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Fungal Infections Key Facts (2016 – 2018)

GLOBAL PROBLEMS
- 1 billion + Infections per year
- 1.5 million + Deaths per year

CHALLENGES
- Limited antifungal drugs
- No vaccines
- Difficult to detect/diagnose
- Antifungal resistance

LARGEST UK INVESTMENT IN THE FIELD
- 1 billion +
- 1.5 million +
- Joint investment UoA/MRC

28 posts
Training Basic Scientists & Clinicians

↑12 Academic Staff
+ 3 Early Career Fellows

AFGrica Unit

2 New clinical guidelines

1 Spinout company to be registered in 2019

97 Publications
+ 542 Citations
(since 2016)

PATENTED
2 Patents

12 public events engaging 20,000 people

77 global collaborators
Aberdeen Fungal Group
The Medical Research Council Centre for Medical Mycology (MRC CMM) was established in July 2016 at the University of Aberdeen. This Centre capitalises on the world-renowned expertise of the Aberdeen Fungal Group (AFG), and represents a joint investment of £6.5 million by the MRC and the University of Aberdeen. The creation of the MRC CMM represents one of the most ambitious strategic investments in UK medical mycology. This award empowers the AFG, enabling this group to utilise and expand its critical mass, promoting pioneering cross-disciplinary research that covers areas of scientific, translational and clinical importance. A major activity of the Centre is to increase future UK capacity in basic and clinical research through training programmes aimed at various levels, from medical students to early career researchers. This award is also facilitating strategic interactions with other national and international groups and promotes public engagement and understanding of our science.

The AFG is one of the largest medical mycology groupings worldwide. The principal investigators (PIs) within the AFG represent a broad umbrella of expertise from fundamental research into the biology of fungal pathogens to patient care and translational science. This wide-ranging expertise enables the development of unique synergies within the AFG, facilitating the simultaneous analysis of both the host and pathogen to determine their individual contributions to the pathogenesis of disease. Originally located at different locations on the Foresterhill site, the formation of the Centre saw the relocation of all AFG members into contiguous laboratory and office space in the Institute of Medical Sciences building (IMS) to optimise interaction and collaboration.

The IMS which sits in the School of Medicine, Medical Sciences and Nutrition, is a cutting edge £50 million biomedical research institute that boasts a well-integrated interdisciplinary research infrastructure that includes state-of-the-art genomics, proteomics, microscopy, histology, cytometry and animal care facilities. Within the IMS, the Kosterlitz Centre for Therapeutics provides expertise in the development of novel drugs and clinical targets. Adjacent to the IMS, the Institute of Applied Health Sciences (IAHS), is a major research centre in health services research that provides complementary expertise in health technology assessments (including in diagnostics), evidence synthesis, clinical trials, health economics and medical statistics. The IMS is also located next to the Aberdeen Royal Infirmary (ARI), which serves one of the largest geographical areas of any hospital in the UK. The Rowett Institute (RI) is also immediately adjacent to the IMS providing
further sources of complementary expertise in human nutrition and health. The collocation of the IMS, the RI, the Suttie Centre for Teaching and Learning in Healthcare, the IAHS, and the ARI provides a tightly integrated biomedical centre for basic, clinical and translational medical research. There are also on-site incubator facilities for translational research and the development of biotechnology-based spin-out companies.
Of all microbial pathogens of humans, fungi are the least well studied and understood. Fungal infections of the nails, skin and mucosae, affect approximately one quarter of the world’s population. In addition, around 3 million individuals suffer from life-threatening invasive infections that are difficult to diagnose and treat [1, 2]. Moreover, these infections often have mortality rates that exceed 50%, even when antifungal drugs are available. Fungi also contribute substantially to morbidity associated with asthma and other allergies, infection-related blindness and debilitating and disfiguring chronic subcutaneous infections. A complicating factor in treating fungal infection is the increasing emergence of pathogenic fungi which are resistant to the limited number of antifungal drugs [3]. Collectively the cost of diagnosing, treating and providing prophylactic protection from fungal infections has major economic impact.

Three areas require our urgent attention:
1. We need to generate safer and more effective antifungal drugs.
2. We need to improve our ability to detect fungal infections, by developing robust, rapid, simple and cheaper diagnostics.
3. We need to better understand fungal virulence and host antifungal immunity, and to exploit these discoveries to help tackle these devastating infections.

References:
Our ability to tackle these urgent challenges is considerably constrained by a worldwide lack of capacity in basic and clinical mycology. The MRC CMM helps to meet this strategic need by facilitating pioneering cross disciplinary research addressing the priority areas of research, and by increasing UK capacity for basic and clinical research for the future.
The overarching vision of the MRC CMM is to facilitate innovative and world leading multidisciplinary research that will substantially advance our understanding of fungal pathogenesis and host immunity, enabling the generation and utilisation of knowledge that will improve the prevention, diagnosis and treatment of fungal diseases in the future.

Our vision is being achieved by continuing to deliver on the following objectives over the next three years:

- New appointments have been made in bioinformatics and antifungal immunity that will catalyse new interdisciplinary activities.
- Enhancing and integrating the broad and complementary expertise of the AFG to achieve synergies across six themes of innovative interdisciplinary research.
- Delivering a strong cohort of basic and clinical researchers through our bespoke training programmes.
- Facilitating and promoting collaborations with industry and the clinic.
- Promoting medical mycology within the broader academic community and the general public.
Delivering the Vision:

1. Research – Innovative and Interdisciplinary

Research in the MRC CMM refocused existing synergies within the AFG into 6 key themes, generating integrated cross-disciplinary programmes of research that address the major challenges facing this field.

Research Themes:

1. Fungal cell surface dynamics and its impact on antimicrobial chemotherapy and host immunity.
2. Fungal components as antifungal drug targets, diagnostics, vaccine antigens and adjuvants.
3. Fungal growth, adaptation and morphogenesis in the context of infection.
4. Temporal host-fungal interactions and key mediators that influence disease establishment and progression at molecular, cellular and organismal levels.
5. Exploiting emerging technologies to generate global perspectives that broaden our mechanistic understanding of host-fungal interactions.
6. Unravelling patient susceptibility to enable directed diagnosis, treatment and prevention of fungal disease.
2. Training and Capacity Building

The creation of the MRC CMM is enabling us to address the shortage in medical mycology expertise in the UK, by training excellent basic and clinical scientists, and consolidating our position as an international ‘Centre of Excellence’ for training in this field. A central component of this programme is the development and mentoring of our trainees, with the ultimate aim of helping them to establish themselves as independent researchers in this field in the UK in the future. We have a track record of over 30 postdoctoral fellows and students trained in the AFG, who now hold permanent research positions or fellowships in medical mycology across the UK and worldwide.

We offer the following bespoke training programmes over the 5 years:

- **13 MRes-PhD Studentships**
  - 9 recruited

- **5 Academic Clinical Training Fellowships**
  - 3 recruited

- **3 Early Careers Fellowships**
  - 1 recruited

- **10 Medical Student Summer Scholarships**
  - 6 recruited
3. Translation to Clinic and Industry

The strong foundational science base of the MRC CMM scientists have led to translatable opportunities, which have been significantly enhanced by the formation of the MRC CMM. Support for these translational activities is provided by the University of Aberdeen which has active pipelines for facilitating commercial exploitation of promising research results and encourages the formation of spin-out companies, collaborations with industry and other knowledge exchange activities. Early stage translational activities are supported by a Wellcome Trust Institutional Strategic Support Fund (ISSF).

**Our objectives include:**
- Increasing and promoting opportunities for translation of Centre research.
- Increasing collaborations and other interactions with industry and the clinic.
- Increasing the numbers of patents and commercial contracts.

**Achievements to date:**
- Patent: “Antibody Molecules and Uses Thereof” - has entered the Nationals Phase filed in Europe, USA, Australia and Canada on 6th September 2017 (GB 1503812.8; PCT/GB2016/050577). The inventors on the patent application are Neil Gow, Fiona Rudkin, Lars Erwig and Allan Jensen.
- mycoBiologics, a spin out company with Fiona Rudkin as CEO is to be registered in 2019.
- The number of international collaborators exceeds 75.
- AsperCF, a research consortium has been created by Professor Adilia Warris to focus on stratification of Aspergillus disease in paediatric and adult cystic fibrosis patients to enable targeted treatment and improve clinical outcomes.
4. Communication – Public Engagement and Scientific Dissemination

Our objective is to raise general awareness of the importance of medical mycology and to communicate the research and training being carried out in the MRC CMM. This is being achieved with several live events for public audiences and visiting schools through our outreach programme. Many of our research highlights have been reported in online media, thus reaching global audiences.
Biography
Gordon Brown is a Professor of Immunology and Wellcome Trust Senior Investigator. He is Director of the MRC Centre for Medical Mycology and of the University of Aberdeen AFGrca Unit that is based at the University of Cape Town. He is also a co-Director of the Wellcome Trust Strategic Award in Medical Mycology and Fungal Immunology, based at Aberdeen. He maintains a small research group at the University of Cape Town, where he holds an honorary Professorship. His primary research interests are C-type lectin receptors and their role in homeostasis and immunity, with a particular focus on antifungal immunity.
Lay abstract of research

To recognise infection, the immune system utilizes sensors on immune cells called “pattern recognition receptors” which detect invading pathogens. These sensors then trigger a number of responses which are aimed at providing protection against the infection. My group is focused on understanding a particular group of these sensors, called the C-type lectins (CLRs), which stemmed from our discovery of the first receptor in this class, Dectin-1. We have shown that CLRs are able to directly induce immune responses, and have determined the mechanisms that they utilize to trigger these effects. Importantly, we have shown that CLRs play a central role in protective immunity during infection with many microbes and identified genetic variants of CLRs in humans, which can confer susceptibility to disease. We have found that these receptors play a central role in immunity to fungi. Our current research is aimed at gaining a more detailed understanding the role of CLRs during infection, and exploring the roles and functions of new CLRs that we have identified, including MelLec, an unusual receptor that recognises fungal melanin.

Key Publications


www.abdn.ac.uk/staffnet/profiles/gordon.brown/
Biography
Adilia Warris is a paediatric infectious diseases specialist with a specific interest in medical mycology and holds an Honorary Consultant position in Paediatric Infectious Diseases at the Royal Aberdeen Children's Hospital. She is a principal investigator of the Aberdeen Fungal Group and co-director of the MRC Centre for Medical Mycology at the University of Aberdeen.

Prof Warris’ research profile has a strong translational focus and specific areas of interest include the host-fungus interaction in specific patient groups with an emphasis on Aspergillus species, the unique interaction of A. nidulans and the CGD host, Aspergillus infections in people with cystic fibrosis, the development of new management strategies for invasive fungal disease in children, the epidemiology of invasive fungal infections in children, and the pharmacology of antifungals in paediatrics. She chairs the European Paediatric Mycology Network (EPMyN) through which post-graduate courses in Paediatric Mycology are coordinated as well as multicentre European studies to obtain a better insight in the fungal and clinical epidemiology of fungal infections in neonates and children.
Lay abstract of research

My research is aimed at unravelling unique host-fungus interactions based on clinical observations.

Patients with chronic granulomatous disease (CGD), suffering from an inborn error in the function of white blood cells, have an extremely high-risk of developing invasive aspergillosis and often these infections are fatal. Invasive aspergillosis in patients with CGD is caused by 2 different Aspergillus species, Aspergillus fumigatus and Aspergillus nidulans, with the latter having a unique predilection for this specific patient group. Our studies are focused on the molecular interaction between immune cells from CGD patients and those fungi, with the ultimate goal to find new targets to improve treatment. In addition we are researching how A. fumigatus can persist and adapt in the lungs of patients with CGD, leading to recurrent infections and the fungus becoming resistant to antifungal therapy.

Comparable studies are done with immune cells from people with cystic fibrosis (CF). Half of the people with CF will be infected with A. fumigatus in their lungs leading to exacerbation of lung disease. The pathophysiology of Aspergillus infections in people with CF is not well understood and in addition to the presence of the thick sticky mucus entrapping the fungal spores in the lungs of people with CF, their immune cells respond abnormally to the presence of A. fumigatus. By studying the interaction between CF immune cells and A. fumigatus we aim to increase our insight into this specific host-fungus interaction and to find new treatment modalities to preserve lung function.

My clinical research focuses on the fungal and clinical epidemiology of invasive fungal diseases in neonates and children (EPMyN-EUROCANDY study) and paediatric antifungal stewardship (PASOAP study).

Key publications


www.abdn.ac.uk/staffnet/profiles/a.warris
Biography
Al Brown studied Biochemistry at the University of Aberdeen, and then worked in Surrey and at MIT before returning to the UK to take up his first faculty position in Genetics at Glasgow University in 1983. In 1989 he moved back to Aberdeen University where he is now a Professor of Molecular and Cell Biology in the Institute of Medical Sciences. Together with Neil Gow, he formed the Aberdeen Fungal Group (AFG) in the early 1990s. Since then the Group has blossomed into a large tightly integrated and interdisciplinary team addressing a wide range of questions in medical mycology and fungal immunology. This has led to the development of the Wellcome Trust Strategic Award in Medical Mycology and Fungal Immunology (www.abdn.ac.uk/mmfi: directed by Neil Gow) and the UK Medical Research Council’s Centre for Medical Mycology (www.abdn.ac.uk/cmm: directed by Gordon Brown). Al Brown’s research team combines genomics, molecular biology and modelling to define how Candida albicans adapts to dynamic and complex host niches, and evades immune surveillance, during colonisation and infection.
Lay abstract of research
My group studies the pathogenic yeast, Candida albicans. Candida normally lives in our gut, doing us no harm. However, it can cause common infections such as thrush, and life-threatening infections in intensive care patients. Our aim is to understand what makes this yeast so adept at switching from a harmless component of our microbiota into an aggressive cause of infection. In part this is because Candida is able to rapidly tune its own physiology to different niches within our bodies, and in part this is because it can evade immune surveillance under certain circumstances. We are investigating the molecular mechanisms that mediate these adaptive responses to the local nutrients and environmental stresses in these niches, and how these adaptive responses help the fungus hide from our immune system. This is increasing our understanding of how Candida survives inside us. In the longer term, this will promote the development of better diagnostics and more effective antifungal therapies.

Key publications


Biography

Neil Gow is a microbiologist with specialist research interests in medical mycology and in particular the biology of the fungal cell wall and host-fungus interactions. He trained at Edinburgh, Aberdeen and Denver USA before taking up a position at Aberdeen. He is a founding member of the Aberdeen Fungal Group (AFG). More than 25 of his past laboratory students and postdoctoral researchers now have their own laboratories in the field. He is the Director of a Wellcome Trust Strategic Award that coordinates research and training activity in the field of medical mycology and fungal immunology across the UK and in developing countries. He is also co-Director for research for this MRC Centre for Medical Mycology and is funded via a Wellcome Trust Senior Investigator award and Collaborative Award. He has been elected a Fellow of the Royal Society (FRS) and Academy of Medical Sciences (FMedSci) and is current President of the Microbiology Society.

Professor

Neil Gow
FRS, FMedSci, FRSE, FAAM, FBS

Honorary Deputy Director for Research
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Lay abstract of research

My group is focused on life-threatening fungal diseases. These infections pose difficulties in diagnosis, there are no vaccines for fungal disease, and treatment options are limited. Fungi have a cell wall that is composed of signature molecules that are not represented at all in the human body. The cell wall is therefore the target which the immune system uses to recognise the presence of a fungal invader and it is also an excellent target to aim the design of antifungal drugs. For these reasons my group’s speciality is to understand how the fungal cell wall is made, how it is detected by our immune system and how we might kill fungi by blocking cell wall assembly. To investigate this we use a combination of genetic, immunological and imaging technologies that allow us to explore the structure and function of the cell wall. Most of our work focused on the major human pathogen *Candida albicans* that causes more than 100 million mucosal infections and 250,000 life threatening infections every year. This research is therefore informing the design of new generations of antifungal drugs and diagnostic tests.

Key publications


Biography
Alex Brand is a fungal cell biologist working on how the penetrative filaments of pathogenic fungi are tailored to promote invasive infections. Alex came to science as a second career after taking an Access course at the University of Aberdeen. She graduated in Biochemistry in 2000 and completed a PhD in Microbiology in 2004. She established her research group in 2009 with a Royal Society University Research Fellowship and an MRC New Investigator grant to investigate how fungi regulate invasive traits in response to the physical properties of the environment. Alex was appointed Reader in 2015 and was awarded a Wellcome Senior Research Fellowship in 2017.
Systemic fungal infections kill more than 1 million people a year. Almost half of these deaths are caused by two fungi that produce invasive hyphal filaments. These filaments penetrate deep within human tissue causing cell damage, inflammation and fatal levels of sepsis. A key virulence trait of these filaments is their ability to steer as they grow and respond to physical features they encounter in the environment. Although fungi are relatively simple organisms, we do not yet understand how this information is sensed or how the direction of growth is altered. We have developed an imaging system that enables us to monitor hyphal growth and track the movement of intracellular fluorescent proteins at the same time. By deleting candidate genes, we can compare the mutant strains with normal cells to find out which proteins are important for hyphal steering. Mutants that cannot steer normally are not able to penetrate human tissue so drugs that uncouple the steering mechanism in fungal cells might be effective at halting deep-seated tissue invasion by these fungal pathogens.

Key publications


www.abdn.ac.uk/staffnet/profiles/a.brand/
**Biography**

Deborah Lockhart is a newly appointed Senior Clinical Lecturer & Consultant in Medical Microbiology providing a unique position to bridge the gap between the bench and the bedside. Deborah's multi-disciplinary collaborative scientific research dissects how the manipulation of critical fungal cell wall biosynthetic enzymes could provide new antifungal therapeutic targets. Her clinical special interests include the epidemiology and aetiology of Candidaemia particularly in light of the global emergence of multi-drug resistant *Candida auris*. Deborah did her undergraduate training at the University of Glasgow and completed Microbiology higher specialist clinical training in NHS Greater Glasgow & Clyde becoming a Fellow of the Royal College of Pathologists. Inspired by the difficulties in diagnosing and managing patients with life-threatening fungal infections, she received a MRC Clinical Research Training Fellowship to complete a PhD at the University of Dundee with Professor Daan van Aalten followed by a Wellcome Trust Clinical Postdoctoral Research Fellowship that facilitated her relocation to the MRC CMM at the University of Aberdeen.
Modern medical treatments including advances in cancer therapy and organ transplants weaken the immune system and make patients highly susceptible to infections that would not normally pose a threat. Invasive fungal infections are often fatal in these groups. *Aspergillus fumigatus* is a fungus that produces spores found widely in the environment. In healthy people inhaled spores are harmless and eliminated by the immune system but in certain groups, including those with existing lung problems, they cause disease. The most serious forms lead to life threatening infections that are notoriously difficult to identify and treat. A sugary coat or ‘cell wall’ protects the fungus. Many coat making machines ‘enzymes’ contribute to this process but there are many gaps in our knowledge. I have discovered a sticky pocket on an enzyme essential for *A. fumigatus* growth under laboratory conditions. I am investigating: (1) whether loss of this enzyme stops the fungus causing disease, and (2) developing the chemical anchor binding to the sticky pocket into a longer molecule to block the enzyme and I hope, ultimately, kill the fungus. This work may help uncover starting points for the development of a new class of antifungal drugs.

**Key publications**


Biography
Donna MacCallum graduated from the University of Aberdeen in 1994 with a first class Honours degree in Genetics, then completed a PhD in Microbiology (1998) investigating yeast-hypha dimorphism in *Candida albicans*. From 1999-2009, Donna was a postdoctoral research fellow building expertise in animal models of immune diseases and fungal infections. She became an independent research fellow in 2009 and was promoted to Senior Lecturer at the University of Aberdeen in 2012. Donna is currently the Programme Coordinator of the MSc Microbiology and is the Postgraduate Teaching Academic Lead for the School of Medicine, Medical Sciences and Nutrition. She is the current treasurer of the International Society for Human and Animal Mycology (ISHAM) (term ends in 2018). The focus of her research is fungal pathogenesis and developing the 3Rs in medical mycology. Donna is also very active in public engagement and is a STEM Ambassador.

Dr
**Donna MacCallum**
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Lay abstract of research

Fungal infection models play a vital role in understanding how pathogenic fungi are able to cause disease, how the host responds to fungal cells and for testing new antifungal drugs. Fungi can cause infections of the skin, nails, mouth, genital tract, lungs, brain and even life-threatening, systemic infections. My research develops and characterises models mimicking these different infections, using animal models, insect models, human skin or cells in the laboratory. My research is particularly directed at reducing, replacing and refining the use of animals in medical mycology research (3Rs). My group has previously developed a shorter term mouse fungal infection model, significantly reducing the length of time required to determine whether a fungus is able to cause an infection or not and a laboratory assay mimicking interactions of fungal cells with kidney cells at the beginning of an infection to replace the use of animals. Currently, we are developing fungal reporter strains which allow fungi to be seen and quantified in living hosts, reducing the numbers of animals required to test new antifungal drugs, and we are investigating fungal-skin interactions using a novel human skin infection model.

Key publications


www.abdn.ac.uk/staffnet/profiles/d.m.maccallum
Biography

Carol Munro has over 20 years’ experience studying human fungal pathogens. Her research investigates how surface components contribute to virulence, host interactions and drug tolerance. Her interests span genomics and proteomics-based approaches to gain a better understanding of fungal pathogenicity and cell wall biosynthesis and remodelling. In collaboration with Christophe d’Enfert at Institut Pasteur she has generated a Candida albicans ORFeome library and a bar-coded genome-wide overexpression library is under development for functional genomics.

Professor Munro is deputy Editor in Chief of the journal FEMS Yeast Research and a past Chair of the Advanced Lecture Course on Human Fungal pathogens (2017). She has published over 90 scientific publications and her research has been supported by grants from the European Union, University of Aberdeen, Medical Research Council, Scottish Universities Life Sciences Alliance, British Society for Antimicrobial Chemotherapy and the Wellcome Trust to fund her research. She has mentored over 30 PhD and Masters students.
Lay abstract of research
My research is focused on investigating the protein components of the outer coat of the fungal pathogen *Candida albicans* and the mechanisms that controls their appearance at the cell surface. This outer coat plays an important role in the ability of the fungus to invade and infect the host, to form biofilms, to escape recognition by the host, and contributes to the ability of the fungus to resist antifungal drugs. The potential of outer coat proteins as novel diagnostic and therapeutic targets to detect and block the invading pathogen is being assessed. Another main focus is building important molecular tools and resources for the fungal research community to improve the characterisation of the *Candida albicans* genetic blueprint in order to gain a better understanding of the factors that make this fungus such a successful pathogen.

Key publications


www.abdn.ac.uk/staffnet/profiles/c.a.munro/
Biography
Duncan Wilson studied Microbiology at the University of Glasgow and went on to start his research career in medical mycology with a PhD at the University of Manchester and Pfizer (PhD: 2007) studying cyclic AMP signalling in Candida albicans. From there he moved to the Hans Knöll Institute in Jena, Germany, where he worked on the molecular basis of C. albicans pathogenicity with Prof Bernhard Hube. In 2014 he established his own research group in the Aberdeen Fungal Group with the support of a Wellcome Trust Sir Henry Dale Fellowship. The focus of Duncan’s current research is understanding how pathogenic fungi manage zinc homeostasis during infection.
**Lay abstract of research**

Our immune systems effectively prevent the vast majority of microbes from causing disease. One of the fundamental mechanisms underpinning this defence is called “nutritional immunity”. This is a system in which the human body withholds access to certain essential trace minerals that microbes require for growth. Pathogenic microbes therefore must have evolved strategies to circumvent nutritional immunity in order to grow within their host and cause disease.

Zinc is absolutely essential for the growth of all microbes and my group is trying to understand how the major human fungal pathogen, *Candida albicans*, adapts to zinc restriction during infection. This is important because fungal pathogens are a huge threat to human health, and are responsible for more deaths per year than malaria, and understanding how pathogens feed during infection may pave the way to novel therapeutics.

**Key publications**


Biography
Fiona Rudkin obtained her PhD in microbiology from the University of Aberdeen in 2015. Prior to this, Fiona worked in the Global Biotherapeutics Division at Pfizer on early-stage drug discovery programmes. Her PhD and subsequent work as a Research Fellow in the MRC Centre for Medical Mycology at the University of Aberdeen was focused on generating and validating human antibodies as potential new diagnostics and therapeutics for the major human fungal pathogen Candida. In 2017, Dr. Rudkin was awarded a Royal Society of Edinburgh Enterprise Fellowship to commercialize this research and create mycoBiologics – a new spin out company developing human antibodies to combat the urgent problems in diagnosing and treating serious fungal infections.

Dr
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Lay abstract of research

Invasive fungal infections kill more people every year than malaria. Current antifungal therapy is restricted to only three main classes of drugs and these are relatively non-specific and toxic. This is problematic in a patient population who are often already critically ill from underlying clinical conditions. With such a limited choice of treatment, another major concern is that resistance to these agents is increasing rapidly. Monoclonal antibodies (mAbs) are highly specific proteins produced naturally by the immune systems to fight infections and as a drug class, have a proven track record in successfully treating many cancers and autoimmune diseases. My research is focused on developing antibody-based therapeutics to address the urgent need for new approaches to antifungal therapy. So far, we have generated a panel of mAbs that specifically target Candida – one of the four major human fungal pathogens which causes life-threatening infections in patients with severely weakened immune systems. I am leading the commercialisation of this research which will result in the creation of a new spinout company called mycoBiologics. By harnessing the highly druggable properties of these mAbs, mycoBiologics will be focused on developing a new class of antifungal drugs to provide doctors with a treatment which is safer and more effective at treating resistant infections than current therapies.

Key publications


www.abdn.ac.uk/staffnet/profiles/fiona.rudkin/
Dr **Elena Shekhova**  
Early Career Fellow  
(Recruited 2017)

**Biography**

Elena Shekhova is a biochemist with Master’s degree from Saint Petersburg State University, Russia. After graduation, Elena became interested in investigating pathogenic fungi and came to Germany to pursue her PhD in Microbiology. There, at the Hans Knoll Institute in Jena, she focused on studying different aspects of the stress response system of the human fungal pathogen *Aspergillus fumigatus*. To continue her career, Elena moved to Aberdeen, where she was appointed as the first Early Career Fellow at the MRC Centre for Medical Mycology. Her current research aim is to decipher the redox biology of fungal infections.

**Research Interests**

Responses to oxidative stress are essential for both the survival of fungal pathogens and host pathology during infection. Immune cells produce ROS (Reactive Oxygen Species) that can serve as antimicrobial agents. Also, ROS generated via phagocytosis may modulate host inflammatory programs. To combat the attack of the immune system, pathogenic fungi must possess sophisticated strategies to adapt to various redox conditions. My research aim is to gain more insights into the importance of ROS-driven changes that occur both in the pathogenic mould *Aspergillus fumigatus* and in immune cells during infection.

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Biography
Carolina Coelho completed a degree in Pharmaceutical Sciences at University of Porto, in her native Portugal. Her PhD was overseen by joint-mentorship from Teresa Gonçalves at the University of Coimbra and Arturo Casadevall at Albert Einstein College of Medicine. She received postdoctoral training with Frederic Geissmann, at King’s College London and Arturo Casadevall, now at Johns Hopkins Bloomberg School of Public Health. She is looking forward to initiating her own research group in the MRC Centre, studying immunity to Cryptococcus neoformans infections.

Research Interests
Cryptococcus neoformans is responsible for almost 200,000 deaths each year, more than any other fungal pathogen. Cryptococcal infection is incredibly difficult to treat, sometimes requiring lifelong therapy, and the best medical treatment cannot avoid a mortality rate as high as 30%. My primary research interest is to understand how cells from the innate immune system recognize and kill this pathogenic yeast. My focus is the recently discovered immune functions of mitochondria. By understanding what constitutes an effective fungicidal response, and why this effective response sometimes fails, we will be able to find better solutions to treat this killer disease.

Dr Carolina Coehlo
Lecturer in Antifungal Immunity
(Starting in January 2019)

Biography
Carolina Coelho completed a degree in Pharmaceutical Sciences at University of Porto, in her native Portugal. Her PhD was overseen by joint-mentorship from Teresa Gonçalves at the University of Coimbra and Arturo Casadevall at Albert Einstein College of Medicine. She received postdoctoral training with Frederic Geissmann, at King’s College London and Arturo Casadevall, now at Johns Hopkins Bloomberg School of Public Health. She is looking forward to initiating her own research group in the MRC Centre, studying immunity to Cryptococcus neoformans infections.

Research Interests
Cryptococcus neoformans is responsible for almost 200,000 deaths each year, more than any other fungal pathogen. Cryptococcal infection is incredibly difficult to treat, sometimes requiring lifelong therapy, and the best medical treatment cannot avoid a mortality rate as high as 30%. My primary research interest is to understand how cells from the innate immune system recognize and kill this pathogenic yeast. My focus is the recently discovered immune functions of mitochondria. By understanding what constitutes an effective fungicidal response, and why this effective response sometimes fails, we will be able to find better solutions to treat this killer disease.

Dr Rhys Farrer
Lecturer in Bioinformatics
(Starting in October 2018)

Biography
Rhys Farrer studied Cellular Biology (BSc), and Bioinformatics (MSc) at the University of East Anglia between 2004 and 2008. He received his PhD in Clinical Medicine from Imperial College London in 2012. Between 2013 and 2017, he worked at the Broad Institute of MIT and Harvard as a Wellcome Trust Postdoctoral Fellow. He was appointed as Lecturer in Bioinformatics and will join the Centre in late 2018.

Research Interests
Rhys’s research uses high-throughput/next generation sequencing technologies to study the patterns of genomic, transcriptomic, and gene-regulatory variation between and within populations of microbial pathogens. His current projects include studying the evolution of virulence in the human pathogen, Cryptococcus gattii. Characterising genomic and epigenomic variation in pathogens can provide insights into their virulence mechanisms, and ultimately assist in their mitigation.
MRes/PhD Students in Medical Mycology and Fungal Immunology 2016-2017

Christina Nikolakopoulou (University of Aberdeen)  Zoe Ross (University of Aberdeen)

MRes Projects 2016
Project 1: Do reactive oxygen species influence genome plasticity in the fungal pathogen Cryptococcus neoformans?
Supervisors: Dr Liz Ballou (Professor Adilia Warris)

Project 2: Interaction of CGD murine bone marrow-derived macrophages with A. fumigatus and A. nidulans
Supervisors: Professor Adilia Warris (Dr Jill King)

PhD Project 2017
Characterization of the fungal ligands and physiological functions of MelLec in immunity
Supervisors: Professor Gordon Brown (Dr Janet Willment, Professor Nancy Keller)

Zoe Ross

MRes Projects 2016
Project 1: Is Candida auris a sexual species?
Supervisors: Dr Alexander Lorenz (Professor Neil Gow, Dr Donna MacCallum)

Project 2: The role of macrophage PTP1B in susceptibility to fungal infection
Supervisors: Dr Heather Wilson (Professor Gordon Brown, Dr Janet Willment, Professor Mirela Delibegovic)

PhD Project 2017
Genetic diversity as a major driver of phenotypic variability and virulence in local outbreak strains of the emerging pathogen Candida auris
Supervisors: Dr Alexander Lorenz (Professor Neil Gow, Dr Elizabeth Johnson)
MRes/PhD Students in Medical Mycology and Fungal Immunology 2017-2018

Alexander Currie (University of Aberdeen)

MRes Projects 2017
Project 1: Platelet interactions with Candida species during fungal septicemia
Supervisors: Dr Nikki Mutch (Professors Neil Gow, Adilia Warris, Dr Duncan Wilson)

Project 2: Regulation of fungal phagocytosis by GPCR activation – a potential therapeutic
Supervisors: Dr James Hislop (Dr Donna MacCallum, Dr Dawn Thompson)

PhD Project 2018
Preventing Aspergillus-induced inflammation in cystic fibrosis to reduce airway disease
Supervisors: Professor Adilia Warris (Dr Darius Armstrong-James, Dr Neil Vargesson)

Emily Speakman (University of Aberdeen)

MRes Projects 2017
Project 1: Novel C-type lectin receptors in dendritic cells and their role in Candida infection
Supervisors: Dr Fabian Salazar (Professor Gordon Brown)

Project 2: Impact of adaptive prediction in a major fungal pathogen
Supervisors: Dr Duncan Wilson (Professor Al Brown)

PhD Project 2018
Dendritic cell lectin-like receptors and their role in antifungal adaptive immunity
Supervisors: Professor Gordon Brown (Professor Fiona Powrie)

New MRes/PhD Students in Medical Mycology and Fungal Immunology starting September 2018

Mark Peacock, University of Glasgow, UK
Chloe Pelletier, University of Aberdeen, UK
Dr Tyng Tan, Clinical Immunology Specialist ST4 Trainee, Salford Royal NHS Foundation Trust, UK
Theresa Wacker, George-August University, Göttingen, Germany
MRes Students in Medical Mycology for Clinicians 2017-2018

MRes Projects for Academic Clinical Fellows

**Dr Joanne Calley**
Speciality Registrar (ST3) in Paediatrics & Academic Core Trainee, NHS Grampian, Royal Aberdeen Children’s Hospital.

An investigation into the in-host genetic microevolution of *Aspergillus fumigatus*
Supervisors: Professor Adilia Warris (Professor Al Brown)

**Dr Catherine Mark**
Specialist Registrar (ST5), NHS Northern Health and Social Care Trust, Northern Ireland

Investigating *Candida auris* and *Exophiala dermatitidis* host interactions and drug resistance mechanisms in an ex-vivo human skin model
Supervisors: Professor Carol Munro (Dr Donna MacCallum, Dr Dora Corzo Leon)

New MRes Student in Medical Mycology for Clinicians starting September 2018

**Dr Leonard Farrigua**
ACCS-AM trainee CT3 in the Acute Medicine stem North West Anglia NHS Trust.

Workshop on Clinical and Diagnostic Medical Mycology

An important component of the 1-year MRes in Medical Mycology course (for both the basic science students and Clinical Fellows), is the 2-day workshop on Clinical and Diagnostic Medical Mycology hosted by Dr Elizabeth Johnson and her team at the Mycology Reference Laboratory, Public Health England, Bristol.
8 Week Summer Scholarship Medical Students

2016

Roberta Garau
Characterisation of the role of protein kinases in mediating resistance to reactive oxygen species in the fungal pathogen Aspergillus nidulans.

Laboratory visited: Professor Gustavo Goldman, University of São Paulo, Brazil

Elliot Gemmell
C-type lectins in anti-fungal Immunity - Aspergillus fumigatus

Laboratory visited: Professor Bruce Klein, University of Wisconsin-Madison, USA

2017

Calum Barnetson
Calcineurin pathway regulation of hyphal growth - developing a novel fungal-specific antifungal through understanding the exact mechanisms of invasive pathogenesis and weak areas to target.

Laboratory visited: Professor William Steinbach, Duke University, North Carolina, USA

Anastasiya Kret
The role of the Candidalysin-coding gene ECE1 during interaction of C. albicans with bacteria and the host.

Laboratory visited: Professor Bernhard Hube, Hans Knoll Institute, Jena, Germany

2018

Yagna Bhattacharya
Characterise the associated changes in cell wall composition that occur in isolates from chronically infected patients and how these correlate with fungal genotype and disease severity.

Laboratory visited: Dr Darius Armstrong-James, Imperial College London, UK

Dylan McClurg
Disarming the macrophage: arginases and Cryptococcus

Laboratory visited: Professor Arturo Casadevall, Johns Hopkins University, Baltimore, USA
The major burden of serious invasive fungal infection is borne by low and middle income countries, particularly in sub-Saharan Africa, where around 50% of people diagnosed with invasive fungal infections die as a result of the infection.

To address this issue, the Universities of Aberdeen and Cape Town (UCT) have joined forces to create the world’s first international research centre for tackling fungal infections; the AFGrlica Unit, which opened in Cape Town in August 2017. The University of Aberdeen AFGrlica Unit, directed by Professor Gordon Brown, is based at UCT’s Institute of Infectious Disease and Molecular Medicine, headed by Professor Valerie Mizrahi, and will give our experts a centre of operations in Africa where they can work in collaboration with UCT experts to establish research programmes that can target the priority areas in fungal diseases that are relevant to the African.

Researchers

Dr J. Claire Hoving
Wellcome Trust Intermediate Fellow and Lecturer in the Division of Immunology, University of Cape Town.

Biography
Claire completed a BSc in the Netherlands and a PhD in Immunology and Infectious Disease at the University of Cape Town. She has recently established a research group in Fungal Immunology at UCT. She is a member of the AFGrlica Unit, a contributing investigator of the Wellcome Centre for Infectious Diseases Research in Africa and an Associate Member of the Institute of Infectious Disease and Molecular Medicine, Cape Town. Claire is funded by a Wellcome Trust Intermediate Fellowship in Public Health and Tropical Medicine, the Medical Research Council and National Research Foundation of South Africa and the Carnegie Corporation.

Research interests
Claire’s research aims at understanding host immune responses to HIV-related fungal infections. *Pneumocystis jirovecii* is an opportunistic fungal pathogen of immunocompromised patients and is a common cause of pneumonia and death in patients with HIV/AIDS. Claire’s group investigates the immune response to *Pneumocystis* and other fungal infections prevalent on the African continent and the role other organisms, such as *Mycobacterium tuberculosis* play in infection.
Dr Liliane Mukaremera
Lecturer in the Division of Medical Microbiology, Department of Pathology, University of Cape Town.

Biography
Liliane completed a BSc in Biology at the National University of Rwanda. After working for 1 year as a teaching assistant at the National University of Rwanda, she obtained a scholarship to study for a Master’s in Medical Molecular Microbiology at the University of Aberdeen (UK). She continued her studies and obtained a PhD in Medical Sciences at the University of Aberdeen. She is currently completing a postdoctoral research programme at the University of Minnesota in the USA where she is studying morphological factors that influence the immune response to the human fungal pathogen Cryptococcus neoformans. Liliane was appointed as a Lecturer in the AFGrica Unit in 2018.

Research interests
Born and raised in Rwanda, Liliane experienced first-hand problems related to poverty and infectious diseases. For that reason, Liliane’s career goal is to perform infectious disease-related research in Africa. Sub-Saharan Africa has many critical infectious diseases, high endemic rates of HIV (and HIV-associated diseases), and fungal diseases such as cryptoccoccosis kill nearly as many people as tuberculosis. Liliane’s research interests focus on understanding factors that affect the interaction between fungal pathogens and their hosts, particularly how fungi develop various cell morphologies to evade the host immune system. Liliane’s goal is to establish a translational research programme performing impactful science aimed at improving human health in Sub-Saharan Africa.
Scope of MRC CMM Interactions

UK universities and institutes
Aberdeen, Birmingham, Bristol, Bath, Cardiff, Dundee, Exeter, Glasgow, Kent, Liverpool, Manchester, Newcastle, Oxford and Sheffield, Imperial College London, King’s College London, St George’s University of London, University College London and the Crick Institute.
Dr Elizabeth Ballou  
Lecturer, University of Birmingham, UK  

Biography  
Liz Ballou is a cell biologist and fungal geneticist researching how human fungal pathogens survive and cause disease in the host. Her lab addresses the basic biological processes that allow proliferation and pathogenesis of the fungus Cryptococcus neoformans, which causes meningitis and affects 1 million people worldwide. Liz moved to the University of Birmingham in 2017.

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www.birmingham.ac.uk/staff/profiles/biosciences/ballou-elizabeth.aspx

Dr Megan Lenardon  
Senior Lecturer, University of New South Wales, Australia  

Biography  
Megan Lenardon researches fungal cell wall structure and biosynthesis in the human opportunistic pathogen, Candida albicans, focusing on the regulation of the chitin synthesis. Chitin is found in the cell wall of almost all pathogenic fungi, but not in humans, and so it represents an attractive target for antifungal drugs. There is an urgent clinical need for the development of diagnostics and new therapeutics for fungal diseases which research in Megan’s group aims to address in innovative ways. Megan took up her post at the University of New South Wales in 2017.

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www.babs.unsw.edu.au/staff_academic/dr-megan-lenardon

Professor Lars Erwig  
Senior Director, Discovery Medicine, GlaxoSmithKline, Stevenage, UK  

Biography  
Lars Erwig is honorary Professor of Nephrology at the University of Aberdeen and an experienced Consultant Nephrologist and General Internal Medicine Physician. He investigated the interactions of the innate immune system with fungal pathogens and has conducted the most comprehensive analysis of fungal-macrophage interactions to date using sophisticated 3D live cell imaging. Lars now works at GlaxoSmithKline in early drug development.

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Structure and Management

The Director, Professor Gordon Brown has responsibility for the strategic direction and development of the MRC CMM, in consultation with the International Scientific Advisory Board, Management Board and other centre principal investigators. The Director is supported by three Deputy Directors (Professor Neil Gow [Honorary, research], Professor Alistair Brown [training and technology development] and Professor Adilia Warris [clinical]), plus a Centre Manager (Dr Karen McArdle).
**Management Board (MB)**
The MB meets three times per annum to advise on scientific direction, strategy and training and monitor progress. The MB oversees the research and training programmes, allocation of funding, allocation of students and fellows to cross-disciplinary projects as well as the commercialisation, translation and outreach activities.

**International Scientific Advisory Board (ISAB)**
The ISAB is comprised of national and international experts in medical mycology, including an MRC representative. The ISAB provides the MB with objective, independent advice on our development, scientific strategy and research, training and translational activities. The ISAB receives minutes of all MB meetings, evaluates annual reports and undertakes formal Centre reviews (Years 2 and 4).

**ISAB members**

**Professor Geraldine Butler (Chair)**
University College Dublin

**Professor Judy Berman**
Tel Aviv University

**Professor Axel Brakhage**
Hans Knöll Institute

**Professor Arturo Casadevall**
Johns Hopkins

**Professor Tom Harrison (MRC representative)**
St George’s University London

**Professor Joseph Heitman**
Duke University

**Professor David Laloo**
Liverpool School of Tropical Medicine

**Dr John Rex (ad-hoc)**
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Notes