



Contracts  
and advice

IP protection  
and management

Development  
funding

Drugs, devices,  
diagnostics

Partnering  
with industry

Consortia  
building

Showcasing  
translation of  
Medical Research  
Council science

2016

This publication highlights some of the recent successes in translating the work of scientists in Medical Research Council units and institutes. It demonstrates the breadth of technologies at different stages of development. Each of these projects aims to bring new products to market, provide real improvements to human health or further scientific research.

The MRC has a rich history of impactful translational research, from antibody humanisation in the 1980s, to the development and commercialisation of innovative new platform technologies in more recent years (Heptares Therapeutics Limited and Bicycle Therapeutics Limited).

Bridging the gap between academic research and tangible societal benefit is often a complex challenge. MRC science needs to be effectively translated into powerful new therapies, diagnostics, devices, and research tools. Key to achieving this is to identify intellectual property (IP) generated that has potential commercial value, protect it through patents or other appropriate means, and ensure that it is effectively commercialised.

MRC scientists are supported by MRC Technology in these vital areas:

- Contracts and advice
- Development funding
- IP protection and management
- Drugs, devices, diagnostics
- Partnering with industry
- Consortia building

### Contracts and advice

Contracts are vital in defining the relationship between collaborating organisations, protecting materials and intellectual property (IP) and ensuring effective commercialisation of IP. MRC Technology can assist and advise MRC scientists on contractual matters and agreements relating to technology development and commercialisation such as confidentiality agreements, material transfer agreements, collaboration agreements, licence agreements and spin-out related agreements.

### Drugs, devices, diagnostics

MRC science leads to a broad range of novel medical and scientific solutions. These range from medical questionnaires to diagnostics, drugs and drug delivery technologies. MRC Technology aids this development through IP protection, helping to secure suitable funding and assisting in finding and securing vital collaborators and partner organisations.

### Development funding

Promising research often requires further funding to progress towards commercial and/or therapeutic application. The Development Gap Fund (DGF) is a pre-seed translational fund available to MRC scientists to conduct translational research. Typical projects might include proof of concept studies, target validation components of drug discovery, assay development and device/diagnostic prototyping.

In addition, MRC scientists can collaborate, on a revenue sharing basis, with MRC Technology's Centre for Therapeutics Discovery (CTD) and Centre for Diagnostics Development (CDD), providing access to antibody humanisation, small molecule drug and diagnostic development and validation.

### Partnering with industry

Intellectual property that has been appropriately protected can be licensed to an industry partner with the right expertise and resources to develop it further, advancing the science and benefiting patients by bringing products to the market.

### IP protection and management

The MRC protects intellectual property (IP) created from the research efforts of its scientists using patents, copyrights, designs and trademarks. This IP can then be further developed, sometimes using development funding, and/or can be commercialised. Some technologies can be commercialised without IP protection, for example, cell lines and research reagents. MRC Technology can advise on all aspects of IP protection and is responsible for IP protection and management on behalf of the MRC.

### Consortia building

Promising research can often require expertise in multiple disciplines to progress towards commercial applications. MRC Technology can assist with finding consultants/collaborators and build consortia through its network of contacts within industry and academia.

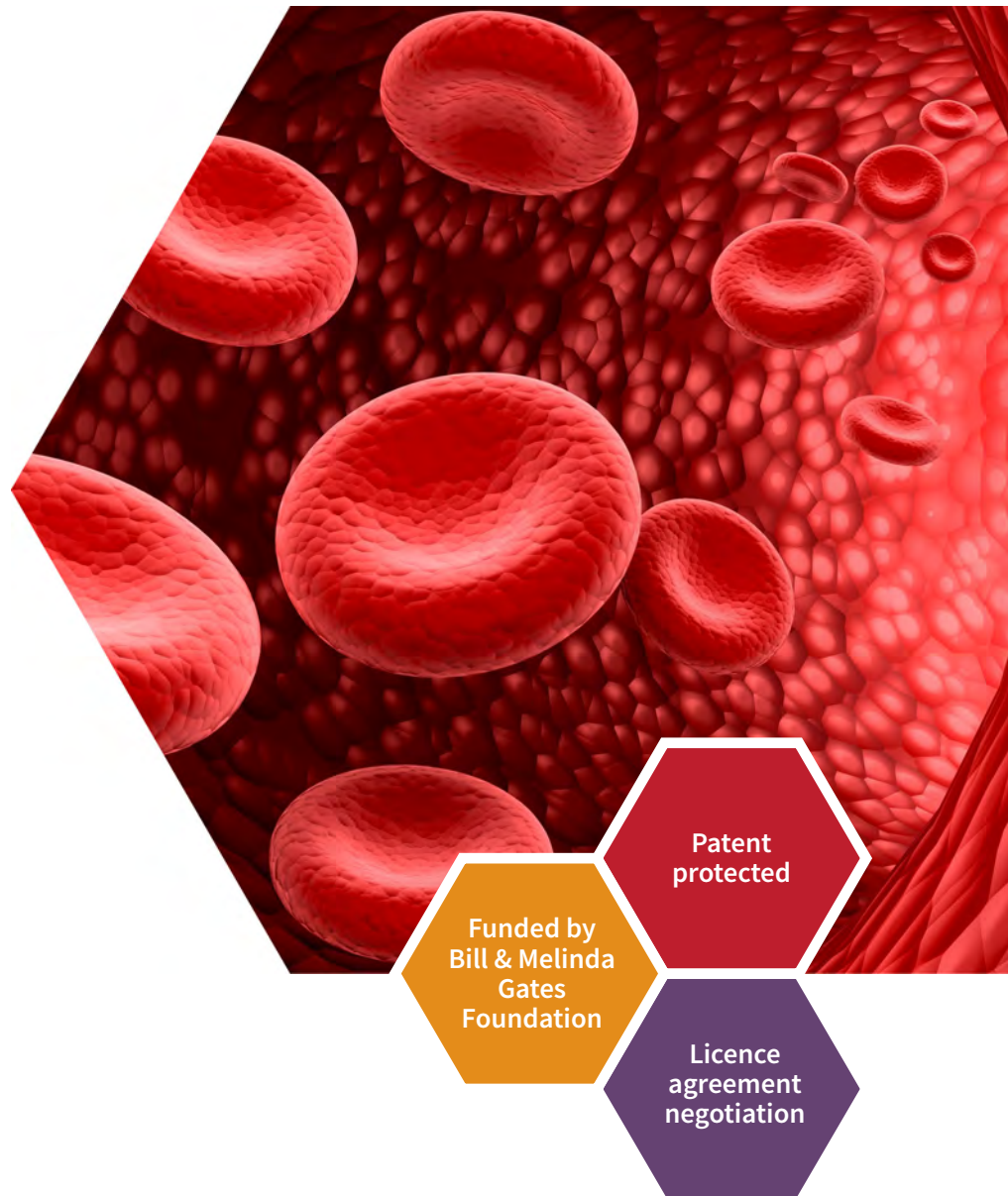
# IHAT – a novel oral iron supplement

## Elsie Widdowson Laboratory (EWL)

Dr Jonathan Powell

Iron deficiency is the most common nutritional deficiency in the world. Children, pre-menopausal women and people with an iron-poor diet which may include the elderly, those in the developing world or even those who lead busy lifestyles are most susceptible to iron deficiency and associated iron deficiency anaemia (IDA). Iron deficiency and IDA is estimated to affect 1 billion people worldwide and is one of the top-10 risk factors contributing to the global burden of disease (WHO's top 10 list for disease cure and prevention).

Current supplements for iron deficiency include ferric compounds which are mostly very poorly absorbed and/or too expensive to reach the majority of people who need them or ferrous compounds which are associated with well recognised toxicity issues that lead to gastrointestinal side effects, poor compliance and additional healthcare costs. Dr Jonathan Powell and his team have developed "IHAT" which is a novel synthetic iron hydroxide adipate tartrate complex that is based on the chemistry of natural, digested dietary iron. Due to its low cost



of manufacture, near equivalent bioavailability to ferrous salts and increased safety profile, IHAT is a commercially viable alternative to ferrous salts for iron supplementation.

IHAT was awarded the Top Emerging Technologies Prize from the Royal Society of Chemistry in 2014 and more recently awarded funding from the Bill & Melinda Gates Foundation to fund a Phase II clinical trial in The Gambia to demonstrate that IHAT safely corrects IDA in children (6-36 months old) in poorly resourced areas. The clinical trial started in late 2016 and is led by Dr Dora Pereira at the University of Cambridge (ex MRC HNR) who, with Dr Nuno Faria (MRC EWL)

and Dr Sylvaine Bruggraber (ex MRC HNR), contributed to the invention of IHAT led by Dr Powell.

The methods of synthesising IHAT are protected by two patent families and MRC Technology is currently negotiating a licence agreement with a company focused on developing and marketing IHAT as a nutritional supplement and onwards as a therapeutic, such that all patients in all different countries may get access to cheap, effective and safe iron supplementation.

# Developing STRIPES\* as a novel psychophysical test for improving speech perception of Cochlear Implant users

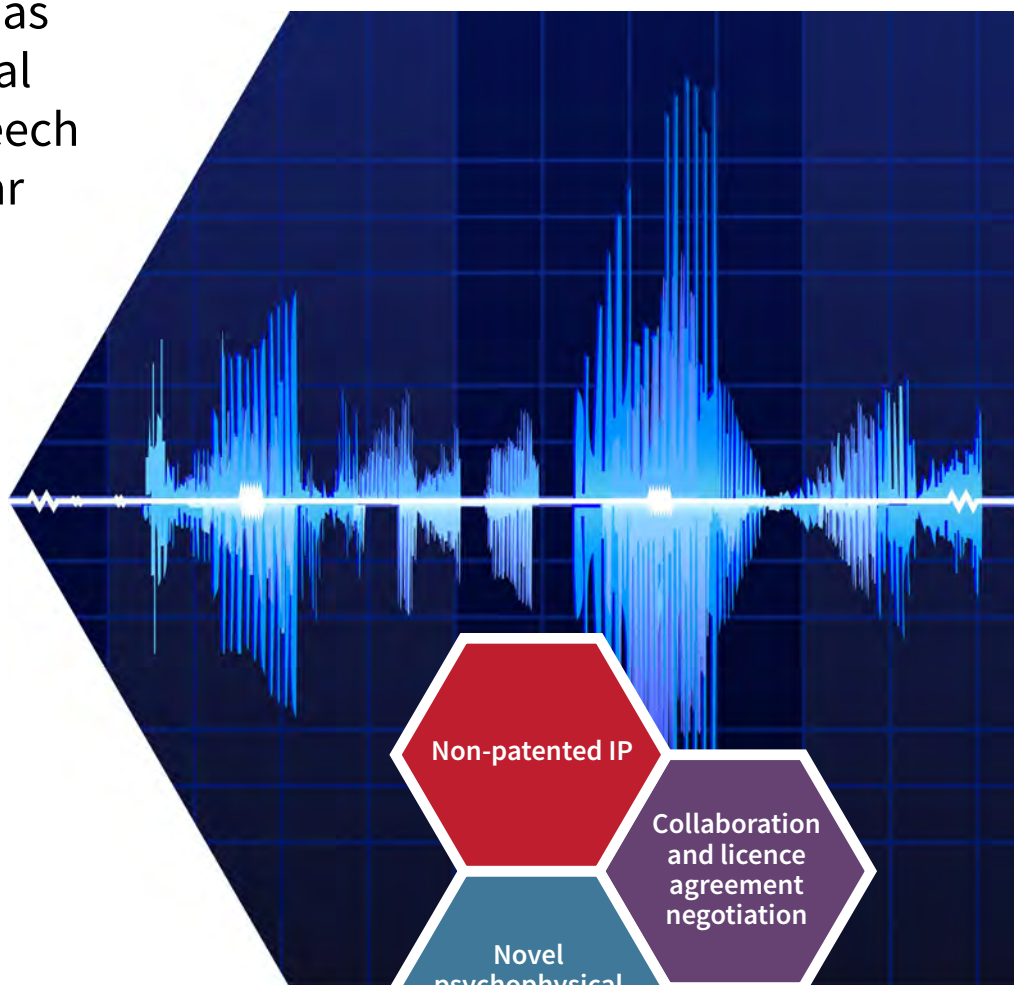
## Cognition & Brain Sciences Unit (CBSU)

Dr Bob Carlyon

Cochlear Implants (CIs) have more than 500,000 users worldwide and about 12,000 in the UK. Although they allow many deaf people to understand speech sufficiently well in quiet environments, they do not help patients perceive speech in noisy situations and offer limited benefit to a substantial minority of patients even in quiet surroundings. In light of this, research efforts have focused on improving speech perception by fine tuning the CIs based on patients' responses when performing a speech test.

Speech tests are, however, subject to learning effects that result in listener bias in favour of previous CI settings that are not optimal and can, therefore, undermine improvement in hearing. To address this problem, Dr Bob Carlyon and post-doctoral scientist Dr Alan Archer-Boyd are working on a psychophysical, non-speech test called STRIPES that does not contain recognisable speech segments.

STRIPES is administered by means of software which presents 3 sounds (per trial) to patients, who are then asked to select the odd-one-out.



During the test, it becomes harder for the patients to distinguish between the sounds and each patient reaches a point (threshold) at which he or she can no longer select the odd-one-out. A new CI setting that produces a higher threshold on the STRIPES test would be expected to result in improved hearing for the CI user.

STRIPES is being developed in collaboration with Advanced Bionics and MRC Technology negotiated the associated collaboration and licence agreement. Under the terms of this agreement, Advanced Bionics will financially support the post-doctoral appointment of Dr Archer-Boyd and Advanced Bionics is granted a non-exclusive licence to STRIPES so that it can be available to patients.

STRIPES\* :  
Spectro  
Temporal  
Ripple for  
Investigating  
Processor  
Effectiveness

# Sequencing 57 monoclonal antibodies for clone preservation and production of recombinant proteins

## External Scientific Staff

Professor Neil Barclay

Monoclonal antibody technology was invented by César Milstein and George Köhler in 1975 at the MRC Laboratory of Molecular Biology (Nobel Prize in Physiology or Medicine, 1984).

The process involves the generation of a hybrid cell (hybridoma) consisting of the desired antibody-producing B cell and an immortalised fusion partner. The resulting antibodies secreted from hybridomas recognise a certain target molecule and are widely used in diagnostic kits and also as research tools for the detection, purification and blocking of specific protein targets.

Hybridomas, as with any other cell line, are however subject to genetic drift and accidental cell death caused by, for example, infection or inadequate storage. An understanding of the antibody sequence can preserve the value in these hybridomas, allowing the production of recombinant antibodies based upon these sequences. Furthermore, recombinant antibodies can be improved by means of molecular engineering. For instance, targeted mutagenesis can be used to increase the affinity of antibodies

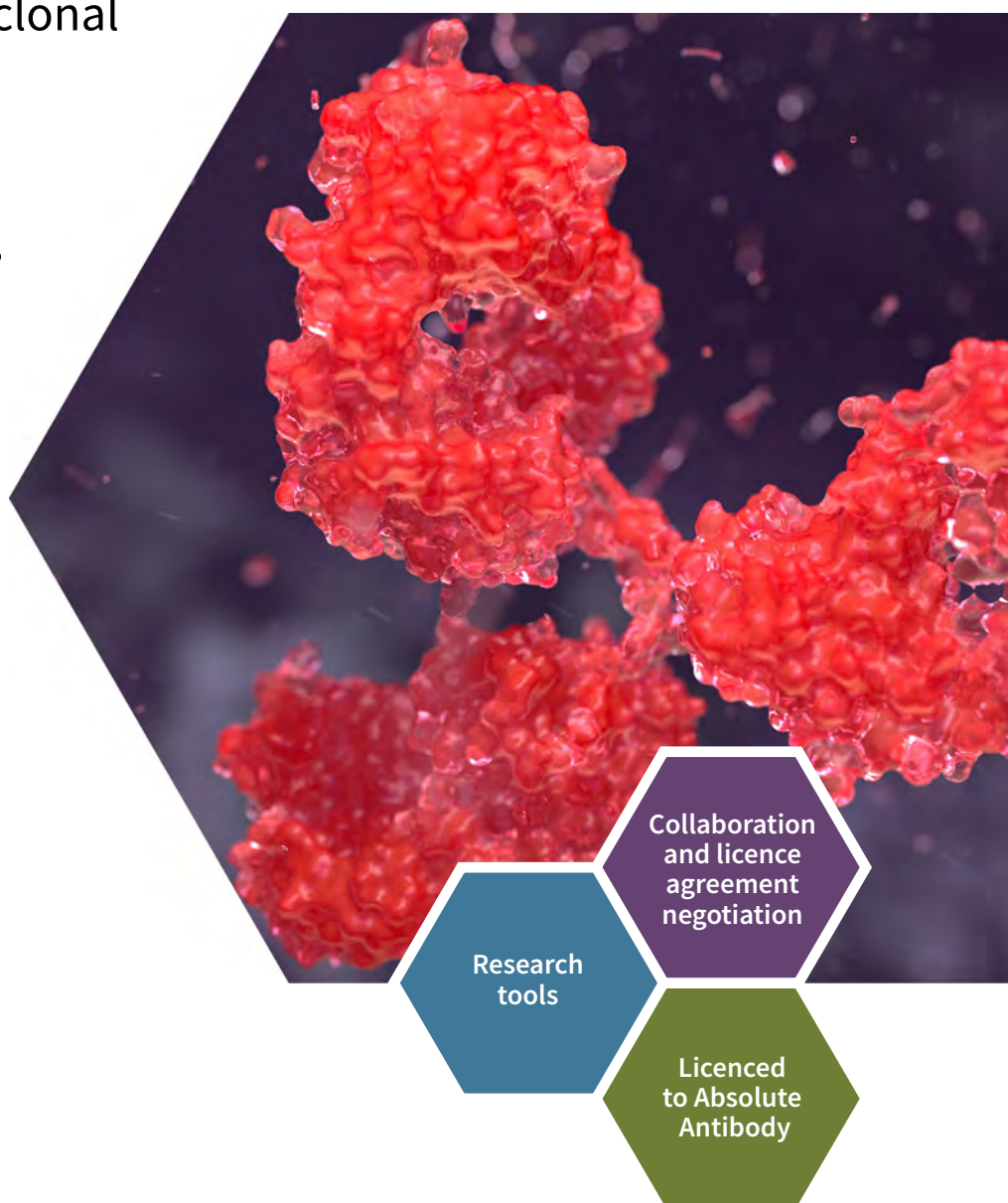
for their targets. It is, therefore, advantageous to have genetic information of clones for antibody preservation and recombinant manufacturing.

The MRC is collaborating with Absolute Antibody, a company which specialises in antibody sequencing, engineering, and recombinant production, for the sequencing of 57 clones.

Twenty of these clones have already been sequenced and include the OX86 clone (specific for mouse CD134) and the OX104 clone (specific for human CD200).

The rest of the antibodies will be sequenced within the next two and a half years.

MRC Technology negotiated a collaboration and licence agreement with Absolute Antibody according to which the company will carry out the DNA sequencing and is granted a non-exclusive licence to use the genetic information for manufacturing and selling recombinant antibodies in return for royalty payments from the sale of any antibodies.



## Mini G proteins: Tools for studying GPCRs in their active conformation

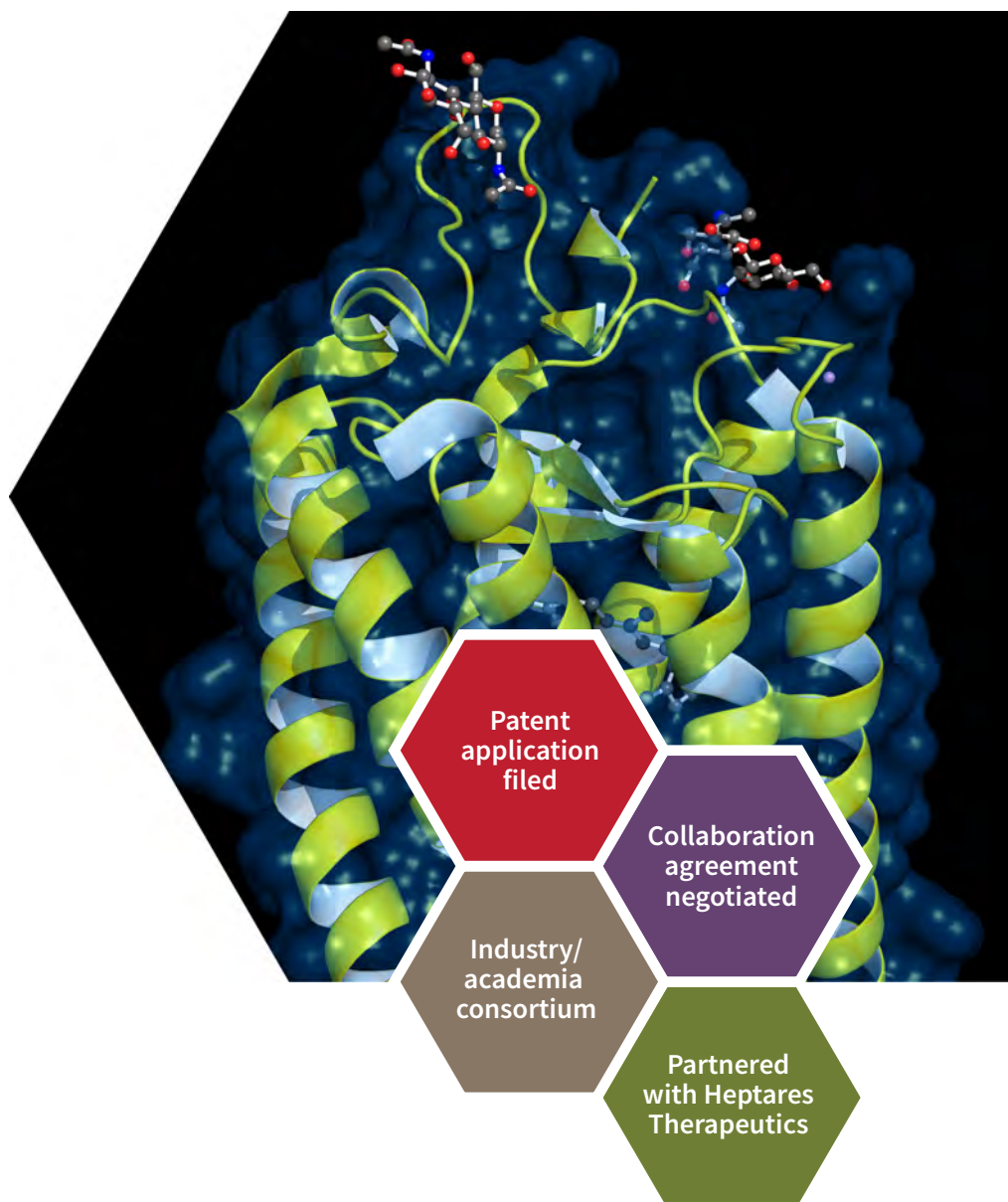
### MRC Laboratory of Molecular Biology

Dr Chris Tate

G protein-coupled receptors (GPCRs) represent a large family of cell surface receptors that respond to a diverse range of external stimuli and play a major role in pharmacology due to their significant function in cell communication, with approximately 30% of the drugs currently on the market targeting GPCRs. Binding of ligands such as hormones to a GPCR activates the receptor, which in turn activates the bound G protein on the intracellular-side of the membrane which can then go on to activate distinct downstream effectors.

To date there has been great progress in the structure determination of GPCRs; however, it is still a major challenge to determine the structure of these receptors in their fully active state due to the instability of activated GPCRs and receptor-bound G proteins.

Work in the laboratories of Chris Tate and Richard Henderson at the MRC Laboratory for Molecular Biology has previously led to the development of stabilised receptor (StaR®) technology, which allows the generation of thermostabilised membrane proteins



for structural analysis and rational drug design. This technology was spun-out of the MRC in 2007 into Heptares Therapeutics, a company focussed on applying this approach to G protein-coupled receptors (GPCRs).

Chris Tate and his team have now applied this approach to G proteins by engineering the GTPase domain of the  $G\alpha$  subunits to create mini-G proteins for all the major  $G\alpha$  families. Given the small size and stability of mini-G proteins, and their ease of expression and purification, they are ideal for structure determination of GPCRs in their fully active state, which will ultimately expand on the knowledge

of the signalling of GPCRs as well as providing useful receptor structures for rational drug design.

A collaborative agreement with Heptares was concluded, who provided funding to Chris Tate's laboratory to develop the mini-G proteins. A patent application claiming these mini-G proteins and the methods for making them was subsequently filed by Heptares in 2016.

## Update: An inexpensive point-of-care diagnostic for tuberculosis

### MRC Unit The Gambia

Dr Jayne Sutherland

The diagnosis of tuberculosis (TB) still represents a major challenge and a significant unmet medical need.

Currently only 16% of the TB patient population receive a laboratory confirmed diagnosis. This leads to missed opportunities to treat patients with TB as well as over-diagnosis in some cases, resulting in inappropriate treatment of those with other respiratory infections. This in turn has direct effects on transmission rates and also potentially drug resistance.

Dr Jayne Sutherland has looked to develop a test that can be used at the point-of-care and provides a yes/no diagnosis of TB, meeting this unmet need. Dr Sutherland's initial work identified a relatively simple set of biomarkers that accurately distinguish TB from other respiratory diseases and is ideally suited to rapid, simple diagnostic platforms.

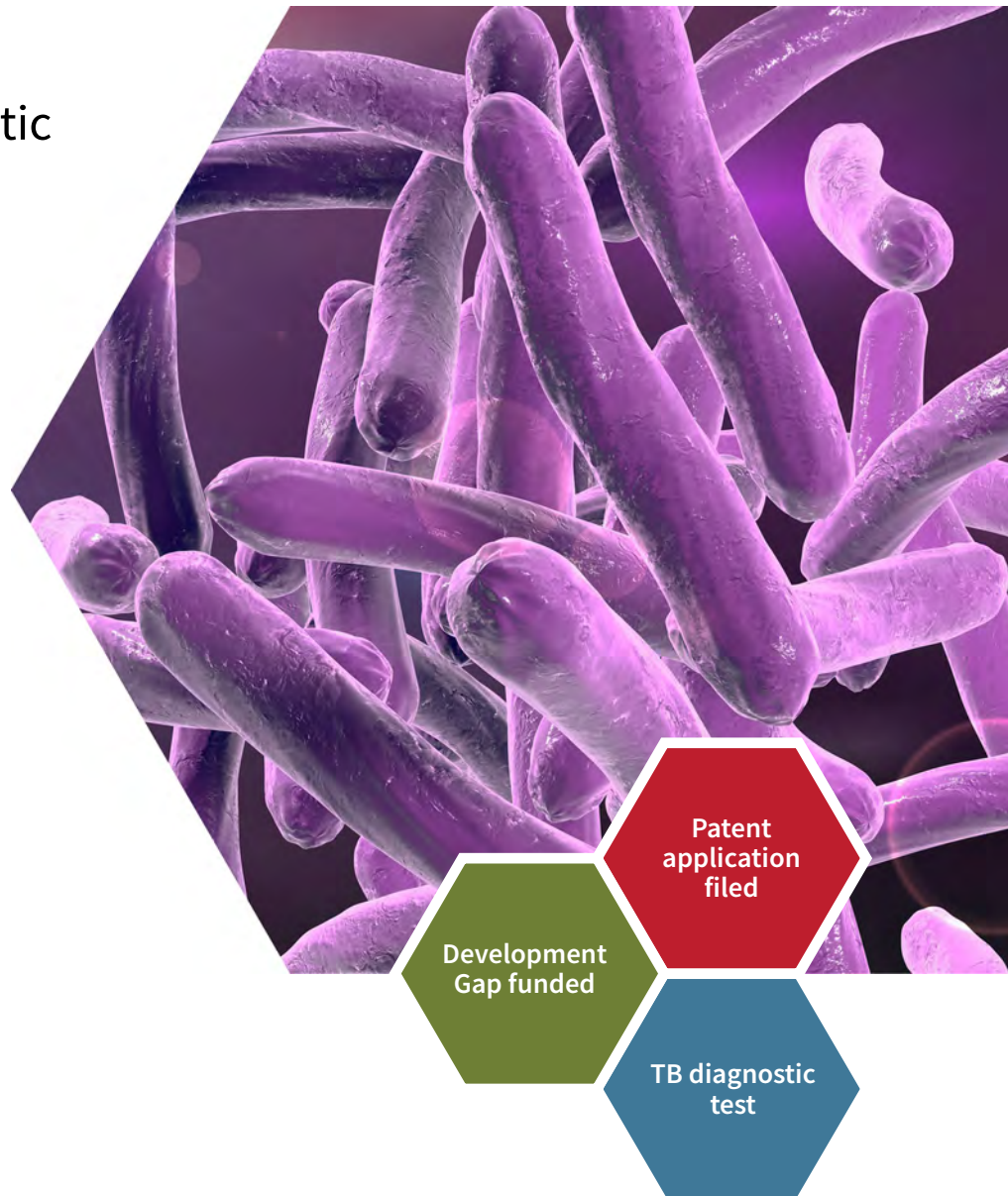
In particular, the test would be very well suited to a lateral flow immunoassay platform. This 'dip-stick' based approach is simple, robust, reliable and inexpensive. As a result, it is very well suited to resource

poor settings, as well as a range of point-of-care situations. Such a test would improve access to TB diagnosis as well as faster results, meaning that diagnosis could be provided in a single clinic visit. MRC Technology has worked with Dr Sutherland to patent protect this signature and to market the approach, garnering industry interest and valuable input into the development of the technology.

In 2016 Dr Sutherland secured £100,000 of funding from MRC's Development Gap Fund (DGF) scheme.

The aim of this work is to take the diagnostic signature into a larger, more varied validation cohort, providing

funding to allow processing and biomarker assessment in patient samples. The work will be performed in early 2017 and should quickly provide supporting data to aid translational development, representing a key step on the path to transferring this signature to a point-of-care diagnostic test.



# Multimedia informed consent for low literacy populations

## MRC Unit The Gambia

Dr Muhammed Afolabi

Informed consent is fundamental to clinical research. The process is required to ensure that participants enter into a clinical study freely and with full knowledge and understanding of the study process, including all risks and benefits.

Although it is a relatively simple task to provide a participant with all necessary study information, ensuring the participant has a full understanding of this information is a more nuanced task, requiring careful consideration of the cultural and societal requirements of different study settings. Empirical evidence from sub-Saharan Africa for example has consistently shown poor comprehension among study participants. This even extends to basic study concepts, such as placebo, randomisation and blinding.

Dr Muhammed Afolabi has developed a multimedia consent tool for achieving informed consent in low to non-literate settings, where the study participants' first language is frequently non-written. In award winning research (MRC CEO Award – Driving Change) the tool was trialled in

the field and was demonstrated to significantly increase comprehension and elicited a statistically significant increase in recall and understanding and led to high levels of participant satisfaction.

This work builds upon a number of studies in a range of settings which demonstrate that moving the informed consent process to a multimedia platform leads to a significant benefit in ensuring participants are truly informed.

Importantly, the work of Dr Afolabi has demonstrated that these concepts can be adapted and extended to settings which present unique and complex challenges to the informed consent process.

MRC Technology has been working with Dr Afolabi to increase the visibility of this tool and to find suitable partners to help increase uptake of the approach and to develop the tool into a product with broader application, building upon the existing strong translational efforts.



# Mouse models of immunological disease

## MRC Laboratory of Molecular Biology

Dr Andrew McKenzie

Interleukins (ILs) are a group of cytokines that modulate the growth, differentiation and activation of immune system cells by binding to high affinity receptors located on a target cell. The exact cellular response elicited will depend on the ligand, receptors expressed on the cell surface and the consequent signalling cascade activated. ILs are critical in the physiological response to an infection and their dysregulation plays a significant role in the pathophysiology of a wide range of disorders, including asthma, ulcerative colitis and leukaemia, making them important therapeutic targets.

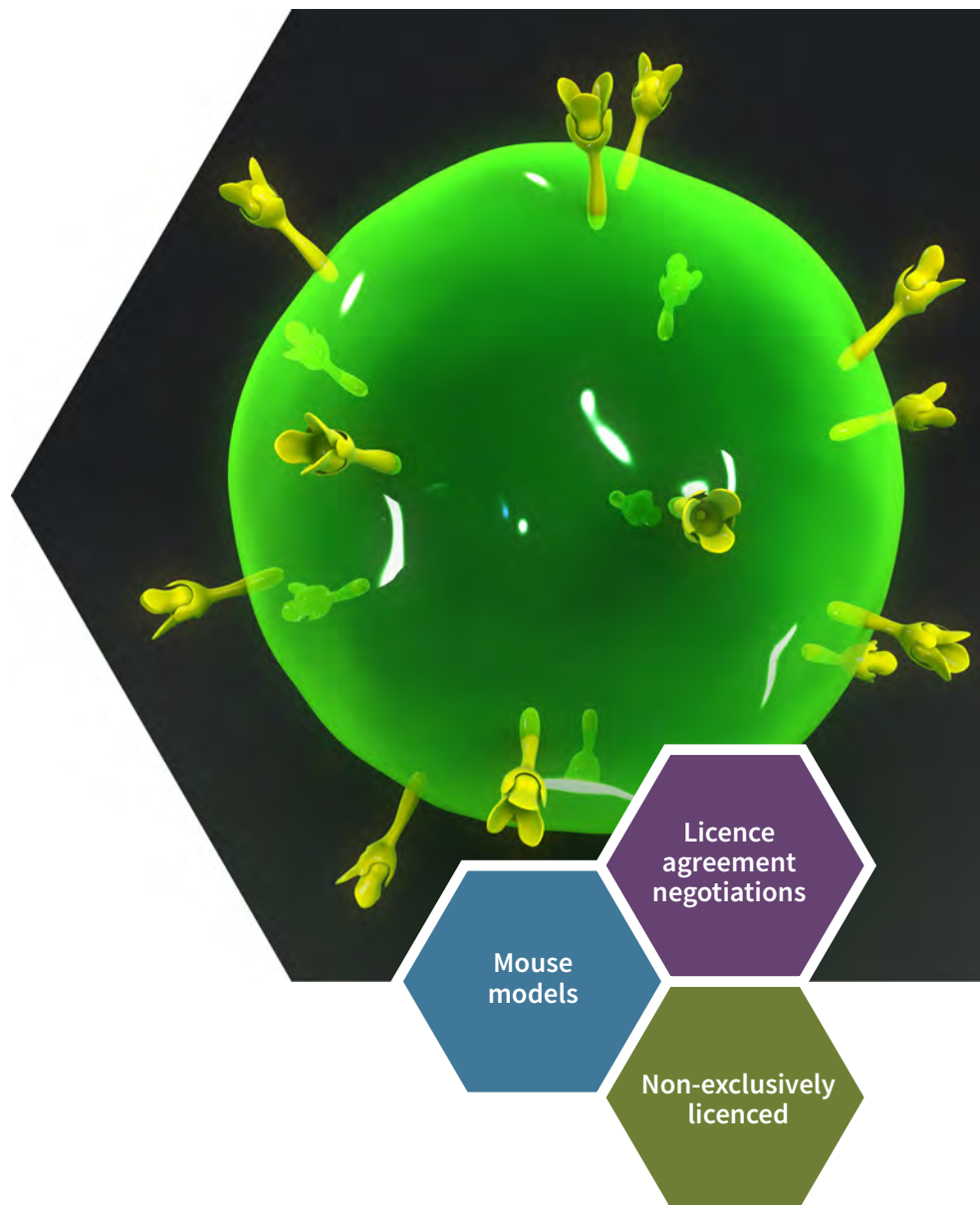
Dr Andrew McKenzie is a world expert in the study of interleukins and their modulation of several immune response pathways. His research into the function of interleukins has uncovered entirely new elements of the immune response such as group 2 innate lymphoid cells (ILCs), which play a critical role in tissue damage and infection. ILCs belong to a family of cells that form part of the innate immune system and generate an adaptive immune response when activated. They are activated by a range

of “alarmin” interleukins, including IL-25, IL-33 and TSLP which are in-turn generated in response to parasitic infection, viral infection or allergen tissue damage. Their function is phenotypically similar to that of T cells except they lack acquired antigen receptors and do not undergo expansion upon activation. Instead they secrete cytokines that direct an immune response proportional and adaptive to the damage or infection of tissues.

Dr McKenzie's work has elucidated the complex interplay behind this adaptive immune response, which can now be used to modulate the immune system as part of disease prevention and therapy. Over the course of this research the

McKenzie lab has generated a number of invaluable mouse models, where the interleukin or cytokine system has been modified, in order to further our understanding how diseases of the immune system can be combatted. These include mice with a deficiency in ST2, a gene that modulates t-helper cell cytokine responses, and IL-17RB, a receptor that plays a role in the inflammatory response.

A number of these mouse models have been non-exclusively licenced to other organisations, which will use them in their own drug discovery and development programmes.



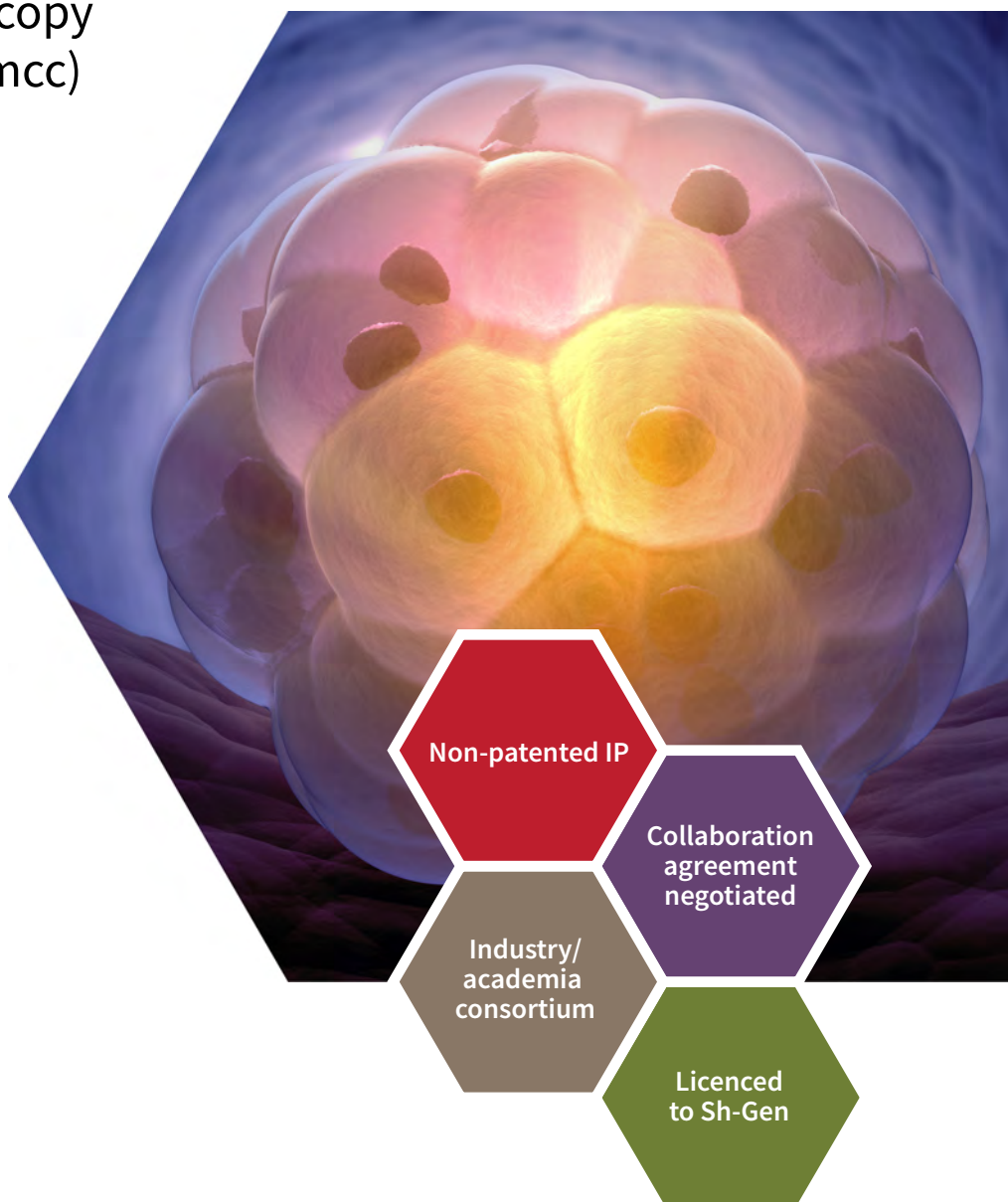
# Single cell molecular copy number counting (scmcc) in pre-implantation genetics

## MRC Laboratory of Molecular Biology

Dr Paul Dear

Aneuploidy is observed in approximately 30% of oocytes in young women. This number increases with age to reach 95% in women over the age of 42. Abnormal chromosome number and other genetic abnormalities have a large effect on the levels of pregnancy and formation of healthy embryos. Recent advances in the area of sequencing technology have led to the development of new ways to overcome these issues. During IVF it is now possible to conduct pre-implantation genetic screens on the polar body of the oocyte or newly formed embryo.

Unfertilized oocytes have the full complement of chromosomes in a diploid state. Upon ovulation the oocyte goes through meiosis 1 and excludes one complete copy of all chromosomes as a polar body. Thereafter when the oocyte is fertilized it completes meiosis 2 and expels a second copy of its chromosomes, to produce a second polar body. Polar body biopsy from oocytes or fertilized eggs and subsequent analysis of the chromosomes inside, allows for aneuploidy and genetic abnormalities to be identified.



Sh-Gen is a German company specialising in pre-implantation genetic screening through the polar body biopsy technique. Identification of aneuploidy in polar bodies is achieved through single cell Molecular Copy number Counting (scMCC).

This technique is based on PCR and allows for multiplexed analysis of a single cell or polar body to determine if there are any chromosomal duplications and the number of copies.

Dr Paul Dear in collaboration with Sh-Gen, developed a number of marker sets that facilitate the identification of chromosomal copy number abnormalities in polar bodies.

The marker sets developed as part of the collaboration were successfully licenced to Sh-Gen as part of a know-how package, in 2016. These marker sets will form some of the 20 probes used on each chromosome and will help to identify potentially embryonically lethal aneuploidy events, resulting in increased levels of successful IVF treatment.

# Protecting and translating research with MRC Technology

MRC Technology was set up as an independent company and charity by the Medical Research Council in 2000 to look after the MRC's intellectual property (IP) and technology transfer needs. It now also offers these services to other medical research charities and organisations.

MRC Technology assists MRC scientists to protect their work, achieve its potential and maximise impact. IP can be protected in order to facilitate investment in further development through patents, copyright, designs or trademarks. Protected or unprotected IP can then be licensed to an industry partner with the aim to develop it into a product for patient benefit or further scientific research.

Drug targets and diagnostics can be advanced through MRC Technology's Centres on a revenue share basis. The Centre for Therapeutics Discovery (CTD) which has world-class skills in antibody humanisation and small molecule discovery and development, while the Centre for Diagnostics Development (CDD) offers collaborative diagnostic assay development and validation.

Every MRC scientist is partnered with an MRC Technology Business Manager, who will keep in regular contact to maintain awareness of research progress and they will advise if the research has commercial potential. Business Managers can also assist when scientists discuss their research with other organisations and are readily available to aid researchers in their interactions with industry.

To find out more, please contact your Business Manager

**020 7391 2700**

**info@tech.mrc.ac.uk**

**mrctechnology.org/  
our-people**

## Populating the MRC Reagents Catalogue

Make your monoclonal and polyclonal antibodies, mice, vectors and cell lines available to the wider scientific community without having to deal with enquiries directly.

On behalf of the MRC, MRCT commercialises research reagents created by MRC researchers via partnerships with several major reagents companies. These companies sell the reagents via their catalogues, generating approximately £250,000 per year for the MRC to reinvest in research. In addition, income generated from such licences may be eligible for the MRC Award to inventors scheme (for reagents created after 1 April 2012).

Depositing your reagents with suitable repositories e.g. with ECACC for antibody hybridomas or MRC Harwell Archive for transgenic mice means that these research tools only need to be provided once, saving you from the burden of continued delivery and ensuring safe back-up storage.

MRC scientists have already deposited more than 90 antibody hybridomas with ECACC and these are made available to the wider scientific community (free-of-charge to academics and under income-bearing licences to companies).

For more information about the commercialisation process or to discuss making reagents available, please contact:

**Antonia Chatzopoulou**

**antonia.chatzopoulou@tech.mrc.ac.uk**

Alternatively, submit your reagents for consideration using the forms available from

**mrctechnology.org/reagents**



If you have any  
questions about:

Development  
funding

PROTECTING  
YOUR WORK

IP protection and  
commercialisation

Distributing  
reagents

MAXIMISING  
ITS IMPACT

Potential  
therapeutics

Diagnostics

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