A BREADTH OF SCIENCE

UKCMRI will study the basic biology that underlies human health and disease. The size of the institute will enable it to take a broad approach to biology, and one that allows all levels of analysis, from molecule to the whole organism.

Progress in biomedical research is rapid, so UKCMRI's research programme will not be defined in detail until closer to its opening in 2015. Nevertheless, the research being carried out in the founder institutes, together with existing medical priorities and emerging scientific opportunities, means that some general comments can be made even at this early stage.

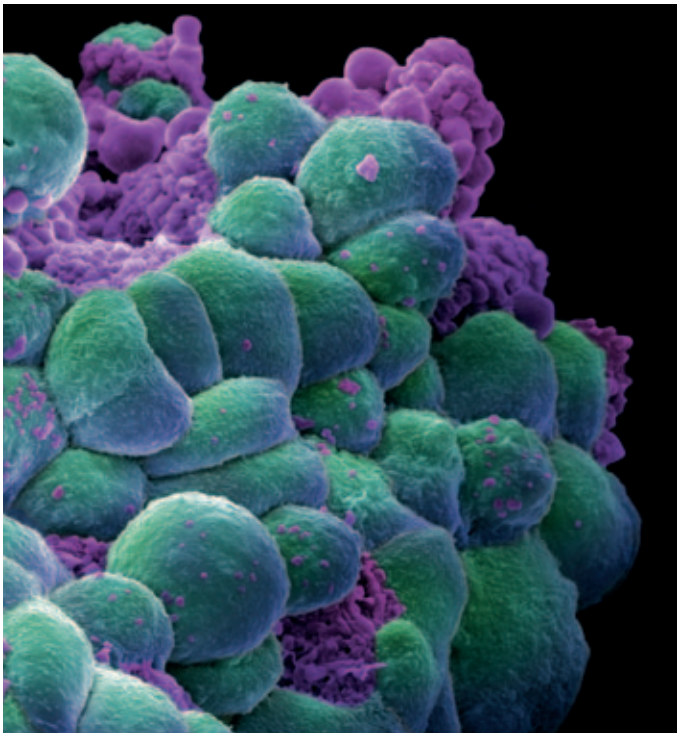
The medical drive will reflect burdens of disease in the UK and throughout the world. Cancer will naturally be a strong focus. So too will be circulatory conditions such as heart disease and stroke – with cancer, the UK's biggest killers – as well as infections and conditions linked to an overactive immune system. Diseases of the nervous system, particularly those of later life, are likely to figure strongly. Less common disorders may also be studied, as they often generate insights of more general importance.

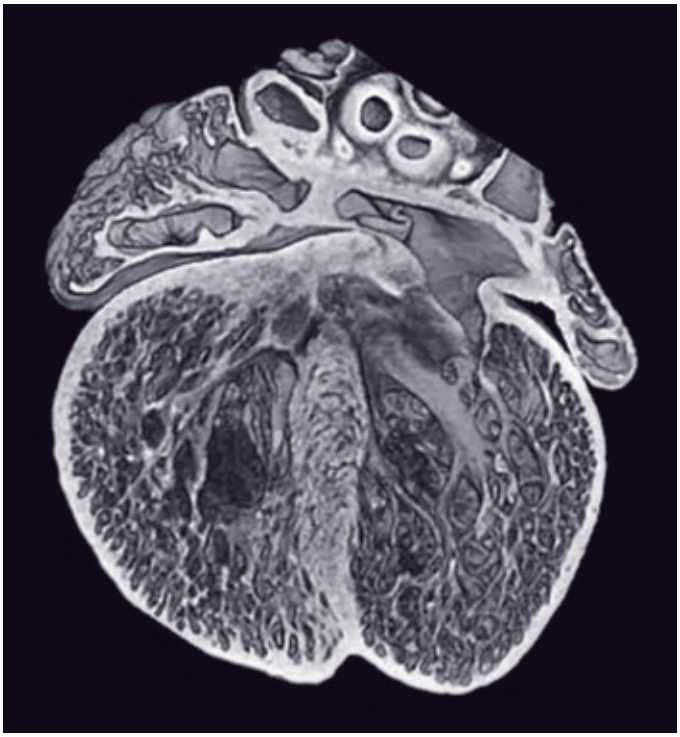
SCIENTIFIC OPPORTUNITIES

While medical needs provide the ultimate driver of research, UKCMRI's principal aim will be to generate new insights and knowledge about the biological mechanisms controlling cell, tissue and body function. The emphasis will be on integrative, systems-led approaches to unravel the interacting networks of genes, molecules and cells underpinning living processes. With this knowledge comes the potential to manipulate cellular processes to tackle the root causes of disease. UKCMRI's scientific focus will include:

Genetics and the genome: Sequencing of the human genome and those of model organisms such as the mouse have transformed biomedical research. The search for genes affecting human disease has borne rich fruit and the focus now is on identifying their physiological functions, finding ways in which their activity might be modified for therapeutic ends, and understanding the impact of variation in these genes on health.

IMAGE
Working on uncharacterised essential cell cycle genes in fission yeast *Schizosaccharomyces pombe* at LRI.





Cell biology: Most diseases arise from the altered behaviour of cells and how they interact with one another, cancer being the most obvious example. Great strides are being made in understanding the complex intracellular networks that control cell behaviour, including division and migratory properties, and how these are influenced by external signals.

Stem cells, developmental biology and regenerative medicine: Progress is being made in understanding how stem cells generate a constant supply of new cells and how the fate of these cells is controlled during development and in later life. This raises the exciting possibility of generating new cells to replace damaged tissue, feeding into the emerging field of regenerative medicine.

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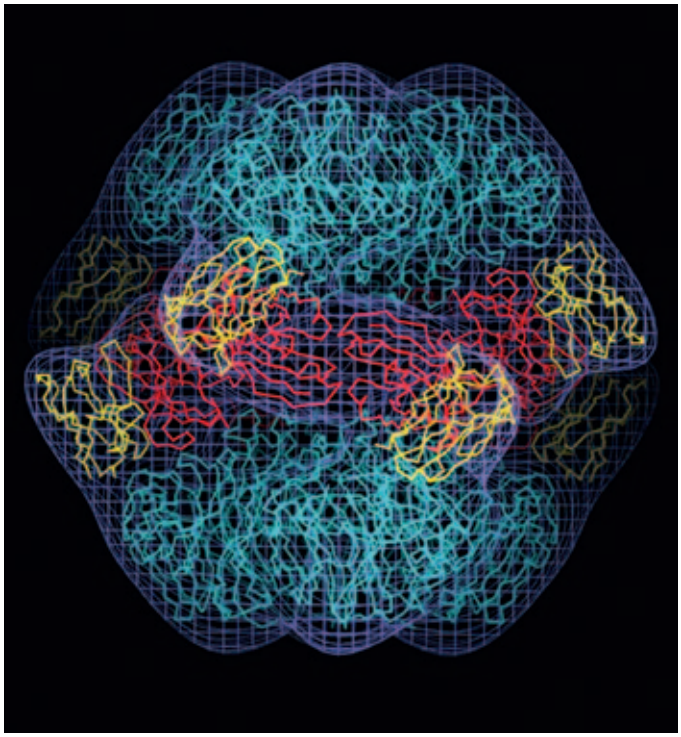
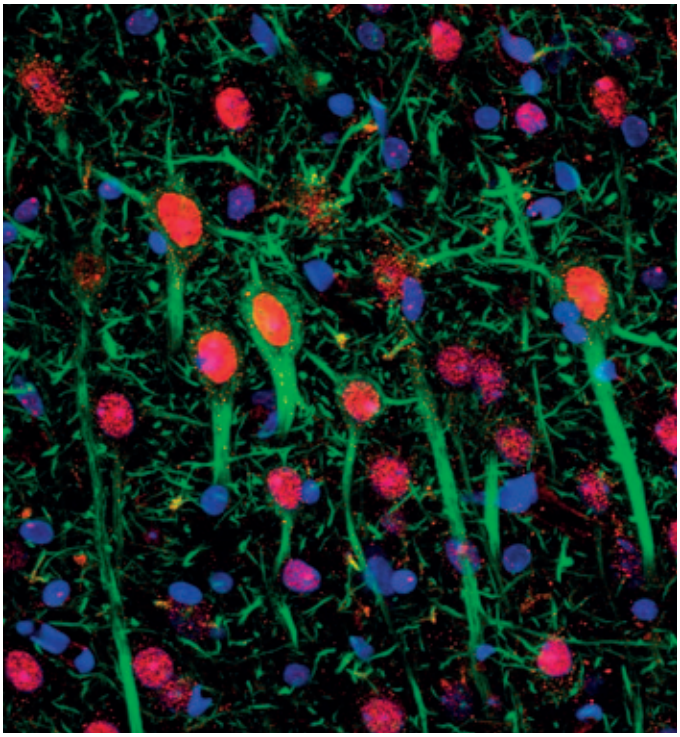
Organ function and whole-animal physiology: While cells are the fundamental units of life, biological functions depend on their coordinated interactions in tissues and organs, in response to the needs of the whole organism. These interactions can be studied in model organisms such as the mouse, but UKCMRI will also explore the use of human tissue and tissue derived from induced pluripotent stem cells.

Infections and the immune system: Many pathogens remain difficult to tackle – including highly variable viruses, antibiotic-resistant bacteria and the evasive malaria parasite. Moreover, the immune system that defends the body is also the cause of some diseases, from allergies to autoimmune conditions.

Neurons and the nervous system: A breakdown in neuronal function is characteristic of many of the most challenging diseases, from neurodegenerative conditions such as Alzheimer's disease and motor neuron disease to behavioural disorders such as schizophrenia, depression and autism. These conditions remain poorly understood, hindering the development of new treatments.

IMAGES
Top left: Breast cancer cells.
Top right: 3D modelling of early mouse heart development.





TECHNOLOGIES AS FACILITATORS
Key to UKCMRI's success will be the development and rapid adoption of innovative new technologies. It is too early to make firm predictions, but some likely applications can be envisaged:

Model organisms: The ability to engineer precise genetic changes into well-characterised models is generating a wealth of data on the functions of molecules and cells in the living body. Particularly exciting is the growing ability to explore aspects of human biology, such as immune system function, in animal models.

Stem cell manipulation: Stem cell biology is a particularly dynamic area of biomedical science. Reprogramming of adult cells to create induced pluripotent stem cells is generating a limitless supply of cells for study, including cell lines derived from patients with particular medical conditions.

Imaging: The ability to follow biological processes continuously, in real time, is transforming our understanding of living systems. The interdisciplinary nature of UKCMRI will allow chemistry, computing, physics and engineering input into the development of imaging technologies, to provide unprecedented insights into biology.

Chemical biology: As well as genetic manipulation, chemical probes can be used to interfere with biochemical pathways, to assess their role in biological processes. UKCMRI's interdisciplinary links will allow increasingly sophisticated probes to be developed, thereby expediting the development of new drugs.

Systems biology and mathematical modelling: While 'wet' biology will underlie much of UKCMRI research, computer-based approaches will draw upon advances in systems biology and mathematical modelling.

Synthetic biology: The application of engineering principles is opening up increasingly sophisticated forms of genetic engineering, in which different cellular components can be put together in precise combinations to build biological systems with specified and desirable characteristics.

IMAGES
Top left: Structure of an influenza neuraminidase-diabody complex.
Top right: Neuropeptide receptors in the brain.

WHERE PEOPLE DRIVE INNOVATION

UKCMRI will be founded on the principle that people come up with the ideas, make the conceptual leaps and have the creative insight to advance medical science. UKCMRI will provide the framework to enable outstanding researchers to develop themselves and their research for extended periods before moving on to leadership positions in the UK or elsewhere.

UKCMRI will be a science-led institution, recognising that science is a human endeavour that relies upon the creativity and effort of individuals. It will be set up to empower its researchers, enabling them to focus on research, develop their skills and follow ideas for extended periods, and thereby fulfil their potential while contributing to the success of the institute.

UKCMRI will select from a global pool of scientific talent, as well as the best from the UK. It will recruit only the most able researchers with the potential to make significant contributions in the future.

Its researchers will be given long-term support, generous resources, access to core facilities, unrivalled training opportunities and mentoring support from senior colleagues. With this backing, they will be able to tackle ambitious, long-term projects that will generate significant advances in knowledge.

Most importantly, UKCMRI will be brave and imaginative in its appointments, recognising that the unusual candidate with the unorthodox ideas may be the one who has most original insight and the greatest likelihood of success.

Training opportunities

Researchers at UKCMRI will be in an environment of constant professional development. Formal training will be delivered through a four-year PhD programme and clinical PhD programme, along the lines of those pioneered by the Wellcome Trust. These will enable young scientists to spend time in a range of UKCMRI labs during their training before choosing a final lab and supervisor for their PhD project.

Scientists without a clinical background will undergo training to familiarise them with the key aspects of human biology and pathology, to encourage greater focus on the translatability of their research.

Researchers will also have an opportunity to learn from visiting fellows and industry scientists who spend short periods at UKCMRI to

IMAGES
Left: Exploring gene expression in cells of the immune system at NIMR.