



Translational Science at the Cambridge Research Institute

The aim of the CRI is to build from a platform of basic cellular and molecular biology to practical clinical application.

The composition of our research groups reflects this. Just under half are in basic biology – in particular, in epithelial cell biology and gene regulation. We also have groups with a strong base in genomics, molecular imaging, pharmacology, chemistry, mouse modelling and biomolecular computing, and (overlapping with these) a series of groups focussed on experimental cancer medicine and on the normal and cancer biology of particular tissues, currently breast, pancreas, prostate and ovary, and on related clinical studies. The idea is that a group focussed on a particular cancer type should be able – and encouraged through the use of discretionary funds – to access the relevant basic or technological expertise, apply it to the problems of the cancer in question and take that application through to the clinic.

Clinical research infrastructure is supported by Cancer Research UK and by funds from NHS Research and Development through the Experimental Cancer Medicine Centre and the Cambridge Biomedical Research Centre. A virtual Cambridge Cancer Centre provides a framework to build interactions with researchers in different disciplines across the University and beyond. These University links are further strengthened by several joint appointments: Fiona Watt with the Wellcome Trust Centre for Stem Cell Research, Kevin Brindle with the Department of Biochemistry, Simon Tavaré with the Department of Applied Mathematics and Theoretical Physics, and Shankar Balasubramanian with the Department of Chemistry. Almost half our group leaders are medically qualified, and most of these are clinically active. We have broadened our clinical base still further through appointments of clinician scientists based elsewhere on the Addenbrooke's campus as CRI adjunct faculty.

Medical Imaging

A state of the art experimental imaging facility within the CRI, which includes PET/CT, 9.3 and 7.0T MRI, mass spectroscopy, fluorescent and ultrasound imaging, is being replicated on a clinical scale within the hospital. This year a collaboration between Addenbrooke's Hospital, the pharmaceutical company Merck Sharp and Dohme, the University of Cambridge and Cancer Research UK has provided a clinical PET/CT dedicated for research use, adding to our existing 3T MRI. Kevin Brindle's group published the use of ^{13}C hyperpolarised reporters to increase the sensitivity of MRI by up to 10,000-fold, allowing the real-time imaging of pH and other metabolic changes in mouse tumours *in vivo*. Investigations of the clinical application of this technique are planned, jointly with the University Department of Radiology, in the coming year.

Drug Discovery and Development

Our resources in imaging and genomics will combine with the Mouse Hospital (led by David Tuveson and further developed by a three-way collaboration with the Netherlands Cancer Institute and the

Wellcome Trust Sanger Institute), and with the Early Clinical Trials Programme (led by Duncan Jodrell) to create a strong programme in drug development. We aim to build collaboration with pharma to investigate promising compounds in areas in which we have biological expertise. The recent appointment of Shankar Balasubramanian to a senior group leader position shared with the Department of Chemistry will strengthen this programme and also nucleate research within CRI in chemical biology, both for drug discovery and for the development of new tools such as imaging reporters. Through the new Cancer Research UK Cambridge Cancer Centre we will consolidate our collaborations with Ashok Venkitaraman (Hutchison/MRC Research Centre), Chris Abell (Department of Chemistry) and Tom Blundell (Department of Biochemistry) and the Cambridge Molecular Therapeutics Programme, in academic programmes of drug discovery. Initiatives under development within the CRI include one based around miRNA as a therapeutic target in breast cancer, between Carlos Caldas, Simon Tavaré, Shankar Balasubramanian and Eric Miska (Wellcome Trust/Cancer Research UK Gurdon Institute).

The practical application of genomics in cancer management, matching the treatment to the individual cancer, is also a major theme, especially in breast cancer (Caldas laboratory). A major international collaboration involving samples from over 2,000 cases of breast cancer with at least five years follow-up (METABRIC) will report next year and is expected to provide definitive information to relate genomic features to clinical outcome.

Early Diagnosis, Screening and Prevention

Several strong programmes exist in this area within Cambridge, and these will be brought more closely together within the new Cambridge Cancer Centre. In the medium term, we will aim to bring together CRI's expertise in epithelial cell biology, mouse modelling, genomics and imaging with the expertise in genetic epidemiology and public health, and the access to populations, based within the Departments of Oncology and Public Health at the Strangeways Research Laboratory. Our goal will be to assemble cohorts of individuals at increased risk for studies of early detection and intervention. A programme in early detection of Barrett's oesophagus led by Rebecca Fitzgerald (Hutchison/MRC Research Centre) is already well established, and we are developing plans for a similar programme in lung cancer based on work done by John Potter during his recent sabbatical at the CRI. David Neal (prostate) and Bruce Ponder (breast) continue to work with Doug Easton and Paul Pharoah (Strangeways Research Laboratory) on the identification of loci for predisposition to the common cancers, and the potential application of this knowledge to programmes of screening and prevention.

Future Developments

The CRI is in its second year. Our immediate tasks are to consolidate our programmes and further build the resources within the hospital and the Anglian region for the conduct of clinical research. We will continue to focus on two broad areas. The first is drug development, in particular the determinants of response and resistance in individual cancers, and evaluating the application of this knowledge in routine clinical practice. The second is the potential for detection and prevention based on high risk groups. The first step here is the practical definition and assembly of appropriate cohorts, which we will next explore in lung cancer.

Bruce Ponder