The UCL Cancer Institute is now fully established with 50 scientific group leads, 32 clinical scientists, 50 honorary clinical consultants and a total staff FTE of 317.

During the past 3 years our total research grant income has increased by 40% to nearly £50 million.

During the next year a number of exciting developments will affect cancer research at UCL: the completion of the £100 million UCH Macmillan Cancer Centre opposite our main research hub in Huntley Street; the recruitment of a radiation oncology lead to develop the proton treatment facility with UCLH and the expansion of molecular pathology research, supporting personalised cancer clinical trials and care.

I hope that this newsletter will give you a sense of the exciting new developments.

Chris Boshoff
Director, UCL Cancer Institute

Spirogen News

Professor John Hartley is one of the founder scientists of Spirogen Ltd (www.spirogen.com). This company is pioneering the discovery and development of a unique class of low molecular weight sequence specific DNA-interactive drugs. Spirogen’s proprietary chemistry-based platform technology, based on the modification of members of a group of natural antibiotics called pyrrolobenzodiazepines (PBDs), forms the basis of a research effort that began over a decade ago to develop novel therapeutics with potential application in a number of markets. Spirogen’s lead oncology drug SG2000 (SJG-136) has completed Phase I studies in the USA (through the NCI) and Europe (through Cancer Research UK). A Phase II study in cisplatin refractory ovarian cancer is underway in the USA, and a haematological Phase II study is planned in Europe for early 2011.

In January, Spirogen announced a multi-year research collaboration and license agreement with Genentech, a member of the Roche Group. The two companies will collaborate on the discovery and development of antibody drug conjugates (ADCs) as potential anticancer agents, using Spirogen’s proprietary PBD drugs and associated linker technology. Under the terms of the agreement, Spirogen will be primarily responsible for synthesising and manufacturing drug reagents, while Genentech will use Spirogen’s drug reagents to generate ADCs and evaluate their potential therapeutic utility.
Hilary Calvert part of winning team

A team led by Hilary Calvert, before he was recruited to the UCL Cancer Institute, won this year’s NCRN Translational Cancer Research Prize.

The story of the Newcastle PARP inhibitor study team’s achievement begins in 1980 with an initial scientific observation by Dr Barbara Durkacz that there was a poly-ADP ribosylation reaction, catalysed by a protein called PARP, associated with DNA damage. If this reaction was blocked, it increased the killing effect of the DNA damage on cancer cells.

In 1990, the newly formed Newcastle drug discovery team undertook its first project - the development of a PARP inhibitor. The team conducted the first ever clinical trial of a PARP inhibitor in cancer patients in 2003. Over the subsequent years, the team has made significant contributions to compound identification, preclinical testing, design of clinical trials and the subsequent clinical development of multiple compounds in this exciting new class of drugs. Today, PARP inhibitors are a major new class of therapeutic’s for cancer.

The 2010 European Society for Medical Oncology (ESMO) Lifetime Achievement Award was also presented to Professor Hilary Calvert. The 2010 award to Prof Calvert was given in recognition for his seminal work on the introduction of carboplatin as a major anti-cancer agent and the development of a dosing formula based on its pharmacokinetics and its subsequent clinical use in ovarian cancer.

Reviving ‘tired’ immune cells gives blood cancer treatment a boost

Cancer Institute researchers, led by Dr. Ronjon Chakraverty, a bone marrow transplant physician at the Royal Free Hospital, have discovered a way of improving the effectiveness of bone marrow transplantation, a key treatment for many patients with blood cancer, by providing an extra ‘boost’ to the immune system.

Each year in the UK, over 1000 patients receive blood or bone marrow transplants from a healthy donor as treatment for leukaemia or lymphoma. This therapy not only provides the patient with a new bone marrow but also a new immune system. This means that immune cells from the donor can attack the blood cancer, an effect called the ‘graft-versus-leukaemia’ effect. Killing residual blood cancer cells is a critical part of the transplant process and is almost certainly necessary to achieve a cure.

Our researchers, together with collaborators at Harvard and Columbia Universities in the US, examined why blood cancers come back in some patients who receive a transplant. In a study funded by the charity Leukaemia & Lymphoma Research, and published in the prestigious Journal of Clinical Investigation (2010), the scientists showed that cancer-targeting immune cells can become ‘worn out’ and stop working. This means that the graft-versus-leukaemia effect may be lost. Importantly, a new treatment can revive the ‘tired’ immune cells and get them to start working again.

By using clinically relevant mouse models of bone marrow transplantation, the researchers found that normal tissues outside the bone marrow were responsible for causing ‘exhaustion’ of the immune cells. This occurred because the normal cells have a molecule on their surface that eventually switches off the immune cells. They went on to show that treatment with an antibody could block this molecule and re-invigorate the immune system. Importantly, this could be done safely without any harmful side effects.

Setting the new standard-of-care for a rare cancer

Finding new treatments for rare and hard to treat cancers is fundamental to cancer research. Clinical trials are one of the best ways to test out new treatments and they do so by comparing the potentially better option with the standard treatment already available.

A team led by Dr John Bridgewater, have carried out the largest ever phase III clinical trial for advanced gall bladder and bile duct cancer which can’t be operated on. Until now there has been no standard treatment for this group of cancer patients. The researchers set out to test whether patients with this type of cancer who were given both the chemotherapy drugs gemcitabine and cisplatin responded to treatment better than those patients who just received gemcitabine.

Over 400 patients in the UK took part. They were split in to two groups, one group was given a combination of the two drugs and the other had just gemcitabine. The treatment lasted for 24 weeks. The combined drug treatment improved survival by a third. And the patients having this treatment lived on average over three months longer.

What’s exciting about the results is that they have changed how treatment is given to patients in hospitals across the world. The study results were published in the New England Journal of Medicine (2010).
**UCL Cancer Research UK Centre**

The University College London (UCL) Cancer Research UK Centre – was the first Centre to be opened in London – it aims to foster world class research into the causes of cancer, using this knowledge to discover and develop new cancer treatments.

The UCL Cancer Research UK Centre is a partnership between UCL, UCL Hospital NHS Foundation Trust, Great Ormond Street Hospital, the Royal Free Hospital, Moorfields Eye Hospital, the London School of Pharmacy and Cancer Research UK.

Research at the Centre includes drug discovery and the development of new treatments such as gene therapy. Scientists will focus on research into the biology and treatment of head and neck, ovarian, lung and blood cancers, as well as sarcomas and brain tumours, which will help to provide more effective treatments for these diseases in the future. Researchers at the Centre are also studying the effect of lifestyle factors - such as smoking and obesity - on cancer risk.

Cancer Research UK already funds an extensive programme of research at UCL and its affiliated Institutes, but the launch of the new Centre will see the charity increase its contribution by almost £1 million a year to research at this Centre, including the funding of clinical and non-clinical PhD studentships. Professor David Linch leads the UCL Cancer Research UK Centre.

For more information, see:
http://centres.cancerresearchuk.org/find-a-centre/london/ucl/

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**UCH Macmillan Cancer Centre**

University College Hospital (UCH) plans to open its new Cancer Centre in Spring 2012. Working closely with the UCL Cancer Institute, UCLH is implementing a programme of change and investment to make UCL and UCLH one of the top Cancer Centres in Europe. Based in Huntley Street, opposite (and connected to) the UCL Cancer Institute, this purpose-built facility cost in the region of £100million to build. Macmillan Cancer Support has invested £10million and The UCLH Charitable Foundation a further £30million towards the cost of this Centre. This ambulatory Cancer Centre will be the first of its kind in the NHS and redefines the way patients are treated, using the best diagnostic and treatment techniques to improve survival rates.

With the expertise of the award winning architects Hopkins, the design will be a patient-focused and environmentally friendly building that will offer not just treatment for cancer, but practical and emotional support for the issues that may arise from living with cancer. The Centre will also feature a roof garden. Macmillan will provide a Wellbeing Centre, providing information and support, including advice around coping with the personal and financial impact of cancer. The Wellbeing Centre will also offer access to complementary therapies.

http://www.uclh.nhs.uk/OurServices/OurHospitals/CC/Pages/Home.aspx
**UCL Cancer Institute and The Sarah Cannon Research Institute**

UCL Cancer Institute and The Sarah Cannon Research Institute (SCRI) (operated by Hospital Corporation of America®, HCA) have signed an agreement to develop a partnership between their new early phase clinical trials unit at 93 Harley Street and the UCL/UCLH Cancer Clinical Trials Facility, bringing together the strengths of both organisations.

**This collaboration will allow:**

- Expansion of current early phase clinical trials at the UCL/UCLH Cancer Research Facility (CRF)
- Access to the Phase I/II clinical trials portfolio of SCRI
- Sharing of expertise to develop and implement early phase clinical trials
- Access by SCRI to the research infrastructure of the UCL Cancer Institute
- Access by UCL/UCLH staff to training opportunities, and staff development at SCRI
- UCL, UCLH and SCRI have complementary resources which can enhance the ability, quality and cost-effectiveness of all three in early phase cancer clinical trials
- Access by NHS patients to drugs only available at SCRI Trials Facility
- Access by private patients to the UCL/UCLH CRF and associated clinical studies

SCRI is a US-based strategic research organisation focusing on advancing therapies and accelerating drug development. It is an internationally known organisation, conducting early phase clinical trials, and one of the foremost such centres in the world. SCRI is amongst the top 5 US centres for recruitment to early phase cancer trials, and is known for their ability to deliver these studies in a timely manner, and to the highest standards. It is one of the largest cancer clinical research programmes in the US, conducting community-based clinical trials, mainly in oncology, but also in cardiology, gastroenterology and other therapeutic areas.

We have recruited Dr Tobi Arkenau to lead and develop this partnership. Tobi was employed as the Director of the Clinical Trials Network and Team leader of the clinical oncology drug development group at the University of New South Wales Prince of Wales Medical School, Sydney, Australia.

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**Cancer Trials in Central and North London**

The North London Cancer Research Network (NLCRN) had a successful year in 2009/10, where national targets were met by recruiting 15.4% of patients to an NIHR approved study (8% to a Randomised Controlled Trial). The NLCRN has built on this achievement and anticipates in 2010/11 increasing overall recruitment from 1082 by approximately a further 100 subjects. For 2010/11 it is anticipated that University College Hospital and the Royal Free Hospital will contribute 545 and 185 patients respectively, but all other Trusts within the Network are actively contributing as well.

NLCRN clinicians affiliated with the UCL Cancer Institute were the Chief Investigators for 21 of 113 trials open across NLCRN sites in 2010/11. Much of the success can be attributed to further investment in research infrastructure from the Comprehensive Local Research Networks (CLRN) and continuing to develop this relationship with NCLRN is a key component of the NLCRN work programme. Other on-going work includes improving the local governance for cancer studies, working with Trust R&D Departments to improve approval times and promoting NIHR Industry studies. These work streams have benefited by the appointment of a dedicated QA Manager, as well as a newly appointed Industry Manager.

For further information on the NLCRN please contact James Lyddiard email: james.lyddiad@cancer.ucl.ac.uk
**UCL Cancer Institute and The London Clinic Biobank**

The UCL Cancer Institute and The London Clinic are working together to establish a joint tissue bank to aid cancer research and provide scientists with material otherwise not available.

Cancer patients referred to The London Clinic present types of tumours, which are underrepresented at our affiliated Hospitals. This initiative would enhance our cancer Biobank collections in certain tumour types, including colon, prostate and breast cancer.

The tissue Biobank’s aim will be to facilitate discoveries by making well-characterised human material available to the research community aimed at discovering the causes and better treatment of cancer. Research from tissues obtained form this Biobank could help in early diagnosis and improved treatment of cancer.

The primary objective will be to establish a tissue bank of tumour and normal tissues from patients being operated on at The London Clinic. Secondary objectives are to assess the types and frequencies of genetic changes (somatic changes) in specific cancers; to correlate these tumour-specific changes, to germline genetic variations in normal tissues (e.g. blood samples) and to investigate the relationship between somatic and germline genetic variations, clinical characteristics and outcome.

The London Clinic is funding 2 staff to manage the service, equipment to support the storage of the samples, facility and running costs totalling £720K over 5 years.

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**The Cancer Institute Research Trust**

The Cancer Institute Research Trust (CIRT) is the official charity of the Cancer Institute. They have recently appointed a new chairperson, Mr Richard Sutton-Mattocks. Richard was previously a senior partner at the law firm Clifford Chance LLP.

The CIRT recently committed £2.5 million towards the Cancer Clinical Research Facility for early phase clinical trials. They have also committed £1.4 million to fund a research clinical single photon emission computed tomography (SPECT CT) scanner.

The CIRT manages the ‘Debbie Fund for Cervical Cancer’, this fund was set up following the death of Debbie Phillips in February 2010 to cervical cancer. The fund has so far raised over £472K and they will be holding a fund raising Ball later this year. For further information and how you can support this fund please visit: [http://www.debbiefund.org/](http://www.debbiefund.org/)

Each year the Trust enters a number of runners into the London Marathon to raise funds for the charity, many of these have been staff or students at UCL or UCLH. For further information on how you can support the CIRT please contact: charity@cancer.ucl.ac.uk
Professor Paolo Salomoni

Professor Paolo Salomoni leads the Samantha Dickson Brain Cancer Unit, the first research centre fully dedicated to brain cancer research in the UK, funded by the Samantha Dickson Brain Tumour Trust (SDBTT). High-grade brain tumours affect patients of any age, and represent one of the leading cancer-related deaths in both the paediatric and adult populations. Prognosis is in most cases very poor, as a result of tumour aggressiveness, limited therapeutic window and resistance to therapy.

The Group studies mechanisms underlying tumour initiation and resistance to therapy, with a particular focus on neural stem cells and brain tumour-initiating cells. His recent work has shown that a growth suppressor originally implicated in leukaemia, called promyelocytic leukemia protein, plays a key role in regulating cell fate in neural stem cells. Furthermore, his laboratory has revealed a role for the intracellular degradation pathway autophagy in the promotion of survival in tumour-initiating cells. This latter study has led to a Phase II cancer clinical trial which started in Spring 2010.

Paolo Salomoni recently co-organised a conference on glioma research (Glioma Club 2010) for the London/Cambridge/Oxford area, sponsored by Cancer Research UK and the SDBTT.

http://www.ucl.ac.uk/cancer/research-groups/samantha-dickson-brain-cancer-unit/index.htm

Professor Hiro Yamano

Professor Hiro Yamano joined UCL in January 2010. Previously he was a senior group leader at the Marie Curie Research Institute (Oxted, Surrey). He did his post doctoral fellowship with Nobel Prize winner, Sir Tim Hunt. Professor Yamano’s Group studies the basic principles of how cells divide and proliferate. Uncontrolled cell division is a key characteristic of cancer. In particular, the Group studies how the cell cycle and cell differentiation are controlled by ubiquitin-mediated proteolysis. Many key proteins have to be destroyed at specific times in the cell cycle. The process needs to be precisely regulated. They are looking into how this selective destruction of particular proteins occurs. At the moment, their focus is on an ubiquitin ligase called the anaphase-promoting complex/cyclosome (APC/C), which plays an essential role in dividing and non-dividing cells.

In the late 20th century after the central dogma of molecular biology (DNA->RNA->Protein) was articulated, scientists rushed to study protein synthesis, not proteolysis, because it was not considered a key element of the central dogma. However, synthesized proteins have to be degraded at the correct time and place. Proteins in our body are in a dynamic state. Proteolysis has a very important role in regeneration of cells and tissues, which constitute the healthy body. That is why the study of proteolysis is now so competitive.

“The UCL Cancer institute has various investigators studying fundamental aspects of normal versus cancer cells. Their focus, resources, systems and techniques would greatly benefit my research and interacting with these researchers will stimulate my research program. It’s a great environment, no doubt we will have great outcomes from here.” Hiro Yamano.

http://www.ucl.ac.uk/cancer/research-groups/cell-cycle-control/index.html
The UCL Cancer Institute has had a very successful start and has recruited many new group leaders with their own fellowships as well as attracting some distinguished established scientists to join us.

Barbara Jennings is a new group leader supported by an MRC Career Development Award. She was also awarded a Wellcome Trust Project Grant. The goal of the Jennings laboratory is to understand the molecular mechanisms underlying transcriptional regulation in response to contextual cues during cell fate determination and differentiation. Her research is centred on repression of gene expression during development and central questions are: Which proteins are involved? How do these proteins interact with each other to control the activity of the RNA polymerase complex? Her group is currently focussing on two models of gene repression in the model organism Drosophila melanogaster; repression via transcriptional pausing, and repression mediated by Groucho family proteins.

Alex Hergovich is a new Wellcome Trust funded group leader. His laboratory studies Hippo signaling, in particular dissecting the molecular mechanisms and functions of the NDR/LATS family of kinases. During cancer development the coordination of cell death and proliferation is misbalanced, which combined with genetic instability, can result in aggressive tumour growth. They are interested in understanding how it is packaged. Errors in where and when telomeres and telomerase activity are expressed can result in chromosome instability. Hergovich's group is interested in how telomeres and telomerase activity affect chromosome organization, and employ engineered yeast models and computational techniques to study chromatin localization during development, at both specific loci and genome-wide to understand how gene expression, and modifications are controlled. Gene expression is controlled through modifications to our genetic material that, while leaving the underlying sequence information unchanged, affects how it is packaged. Errors in where these modifications occur throughout the genome play an important contributing role in the development of diseases such as cancer.

Sue Hadjur, a newly appointed MRC Career Development Fellow, studies the molecular regulation of cohesins in pluripotent stem cells, including ES cells. Her laboratory will use molecular and computational techniques to study chromatin topology and cohesin localization during development, at both specific loci and genome-wide to gain insight into the role of cohesins in gene regulation. Overall, her group will investigate a role for cohesins in chromatin folding in mammalian cells and the effect on gene expression, and employ genome-wide cohesin mapping in ES cells and differentiated progeny. Sue was also recently successful in obtaining an additional MRC Project grant.

Steen Ooi was awarded a BBSRC David Philips Fellowship. His group uses genetic, cell and molecular biological approaches to understand how gene expression and modifications are controlled. Gene expression is controlled through modifications to our genetic material that, while leaving the underlying sequence information unchanged, affects how it is packaged. Errors in where these modifications occur throughout the genome play an important contributing role in the development of diseases such as cancer.

Kazunori Tomita is a newly appointed CR-UK Career Development Fellow. His group is interested in how telomeres utilize the DNA damage response and cell cycling factors to maintain telomeres and participate in cell cycle regulation. Elucidating systems and functions of telomeres is essential for our understanding of cancer cell immortality as well as cellular ageing. Employing a fission yeast model system, his group aims to uncover mechanisms at a molecular level. They hope this will lead to the development of advanced cancer treatments and techniques to aid with diagnosis.

Sergio Quezada a CR-UK Career Development Fellow has joined us from the Memorial Sloan Kettering Cancer Center, New York. His group investigates the cytolytic activity of the tumour-reactive CD4+ T cells he recently described. CD4+ T cells are well known for their helper and regulatory functions, whereas clear demonstration of in vivo cytotoxicity has been more elusive. The newly described acquisition of cytolytic activity by tumour reactive CD4+ cells raises numerous questions regarding CD4+ T cell function and plasticity. In this regard Dr. Quezada’s group will study the cellular and molecular basis for acquisition of cytotoxic activity by CD4+ T cells in both mouse models of cancer as well as in human lymphocytes. This is an extremely novel and exciting field in tumour immunology, that could lead to new immunotherapeutic avenues to treat cancer.

Tariq Enver has joined the Institute as ‘Professor of Stem Cell Biology’. He previously led a research team at the MRC Molecular Haematology Unit at Oxford University. We are currently in the process of transferring his team to the Cancer Institute. Professor Enver is internationally known for his work on haematopoietic and leukaemic stem cells. His team has made a series of important conceptual and practical advances in the study of blood stem cells and leukaemias. His studies of normal blood stem cells have established the principles of how stem cells are configured in terms of their genetic circuitry. These studies have already identified new genes that may be used to expand stem cells present in cord blood – a procedure that would significantly broaden the use of cord blood stem cells for transplantation of adults with leukaemia. Professor Enver is currently applying the methodologies of the emerging interdisciplinary field of systems biology to develop these studies which should further enhance our ability to devise rational strategies to control stem cells and get them to behave in the way we would like them to both in the laboratory and in the patient.
**Selected Funding Awarded**

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<tr>
<th>Sponsor</th>
<th>Title</th>
<th>Amount</th>
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<td>NHS Blood Transplant</td>
<td>Support for the position of Director of CLL Research</td>
<td>£384,000</td>
<td>Dr Amit Nathwani</td>
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<td>Cancer Research UK</td>
<td>UCL CRUK Centre Clinical Training Account</td>
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<td>Cancer Research UK</td>
<td>UCL CRUK Centre Non-clinical Training Account</td>
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<td>Astra Zeneca (UK) Ltd</td>
<td>A randomised phase II study of Cediranib vs placebo</td>
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<td>Mologic</td>
<td>Antibody directed enzyme prodrug therapy systems</td>
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<td>Children with Leukaemia</td>
<td>Infrastructure support award</td>
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<td>Leukaemia &amp; Lymphoma Research</td>
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<td>MRC</td>
<td>Preclinical evaluation of rAAV encoding a novel highly expressed Factor VIII molecule for haemophilia A gene therapy</td>
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<td>MRC</td>
<td>MRC industry collaboration award</td>
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<td>Dr Suzana Hadjur</td>
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<td>Cancer Research UK</td>
<td>GEDDIS (Gemcitabine and Docetaxel Versus Doxorubicin in Sarcoma)</td>
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<td>Dr Jeremy Whelan</td>
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<td>European Union FP7</td>
<td>HEROIC - High Throughput Epigenetic Regulatory Organisation in Chromatin</td>
<td>£547,700</td>
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<td>MRC</td>
<td>Lentivirally Modified Stem cells to treat Duchenne Muscular Dystrophy</td>
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<td>Prof Olivier Danos</td>
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<td>Marie Curie Cancer Care</td>
<td>Transitional programme grant</td>
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<td>Prof Hiro Yamano</td>
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<td>European Union FP7</td>
<td>IMAGINT (Imaging &amp; Molecular Interaction Mapping in Breast Cancer)</td>
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<td>NIHR via NHS Blood Transplant</td>
<td>Molecular and Tissue Engineering: Programme A</td>
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<td>European Union FP7</td>
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<td>MRC</td>
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<td>Bayer PLC</td>
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<td>Wolfson Foundation</td>
<td>UCL Cancer Institute capital equipment</td>
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<td>Cancer Research UK</td>
<td>Identification of molecular link between telomeres and telomerase and investigation of the mechanisms underlying telomerase recruitment and activation</td>
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<td>Leukaemia &amp; Lymphoma Research</td>
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<td>Welcome Trust</td>
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<td>Investigating a Role for the Cohesin Complex in Chromatin Looping, Gene regulation and development</td>
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<td>Kay Kendall Leukaemia Fund</td>
<td>Role of MicroRNAs in T-Cell Acute Lymphoblastic Leukaemia and their regulation by TAL1 and NOTCH</td>
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<td>Department of Health</td>
<td>Gene Therapy for Haemophilia B using AAV8 pseudotyped vectors</td>
<td>£300,000</td>
<td>Dr Amit Nathwani</td>
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**EVENTS & FUNDING**

**The UCL Cancer Institute is hosting an international symposium** highlighting the function and regulation of microRNAs and other non-coding RNAs during cancer development and progression.

**12th April 2011**
University of London Senate House

**Speakers**
Carlo Croce (US), Antonio Giraldez (US), Eran Hornstein (Israel), Gyorgy Huvtagner (UK), Richard Jenner (UK), Sakari Kauppinen (Denmark), Kevin Struhl (US), Martin Turner (UK), Mihaela Zavolan (Switzerland), and Pier Paolo Pandolfi (US)

For more information and to register and submit an abstract please visit: http://www.ucl.ac.uk/cancer/noncodingRNA2011/

**The UCL Cancer Institute visit to Yale University**
31st May - 1st June

12 scientists from the UCL Cancer Institute will visit Yale University as part of the UCL-Yale partnership. Cancer clinician scientists and scientists are co-developing research programmes between our two universities.

This visit follows on from the successful visit from Yale cancer researchers to UCL during 2010.

Dr Thomas Lynch is the Director of the Yale Cancer Centre.