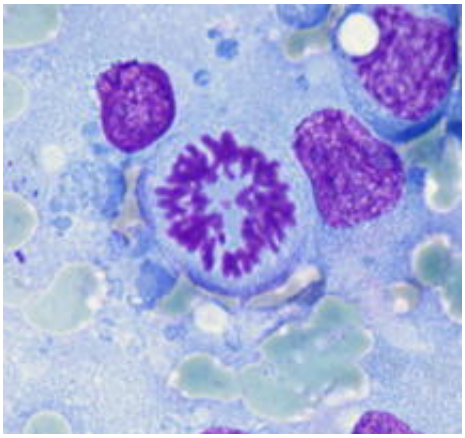
Researchers run rings round cell division

July 3 2008



Cell division, or mitosis, produces new cells through the growth and division of existing cells. Credit: Oxford University

A puzzle in the control of cell division, one of the most fundamental processes in all biology, has been unravelled by Oxford University researchers.

Although the steps of cell division are familiar to all pupils studying biology in schools, the details of how cell division is controlled and errors avoided have still to be sorted out.

In a paper appearing in *Nature* this week, the Oxford team show that a protein ring is used to hold two sister copies of each DNA molecule together physically until they are ready to be segregated into each daughter cell after division.

Understanding the mechanics of cell division is important: mis-separation of chromosomes can be one of the defining characteristics of cancerous cells, and such errors are also a leading cause of infertility in women as they get older. Down's syndrome – the presence of an extra copy of chromosome 21 – is one example of what can happen when chromosome segregation goes wrong.

'DNA replication and cell division provides the mechanism for evolution,' explains Professor Kim Nasmyth, head of the Department of Biochemistry at the University of Oxford. 'It is the most fundamental process in biology, and chromosome segregation is one of the driving forces.'

Cell division, or mitosis, produces new cells through the growth and division of existing cells. The process begins with the replication of the genetic material held in the chromosomes of the cell. The pairs of sister DNA molecules or chromatids are lined up before being pulled in opposite directions to different sides of the cell. Partitioning of the original cell then gives two new daughter cells each with the full complement of chromosomes.

'Three steps are essential for mitosis,' says Professor Nasmyth. 'The sister DNA molecules must be held together. Next you need to tell when all the chromatids have been paired up. Then, and only then, the associations must be broken and the sister DNAs pulled apart.'

A protein ring called cohesin is known to mediate this process, holding the sister DNA molecules together until an enzyme called separase snips through cohesin and releases the sister DNAs for segregation into the two daughter cells. Professor Nasmyth and colleagues devised an experiment that would conclusively show how cohesin manages this process.

Cohesin consists of three proteins held together in a ring. The researchers suspected that this ring encircled the two sister DNA molecules, physically pairing them up. The separase enzyme would release them on command by breaking the ring in just one place. Their only difficulty was how to show this model was correct.

The team made use of tiny circular chromosomes isolated from yeast in which the three constituent proteins of the cohesin ring had been modified so that they could be chemically linked together. According to the model, chemical linkage would trap the circular sister DNAs inside circular cohesin molecules like a set of Olympic rings. In this form, harsh chemical treatments would not be able to break them apart. This is indeed what they found.

The cohesin and circular yeast chromosomes survived the harsh chemical treatment, proving that cohesin does indeed form a ring around sister DNA molecules.

‘Understanding the critical stages of fundamental biological processes like this may not result immediately in new treatments and cures, but future progress will rely on the knowledge gained from advances of this kind,’ adds Professor Nasmyth.

Source: Oxford University