PRESS RELEASE

Singapore, 4 October 2002

OF YEAST, CANCER AND DEVELOPMENT

Singapore, 4 October 2002 – Temasek Life Sciences Laboratory (TLL) is pleased to announce the discovery of an important control mechanism functioning in mitosis by Dr Snezhana Oliferenko and Associate Professor Mohan Balasubramanian. Mitosis is a fundamental process of life, which distributes full sets of chromosomes from a parent to two daughter cells. The events during mitosis are tightly coordinated to ensure that the partitioning of the duplicated chromosomes into daughter cells occurs properly during cell division. Disruptions of such cell cycle controls have significant implications in development and disease. The newly discovered checkpoint ensures that the chromosomes are in the correct position before they can be segregated into daughter cells. These findings have been published in the October issue of *Nature Cell Biology*.

In organisms ranging from yeast to humans, duplicated chromosomes are segregated with stunning precision through the use of a specialized molecular machine, a microtubule-based mitotic spindle. Correct orientation of the mitotic spindle controls subsequent events that are crucial for developmental decisions and faithful chromosome segregation. Also, in order to prevent genetic damage, chromosomes should be segregated in the direction perpendicular to that of the physical division of the cell. Yet at the moment it is poorly understood how proper spindle orientation is achieved.

Studies by Drs Oliferenko and Balasubramanian suggest that the unicellular fission yeast *Schizosaccharomyces pombe* may be an excellent system to study this question. In this cylindrically shaped organism, chromosomes should be segregated along the long axis of the cell to preserve DNA during cell division. TLL scientists have identified a yeast mutant that is defective in forming asters, which are a certain type of microtubules. While this mutant is perfectly capable of assembling the functional mitotic spindle, it fails to orient it along the long axis of the cell. As a result, these mutant cells undergo a prolonged delay during early cell division, whilst attempting to orient their spindles. Having more time to do so allows them to keep an uneven chromosome segregation at bay and, ultimately, to survive. Thus, this time lag serves as a checkpoint, that delays progression through the cell cycle when spindles are not properly oriented. When the components of this checkpoint machinery are also damaged in mutant cells, they continue to divide without orienting their spindles. This defect results in chromosomal abnormalities and increased cell death.

This simple model system may allow us to glimpse into the workings of very complex organisms such as humans. Hopefully, understanding this control mechanism at the molecular level in yeast will allow us to expand our knowledge of the mechanisms involved in human development and diseases such as cancer, which in part results from improper chromosome segregation, as it happens in the mutants described by the TLL scientists.

The importance and potential of this work has been highlighted by Dr Dannel McCollum of the University of Massachusetts Medical Center in the commentary article in the “News and Views” section of the same issue of *Nature Cell Biology*.

This work, initiated at the Institute of Molecular Agrobiology, is currently being continued at Temasek Life Sciences Laboratory, which is affiliated to the National University of Singapore and Nanyang Technological University.

For media queries, please contact:

Shireen Lian
Assistant Manager (Corporate Services)
Temasek Life Sciences Laboratory
DID: (65) 6872 7010
Fax: (65) 6872 7012
Email: shireen@tll.org.sg