at *PLoS ONE*, which describes **the most extensive survey of the chicken microbiome ever performed**, incorporating >10 Gb of shotgun metagenomic data. We have now completed molecular barcoding studies of the chicken caecal microbiome under different conditions (age, breed, with or without various infections or interventions) and are currently writing this work up.

I am involved in several other microbiome studies, including investigations of

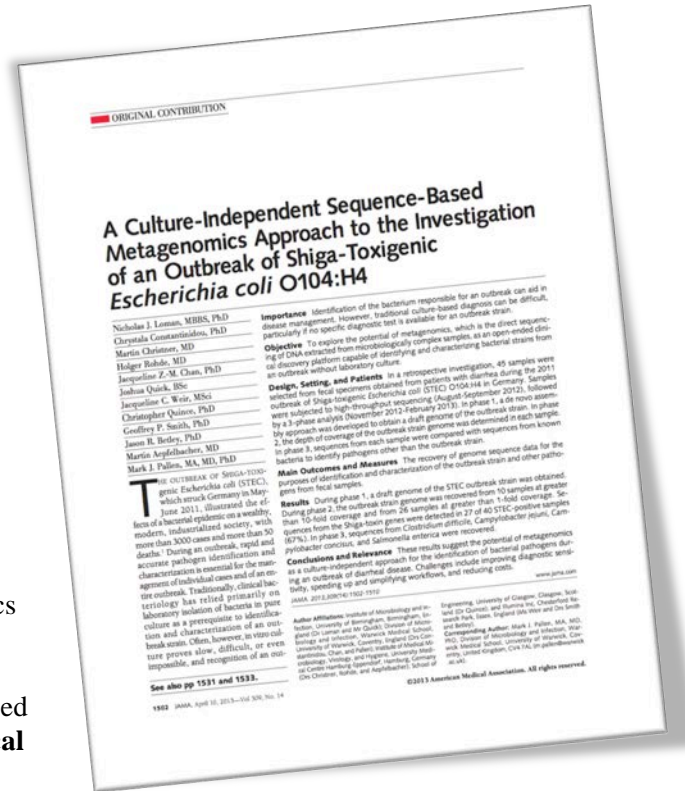
- the human gut microbiota in **primary sclerosing cholangitis** (with David Adams, Birmingham)
- the human gut microbiota in before and after treatment of **schistosomiasis** (with Francisca Mutapi, Edinburgh)
- the gut microbiota in IL17A knockout mice (with Ulrich Wenzel, Hamburg).

In response to a recent BBSRC call on metagenomics, I have submitted a research grant proposal for the January 2014 deadline to improve the detection and characterisation of **resistance determinants on UK pig farms**, in collaboration with Muna Anjum at the Animal Health and Veterinary Laboratories Agency.

## Diagnostic Metagenomics

Diagnostic bacteriology has relied on microscopy and culture since the time of Gram and Koch, despite numerous drawbacks to the use of these nineteenth-century approaches in the twenty-first century. In my group, we have been developing an **innovative culture-independent paradigm** for the detection and characterization of bacterial pathogens, which we term “diagnostic metagenomics”. This approach avoids the complex and unreliable workflows associated with culture of bacteria or amplification of DNA and draws on the extraordinary throughput and ease of use of modern sequencing approaches.

Working with collaborators in Hamburg, we performed **metagenomics analyses of faecal samples collected during the German STEC outbreak**. We developed a novel *de novo* assembly approach to obtain a draft genome of the outbreak strain. We recovered the outbreak strain genome from ten samples at greater than 10X coverage and from 26 samples at greater than 1X coverage. From STEC-negative samples, we recovered sequences from *Clostridium difficile*, *Campylobacter jejuni*, *Campylobacter concisus* and *Salmonella enterica*. These results emphasize the potential of metagenomics as a culture-independent approach for the discovery, detection and characterisation of bacterial pathogens directly from clinical samples. This work was published in April 2013 in the **Journal of the American Medical Association** (Impact Factor 30) [10].



More recently, working in collaboration with **Liz Wellington** at Warwick, we have shown that we can obtain 2X coverage of a *Mycobacterium bovis* genome directly from the **metagenome of badger faeces**, without culture or capture of target cells (unpublished). I am co-applicant on a proposal of Liz Wellington’s to incorporate metagenomics into the study of bovine tuberculosis, which is currently under review at the BBSRC.

In collaboration with Martin Antonio at the MRC Gambia, I have a PhD student, Emma Doughty, who is exploring the potential for obtaining *M. tuberculosis* genomes from **sputum metagenomes**.



## Historical and Ancient DNA

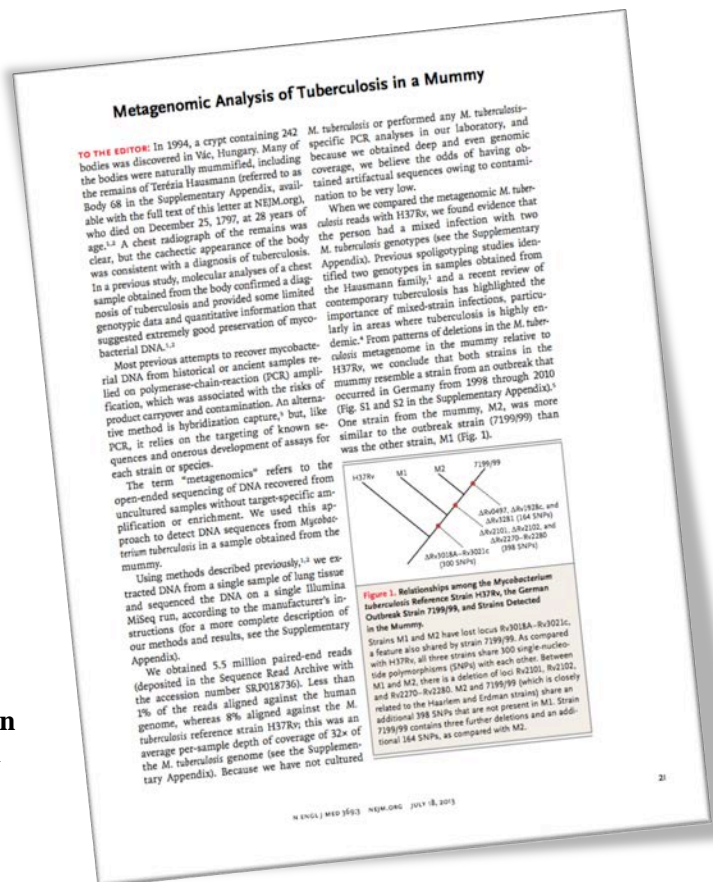
In collaboration with **Helen Donoghue** (UCL) and **David Minnikin** (Birmingham), I have been applying metagenomics to historical specimens.

In an initial pilot study, we recovered *M. tuberculosis* genome sequences from a metagenome obtained from mummified lung tissue from a Hungarian woman, Terézia Hausmann, who died aged 28 on 25 December 1797. Her mummified remains were recovered from a crypt in the town of Vác, Hungary. When the crypt was opened in 1994, it was found to contain the naturally mummified bodies of over 200 people. This pilot study, which was published in the *New England Journal of Medicine* [5], showed that Terézia Hausmann suffered from a mixed infection with two different strains of the TB bacterium. This was the **first demonstration that an *M. tuberculosis* genome could be obtained from human material using shotgun metagenomics**, without culture or capture, and opens up new avenues of research on ancient DNA.

We are now performing a much more ambitious metagenomics study of around two-dozen samples from the Vác crypt, with the aim of reconstructing the **epidemiology of tuberculosis in this eighteenth-century population**—a time when tuberculosis was probably at its peak prevalence in Europe. We anticipate publication in a high-impact journal (e.g. *NEJM*).

We have also established a research collaboration with **Raffaella Bianucci** (Turin/Oslo), who is providing us with samples from a **range of mummies** from Europe and, we hope, from Egypt.

Working with **Vince Gaffney** (archaeologist at University of Birmingham) and **Robin Allaby** (ancient DNA expert at Warwick), I have initiated a groundbreaking study in which shotgun metagenomics is applied to DNA extracted from **ancient sediments** from the submerged landscape of the North Sea basin (**Doggerland**). We have analysed eight samples from ~8Kya and the results look promising in that we have found DNA that appears to originate from land animals and plants, so we are optimistic of achieving a **high-impact publication**.



## MRC Consortium For Medical Microbial Bioinformatics (CMMB)

As *Principal Investigator/Director*, I led the proposal to establish this exciting new **£9m initiative**, in collaboration with co-Director Sam Sheppard (Swansea), Tom Connor (Cardiff) and others. The decision to fund this national consortium was made in late December 2013 and the funding will begin in April 2014.

The CMMB will enhance UK capability and infrastructure in microbial bioinformatics and will allow us to recruit three highly talented individuals into UK medical microbial bioinformatics from careers outside the discipline or the country.

Through this project, we will develop a **distributed computing infrastructure** that will operate together to provide:

- **an agile, scalable system** available to consortium members that can be dynamically provisioned to handle different workloads/projects as needed; this will include:
  - four clusters (one on each site) providing a heterogeneous mix of high-memory/low CPU and low-memory/high CPU servers suitable for both memory-intensive tasks (e.g. metagenomic assembly) and CPU-intensive activities.
  - substantial storage (>2 petabytes).
  - sufficient network capacity for each site to operate at 10 gigabit/second connectivity.
- an instance of the **Galaxy platform** customised for medical microbial research.
- **a freely accessible** database of relevant workflows, pipelines, scripts, programs, virtual machine images built on Galaxy/Github and mirrored across our sites.
- a **data archive** of relevant microbial (meta)genomes
- a **computational infrastructure** for linking patient metadata with microbial (meta)genomic data.

We also intend to develop an ambitious and exciting **training programme** that will include **bootcamps, hackathons, workshops, modules and courses**, suitable for a wide range of users from professional bioinformaticians to undergraduate students.

We will strengthen national microbial bioinformatics research through **community-building activities**, encouraging knowledge transfer and dissemination of best practice. We will exploit pump-priming funds together with externally funded research activities to "stress our systems", confirming that the facilities that we have created work as planned and/or priming iterative refinements to our infra-structure.

## Type III Secretion

For the decade after I left Imperial, much of my research concentrated on **Type III secretion**, a bacterial protein secretion mechanism common to a wide range of bacterial pathogens of humans, animals and plants. In 1998, I was part of the team that described a novel component of a type III secretion system in *E. coli* (the EspA filament), which resulted in a paper in *EMBO Journal* (**cited >430 times**) [129].

In the decade that followed, I published over two-dozen papers on type III secretion [<http://tinyurl.com/9rnfb7p>], ranging widely over the subject and using **bioinformatics analyses** to make numerous exciting discoveries:

- the presence of **tetratricopeptide repeats** in T3SS chaperones (77, 101)
- the presence of an **FHA domain** within the cytoplasmic portion of YscD [86, 105].
- homologies between specificity-switching proteins and their partners in different T3SSs [39, 86]
- homology between ATPase-binding proteins from T3SSs (e.g. YscL/FliH) and second-stalk components of **F-type ATPases** [75].
- the observation that the **ETT2 gene cluster**, encoding a second type III secretion system from *E. coli*, is present in the majority of strains but has undergone attrition in most cases (93).
- the realisation that the **Flag-2 locus** is potentially associated with a novel flagellar system from *E. coli*, but is degenerate in most strains (88).

In 2005, I led an Anglo-Japanese collaboration, assembling bioinformatics and experimental evidence for a **massive expansion in the number of known type III secretion effectors** in *E. coli* and highlighting a key role for bacteriophages in the evolution of the effector repertoire. This work culminated in a last-author **paper in PNAS** [69], which has been cited >200 times. This programme of work was supported by a grant from the BBSRC and my collaborator Gad Frankel went on to characterise several new effectors and, with help from lab, investigated the role of type III secretion in bacterial attachment to plants [49, 55, 56].

I have also studied **gene regulation** in type III secretion systems, with support from three BBSRC grants and in **collaboration with Steve Busby**—this line of work has resulted in several publications [4, 27, 31, 34, 39]. Most recently I have joined Busby and his collaborator David Grainger as a co-investigator on a BBSRC-funded study of the **bacterial nucleoid** in the model organism *E. coli*.

## Other Protein Secretion and Targeting Systems

In addition to type III secretion, my interests have ranged widely over other protein secretion and targeting systems in bacteria. I have published several reviews or commentaries incorporating bioinformatics analyses that have transformed our understanding and opened up new avenues of enquiry, as evidenced by high citation rates:

- A 2008 review on Type VI secretion [57] in *Current Opinion in Microbiology* that has been **cited >200 times**.
- A 2002 article in *Trends in Microbiology* on Esx secretion [107] that has been **cited >180 times**; several of the predictions in this paper have been confirmed by the Missiakas lab.
- A 2001 article in *Trends in Microbiology* on sortases [112] that has been **cited nearly 200 times**; an allied research paper on sortase substrates in *Staphylococcus aureus* [102] has been cited over a hundred times and a patent has been granted on this work [96].

## Recent Research Presentations

I have been invited to organize or participate in numerous meetings on the topic of high-throughput sequencing (recent talks are available as Slidecasts on YouTube):

- two-day genomics conference at the **MRC Gambia**, which I organized in 2008
- session at the *Society for General Microbiology* April 2009 meeting in Harrogate.
- two infectious disease research network meetings
- talk at the *African Society for Bioinformatics* conference in **Cape Town**, Mar 2011
- session at the ASM annual meeting in **New Orleans**, 2011.
- talk at the BSAC 40th Anniversary Conference, Birmingham, Summer 2011
- talk at the Prokagenomics conference, **Göttingen**, Sept 2011  
(<http://www.youtube.com/watch?v=HyN2BZPItrg>)
- talk at workshop on *Applying Advanced Molecular Techniques to Healthcare-associated Infections*, Hinxton, Oct 2011
- seminar at the Dunn School of Pathology in **Oxford**, Oct 2011  
(<http://www.youtube.com/watch?v=HjIWzpuHSaY>)
- talk at Seqahead workshop in Uppsala, June 2012  
(<http://www.youtube.com/watch?v=tKTADKq6efQ>)
- talk at workshop on *The Science and Applications of Microbial Genomics* in **Washington, DC** Jun 2012 (<http://www.youtube.com/watch?v=2vBd5CdtU4w>)
- session at ICAAC, **San Francisco** and a talk at Stanford University, Sept 2012  
([http://www.youtube.com/watch?v=fdZ9nuS\\_RKI](http://www.youtube.com/watch?v=fdZ9nuS_RKI))
- talk at the DGHM2012 meeting in **Hamburg**, Oct 2012  
(<http://www.youtube.com/watch?v=JWBGBHH5Ros>)
- *Metagenomics of ancient and historical material: From mummies to microbes*, UK Genome Science meeting, **Nottingham**, Sep 2013  
([http://www.youtube.com/watch?v=PeR1\\_9qRauc](http://www.youtube.com/watch?v=PeR1_9qRauc))
- *Diagnostic Metagenomics* at British Society of Parasitology, **Liverpool**, Sep 2013  
(<http://www.youtube.com/watch?v=wtC4EBZt6lM>)
- *Adventures in translational genomics and metagenomics, Inaugural symposium*, Division of Microbiology and Infection, **Warwick**, Sep 2013  
(<http://www.youtube.com/watch?v=qK0iQFb9lGc>)

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## Publications

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My publications via Google Scholar <http://goo.gl/c3FCx>  
 My publications via PubMed: <http://pubmed.gov/?term=pallen%20m>  
 H-index according to Google Scholar: 49

Citation numbers are from Google Scholar.

Papers cited >100 times or in journals with impact factor >20 shaded in grey.

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2. Sergeant MJ, Constantinidou C, Cogan TA, Bedford MR, Penn CW, **Pallen MJ** (2014) Extensive microbial and functional diversity within the chicken cecal microbiome *Under revision at PLoS One*
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## Regular Columns

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## Academic Leadership

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During my time at Barts, I attended a **Course in Management for Registrars and Senior Registrars in Pathology** at the University of Keele, sat on various working groups on informatics and participated in Divisional steering group meetings. I also set up a web-based system for collating staff publications for the Research Assessment Exercise.

I gained additional experience of university governance and management as **Head of Department** at **Queen's University Belfast** (1999–2001). Here, I took over a department that had been without effective leadership for several years and implemented steps to improve the situation:

- I established a **monthly departmental committee meeting**, with representatives from all grades of staff. As all academic staff were required to report on publications and grant proposals, these meetings also served as a gentle priority-setting exercise, reminding them of the obligations to get money in and papers out.
- I set up a **weekly departmental seminar series**, injecting new intellectual life into the department by bringing in speakers from outside Northern Ireland
- I performed **appraisals** of academic staff, **raising their aspirations** by encouraging them to seek external funding and/or collaborations (e.g. on my suggestion, Sheila Patrick became involved in a genome-sequencing project, which culminated in a *Science* paper and a chair for her).
- I carried out a **technical staff review** and set up a staff development programme.
- **I recruited a talented non-clinical lecturer**, Ian Henderson.

### Academic Leadership In Birmingham

In Birmingham, my efforts at academic leadership included:

- **recruiting high-quality staff to the campus:** I persuaded **Ian Henderson** to come with me from Belfast (he is now a professor and Director of Birmingham's Institute of Microbiology and Infection), **Nick Loman** (now on his own MRC fellowship), **Pauline Jumaa** (Consultant Microbiologist and now head of microbiology service at QEHB); I helped recruit **Tim Mitchell** (Professor of Microbial Infection) and **David Simmons** (immunologist with experience of pharma).
- **giving talks on grantsmanship**, explaining to my fellow academics the tricks of the trade. (<http://www.youtube.com/watch?v=K3q62MgV8ek>)
- catalysing moves towards the **establishment of an Institute of Microbiology and Infection** by organising an away day for the University's bacteriologists in 2008, where the idea of an institute was first formulated.
- organising Darwin Day meetings (see next section).
- establishing high-throughput sequencing on campus (see above)

By late 2011–early 2012, I had taken on a number of important leadership roles:

- **Microbiology Theme Lead for the School of Biosciences**, coordinating internal peer review of grant proposals and helping staff improve the structure and presentation of their proposals. I played a **decisive role in re-drafting and/or re-organising three successful research proposals** (BBSRC project grant proposals for Steve Busby and Pete Lund; Leverhulme fellowship application for Liz Fullam)
- Project Champion for a fundraising **initiative in Global Infection**; this led to me drafting, with Del Besra and Luke Alderwick, a **successful bid to the Wolfson Foundation**, which brought in £500,000 towards creation of a BSL3 laboratory and ended a long period of failed attempts by the University to engage with this funding body.

- Microbiology Theme Lead in our £10m **NIHR Surgical Reconstruction and Microbiology Research Centre** (see above)
- Microbiology Lead for the **Birmingham Fellows initiative** in 2011, which meant dealing with enquiries from applicants, contributing to long-listing and short-listing and sitting through an exhausting 29 hours of interviews.
- **Director of Research** for the School of Biosciences, which included **responsibility for the REF return**; in this role, I interviewed >30 staff within the School about their REF status and reorganised research meetings within the School. I also contributed to a university initiative to establish links with the **BGI** (the Chinese genomics institute).

During this period, I also demonstrated my ability to think strategically by **recruiting Dr Alice Roberts** to a Chair in Public Understanding of Science at the University (see below).

In April 2012, after a competitive selection process, I was appointed Director of the **Institute of Infection and Microbiology (IMI)**. In this role,

- I established an effective IMI Executive Management Group
- I led a **successful £200K bid** to the University's Dynamic Investment Fund
- I recruited support staff to the IMI: a research technician and an IMI facilitator
- I organised an **IMI Inaugural Symposium** for Dec 2012, with Keynote Speakers from Stanford, Berkeley, Chicago, Princeton and the Institut Pasteur.
- I ran an interdisciplinary **Workshop on Infection** in July 2013, under the auspices of the university's Institute of Advanced Studies, including participants from the Arts and Humanities, the armed forces and other universities (Nottingham, UEA, Warwick).

In late 2012–early 2013, I took part in the University's **Senior Leadership Programme**, which included ten one-day workshops and a 360° appraisal. This provided valuable insights into the strengths and weaknesses of my own management style.

My contributions to academic citizenship and leadership in Birmingham were recognised by the award of **pay increases or bonuses** for three consecutive years and by categorisation as a **Band 3 Professor** (the highest level) within the University's new Professorial Banding scheme in 2012.

## Academic Leadership In Warwick

On arrival in Warwick in April 2013, I established and headed a **new Division of Microbiology and Infection** within Warwick Medical School (WMS). In this role, I:

- recruited seven talented new members of academic staff, including a world leader in bacterial population genomics, **Mark Achtman**.
- created a new Divisional web site (<http://www2.warwick.ac.uk/fac/med/research/microinfect>), a blog (<http://blogs.warwick.ac.uk/microbialunderground>) and a Twitter feed (@WarwickMicrobio)
- delivered **REF uplift** to WMS, with four four-star publications from Achtman alone plus my papers in *NEJM*, *Nature Biotechnology* and *JAMA* and several other four-star papers from new staff.
- supervised the establishment and equipping of a new **molecular bacteriology laboratory**, including purchase of a new Illumina MiSeq and a high-end server.
- established a divisional **seminar programme** that brought world-class researchers to the WMS campus, e.g. Susan Lea from Oxford, Petra Oyston from DSTL and Paul Keim from Northern Arizona University.
- organised an **Inaugural Symposium** for the Division in Sept 2013, with a keynote address from Gad Frankel (Imperial) and entertainment from Canadian science rapper, Baba Brinkman; videos and live-tweets from the event have been storified here: [http://storify.com/mjipallen/inaugural-symposium-warwick-micro-and-infection?utm\\_source=embed\\_header](http://storify.com/mjipallen/inaugural-symposium-warwick-micro-and-infection?utm_source=embed_header)

I set about ensuring that the Division was able to recruit grant income. As soon I arrived, I started co-ordinating a now-successful **£9m MRC bioinformatics infrastructure proposal**, working with co-investigators in Birmingham, Swansea and Cardiff (see above). I also co-wrote a **BBSRC bioinformatics infrastructure proposal** with Mark Achtman. In July 2013, I organised a **Divisional Away Day** in Malvern, with input from Charles Penn (Birmingham) and Rick Titball (Exeter); this provided **training for new investigators on grantsmanship** and laying the ground for high-impact publications. In recent months, I have helped newly recruited staff draft well written and persuasive new-investigator proposals. We have seen our first modest success, with the recent award of a £50k Noreen Murray grant to Emma Denham and Chrystala Constantinidou.

I have also sought to connect the new Division to the wider world by

- forging collaborative links with academics in the **School of Life Sciences**, including involvement as co-investigator on a NERC grant proposal from Liz Wellington and bringing together ancient DNA expert Rob Allaby and archaeologist Vince Gaffney (Birmingham) on a highly promising collaborative sedimentary DNA project
- re-establishing collaborative research links with former colleagues on the Birmingham campus by creating **honorary academic positions** for Beryl Oppenheim (UHB) and Nick Loman (Birmingham) within the new Division.
- establishing new links with local NHS trusts through research meetings and participation in the Grand Round at Coventry.
- linking up with academics outside the medicine/life sciences, including classicist and TV personality **Michael Scott**, Roberta Bivins (history of medicine) and Stuart Croft (DVC; political science)
- introducing TV medical journalist **Michael Mosley** to Warwick, preparing the way for his participation in the university's fifty-year anniversary celebrations in 2015.
- speaking at the RSM's Military Medicine Section Colt Foundation research meeting in Dec 2013 (<http://www.rsm.ac.uk/academ/use02.php>), building on my good standing with the military.

## Additional Evidence of Academic Citizenship

I have received training in interviewing and in equal opportunities legislation. I have served on numerous **appointments panels** within the academic sector or within the NHS representing the university or the Royal College of Pathologists. I have also received training **in health and safety** and have conducted lab inspections and formulated risk assessments.

I have gained useful insights into the dynamics of research grant panels, by serving as an evaluator

- on the **Life Sciences Panel** for the Irish Basic Research Grants Scheme, organised by Enterprise Ireland in 2000
- on a **BBSRC panel** on Synthetic Biology in 2012
- for the **Norwegian Research Council** in Oslo in Oct 2013
- on an Food Standards Agency tender for *Campylobacter* genomics

I have peer-reviewed grant applications for the Wellcome Trust, BBSRC and MRC. I have peer-reviewed publications for numerous journals; in the 1990s I served on the "hanging committee" for the *BMJ's Information in Practice* section. After my arrival in Birmingham, I served as Editor for two years for the journal *FEMS Microbiology Letters*.

In 2012-13, I served on a **Blackett Review**, at the invitation of Sir John Beddington, Chief Scientific Adviser to HM Government, to consider new approaches to Biodetection. This involved attending three meetings with other academics and opinion-formers and working with BIS staff to draft the report.

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## Communicating and Defending Science

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### Media and Outreach

While at **Imperial College**, I selected and led a team of scientists to victory in the 1995–6 series of the national quiz competition, **University Challenge** (<http://www.youtube.com/playlist?list=PL1CF5C66011C99067>), projecting a positive image to the public of science and scientists. As a result, I was awarded **social colours** by Imperial.

Since my arrival in **Birmingham**, I have participated in various science-communication and media events, including:

- a play for children on the eradication of smallpox (<http://www.youtube.com/watch?v=k7ZpC6XgN5o>)
- radio and newspaper interviews during the Darwin bicentenary year 2009.
- contributing a chapter to a pop-sci book *What are you optimistic about*.
- joining **Melvyn Bragg** on **BBC Radio 4's In Our Time** (estimated audience 2 million) to discuss *The Origins of Infection* in June 2011 (<http://www.bbc.co.uk/i/b011pldm>).
- two talks at Malvern churches evolution weekend (<http://www.youtube.com/watch?v=XtU7WbLLJDe>)  
(<http://www.youtube.com/watch?v=UijJlt3SU5M>)
- a University open day talk ([http://www.youtube.com/watch?v=ua\\_pFKFUKcM](http://www.youtube.com/watch?v=ua_pFKFUKcM))
- contributing to the University of Birmingham Community Day, 2012
- a public talk as part of Thinktank's Genetics week in Oct 2012 (<http://www.youtube.com/watch?v=3nAPIYXXIMQ>)

### Digital Scholarship

For over two decades, I have been an **early adopter engagement with digital technologies**. In 1995, I wrote a series of articles, **Guide to the Internet**, for the **BMJ** (later turned into a booklet, right). Throughout the late 1990s, I communicated the potential of the Internet to health workers through publications, talks and workshops [131-132, 137-140, 142-146].

In recent years, my group has led the way in exploiting social media in science communication. Two blogs that I established have together featured hundreds of blog posts and have received over **90,000 hits from >120 countries**:

- <http://roughguideto evolution.blogspot.com>
- <http://pathogenomics.bham.ac.uk/blog>

(note the latter is now run by Nick Loman)

I have >1200 followers on **Twitter** and have produced >3700 tweets and live-tweeted numerous meetings.

I have >260 subscribers to my **YouTube** channel, with over 100,000 views. My Klout score is 51 (<http://klout.com/#/mjpallen>).



## Evolution and Darwiniana

Since 2003, I have organized a local **Darwin Day** symposium or lecture, kicking off with some readings of anti-slavery prose and poetry by local Rastafarian poet, **Benjamin Zephaniah** (whom I later chaperoned during the award of his honorary degree). Through these Darwin Day events, I have entered into collaborations that have resulted in publications:

- an **encyclopedia entry on *Darwin and Religion*** with Alison Pearn of the Darwin Correspondence project [13]
- a **peer-reviewed research article** with John van Wyhe on the **influence of Darwin's daughter's death on his religious views**. [21]
- several papers on the **evolution of the bacterial flagellum** (a preoccupation of ID-creationists) including a highly cited paper [70] with Nick Matzke, who provided scientific advice at the landmark Dover trial in 2005.

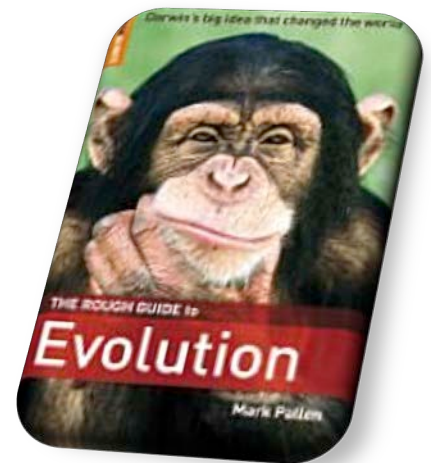
I organized Darwin-related tours for visiting speakers, including

- the **Darwin's Pilgrim's tour**, which took Lauri Lebo, a journalist involved in the Dover Trial, on a lecture tour of Cambridge, London, Birmingham and Shrewsbury (<http://www.youtube.com/watch?v=GCf3Kg3ekeY>)
- two visits to **Down House**, hosted by Darwin descendent **Randal Keynes**, for Eugenie Scott in Feb 2011 and Ken Miller and John Hawks in Sept 2011.

In the run-up to the Darwin bicentenary in 2009, I wrote **The Rough Guide to Evolution**, a popular and wide-ranging introduction to Charles Darwin, the theory of evolution and its ramifications in science and society. The book's 100,000 words—the equivalent of two PhD theses—were written in my spare time in less than six months. The book was publicised in *Nature* and the *Guardian*, adopted by the US National Center for Science Education and has **seven 5-star reviews on Amazon**.

After a competitive selection process, *The Rough Guide to Evolution* was selected for the first **Great Read in Birmingham initiative** and was **distributed to > 6000 undergraduates** in Sept 2011. This initiative was accompanied by keynote seminars in evolution (<http://www.youtube.com/playlist?list=PLDA93D52E7F58B09E>).

In late 2011, I recruited anatomist and TV presenter **Dr Alice Roberts** to a **Chair in Public Engagement in Science** at the University of Birmingham. That same year, I proposed and chaperoned Randal Keynes as an honorary graduand (<http://tinyurl.com/9ghngkg>).



My interest in evolution has led to involvement in a number of SciArt projects

- The **Rap Guide to Evolution**, a celebration of Darwin's legacy in music and words written (with my help) and performed by Canadian rap artist Baba Brinkman. This show won an award at the Edinburgh fringe, gained **positive reviews in *Science* magazine and the *New York Times*** and had a run **off Broadway**. Videos have been created to accompany the tracks (<http://rapguidetoevolution.co.uk>); Chris Stringer and I play cameo roles.
- The **Evolving Words Project**, a Wellcome Trust project to engage young people in Darwin-related poetry during 2009.
- **The Origin of Species in Dub** (<http://pathogenomics.bham.ac.uk/Dub/Videos>), a celebration of Darwin's work through the medium of reggae music.

I was invited to speak at a SGM *Tree of Life* symposium at Herriott-Watt in 2009 and to give an after-dinner speech on the *Great Trees of Life: Genes, Gospels and Languages* in March 2013 at a **meeting of New Testament scholars** in Birmingham (<http://www.youtube.com/watch?v=8Ykj5wQs7vU>)

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## Teaching Experience

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Throughout my career, I have enjoyed teaching and have sought to bring to my teaching the same **enthusiasm** and standards of **rigour** that enlighten my research. I have been involved in **all aspects of teaching**, including **course design, organisation and implementation, delivering lectures, small-group teaching and assessment**.

### Undergraduate Teaching

As Lecturer and then Senior Lecturer at Barts in the late 1980s and early 1990s, I was responsible **for planning and organising the course in Medical Microbiology for medical students**. I oversaw the transition to a new undergraduate curriculum, restructuring the timetable, rewriting lectures and devising new problem-based learning sessions. In 1992 and 1993, in polls organised by medical students, I was judged **Best Teacher of Pathology** at St. Bartholomew's Hospital Medical College. I attended a one-day workshop on **Problem-Based Learning** in March 1999.

At Queen's University Belfast I **re-organised medical student teaching of microbiology**, restructuring the timetable and improving the ways in which teaching was delivered (e.g. replacing large practical classes with small group teaching, putting teaching material on the web). I broadened the involvement of local microbiology staff in the teaching, getting them all involved in the small group teaching.

Working within the **medical school in Birmingham** (2001–2008),

- I organised and delivered **medical microbiology teaching to medical, dental and nursing students**, coordinating and delivering lectures and small group teaching, writing and marking exam questions; conducting vivas
- I acted as a **personal tutor** for medical students
- I sat on working parties in medical education, which including establishment of a **Graduate Entry Course** and a review of Years 1–2 Teaching.
- I lectured and examined on BMedSc microbiology modules.
- I acted as **external examiner in Pathology** at Barts/London.

Working for the **School of Biosciences** in Birmingham (2004–2012):

- I ran a **second-year module** on the **Bioinformatics BSc** for five years until 2009.
- I lectured on the **human genome evolution** on second- and third-year modules
- During 2009-10, I led a far-reaching review of microbiology teaching within the School of Biosciences, which led to the **establishment of three new modules**, which resulted in me giving over 20 new lectures in 2010–2011.
- I set up a third-year module on the **Molecular Basis of Bacterial Infection**.
- I lectured on global infection on a third-year **Applied and Environmental Microbiology** module.
- I acted as **tutor** to Natural Science and Biosciences students and answered questions from applicants and their parents during University Open Days
- I performed school visits to Queen Mary's Grammar School, Walsall

At Birmingham, I was nominated for the **Head of School Award for Excellence in Teaching 2010–11** by two third-year students and narrowly missed obtaining this award.

Since my arrival at the **University of Warwick** I have given lectures to medical students on the MBChB course and to Life Sciences students on a second-year module on clinical microbiology. I have also set up a student-selected teaching module for medical students.

## Postgraduate teaching

In 1989–90, I helped run a 22–week evening class and a two-week practical course, both on the **Molecular Biology of Bacterial Pathogens**. In 1993–1994, I organised **Revision Courses for the Practical MRCPATH Examination** (two mock examinations and five tutorials), bringing over £1,500 into the Department. In 1993, I attended a workshop on **Effective Supervision of PhD Students**.

After my arrival in Birmingham, I **lectured on MSc courses** at the Royal London Hospital, the London School of Hygiene and Tropical Medicine, the University of Oxford and at Imperial College and acted as **external examiner** for several years on a microbiology MSc at the London School of Hygiene and Tropical Medicine. For four years after my arrival in Birmingham, I ran a **two-week module on the Infection and Immunity MSc**.

I have supervised and examined numerous PhD students; notable former PhD students include **Martin Antonio** (now Molecular Biologist and Head of TB diagnostics laboratory, MRC Gambia), **Helen Hampikian** (now Assistant Professor of Biology at Clarion University) and **Nick Loman** (now on his own MRC Fellowship).

## Innovative approaches to teaching

Throughout my career, I have enthusiastically adopted innovative approaches to teaching, using **digital tools**, and, more recently, **social media**. This began in the late 1980s, with the use of Apple Macintosh computers to produce visually appealing slides and handouts.

A couple of years ago, I ran a **special study module** on Evolutionary Medicine, in which **medical students were required to file blog postings** on evolutionary topics, gaining experience of blogging in an academic setting (<http://darwinstudents.blogspot.com/>).

During the last year, in the spirit of **open scholarship**, I have recorded almost all my lectures and research seminars and have made them publicly available on YouTube as **slidecasts**. Most of my lectures have been **watched hundreds or thousands of times** online, helping local students with revision and making my teaching available to the world—my YouTube channel has been **accessed from 109 countries**. Examples of my online teaching include:

First-year teaching on Microbiology (Birmingham):

<http://www.youtube.com/playlist?list=PL3118E4689AA9D4D5&feature=plcp>

Second-year teaching on Human Evolution (Birmingham):

<http://www.youtube.com/playlist?list=PL653C003004B33A0E&feature=plcp>

Third-year teaching on Human Evolution (Birmingham):

<http://www.youtube.com/playlist?list=PL2E8AD7EC29AB0F71&feature=plcp>

Third-year teaching on Global Health and Diagnostic Microbiology (Birmingham):

<http://www.youtube.com/playlist?list=PLB9A7EA033B57D9A8&feature=plcp>

Third-year teaching on Molecular Basis of Bacterial Infection (Birmingham):

<http://www.youtube.com/playlist?list=PL837F8A36C9E16B47&feature=plcp>

MBChB teaching in Warwick:

<http://www.youtube.com/playlist?list=PLrc5DGP6JJKL3TKVXohx7gGGzJBecni6w>

Life Science/Clinical Microbiology teaching in Warwick:

<http://www.youtube.com/watch?v=pbONqQxNCrg>

[http://www.youtube.com/watch?v=98\\_15EHBT-M](http://www.youtube.com/watch?v=98_15EHBT-M)



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## Clinical Experience

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I completed my specialist training in Medical Microbiology as SHO, then Registrar, at the **Royal Free Hospital** (1986–8) and as Lecturer/Honorary Senior Registrar at **St. Bartholomew's Hospital** (1988–92). During my training I gained experience of a range of clinical duties, including:

- signing out laboratory reports and supervising laboratory diagnostic procedures
- discussing diagnostic and therapeutic problems with clinicians
- daily visits to the ICU
- advising on nosocomial infections
- advising oncology staff on the management of febrile neutropenics
- advising on community-acquired and imported infections
- hospital infection control and follow-up of community-acquired infection
- participation in the on-call out-of-hours rota

I passed my MRCPPath final examination in 1991 and was promoted to Senior Lecturer the following year.

As a Senior Lecturer at Barts I held **an honorary consultant contract** with the NHS, carrying out various clinical duties:

- out-of-hours consultant service on a one-in-three rota throughout the year.
- full-time consultant microbiology service for eight weeks a year.
- participation in weekly clinical case conferences.
- training of specialist registrars (e.g. organised MRCPPath Revision courses in 1993–4, monthly training in management meetings Jul-Dec 1998).
- attendance at monthly microbiology clinical directorate meetings.

Initially, after my arrival in Birmingham, I provided one programmed activity to the **University Hospitals Birmingham NHS Foundation Trust**, which covered:

- training of junior medical staff—I ran **MRCPPath examination preparation tutorials** for seven local SpRs.
- contributing to **NHS research activities**, which led to several papers [1, 15, 23, 41].
- contributing to the local **CPD programme**.

In February 2007, I transferred to a **non-clinical professorial contract** and have recently voluntarily withdrawn from the medical register and Royal College of Pathologists. However, I remain committed to building an effective interface between academia and the health service, as evidenced by my efforts in establishing the NIHR Surgical Reconstruction and Microbiology Research Centre and through my on-going collaborations with colleagues in the NHS and Public Health England and through links to other healthcare genomics centres/activities (on good terms with Sharon Peacock, Danny Wilson, Derrick Crook, Mark Caulfield).