MRC Funding and Translational Research

Dr Catriona Crombie
The Medical Research Council is dedicated to improving human health through the best scientific research.

Its work, on behalf of the UK taxpayer, ranges from molecular level science to public health medicine and understanding of the human body in health and disease.
MRC mission

- Encourage and support high-quality research with the aim of improving human health
- Produce skilled researchers
- Advance and disseminate knowledge and technology to improve the quality of life and economic competitiveness in the UK [and worldwide]
- Promote dialogue with the public about medical research
Funding Categories

• “Response mode” grants (includes highlight notices)
  • Research grants (project, inc. New Investigator Research Grants)
  • Programme grants

• Strategic Initiatives and Calls for Proposals
  • Specific schemes for areas of identified strategic need

• Fellowships and studentships
MRC support at different career stages

**Educational Stage**
- Acquisition of knowledge, skills and competencies through systematic instruction

**Training Stage**
- Acquisition of knowledge, skills and competencies, technical and transferrable through original research

**Consolidation Stage**
- Consolidation of research skills and confirmation of medical research as personal career choice

**Exploration Stage**
- Exploration of personal capacity and aptitude for independence

**Progression Stage**
- Leading independent research plans and establishment of research team

**Independence Stage**
- Leadership and management of own programme, team and resource

**Leadership Stage**
- Setting strategic direction, leadership and management of multiple programmes, teams and resources

**MRC Units and Institutes**

**Studentships**

**Skills Development Fellowships**

**Post-docs on grants**

**New investigator grants**

**MRC intermediate Fellow: “Transition to Independence”**

**MRC Senior Fellow “Transition to Leadership”**

**Grant support**

**MRC support at different career stages**
- Studentships
- Skills Development Fellowships
- Post-docs on grants
- New investigator grants
- MRC intermediate Fellow: “Transition to Independence”
- MRC Senior Fellow “Transition to Leadership”
- Grant support
MRC Industrial Collaboration Applications (MICAs)

- If your team includes industrial collaborators, you will need to submit a MRC Industrial Collaboration Application (MICA) form and a completed Heads of Terms document.

- MICA proposals are assessed in parallel with other proposals and the quality of the proposal is of primary importance.

  - Questions that apply particularly to MICA proposals are:
    - Would MRC funding support work that would otherwise not be undertaken at the required quality level or timescale?
    - Is the project truly collaborative and intellectually led by the academic PI?
    - Is there long-term freedom to operate?
    - Are the IP distribution arrangements within the MICA rules?

http://www.mrc.ac.uk/Fundingopportunities/Grants/MICA/Specification/index.htm
Proximity to Discovery

- Model for discovery partnerships with Pharma and Biotech to promote, enable and facilitate pre-competitive collaboration:
  - Pre-competitive scientific excellence
  - Partnership for target discovery
  - Proximity to critical mass

- Our vision is for discovery teams, ranging from a small team to a large facility, to engage with MRC-funded, pre-competitive world-leading academic discovery environments.

- Aiming for a step-change in the quality of interaction between discovery academics and research leaders in Pharma and Biotech, and the wider Life Sciences sector, both in the UK and more widely.
MRC / Industry Asset Sharing 2015

- Researchers can use industry compounds in experimental medicine studies to understand disease mechanisms and explore treatment opportunities
- 68 compounds, with at least 21 CNS-penetrant, across 61 mechanisms of action

[Logos of participating companies]
MRC/AstraZeneca Centre for Lead Discovery

- Access to AstraZeneca’s 1.9m screening collection and technology platforms
- Use to discover probes and biologically-relevant small molecules
- MRC-funded scientists alongside AZ researchers, working on MRC selected projects
MRC/UCB Initiative offering access to UCB’s novel antibody discovery platform

- Using UCB’s innovative technology platform, MRC funded scientists will be able to efficiently sample the immune repertoire, potentially assessing over a billion antibody-producing B-cells.
- These antibodies will enable scientists to research the mechanisms of human disease, identify novel therapeutic opportunities, and may provide the initial starting points for new treatments.
MRC and translation

- The Aim: turning discoveries into clinical benefits, while maintaining the basic research that drives it
- MRC research expenditure
  - Discovery research ~75%
  - Translational and applied research ~25%
- Strong discovery science and talented, flexible researchers underpin everything
- Creative and reciprocal co-operation with industry
  - Partnerships to tackle complex fields
  - Public funding, project by project, to bridge the valley of death
- Partnerships with Universities, charities, RCs and Innovate UK
MRC’s Translational Research Funding

Translational Research Support

- BMC: Confidence in Concept
- Biomedical Catalyst: DPFS
- Biomedical Catalyst: RMRC
- BMC: Major Awards Committee
- Efficacy, Mechanism and Evaluation Programme
- Health Technology Assessment Programme

Innovate UK

- Basic research
- Prototype discovery & design
- Pre-clinical development
- Early clinical trials
- Late clinical trials
- Health Technology Assessment

MRC Lead

NIHR Lead

MRC/NIHR Methodology Research Programme

BBSRC & EPSRC

Medical Charities
Biomedical Catalyst (BMC)

• Four-year £240 million translational programme open to academia and SMEs jointly managed by the MRC and Innovate UK

• Aims to deliver growth to the UK life sciences sector through supporting the development of innovative products and services

• Industry-led applications are submitted via Innovate UK

• Three categories of grant: Feasibility, Early- and Late-stage
  • Confidence in Concept is the MRC equivalent of the Feasibility award.

• Academic-led applications for Early and Late-stage academic-led projects are made via the BMC: DPFS and BMC: RMRC schemes.
BMC: Developmental Pathway Funding Scheme

• Cornerstone of the MRC’s Translational Strategy: www.mrc.ac.uk/Fundingopportunities/Grants/DPFS

• £35m/year, deadlines 3 times/year

• Different to Research Grants
  • Goal oriented and funding is milestone-based
  • Allows MRC to provide a long-term commitment to inherently risky projects
  • Downstream reporting helps MRC develop a strong evidence base on outcomes
  • Investigators are required to submit
    • quarterly reports, to inform MRC of project progress,
    • milestone reports, to secure continued support
Major Awards Committee (MAC)

- Assesses commercially focused/driven awards submitted to the BMC:DPFS scheme

- MAC membership is composed of individuals from academia, industry and the investment community [as for the DPFS Panel].

- Commercial development and exploitation will be enabled through:
  - Increased exposure to the commercial sector and investor community
  - Tailored guidance and mentoring provided to applicants by the experts on the MAC.

- MAC assessment includes an interview stage.
BMC: DPFS application process

- Two step decision process
  - Outline application: DPFS Panel review
  - Full Application: Expert referee and Panel review
- Full stage applicants have six months in which to submit their application

Outline review (c.6 weeks)
DPFS Panel meeting outline decision
Panel meeting (DPFS/MAC) full decision

Applicant writes full application (c.8 weeks)
Full application review (c.8 weeks)

Elapsed time c.24 weeks
As of February 2015, 169 projects have been supported with a total commitment of more than £145m:

- 103 therapeutic interventions including
  - 34 small molecule
  - 20 protein/peptide
  - 14 gene therapies
  - 12 antibodies
  - 7 cell therapy
- 32 diagnostics
- 16 vaccines
- 10 medical devices
- 8 other
Pathway

DPFS project aim: to get the evidence needed to justify doing for phase 2?
What are the tasks needed to get to the aim?
What resources, particularly what team, is needed?

Find out what this is
e.g. talk to likely phase 2 players
Preparation of the proposal

- Key aims of the application:
  - What is the underpinning problem or need?
  - Where are you now?
  - What, specifically, will this project achieve?
  - What are the alternatives and why is this better?
  - What are the risks to the project and how will these be managed?
  - What is the long-term plan?
Preparation of the proposal

- **Tailor the proposal to the audience**
  - Your outline application will be reviewed by the Panel
  - Your full proposal will be peer reviewed by relevant experts
  - Final decisions are made collectively by the DPFS Panel, who have broader expertise
  - Your proposal must address an expert and a general scientific audience
Target Product Profile – Linking Need to Rationale

- What –
  - what you hope your product/solution will look like
  - the essential attributes of a clinically (and potentially commercially) successful product, which can form the basis of a development plan

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Desired</th>
<th>Acceptable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of Action</td>
<td>Multitarget</td>
<td>Unique target (but not uptake via P2-transporter only)</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Crani</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Effective against stage 1 and 2</td>
<td>Effective against stage 2</td>
</tr>
<tr>
<td></td>
<td>Broad Spectrum (gambionte and imidazole)</td>
<td></td>
</tr>
<tr>
<td>Efficacy &amp; product benefit</td>
<td>Clinical efficacy &gt; 95% at 18 months follow up</td>
<td>Clinical efficacy no worse than current treatments</td>
</tr>
<tr>
<td></td>
<td>Effective in meconoprol refractory patients</td>
<td></td>
</tr>
<tr>
<td>Safety &amp; tolerability</td>
<td>&lt;0.1% drug related mortality</td>
<td>1% drug related mortality</td>
</tr>
<tr>
<td></td>
<td>Safe during pregnancy and for lactating women</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No monitoring for AEs</td>
<td>Weekly simple lab testing (field testing)</td>
</tr>
<tr>
<td>Dosing / administration / regimen</td>
<td>Formulation adoped to adults and children</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 7 days p.o., once daily (DOT)</td>
<td>&lt; 20 days p.o. (DOT)</td>
</tr>
<tr>
<td></td>
<td>&lt; 7 days i.m., once daily</td>
<td>&lt; 20 days i.m.</td>
</tr>
<tr>
<td></td>
<td>&lt; 9 days i.v. if no toxicity</td>
<td></td>
</tr>
<tr>
<td>Delivery system / product presentation / market configuration</td>
<td>Stability in Zone 4 for &gt; 5 years</td>
<td>Stability in Zone 4 for &gt; 12 months</td>
</tr>
<tr>
<td>Pricing / cost of goods (COGs)</td>
<td>&lt; 30 € / course (only drug cost)</td>
<td>&lt; 100 € / course</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 200 € / course ok if very good on other criteria</td>
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</tbody>
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At the early stages in the development process the TPP is a bit of a wish list but, over time, it will come to define the product.
Milestones

• Milestones are a key feature of DPFS proposals and allow MRC to mitigate risk.

• Milestones are often put at the end of a stage to mark the completion of a work package or phase:
  • Can be part of a risk mitigation strategy before the end of a phase to allow for corrective actions.

• Not a list of tasks:
  • Must be quantifiable/objective tests.

• Should be key markers of the critical path to your aim.

• Failing to achieve a milestone indicates that you are unlikely to get the evidence you need for the pathway to your ultimate ideal goal.
## Milestone Examples

<table>
<thead>
<tr>
<th>POOR</th>
<th>GOOD</th>
<th>Specific</th>
<th>Measurable</th>
<th>Achievable</th>
<th>Relevant</th>
<th>Timely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establish fit for purpose primary screening assay</td>
<td>Primary screening assay established with transient transfection in 384 well format with $Z' &gt; 0.7$ (acceptable 96 well assay, $Z' &gt; 0.5$) at month 6</td>
<td></td>
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<tr>
<td>Evaluate hits from HTS</td>
<td>Re-evaluate hits in single shot and full EC50 mode in primary assay. Re-confirmed hits ranked according to EC50 and chemical characteristics (see target product profile for measurables). Completed at month 12</td>
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</table>
What do the Panel want?

- Clearly defined, well written **applied** project
  - Don’t be repetitious
- Strong scientific rationale
  - Convincing preliminary data
- Meets a medical need
- Competitive
- Well structured project plan that will yield suitable evidence for onward decisions
  - Don’t slip in some basic scientific investigations
  - Work on critical path items and work in a logical order
- Feasible
  - Clear risk/benefit
  - Can be high risk as milestones in place
Competitive situation

- Don’t take a narrow view
  - What is the true ‘market’ competition?
  - Consider other competing approaches - not just your specific approach
  - What’s already on the market?
  - What’s already in development
    - Use Google, Patent databases, Clinical trials databases
- Use your Institution’s patent/tech transfer expertise
- “We have freedom to operate”
  - Recognize difference between freedom to operate for fundamental research and DPFS project
- Consider IP and FTO now
- What are the possible barriers if your project is successful?
Common failure modes

Project team is weak in some key area

Pilot data not convincing or not relevant to final aim

DPFS Grant

Evidence needed for phase 2

Plan not likely to yield the required evidence

Phase 2

Phase 2

Ultimate ideal goal

Proposed solution has a problem

Pilot data
Details of all funding schemes can be found on the website

http://www.mrc.ac.uk/funding
Contact Details

- If you have any questions:

Dr Catriona Crombie
Phone: 0207 395 2220
Email: catriona.crombie@headoffice.mrc.ac.uk

DPFS&DCS@headoffice.mrc.ac.uk