

## London Research Institute

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### London Research Institute

Lincoln's Inn Fields and Clare Hall Laboratories  
Cancer Research UK  
PO BOX 123  
61 Lincoln's Inn Fields  
London  
WC2A 3PX  
United Kingdom

Telephone: +44 (0)20 7242 0200  
Email: [lrinfo@cancer.org.uk](mailto:lrinfo@cancer.org.uk)

Registered Charity Number: 1089464

Image source: Denise Sheer and Radost Vatcheva



### Takashi Toda

*Cell Regulation Group*

The mitotic spindle, which is formed only during mitosis, plays a pivotal role in equal partition of genetic materials and is, therefore, directly involved in genome stability. Any errors in forming this structure lead to chromosome segregation defects that result in the production of aneuploid progenies, a hallmark of many cancerous cells. We aim to understand the molecular pathways leading to mitotic bipolar spindles.

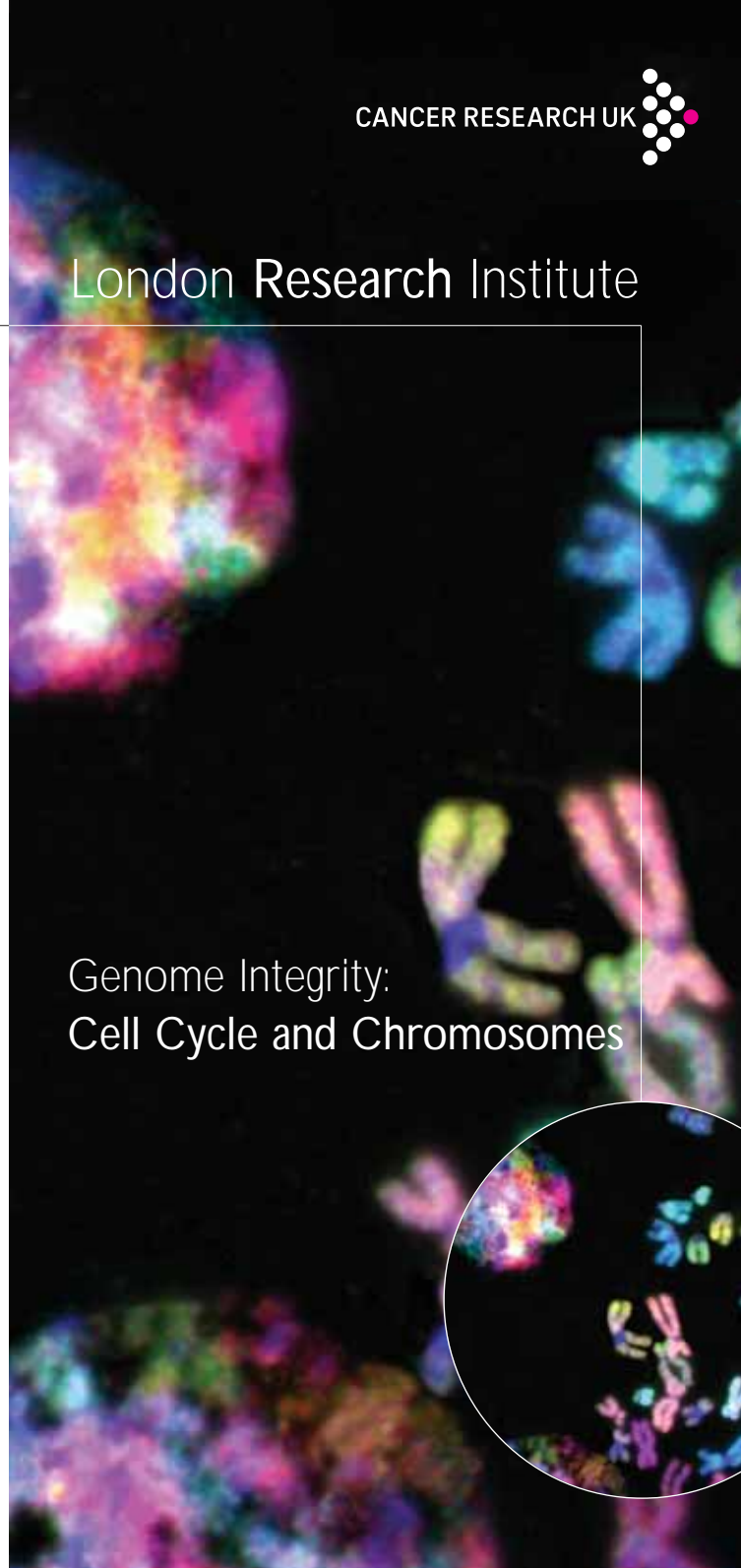


### Frank Uhlmann

*Chromosome Segregation Group*

The chromosomal 'cohesin' complex holds sister chromatids, the products of eukaryotic genome replication, together after their synthesis. This allows the mitotic spindle in metaphase to recognise pairs of replication products for segregation into opposite directions. Our studies use the budding yeast *Saccharomyces cerevisiae* as a model. Cohesin and separase also regulate chromosome segregation in higher eukaryotes, including man, making these studies important in a broad context.

Genome Integrity:  
Cell Cycle and Chromosomes



The Cancer Research UK London Research Institute has an international reputation for research into the basic biology of cancer. Themes of research are signal transduction (biology of tissues and organs, and molecular cell biology) and genome integrity (cell cycle and chromosomes, and DNA repair). Our group leaders who work on genome integrity, specifically the cell cycle and chromosomes, have outlined their laboratories' research below.

**Julia Promisel Cooper**

*Telomere Biology Group*

Telomeres have become a particular focus of research on tumourigenesis, which is associated with genomic instability and telomerase activation and ageing, which is accompanied by a gradual decline in telomere length. Our research focuses on understanding the components of telomeres, the mechanisms and spectrum of telomere function, and the events that follow telomere loss.



**Vincenzo Costanzo**

*Genomic Stability Group*

Genome stability is ensured by complex mechanisms that coordinate DNA replication, DNA repair and chromosome segregation. When these mechanisms fail, cells lose their identity and acquire features of cancer cells such as uncontrolled proliferation and invasiveness. We are developing systems based on the *Xenopus laevis* egg to study the biochemistry of the pathways involved in maintenance of genomic stability.



**John Diffley**

*Chromosome Replication Group*

In each cell cycle, eukaryotic cells must replicate vast amounts of genomic DNA distributed on multiple chromosomes. Mistakes in either DNA replication or chromosome segregation can result in loss or duplication of this genetic information. These events can play an important role in the genesis of cancer cells. We aim to understand the mechanisms of DNA replication in eukaryotic cells and how DNA replication is regulated at every level.



**Tim Hunt**

*Cell Cycle Control Group*

Various questions on cell cycle control preoccupy us. Which proteins need to be phosphorylated in order to enter S-phase or mitosis? How do different combinations of cyclins and CDK recognise their substrates? We are also interested in how particular cyclins are recognised for degradation, with such high specificity, at the right times in the cell cycle, and how their proteolysis is regulated.



**Paul Nurse and Jacky Hayles**

*Cell Cycle Group*

We aim to gain a thorough understanding of how the cell cycle is controlled and how cell division generates two spatially organised cells from the original single cell. Using the single celled eukaryote, *Schizosaccharomyces pombe* or fission yeast, we hope to establish the relevance of these controls for cancer.



**Gordon Peters**

*Molecular Oncology Group*

Senescence was originally described as a mechanism that limits the proliferative lifespan of primary cells in tissue culture, but is now recognised as a more general response to a variety of cellular stresses, including oncogenic mutations. We wish to increase our understanding of senescence as a mechanism of tumour suppression and an opportunity for therapeutic intervention.



**Martin Singleton**

*Macromolecular Structure and Function Group*

We aim to determine the three-dimensional structures of some of the multi-protein complexes that comprise the kinetochore. Particular areas of interest include the proteins involved in binding centromeric DNA and the complexes implicated in generating the spindle checkpoint signal at the kinetochore. Structural information combined with suitable functional studies should allow us to build up a model of kinetochore operation.



**Jesper Svejstrup**

*Mechanism of Gene Transcription Group*

RNA polymerase (RNAPII) transcribes all protein-encoding genes in eukaryotes and is the endpoint for a plethora of cell regulatory pathways. We aim to understand the basic mechanisms underlying transcription by RNAPII, in particular transcript elongation. We believe that a detailed insight into this process will allow us to understand the mechanisms underlying multiple human diseases.

