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Babraham in leukaemia breakthrough

by John Fenton

SCIENTISTS at the Babraham Institute have discovered a completely new mechanism behind the development of a certain type of leukaemia, according to research published in the online edition of *Nature Immunology*.

The research, funded by BBSRC, Cancer Research UK and the MRC, revealed that mice missing two key genes develop an aggressive form of leukaemia that is similar to Acute Lymphoblastic Leukaemia, the most common form of leukaemia in children.

Without these genes, the mice are unable to produce 'silencer' proteins, which normally regulate the activity of other genes to ensure the development of a healthy individual.

How cells grow and multiply is controlled by a set of instructions stored by the DNA inside the cell's nucleus. These instructions are copied into messengers (messenger RNA or mRNA), which deliver instructions from the nucleus for the production of proteins which control cell behaviour.

It is known that mRNA has to be copied from DNA at the right speed - too fast or slow and diseases like cancer can occur. This research shows for the first time that 'silencer' proteins acting directly on specific mRNAs also provide critical control against cancer.

It demonstrates the significance of regulation at the post-transcriptional level (the destruction and inactivation of mRNA) and reveals that defects in this regulation lead to the development of malignancy.

This new knowledge may pave the way for new medicines and therapeutic strategies to tackle cancer.

The researchers identified this new pathway by looking at relatively unknown genes, which produce proteins that ensure the timely destruction of specific mRNAs after they have successfully delivered their message to the cell's machinery responsible for growth.

The two genes, *Zfp2611* and *Zfp2612*, produce 'silencer' proteins, which regulate gene expression by acting on mRNA the critical intermediate between DNA and protein.

Without these 'silencer' proteins the 'messenger' produces excessive amounts of



protein. In this case the target mRNA directs the production of a protein called Notch1, which plays a key role in the development of a type of white blood cell called the T cell.

Absence of the silencers therefore causes higher levels of Notch1 to be produced than is needed for normal growth; consequently the cells multiply out of control, leading to leukaemia.

Dr Martin Turner, head of Babraham's Laboratory of Lymphocyte Signalling & Development and senior study author said: "This is a completely new mechanism for the control of normal T cell development that, when corrupted, causes leukaemia."

Dr Daniel Hodson, a Cancer Research UK Clinical Research Fellow and lead author added: "We have known for some time that switching on Notch1 is an important step in the development of leukaemia, but this 'missing silencer' is a completely new step through which Notch1 is controlled. We need to now identify whether this aspect of Notch1 control is faulty in human leukaemia and in other types of human cancer."

Dr Lesley Walker, director of cancer information at Cancer Research UK said: "Acute Lymphoblastic Leukaemia is the most common form of leukaemia in children but also occurs in adults. It can be difficult to treat because

cancer cells spread throughout the body so surgery is not an option.

"This exciting work, finding how the control of Notch 1 levels can lead to leukaemia in mice, could provide scientists with important new leads for treatments."

It is known that the expression of such silencer proteins is suppressed in a number of human cancers, including breast cancer, so this may be a mechanism contributing to the pathogenesis of other different malignancies.

Manipulating the stability and destruction of mRNA may therefore be a useful strategy for developing anti-cancer agents and the treatment of human leukaemia.

How does broccoli stop prostate cancer?

LIGHT has been cast on the interaction between broccoli consumption and reduced prostate cancer risk.

Researchers writing in *BioMed Central's* open access journal *Molecular Cancer* (www.molecular-cancer.com) have found that sulforaphane, a chemical found in broccoli, interacts with cells lacking a gene called PTEN to reduce the chances of prostate cancer developing.

Richard Mithen, from the Institute of Food Research, an institute of BBSRC, worked with a team of researchers on Norwich Research Park, UK, to carry out a series of experiments in human prostate tissue and mouse models of prostate cancer to investigate the interactions between expression of the PTEN gene and the anti-cancer activity of sulforaphane.

He said: "PTEN is a tumour suppressor gene, the deletion or inactivation of which can initiate prostate carcinogenesis, and enhance the probability of cancer progression. We've shown here that sulforaphane has different effects depending on whether the PTEN gene is present."

The research team found that in cells which express PTEN, dietary intervention with SF has no effect on the development of cancer.

In cells that don't express the gene, however, sulforaphane causes them to become less competitive, providing an explanation of how consuming broccoli can reduce the risk of prostate cancer incidence and progression.

Mithen said: "This also suggests potential therapeutic applications of sulforaphane and related compounds."

Earth could be younger than previously thought

THE Earth could be up to 70 million years younger than scientists previously thought, a study has found.

An international team of researchers used geochemical information taken from the Earth's mantle and compared it with similar data from meteorites to create a new set of models showing how the planet might have been born.

The results suggest that the length of time between the date at which the solar system was formed, about 4.567 billion years ago, and the point at which the Earth reached its present size, may have been far longer than traditionally presumed.

Scientists have typically suggested that the Earth's development - a process known as "accretion" - happened over the course of

30 million years.

Writing in *Nature Geoscience*, however, the researchers argue that while the Earth probably grew to 60 per cent of its size relatively quickly, the process may well have then slowed, taking about 100m years in all.

"The whole issue hinges on working out how long it took for the core of the Earth to form, which is one of the big unknowns in this area of science," said co-author Dr John Rudge, from the University of Cambridge.

"One of the problems has been that scientists usually presume Earth's accretion happened at an exponentially decreasing rate. We believe that the process may not have been that simple and that it could well have been a much more staggered, stop-start affair."