

Cambridge BioResource

>> Cambridge BioResource is understand what these genes do in 'normal' people."

Prof Todd believes the BioResource is good for Cambridge. He says: "It will attract other researchers to Cambridge because it is a unique resource. And there is a local impact in that it draws in the public, getting them to understand a little bit more about important medical research at Addenbrooke's and the University's Clinical school."

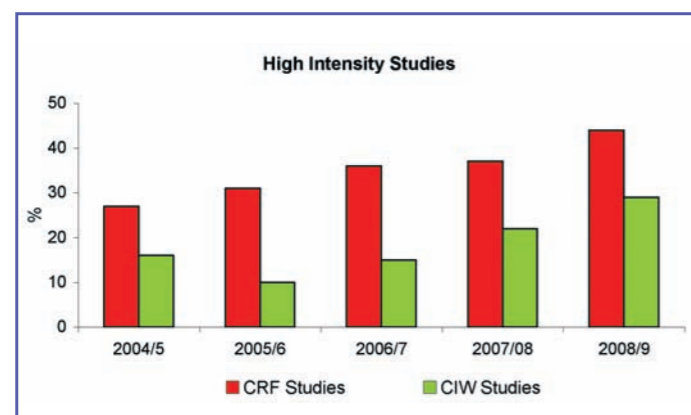
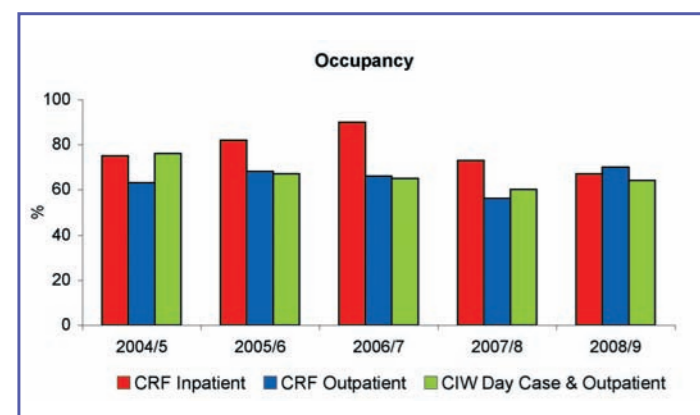
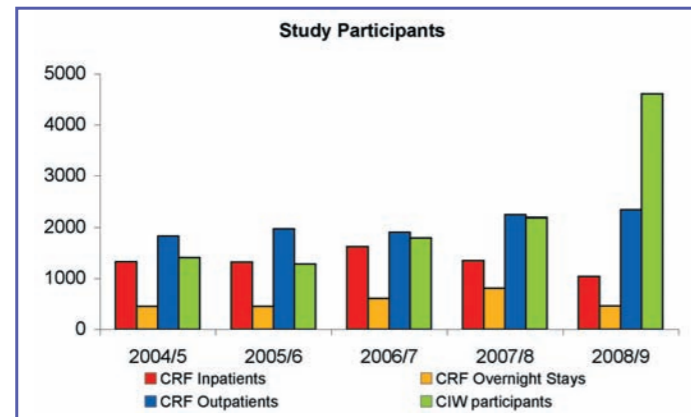
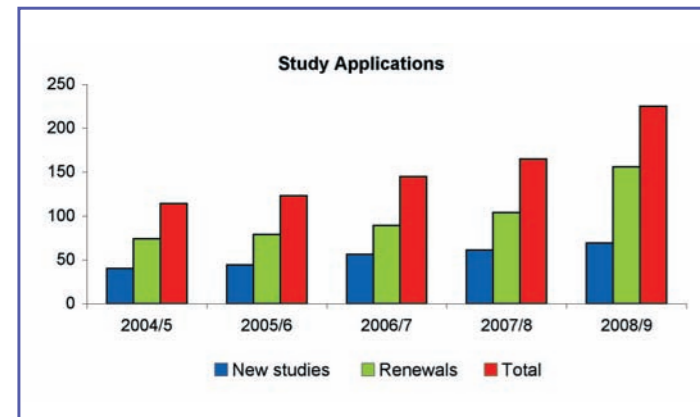
Joining the BioResource is easy – it just requires an initial blood or saliva sample from which a DNA sample is extracted and stored for genotyping. With CBR now working in partnership with the ACRC, volunteers recruited to CBR are able to visit the WTCRF to donate

their sample. In addition to taking the blood samples, WTCRF staff are also trained to take informed consent from volunteers, which mean that the visit can happen without a member of the CBR team being present, freeing up more time for the CBR research team to spend recruiting out in the field.

For further information about joining the CBR please email bioresource@cimr.cam.ac.uk or contact the CBR study office on 01223 769 215.

Access to the CBR is also open to applications from researchers from across the Addenbrooke's campus, with ethically approved research studies. For more information please email Sarah Nutland, the study coordinator at sarah.nutland@cimr.cam.ac.uk

Study Activity



Key dates and contacts

How to apply to use the facilities

All research undertaken within the ACRC is reviewed by the Scientific Advisory Board (SAB). The composition of the SAB is broad-based to optimise the assessment of applications from diverse disciplines. Studies are assessed in detail for scientific merit by a nominated SAB member, and the Board as a whole also considers and approves the appropriate allocation of ACRC resources for the project. The SAB meets on a monthly basis.

Submission dates for Scientific Advisory Board meetings

Application submission dates for 2009 Scientific Advisory Board Meetings (Submission dates 3 weeks prior to SAB)

Deadline for New Applications	Date of SAB meetings 2009
15th January	5th February
12th February	5th March
12th March	2nd April
16th April	7th May

Key contacts

If you have any suggestions, comments on this newsletter please contact Gayle Lindsay as below and she will pass on any comments/suggestions you may have to the relevant people.

Contacts	Secretary	Phone No	E-mail
Professor VKK. Chatterjee , Director	Teresa Wallman	c.3362618	kkc1@mole.bio.cam.ac.uk tdw30@medschl.cam.ac.uk
Caroline Saunders , Head of Clinical Operations	Gayle Lindsay	x 6055	caroline.saunders@addenbrookes.nhs.uk
Kornelia Hathaway , Education and Training Manager	Pam Sole	x 58986/6779	kornelia.hathaway@addenbrookes.nhs.uk pam.sole@addenbrookes.nhs.uk
Polly Tarrant , Lead Research Nurse	Gayle Lindsay	x 6055	polly.tarrant@addenbrookes.nhs.uk
Stewart Fuller , Senior Charge Nurse, CRF	Gayle Lindsay	x 6055	stewart.fuller@addenbrookes.nhs.uk
Bev Spencer , Senior Sister, CIW	Gayle Lindsay	x 4314	bev.spencer@addenbrookes.nhs.uk
Gayle Lindsay , Administration Manager		x 6076	gl250@medschl.cam.ac.uk or gayle.lindsay@addenbrookes.nhs.uk

Useful links

<http://www.addenbrookes.org.uk>
Addenbrooke's website

http://www.cuh.org.uk/research/research_index.html
Research & Development at Addenbrooke's Hospital

<http://www.wtcrf.cam.ac.uk/>
Cambridge Wellcome Trust Clinical Research Facility website

<http://www.medschl.cam.ac.uk/>
Clinical School website

14th May	4th June
11th June	2nd July
16th July	6th August
13th August	3rd September
10th September	1st October
15th October	5th November
12th November	3rd December

ACRC Application Forms have been updated. If you require an application pack or need further information please contact Caroline Saunders (Head of Clinical Operations) on 01223 596057 (Ext. 6057) or Gayle Lindsay (Administration Manager) on 01223 5960576 (Ext 6076) alternatively you can e-mail us as below. A preliminary discussion with the Head of Clinical Operations or Director is always welcomed.

STUDY PARTICIPANT BOOKINGS

Please note e-mail bookings can only be made from an Addenbrooke's.nhs.uk account. All other bookings can be made by telephone or fax (01223 596059 Ext 6059).

UK CRF NETWORK

<http://www.ukcrn.org.uk/index.html>
UK Clinical Research Network website

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UK Clinical Research Facility Network
c/o Manchester Interdisciplinary Biocentre
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(please note this is a general fax number)



ACRC news

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Addenbrooke's Clinical Research Centre comprises The Wellcome Trust Clinical Research Facility and The Clinical Investigation Ward

wellcome trust

Addenbrooke's NHS Trust

UNIVERSITY OF CAMBRIDGE

News and information from Addenbrooke's Clinical Research Centre

Service Developments

Clinical research into metabolic disorders to be enhanced

University of Cambridge installs MAGNETOM Verio

The University of Cambridge, has installed a new Siemens MAGNETOM Verio 3T MRI scanner in the Wolfson Brain Imaging Centre (WBIC) located on the Addenbrooke's Hospital campus.

The MAGNETOM Verio is a 3T field strength MRI. It has a wider than conventional design (70cm) and

features Tim™ (Total imaging matrix) in one powerful system. With the strongest magnet field strength used clinically, it can be used for many applications, including spectroscopy and imaging.

The system in the WBIC will be used by a range of investigators from both the University of Cambridge and Addenbrooke's Hospital Trust, including those from the newly-established Institute of Metabolic Science, to undertake Magnetic Resonance Spectroscopy (MRS) in a range of disorders including insulin resistance and diabetes, obesity, endocrine and metabolic storage diseases. MRS technology enables researchers to measure biochemical processes and pathways in tissues without the need for an invasive biopsy. Such knowledge may lead to a better understanding of how



The MAGNETOM Verio is carrying out Magnetic Resonance Spectroscopy (MRS) in a range of disorders including insulin resistance and diabetes, obesity, endocrine and metabolic storage diseases.

metabolic pathways are deranged in various disorders.

"The MAGNETOM Verio will allow us to develop MRS as a biomarker in clinical metabolic research" said Adrian Carpenter, Director of MR and Reader in Imaging Sciences at the WBIC. "The system is performing well and has lived up to all our expectations. We are looking forward to beginning studies on the Verio shortly and are positive it will assist with our research efforts."

"MRS is a highly sophisticated research tool that can be used to shed light on biological pathways in a range of conditions" said Graham Walker, Regional Sales Manager at Siemens Healthcare.



The MAGNETOM Verio at the Wolfson Brain Imaging Centre. (Left to right): Dr. Adrian Carpenter, Director of MR and Reader in Imaging Sciences at the WBIC and Professor Krishna Chatterjee, Director of the Wellcome Trust Clinical Research Facility in Cambridge.

The installation was funded by an initiative from the UK Clinical Research Collaboration (UKCRC) led by the Wellcome Trust. The Clinical Research Infrastructure (CRI) initiative provides funding to enhance facilities for undertaking experimental medicine and translational clinical research in the UK. Under the auspices of the CRI initiative, a consortium of funders including the Medical Research Council, Wolfson Foundation, Wellcome Trust and Department of Health have provided support to strengthen metabolic research >>

Service Developments

>> infrastructure allied to the Wellcome Trust Clinical Research Facility (WTCRF) in Cambridge. The scanner has been installed in a newly-built extension to the WBIC; additional resources have provided a dietetic and nutrition resource within the WTCRF.

“This development is an example of how the Clinical Research Infrastructure Initiative has provided investigators from both Cambridge University and Addenbrooke’s Hospital with cutting-edge technology to enhance understanding of metabolic disorders,” said Krishna Chatterjee, Director of the Wellcome Trust Clinical Research Facility in Cambridge.

Metabolic Research Area (MRA)

The MRA supports research into energy regulation at the whole-body level. Our studies in progress ranging from the influence of thyroid disorders on energy expenditure and body composition, through phenotype description of variants in genes such as FTO, which predispose to increased body mass or obesity, to therapies to moderate appetite in lipodystrophy.

If you have research plans which could benefit from our facilities and support then please do come along and discuss them. Just contact Peter Murgatroyd or Pip Raymond-Barker on (59)6077 (email prm13@cam.ac.uk or pr328@cam.ac.uk)

Early in 2008, the diet kitchen was refurbished and freezer storage increased to expand our ability to provide meals to match the requirements of study interventions.

The MRA has now purchased two universal eating monitors (UEMs). These monitors will enable us to study eating behaviour, such as total food intake, meal duration, initial rate of intake, and deceleration of intake. A study analysing eating behaviour in Prader Willi Syndrome will be the first to use these monitors.

In August 2008, Pip Raymond-Barker joined us as a Research Assistant. Having studied exercise physiology and previously undertaken exercise research with both the athletic and clinical populations, Pip has prior experience of several of the techniques used in the MRA to measure energy expenditure and body composition. As well as recruiting volunteers and performing physiological measurements, Pip’s role involves the analyses of research data for scientific publication. We are continuing to extend our team with the recruitment of a Research Technician. The technician will manage the CRF and CIW laboratories, and will assist with the physiological measurements in the MRA. They will also support the development of protocols relating to eating behaviour using the UEMs.

Our studies continue to require reference data from the metabolically normal population, and so we are asking “normal controls” to undergo measurements of body composition and energy expenditure. If you are interested in taking part then please contact Pip on 59(6077) or email crf-volunteer@medshcl.cam.ac.uk

Education and Training

The new Education Post on ACRC

To maintain excellence in clinical research you need a highly trained workforce. This applies to the researchers as well as to their support staff. As the size of the clinical research operation at the ACRC has expanded over the years it has become more critical than ever to coordinate the training and development of its staff.

It was with this in mind that the post of *Education & Training Coordinator* had been created at ACRC. I was thrilled to be appointed to this new post in the spring of 2008. It turned out to be a unique opportunity for me to combine my passion as a Clinical Research Nurse with my previous work in education and academic study. Right from the start it was apparent that this new role would work best if a collaborative and interdisciplinary approach was taken. Subsequently, I am involved in developing, working on and managing a broad range of research-related educational projects with an ever-wider circle of collaborators from a variety of professional disciplines and in a variety of settings.

Here are some examples:

For the ACRC staff I am building on the existing induction programme which contains training on key elements required for the conduct of clinical research, such as, for example, the need and significance of a research protocol and for ethical conduct at all levels of the research study. Gradually via a combination of in-house training sessions, attending study days, courses and conferences, staff are able not only to expand their study-specific skills but equally gain wider knowledge of research design and on-going developments in the clinical research arena.

In the past year the Cambridge University Hospitals Foundation Trust (CUHFT) has become increasingly aware of the need to

equip clinical staff who are involved in the conduct of research to have early and appropriate basic research skills training. This was to forge tighter links between CUHFT and the ACRC and as a result I am taking forward the managing and delivery of a twice yearly “basic research skills course for Nurses, Midwives and Allied Health Professionals”.

Similarly, the Postgraduate School of Medicine for the East of England approached the ACRC for assistance to provide research skills training for Specialist Registrars working in the Eastern Deanery. This has resulted in a fantastic collaboration of ACRC education staff with experienced University – and NHS-based clinical research academics. The first of the two-day residential “Research Skills for Clinicians” courses starts in April – to be held twice a year. An exciting interactive programme will be delivered by a high-calibre faculty of speakers and the course is already heavily oversubscribed. This course led to further collaboration – this time – although in the early stages - with an academic/industry based teaching programme. Equally, there are plans to commence an ACRC-based monthly seminar series on Research Methods in the autumn under the lead of Professor Chatterjee.

Branching out to include substantial involvement in UK-wide events, projects and beginning to develop an education business group for the Clinical Research Facilities Network, the post of *Education & Training Coordinator* has evolved into that of *Education & Training Manager*. My biggest education project currently underway is the organisation of the UK Clinical Research Facilities 5th Annual Conference in Cambridge on 8th & 9th July 2009.

Kornelia Hathaway

Case Study

Dr Alasdair Coles

Tony’s story

Tony Johnston was a professional golfer in his forties, with six European and 22 US tour victories, when one day in 2002: “my left side went numb, I thought I was having a stroke but it was diagnosed as a viral infection and I was given steroids, which did help for a short while....But two months later, I began to feel dodgy again. My co-ordination deteriorated and my golf game vanished.” He ploughed on, but things came to a head in 2003 at the British Open. He had to abandon the game after nine holes because he could not walk. Shortly afterwards, he was diagnosed with multiple sclerosis. He continued to have attacks and was told he would never play tournament golf again.

Tony was recruited to the CAMMS223 trial testing the experimental drug Campath-1H (otherwise known as alemtuzumab) in people with early multiple sclerosis. He received Campath-1H as a daily infusion, over several hours, for five consecutive days in the CRF. Patients have to be monitored closely for the unpleasant –but treatable and temporary – side effects of Campath-1H infusion. Patients then have another dose, twelve months later.

Since Tony had Campath-1H, he has had no further attacks of multiple sclerosis. Amazingly, his disability has actually improved. He was able to get back to professional golf, now on the Seniors tour, and in June 2008, he won the Jersey Seniors Classic. Looking back, he says the day he decided to take part in the trial was “to use a golfing analogy, the best cut I’ve ever made in my life”.

The early days of Campath-1H in multiple sclerosis

In 1984, Cambridge scientist Cesar Milstein was awarded the Nobel Prize for Physiology or Medicine, jointly with George Kohler, for inventing the

technology to make large quantities of monoclonal antibodies of defined specificity. Further work in Cambridge, by Herman Waldmann and Greg Winter, led to the production of the first humanised monoclonal antibody to be used as a therapy, Campath-1H (“Cambridge Pathology 1 Humanised”). It has since been licensed for the treatment of chronic lymphocytic leukaemia.

In 1991, Herman Waldmann and Alastair Compston, then both at the University of Cambridge, decided it would be interesting to study the effect of Campath-1H in the autoimmune disease multiple sclerosis. The first person with multiple sclerosis to be treated with Campath-1H was a local Cambridge accountant. She received the drug on A4 at the hands of a young neurology registrar called Neil Scolding (now Professor of Neurology in Bristol) and the much revered Sister Fraser. The patient did well initially, and six other patients were treated, by a suave French neurologist who left a year later, several English hearts having been broken, to become a Professor of Neurology in Dijon.

I took over the day-to-day running of the Campath-1H project in 1993 and, over the next five years, struggled to find bed-space in the neuroscience wards to treat a further 50 patients. For there would always be a neurosurgeon insisting their patients came first.... Undoubtedly such success as we had was due to the Irresistible Force that was our research nurse, Jackie Deans, now happily retired. The conclusions from this early work were that Campath-1H is remarkably effective at suppressing inflammation in the brain, but –very sadly- that it did not halt the worsening disability of late (secondary progressive) multiple sclerosis. On the way, we had also learnt that Campath-1H is surprisingly well tolerated, with little in the way of increased infective risk, but curiously 20% of patients developed autoimmune thyroid disease months or years after treatment.

The CAMMS223 trial

Some people suggested we should give up. Others, notably Alastair Compston, argued that we should use Campath-1H in people with early multiple sclerosis, before irreversible disability had been established. We were talking about exposing young adults, at the start of their careers, relationships and family aspirations, to a highly experimental drug. Negotiations were difficult with the successive commercial owners of Campath-1H. But in the end, we found in Ilex, and then in Genzyme, companies who were prepared to take the risk and fund a head-to-head trial of Campath-1H against a standard licensed drug, interferon-beta: CAMMS223. This phase 2 clinical study involved 334 patients followed for three years. We were the principal investigators. Thanks to the CRF, we no longer had to fight for beds on NHS wards and we were the highest recruiters to the study. Compared to interferon, Campath-1H reduced the relapse rate by 74 % over and the risk of sustained accumulation of disability by 71 %. An unprecedented result was that most people who received alemtuzumab had an improvement in their disability, like Tony. This suggests that Campath-1H may allow damaged brain tissue to repair. However, there is a cost to Campath-1H. In addition to thyroid disease, 3% of patients developed ITP, with a risk of bleeding. This has necessitated a complicated monitoring regime. And, very sadly, one of our much-loved patients, a regular attendee at the CRF for five years, died last year of a lymphoma, which we suspect is a rare complication of Campath-1H.

Our work has now shifted up a gear. We are helping Genzyme run two phase 3 trials in 1500 people all over the world, to test whether or not Campath-1H should be licensed as a treatment of multiple sclerosis. For all those people in the CRF who have helped us get this far, we are very grateful.



Cambridge BioResource

Set up in 2004 as a joint collaboration between the University and the MRC Epidemiology Department, the aim of the Cambridge BioResource (CBR) was to establish a resource of volunteers aged between 18 and 65 years from the Cambridge area who would be willing to be approached and invited to participate in a wide variety of local medical research studies, including donation of blood or saliva samples for genotyping.

The last five years has seen the CBR grow into an invaluable clinical resource. Through collaboration with the National Health Service Blood and Transplant Center (NHSBT), CBR now has over 5,000 members on its volunteer panel. In addition to recruitment to CBR through the NHSBT, the CBR team recruits volunteers through local schools and colleges, the Emergency Services, businesses, hospitals, clubs and by holding recruitment stands at local fairs and road shows. Look out for the CBR stand at this year’s Science Festival on Saturday 14th March! It will be located in the Biology Zone in the Large Exam Hall in the Arts School.

The key feature of the CBR is that local volunteers can be approached and invited to participate in a whole variety of research studies, based on selection by genotype, age, sex and other demographic variables, allowing powerful analyses of genotype-phenotype associations. The CBR has already proved successful in inviting and recruiting a large cross section of volunteers on its panel to a number of scientific phase 2 studies including “Genes and Mechanisms in Type 1 Diabetes” led by Professor John Todd at the Cambridge Institute for Medical Research, “Genetic factors affecting the neural coding of emotional signals in humans” led by Dr Andy Calder based at the MRC Cognition and Brain Sciences Unit, “Phenotypes linked to common weight gain/diabetes genetic variants” led by Drs Savage, Farooqi, O’Rahilly, Wareham and Finucane at the University of Cambridge and “Genes and Mechanisms of Cardiovascular disease” led by Dr Willem Ouwehand at the National Health Service Blood and Transplant Center in Cambridge.

Through a recent collaboration with the Cambridge Biomedical Research Centre the CBR has secured NIHR funding for the next 4 years to double the size of its volunteer panel to over 10,000 volunteers, and to assist in the recall of CBR volunteers on the basis of their genotype and/or other phenotypic variable to further local phase 2 scientific research studies.

The CBR benefits not only researchers but also provides members of the public with an opportunity to get involved in local research. Participating in these studies gives volunteers an insight into world-leading research projects going on in Cambridge and gives them a better understanding of the role of research in primary healthcare. It also provides a valuable link between researchers and their local community.

John Todd, Professor of Medical Genetics at Cambridge University, who has used the BioResource in his research into pathways in the human immune system that produce type 1 diabetes says: “What we are trying to do with the >>



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