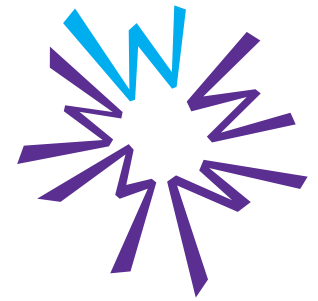


Research Newsletter



WELLBEING
OF WOMEN

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Professor Peter Brocklehurst (Left), Professor Mark Kilby (Right)

SUMMARY

RAC (Research Advisory Committee)

The Research Advisory Committee plays a vital part in the process of choosing which projects to fund.

The peer review process that Wellbeing of Women employs was awarded a 'Certificate of Best Practice in Medical Health Peer Review' by the Association of Medical Research Charities (AMRC).

Applications are subject to external peer review by at least three assessors from either the UK or abroad. Assessors are asked to comment on the significance of the topic to Wellbeing of Women's aims and objectives, the details of the proposal, the people and workplace, value for money, ethical and other considerations, translational potential or potential for clinical outcome.

We have 2 grant rounds per year.

Professor Mark Kilby is the Chairman of Wellbeing of Women's Research Advisory Committee (RAC). He has served in this role for the past 3 years and is handing over to **Professor Peter Brocklehurst** in June 2011 as his term ends.

After qualifying from Guy's Hospital Medical School in 1984, Mark has taken on many significant roles in the medical community, including serving on council for RCOG. He is Lead Clinician of Fetal Medicine at the Birmingham Women's Hospital Fetal Medicine Centre, and was the elected Fetal Medicine representative on the Executive Committee of the British Society of Maternal and Fetal Medicine, (he is also a member of the Perinatal Research Society of the USA, International fetoscopy Working Group, Society of Maternal & Fetal Medicine in USA and Society of Gynecological Investigation in the USA).

Mark's clinical special expertise is in prenatal diagnosis, fetal anomalies, fetal therapy and intrauterine growth restriction and he has published over 120 peer reviewed original articles on these subjects.

Through his role as chairman of the RAC, Mark has raised standards and significantly developed the research strategy and processes. The research projects have been awarded each year with great guidance and scientific rigour. In Professor Peter Brocklehurst he is handing over to an equally safe pair of hands.

Professor Brocklehurst is Director of the Institute of Women's Health and has served as Deputy Chairman of the RAC for 3 years. Peter has led numerous trials in perinatal care as well as a large observational study to evaluate the outcomes associated with planned birth in hospital, midwifery-units and home. He created UKOSS, the UK Obstetric Surveillance System, a system to measure the incidence and outcomes of a range of rare disorders of pregnancy.


Professor Brocklehurst also chairs numerous steering committees and data monitoring committees, and is a member of the executive and board of the NIHR Medicines for Children Research Network and the National Reproductive Health Research Network.

Ian Sargent at the University of Oxford was awarded a grant of £140,231 (over 24 months)

The regulation of immune cells in normal and abnormal pregnancy

The Research Advisory Committee (RAC) felt that this project could make very important new discoveries into why some pregnancies are 'rejected' by the mother. The project arose from work being carried out by a young clinician, Dr. Ingrid Granne and her PHD project. Ian says of her "She has been bitten by the research bug and being a successful co-applicant will help her enormously in her aim to pursue an academic medical career". Dr Jen Southcombe who trained and mentored Ingrid will also work on the project alongside another PHD student - Zahraa Al Yahyai.

The project focuses on the mother's immune system (an early and continuing research interest for Dr Sargent) and how this changes to accommodate the development of the genetically foreign fetus. Changes to immune cells can be detected throughout


 I was absolutely delighted to hear that our application to Wellbeing of Women had been successful, not just because it enables us to carry out some exciting new research but because it impacts on the training and development of three young members of my group.




pregnancy, and it is when these changes fail to occur that an unhealthy or unsuccessful pregnancy results. From a previous study the team have identified increased levels of two particular molecules called ST2L and IL33 - in the blood of pregnant women. The aim of this project is to understand more about these molecules and their relevance to pregnancy success.

The team hope to find out whether these molecules could be used in a simple blood test to predict pre-eclampsia, and early pregnancy loss. By understanding how they work we may be able to medically intervene and develop new treatments that will help women who have miscarriages or pre-eclampsia or are unable to conceive naturally.

Sarah Blagden - Gary Weston Centre, Imperial College awarded a grant of £183,855 (over 36 months) to investigate "The role of Larp1 protein in the development of ovarian cancer chemotherapy resistance"

 In my career as an oncologist I have repeatedly witnessed the terrible destruction that cancer causes, both to patients as well as family and friends. It makes me angry and motivates me to do my bit towards finding a cure. The research itself is full of highs and lows but becomes a tantalising and highly addictive process as we gradually piece together our discoveries.

Sarah Blagden 

The RAC thought that the project had the potential to define a new target for treatment and might also find a marker which could be used to tailor treatment and allow women who are unlikely to respond to platinum-based chemotherapy to be given alternative treatment and avoid the toxicity of ineffectual treatment. The Lead RAC member said: "It is a novel area for research and this is a well-planned, logical project to be performed by a group with an excellent track record."

She says: "I have been interested in the Larp1 (previously called "meteor") since the days of my PhD." Sarah initially, studied the gene in fruit flies, but her research made her realise it was vital for the day-to-day functioning of human cells too.

Cancer cells have the ability to "turn nasty" and leave one part of the body to travel to other areas. This switch to aggressive behaviour is also believed to be the reason that cancer cells become resistant to treatment. This is especially the case in ovarian cancer. Sarah says of her project, "We have shown that Larp1 is crucial for cells to undergo this switch, and that levels of Larp1 are higher in ovarian cancer cells which have become resistant to chemotherapy. We think Larp1 is an important step in this cellular switch. The aim of the project is therefore to investigate how Larp1 is turned on and off in the cell and whether it is the main controller of this aggressive behaviour. Potentially, this means that if we could inhibit or turn off Larp1, we might be able to treat ovarian cancer more easily".

Robert Pickard, Newcastle University
Awarded £151,417 over 36 months
Boosting Immune Defences in Women with
Recurrent Cystitis without Using Hormones

Lead RAC member statement:

They are uniquely placed in conducting this research, the outcome of which could be a safe, effective treatment for cystitis that is based on enhancing natural defence mechanisms.

This project was highly rated by five reviewers and was the highest rated project in the field of 'quality of life' by the Wellbeing of Women Research Advisory Committee.

How did you feel when you found out that your application had been successful?

Initially elated that all the hard work done by the team in preparing a clear and concise application had been appreciated by the Wellbeing board, then mixed feelings of excitement and trepidation for the work ahead. We also realise the responsibility we have to Wellbeing and to everybody who donates to the charity to make sure we give full value from our research.

What made you want to pursue a career in medical research?

Three main things: firstly a desire to try to help ensure that we make best use of the treatments we already have; secondly to identify and investigate areas where new approaches are most urgently needed; and thirdly to make sure that the next generation of doctors talented in medical research are identified, nurtured and encouraged to become the professors of tomorrow.

What attracted you to the specific area of research in the first place?

Both my clinical work as a urologist and my research programme is focused on health problems that although not life threatening do have a major impact on people's well being. Working in urology clinics makes you realise that recurrent cystitis is a very troublesome problem for lots of women making their life miserable and impacting on relationships. This together with the realisation that traditional antibiotics are often ineffective made us begin the search for new treatment targets.

Tell us about this research project. What problem will it tackle? What potential benefits does it have? How will the grant aid you in this?

The ready availability of antibiotics has made us all a bit complacent about how we treat infections and we are now starting to see the drawbacks of this approach such as the emergence of highly resistant bacteria. Cystitis we know is almost always caused by bugs present in the person's own gut. These bugs such as E. coli ordinarily do sterling work in terms of maintaining a healthy gut lining and are actively tolerated, but when they migrate to the bladder they set off the body's defences resulting in inflammation and the typical symptoms of tummy pain, having to pass urine frequently and burning. Having thought about the problem we decided that one way to stop this process would be to prevent the E. coli bugs getting to the bladder.

We have also found out that the female hormone, estrogen, boosts the body's own defences naturally which may explain its protective effect in women suffering recurrent cystitis. Unfortunately estrogen creams are often ineffective and there are concerns about their possible links with cancer in women after the menopause. This project funded by Wellbeing is therefore designed to find new treatments that work better than estrogen at preventing recurrent cystitis without the side effects.

The generous grant from Wellbeing will make this study possible. As well as paying the salary of the scientist doing the main part of the work, it will also pay for the expensive chemical and gene detection kits that make the work

much quicker and more accurate.

Q5 What are your hopes for this project? Once complete, do you foresee future research in this area?

I think it is essential that we find alternatives to traditional antibiotics for the common infections such as cystitis that we see in developed countries like the UK. If we can find ways to enhance these defences naturally, even by a little, this will produce the same benefit in terms of resolving symptoms quickly as traditional antibiotics. These developments will allow a more natural control of the bugs we need in our bodies and

Virginia Beckett, Bradford Royal Infirmary
Awarded £13,500 Over 36 months
Cardiac Arrest in Pregnancy Study (CAPS)

RAC member comment:

The study will be the biggest descriptive study of this rare complication in the world and will guide decisions about how to manage such women in future. Currently this happens without any evidence base. This will provide it.

"I was delighted to find out that we were successful in our application, particularly given that I have been involved in fundraising for Wellbeing in the past. My main interest is in clinical medicine. Fitting research in with this and bringing up my own children is a challenge. This is a project that I feel strongly about, however, and now my children are older, I hope to have a little more time!

I was surprised to discover that, although the number of cardiac arrests in pregnancy seem to be increasing, we have very little data to guide us in how to manage this devastating complication of pregnancy, nor do we really know who is at risk. We are using our Wellbeing grant to gather information on all cardiac arrests (when the heart stops beating) in pregnancy by surveying all obstetric units in the UK for 3 years. At the moment we only know about those cardiac arrests that end in the mother's death, through the Confidential Enquiry. We know that the number of those deaths have been increasing. We want to find out why so that we can begin to act to prevent cardiac arrest in pregnancy. We know that around 15% of women who suffer cardiac arrest in pregnancy survive. We want to know how to improve survival rates, hopefully by establishing guidance on the management of cardiac arrest in pregnancy, based on the evidence we collect. We are using the well established UK Obstetric Surveillance System (UKOSS), so I am confident that we will gather robust data on this important subject. Ultimately, I hope that this work saves the lives of women and their children. In future, we may be able to carry out some more specific work on the outcomes of survivors of cardiac arrest in pregnancy."

Virginia Beckett

Research Grants Manager

Our Research Grants Manager; Philip Matusavage, tells us about his first experience of The Research Advisory Committee for Wellbeing of Women



Having joined Wellbeing of Women as Research Manager immediately after all of the 2010 grants had been awarded, the 2011 Research Project Grant round was my first experience of the process used to choose which research to fund. It was a very busy period for me but one which I found interesting and illuminating.

By the time the call for project applications closed in September 2010, we had received 66. Each one had to be logged and checked to ensure they had included all of the required information and correctly completed the application form. After this a summary of all the applications was sent to the Chair of our Research Advisory Committee (RAC). This is a body made up of 21 experts in various fields of obstetrics and gynaecology, and their expertise is invaluable in this process. Together with the Chair I split the applications between members of the RAC, with each application being allocated to two members. Each application is reviewed by these members, and they also recommend external experts whom I then approach for their opinion (after first checking to ensure that there is no conflict of interest e.g. they work at the same institution as any of the relevant applicants).

I was surprised by just how helpful most of these external experts were. Many quickly agreed to review an application, and most of those who could not recommended alternative names. As a result, I managed to find at least three external reviewers for each application, meaning that every application was reviewed by at least five people. These review scores are collated and only those above a certain threshold progress to the final stage of the process. This ensures that only research projects of a high standard are eligible for funding.

The final stage is the Research Awards Committee meeting, which took place on January 17th. Getting so many busy researchers and clinicians in a room together is no easy feat, so preparations for this meeting were complicated and prolonged. Fortunately, all but two of the Committee were able to attend the meeting in person, and those who could not sent their input. The Committee went through every application in order to ensure that all agreed on the final shortlist of approx 30. These applications were discussed in great detail, with the two Committee members who reviewed it presenting and leading a full discussion. Each member of the Committee then scored the application in secret.

This was a lengthy process which lasted 2 days. I was very impressed by the level of discussion afforded to the projects and I found it hugely informative. It was also heartening to see how passionate the Committee was. I came away with a sense of how robust our processes are. The quality of the application is fundamental in its progression, and by having at least five peer reviewers we are able to ensure that our money goes to only the best and most promising research projects. I was also hugely impressed with, and grateful to, the members of our Research Awards Committee and also the external reviewers. All of these individuals give their time and expertise for free and provide an invaluable service.

The process culminated in four projects emerging ahead of the rest and these were recommended to our Trustees for funding. The Trustees agreed with the recommendation and we have committed to fund them.

Our Research Advisory Committee selects all our research for its excellence, cost effectiveness and expected benefits to women and their babies. We would like to warmly thank all our wonderful supporters, whose generosity enables us to fund this exciting and innovative research to take forward improvements in women's health.



Current Research Advisory Committee gathered for their meeting in May 2011