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Gene may hold key to future cancer hope

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Scientists may have discovered a new way of killing tumours in what they hope could one day lead to alternative forms of cancer treatments.

The University of Manchester research has identified a key gene that appears to play a critical role in the normal process of cell division.

Cells divide creating new cells as part of the body's natural growth, renewal and healing processes but cancer results when cells divide in an uncontrolled way.

What the Manchester team has discovered is that a protein in our cells called 'Bub 1' is essential for normal cell division to take place; if the gene that generates Bub 1 is 'switched off' then the cells are unable to divide successfully.

"Bub 1 is an enzyme that controls several processes required for cell division to occur," said Dr Stephen Taylor, who led the research in the Faculty of Life Sciences.

"We have shown that mouse embryos lacking the Bub 1 gene are unable to develop. Older cell types also failed to divide when the gene is switched off, while male mice lacking Bub 1 became infertile as their sperm cells died."

In fact, deactivating Bub 1 had such a profound effect on cell division at all stages of a cell's life - known as the 'cell cycle' - that the team is hopeful it will have a similar effect on cancer cells.

“Before cells can divide they have to duplicate and then distribute their genetic material so that the two ‘daughter’ cells receive all the genetic information for further growth and development,” said Dr Taylor, whose work is funded by the charity Cancer Research UK.

“The distribution phase has to be done with a high degree of accuracy - just one chromosome segregated incorrectly, for instance, leads to Down’s syndrome - so the cell has a surveillance mechanism which acts as a brake to delay chromosome segregation until accuracy has been guaranteed.”

An important part of this intricate surveillance system is Bub 1. The team found that when the gene is switched off the surveillance mechanism fails and accuracy is lost, resulting in cell death.

Now that scientists understand the precise role of Bub 1 in normal cell division, as well as what goes wrong when the gene is missing, they plan to test their theory on cancer cells.

“Unlike some other genes that become mutated in cancer cells, the Bub 1 gene appears normal indicating that it behaves in exactly the same way in cancer cells as it does in healthy cells.

“If this is the case, then we can be confident that switching it off will stop cancer cells proliferating too. And while our normal cells don’t divide that often, cancer cells divide more frequently, so hopefully by targeting Bub1 we will selectively kill cancer cells.”

Equally exciting, says Dr Taylor, is the fact that drugs are already being developed that are able to block the actions of Bub 1-type enzymes, known as ‘protein kinases’; such kinase blockers or ‘inhibitors’ are already providing a whole new approach to tackling cancer and Bub1 inhibitors may be another weapon in the oncologist's arsenal.

The research, which began in 1999, is published in the journal *Developmental Cell* on Tuesday, October 9.

Source: University of Manchester