

**Meeting Report**  
**MRC strategic review of fungal disease research in the UK**

**20<sup>th</sup> January 2014**

**1. Background**

Fungal diseases are a worldwide problem ranging from superficial infections easy to cure to more invasive life threatening infections that are much harder to diagnose and treat. Recent estimates suggest that invasive fungal infections cause at least as many deaths as malaria and tuberculosis<sup>1</sup>. The burden of fungal disease continues to increase as the number of people with weakened immune system increases (cancer, transplantation and HIV/AIDS patients as well as elderly). In addition to affecting humans and animals, fungi have established themselves as plant pathogens with major threat to agriculture.

There are only limited numbers of available drugs against invasive fungi infecting humans with modest success in reducing high mortality rates. This is due to the lack of early diagnosis of the pathogen as well as the broad spectrum specificity of the drugs, their toxicity and side effects. Flucytosine treatment for serious candida or cryptococcal infections has proved effective and affordable but it is not well used by clinicians, again, due to the lack of good diagnostics. Though rare, antifungal drug resistance is becoming a cause of concern in the treatment of fungal infections. Screening in hospitals and effective disinfection strategies can help in reducing the incidence of fungal infection and thereby reduce morbidity and mortality related to invasive fungal infections.

Despite the need for effective anti-fungal drugs, vaccines and diagnostics, the Medical Research Council's (MRC) mycology research portfolio is relatively small compared with bacterial, viral and parasitic disease (Figure 1). This appears to be a reflection of the limited number of applications made in this area rather than a low success rate (Figure 2). In fact, less than 1% of grant applications to the MRC between 2007 and 2012 involved fungal research. The figures for other funding bodies are similar.

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<sup>1</sup> Brown et.al 2012 – Human fungal infections: the hidden killers. Science Translational Medicine 4, 165rv13

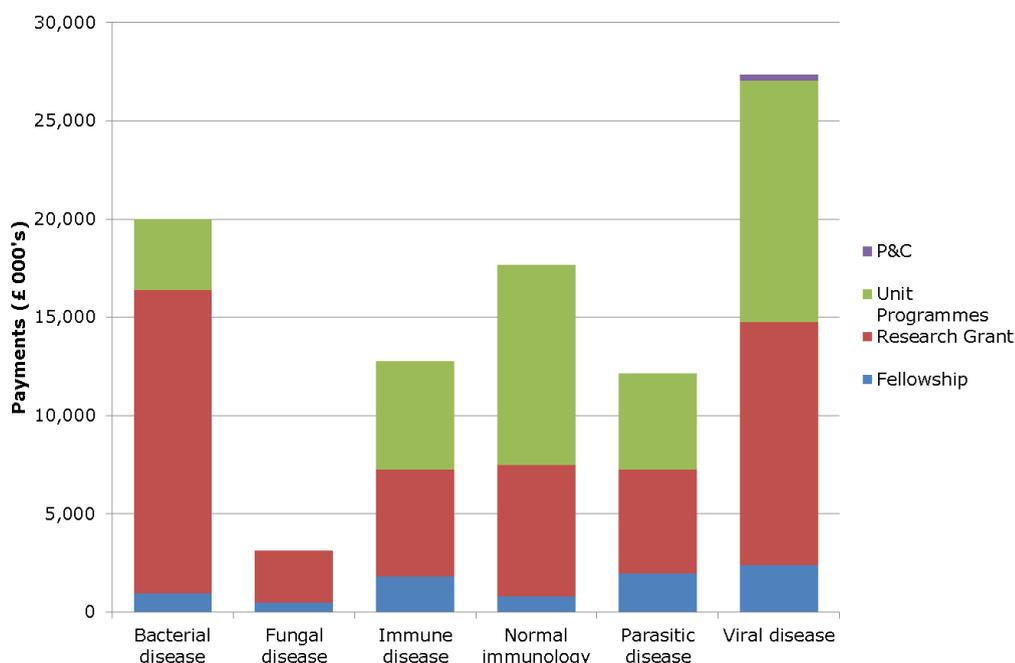


Figure 1: Infection and Immunity portfolio by Board Science and Funding type 2012/13.

Decision Year	Number applied	Awarded	Rejected	Success rate
2008/2009	9	1	8	11%
2009/2010	16	2	14	13%
2010/2011	8	2	6	25%
2011/2012	9	6	3	67%
2012/2013	6	2	4	33%
<b>Grand Total</b>	<b>48</b>	<b>13</b>	<b>35</b>	<b>27%</b>

Figure 2: MRC fungal research success rate since 2008. On average the success rate was 27% above the average MRC success rate of 20%.

To start to identify gaps and opportunities and how to address the challenges highlighted above, the MRC organised, a one day workshop to discuss fungal disease research. The workshop was chaired by Professor David Lalloo and brought together fungal disease researchers from the UK and overseas to discuss the key challenges and to encourage expansion and strengthening of fungal disease research in the UK (Annex 1).

## 2. Format of the day

Forty five participants took (Annex 2) part in the meeting from academia, pharma and the biotech industry with representatives from the UK Funders (BBSRC, NERC, MRC and the Wellcome Trust). The meeting aimed specifically at

- Examining the reasons why fungal infection research is relatively under-represented in the UK when compared with other disease areas;
- Identifying which research challenges can be effectively addressed by UK academic

researchers;

- Encouraging more scientists to take an interest in the field and become fungal research leaders of the future;
- Highlighting the various funding opportunities available through the MRC and other funders;
- Gathering opinions amongst the research community and feed these into the MRC's strategy and
- Encouraging interdisciplinary approaches to tackling fungal disease problems

The workshop was informed by keynote presentations from Prof Joe Heitman (Duke University), Prof Neil Gow (University of Aberdeen), Dr Elaine Bignell (University of Manchester, formerly Imperial College London) and Prof David Denning (University of Manchester). There were also presentations from representatives of the Wellcome Trust, BBSRC, NERC and MRC highlighting the fungal research they support. There were also a number of breakout sessions to discuss how best to expand the UK fungal disease research base, how to promote interdisciplinary research and capacity building and how best to translate basic research to benefit global health. Presentations from key scientists and funders aimed at generating informative discussions at the break-out sessions.

### **Keynote presentations**

Professor Joseph Heitman from Duke University Medical Centre, USA, provided an international perspective to fungal diseases research with a focus on the USA portfolio. Prof Heitman emphasised the need to conduct studies that will increase our understanding of the pathogen from basic to clinical research. More work was needed to develop new and better treatments as well as new preventatives such as vaccines. Better monitoring was important to identify the pathogen and global effort to combat fungal diseases is needed. He highlighted the opportunities offered by big data, citing the role of the Sanger Centre and EMBL in mycology research. He also suggested that there needs to be greater cross talk between the human and plant mycology community and opportunities for both communities to fund joint activities.

Professor Neil Gow summarised the UK experience and the future of fungal diseases research including unmet need for the next 5-10 years. He stressed that the fungal research community in the UK was small and mainly centred around Aberdeen, Manchester and London. There was a need to stimulate and encourage new researchers to work in fungal research to increase capacity in this area. As an example, he cited how some disciplines had benefitted from strong overarching bodies or charities such as Arthritis Research UK in developing the research community – how could this happen for fungal disease?

The capacity building message was echoed by Dr Elaine Bignell. She drew upon her personal experience of progressing into an independent investigator in this field, highlighting opportunities and challenges that young researchers face in fungal disease research. She highlighted the

importance of networking to build skills, access to samples, techniques and technologies and getting support for international meetings. She also emphasised, that the mycology community, although small, was well connected and a mentorship programme could easily be developed to help researchers in the early stages of their careers.

Professor David Denning covered the area of new therapeutics and translating academic research in fungal diseases. He described the current state of engagement with industry, the successes and challenges of anti-fungal drugs and how best industry and academia could work together. Prof Denning presented some of the limitations of the current fungal treatments and the need for more sensitive diagnostics. There are existing links with the pharma sector but these need to be better developed to ensure translation of research for patient benefit. These links should also extend beyond small molecule development into diagnostics and vaccine strategies.

Representatives from the MRC, BBSRC, NERC and the Wellcome Trust presented the various funding opportunities available to researchers working in fungal research.

### **Breakout sessions**

Breakout sessions provided opportunities for attendees to discuss the different issues faced by the fungal disease community. A rapporteur from each session summarised outcomes from discussion groups and presented them to all attendees.

Breakout session 1: Expanding/strengthening the UK research base

Participants discussed the current status of the UK fungal disease research community, the funding opportunities, and what the community needs in the next 5-10 years.

Breakout session 2: Promoting interdisciplinary research & capacity building

Participants addressed how best to encourage research in this area and identified skill gaps. Discussions considered the need to link with other disciplines/partners in their research.

Breakout session 3: translating basic research for global benefit

This session covered the shortfall in effective treatments and diagnostics and how best to boost development of the therapeutics and preventatives. Discussions were around how industry and academia would work together for better patient outcomes.

Through these presentations and breakouts, the participants highlighted a number of emerging challenges in fungal research and how, as a community, they can address them.

### **3. Emerging challenges**

- Lack of capacity in the field

The fungal research community within the UK is relatively small and centred around Aberdeen,

Manchester, London and Exeter (a centre for both human and plant fungal research). The research community is highly collaborative but in general seemed unable to attract larger capacity into this area of work due to the number of basic and medical mycologists diminishing. Discussions at the workshop highlighted the low profile of fungal research on the UK National Curriculum, within Universities and the lack of teaching of medical mycology at medical schools. Despite some very strong research groups working in fungal disease, targeted postgraduate training opportunities in molecular mycology at the Master and doctoral levels were needed. Similar issues were identified in the USA<sup>2</sup> where researchers identified a "training crisis" because of the lack of adequate training programmes, courses and seminars at all levels. It was not clear why so few infectious disease researchers chose a career in mycology – instead choosing virology or bacteriology.

Skills gaps identified at the workshop include clinical mycology as well as system biology, epidemiology, biostatistics, bioinformatics and the fungal biome. As well as addressing these gaps, there needs to be much stronger linkages between basic researchers, clinicians and industry.

- Research challenges:

The following research gaps were highlighted:

- 1) Basic understanding of the bugs and the host pathogen interaction: With over 600 different fungi reported to infect humans ranging from mild to fatal infections, it will be difficult to address the basic mechanisms of fungal infection within such a small community. However, there are some fundamental issues that are still unclear such as what drives the conversion of a non-pathogenic strain to become pathogenic? Given the broad range of fungal species, an opportunity for the community is to better understand the pathogen/host interactions from basic to clinical research. This would include developing a better understanding of disease pathology as well as linking with the UK immunology strengths.
- 2) There are few epidemiological studies looking at the occurrence of disease to provide better understanding of the modes of transmission of the pathogens.
- 3) Suitable diagnostics: Discussions at the meeting emphasized the need for robust, rapid, simple, and cheap diagnostics to allow the best practice in patient management. Most diagnostics still suffer from long assay times and poor specificity and/or sensitivity. These problems, combined with subtle clinical presentations, often result in missed or delayed diagnosis and compromised clinical care. Appropriate diagnostics would immediately affect mortality and reduce morbidity. Such diagnostics would be built on better understanding of the host/pathogen interaction but also the integration of engineering sciences with mycology.
- 4) New therapeutics and preventatives: currently available antifungal compounds have not been ideal due to issues with toxicity, cost, wide spectrum of activities (specificity) and an emerging issue of resistance. New methods of developing antifungal drugs that are safer

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<sup>2</sup> Steinbach et al (2003) Status of medical mycology education, *Med Mycol* **41**: 457-67

and more effective are needed as well as getting antifungal vaccines into clinical trials. The participants noted that there were few spin-outs looking at fungal research. This was probably a reflection of the small community but entrepreneurship should be better encouraged.

- 5) Monitoring and global surveillance: currently there is a very limited mycological surveillance conducted globally. The World Health Organization has no programme on fungal infection, and most public health agencies conduct little or no mycological surveillance. This is hampered by the lack of proper diagnostics. It is therefore important to look at established and emerging pathogens on a global level and study their transmission.

- Lack of knowledge of funding opportunities

Discussions at the meeting highlighted the lack of awareness of funding opportunities available to fungal disease researchers especially those related to translational research, linking with industry and international working. Translational schemes such as the MRC Developmental Pathway Funding Scheme (DPFS), the MRC Confidence in Concept (CiC) scheme and the WT Translation Award in Seeding Drug Discovery theme amongst other schemes were emphasized by the funders as opportunities to the fungal research community along with a number of global health schemes.

#### **4. Mechanisms to address some of the challenges**

- Profile raising:

Fungal research community needs to be mobilised at universities to raise the profile of fungal diseases and encourage research in this area to create momentum for the future. The community needs to increase outreach activities such as workshops, open days, talks to lay audience to highlight the burden of fungal diseases at a societal level. This could be done through the learned societies where fungal researchers could play a greater role through membership of governing boards etc.

- Developing capacity

The small size of the UK fungal research community was seen as a major obstacle to addressing the research challenges. There was very strong preclinical research in the UK but it was thinly spread and focussed on too few pathogens. The field needs to attract researchers at the early stages of their careers and a prospective review of the curriculum was needed with a stronger push for courses in fungal diseases to be taught to both clinical and non-clinical pre and post graduate students. There should also be greater use of project placements or summer school activities to stimulate interest before students have decided their final directions. . Indeed, Professor Heitman highlighted the example of a recent molecular mycology residential course for post graduate students and the interest it had stimulated within Duke. Ultimately, the goal should be to make fungal research as attractive a proposition to young investigators as virology and bacteriology.

In addition to attracting researchers into the field of mycology, discussions also identified the need to promote interdisciplinary research. There was a clear need to strengthen links between basic and clinical research in mycology, but also to bring together the human and plant fungal research communities. There also needs to be better integration of, for example, bioinformatics, epidemiological studies and biostatistical analysis with mycology. Funders will need to work with the research communities to identify opportunities to support interdisciplinary research in mycology either through existing funding mechanisms or through new investments and suggested that an MRC centre type activity would be a powerful tool to attract new recruits as well as fostering interdisciplinarity

- Sharing resources and networking

The fungal research community is small and collaborative, but sometimes too focused and isolated. It is essential for the community to expand its networks linking with other groups nationally and internationally. Sharing resources (such as mutant libraries, data generated, technologies), knowledge and personnel between centres working across human, animal and plant fungi would add real value to a strong research base. Strong links with the relevant learned societies, charities and industry will be required.

## **5. Recommendations**

Fungal research community needs to:

- Raise its profile in the UK primarily within universities to increase capacity in the field of mycology and attract the skills needed to bridge the gap between basic and clinical research in mycology
- Coordinate its activities through networking and sharing resources, technologies and knowledge with other research groups working across human, animal and plant fungal diseases
- Engage with stakeholders such as industry to identify opportunities to translate basic knowledge into products and therapeutics for the benefit of the patients; and local community to highlight the societal burden of fungal diseases
- Engage with Funders to identify opportunities to support research in mycology especially translational research and engagement with industry.

MRC will need to consider:

- How best to encourage submission of fungal research – through better communication with the community and targeted information on the MRC website (web text and highlight notices to encourage submission)
- How best to increase capacity building in this area of research – through existing fellowship and studentship schemes and/or centre of excellence.

## MRC strategic review of fungal disease research in the UK

Monday 20<sup>th</sup> January 2014

### Agenda

- 9:45 Registration and coffee
- 10:00 Introduction from Professor David Lalloo, LSTM (Chair)
- 10:10 Keynote speaker 1 – Professor Joseph Heitman, Duke University Medical Centre, USA
- 10:40 Professor Neil Gow, the University of Aberdeen, UK
- 11:10 Fungal Research – Funders’ perspective (MRC, BBSRC, NERC and WT) with Q&A session – (with coffee and tea)
- 11:45 Dr Elaine Bignell, University of Manchester, UK
- 12:05 Breakout session 1  
Expanding/strengthening the UK research base
- *What is the UK research base in this field? i.e. which people/subjects*
  - *How coordinated is the UK research base?*
  - *Who is currently funding research?*
  - *What can we build on?*
  - *What are the barriers?*
  - *Where does the field need to be in 5-10 years?*
- Promoting interdisciplinary research & capacity building
- *How can we encourage research in this area that will create momentum for the future?*
  - *What are the skills gaps?*
  - *What central facilities are needed/used?*
  - *What other disciplines/partners do you need to work with?*
- 13:00 Networking Lunch
- 13:45 Feedback from Breakout session 1 discussions

- 14:15 Professor David Denning, University of Manchester, UK
- 14:45 Breakout session 2  
Translating basic research for global benefit
- *Current and emerging themes?*
  - *What are the big challenges?*
  - *Why is there a shortfall in effective treatments and diagnostics?*
  - *How do we boost development of drugs, vaccines & diagnostics?*
  - *How should industry and academia team-up to improve this?*
  - *What role can the UK play?*
- 15:40 Coffee and Tea
- 15:50 Feedback from Breakout session 2 discussions
- 16:15 Closing remarks and next steps - Professor David Lalloo

## Annex 2

### List of Attendees

Dr	Darius	Armstrong	Imperial College London
Dr	Ruth	Ashbee	University of Leeds
Professor	Rosemary	Barnes	University of Cardiff
Dr	Tihana	Bicanic	St George's London
Dr	Elaine	Bignell	University of Manchester
Dr	Michael	Birch	F2G Ltd
Dr	Alexandra	Brand	University of Aberdeen
Mr	Michael	Bromley	University of Manchester
Professor	Gordon	Brown	University of Aberdeen
Professor	Alistair	Brown	University of Aberdeen
Dr	Alessia	Buscaino	University of Kent
Dr	Michael	Chew	Wellcome Trust
Dr	Chris	Conlon	University of Oxford
Dr	Brian	Crook	Health and Safety Laboratory
Dr	Stephanie	Deizmann	University of Bath
Professor	David	Denning	University of Manchester
Professor	Matthew	Fisher	Imperial College London
Dr	Campbell	Gourlay	University of Kent
Professor	Neil	Gow	University of Aberdeen
Dr	Ivana	Gudelj	University of Exeter
Dr	Rebecca	Hall	University of Birmingham
Professor	Ken	Haynes	University of Exeter
Professor	Joseph	Heitman	Duke University
Professor	William	Hope	University of Liverpool
Dr	James	Horswill	Medical Research Council
Dr	Joe	Jarvis	London School of Hygiene and Tropical Medicine
Dr	Elizabeth	Johnson	Public Health England, Bristol
Dr	Simon	Johnston	University of Sheffield
Dr	Lizzie	Jones	Natural Environment Research Council
Dr	Maria	Kapi	MSD
Professor	Steven	Kelly	University of Swansea
Miss	Ruth	Kelly	Medical Research Council
Professor	David	Laloo	Liverpool School of Tropical Medicine
Dr	Megan	Lenardon	University of Aberdeen
Dr	Desa	Lilic	University of Newcastle
Dr	Donna	Maccallum,	University of Aberdeen

Professor	Robin	May	University of Birmingham
Dr	Robert	Miller	University College London
Professor	Fritz	Muhlschlegel	University of Kent
Dr	Carol	Munro	University of Aberdeen
Dr	Julian	Naglik	King's College London
Dr	Selinda	Orr	University of Cardiff
Professor	Garth	Papeport	Pulmocide and Imperial College (NHLI)
Dr	Catherine	Pashley	University of Leicester
Dr	Sarah	Plowman	Biotechnology and Biological Sciences Research Council
Dr	Janet	Quinn	University of Newcastle
Professor	Gordon	Ramage	University of Glasgow
Professor	Nick	Read	University of Manchester
Dr	Des	Walsh	Medical Research Council
Professor	Andrew	Wardlaw	University of Leicester
Dr	Ghada	Zoubiane	Medical Research Council