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'Limpet Like' proteins provide secret to DNA Repair

16 December 2009

Research, part funded by the Medical Research Council, has found that a crafty family of 'limpet-like' proteins can play a crucial role in repairing DNA damage – according to two research papers published in Nature* today (Wednesday). These findings could pave the way to the design of new anti-cancer drugs which target this process.

Two teams studied the ways in which cells respond to DNA damage. Failure to repair this damage accurately can lead to cell death and trigger diseases such as cancer.

Both studies independently found that a family of Small Ubiquitin-like Modifier (SUMO) proteins could track down sites in the body where DNA damage has occurred, attach themselves to normal proteins, and guide them in fixing the genetic faults. These proteins could unlock a secret to the body's cancer fighting mechanisms.

It is hoped that this new knowledge may help scientists to develop drugs which work with common cancer treatments, such as chemotherapy and radiotherapy, to kill cancerous cells and allow the body to reproduce healthy new ones. The scientists made this discovery by observing the way cancer cells behave in the laboratory.

Professor Steve Jackson, who led the first study and who is senior group leader at the Cancer Research UK/Wellcome Trust Gurdon Institute at the University of Cambridge, said:

"What's really striking about our discovery is the capacity these SUMO proteins have to locate and help repair DNA damage as it occurs. They can also recruit other proteins to help repair double strand DNA breaks – the most severe type of DNA damage of all. We found these proteins can strengthen the cells' defences against DNA damage. When their work is done, the SUMO proteins then detach themselves and move on - which is quite incredible."

The second study was led by Dr Jo Morris, a Breast Cancer Campaign fellow in the Cancer Genetics Laboratory at Kings College London. This team looked specifically at the role of SUMO in relation to the breast cancer gene BRCA1 – which, when faulty, is associated with a very high risk of breast cancer.

Dr Morris said:

"Our findings showed that after DNA damage, SUMO becomes attached to BRCA1, switching it on and helping prevent breast cancer forming."

"We discovered how the cells in our body co-ordinate the difficult task of repairing potentially breast cancer causing DNA breaks and how they direct BRCA1 to do its job to stop tumours forming."

"This new insight is the first step towards developing drugs which may protect normal cells from the side effects of chemotherapy, or improve the effectiveness of current breast cancer treatments."

Dr Lesley Walker, Cancer Research UK's director of cancer information,

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said:

"DNA damage, particularly double strand DNA breaks, are a fundamental cause of cancer and we know that people who have mutations in the BRCA1 gene have a higher risk of developing some kinds of cancer. Discovering that these 'limpet like' proteins play such an important role in repair may provide new opportunities to stop cancer from growing.

"But this is an extremely complex and intricate biological process so it may be many years before we can use this knowledge to safely intervene and help treat cancer patients."

Ends

Notes to Editors:

* Yaron Galanty et al. SUMO proteins promote responses to DNA double-strand breaks in mammalian cells. Nature. December. 2009. This study was supported by Cancer Research UK.

Joanna Morris et al. The SUMO modification pathway is involved in the BRCA1 response to genotoxic stress. Nature. December. 2009. This study was funded by Breast Cancer Campaign, Cancer Research UK, the Medical Research Council and Breakthrough Breast Cancer.

You can watch a video interview with Dr Jo Morris here:

tinyurl.com/ycepbd6

About Cancer Research UK

- › Cancer Research UK is the world's leading charity dedicated to beating cancer through research.
- › The charity's groundbreaking work into the prevention, diagnosis and treatment of cancer has helped save millions of lives. This work is funded entirely by the public.
- › Cancer Research UK has been at the heart of the progress that has already seen survival rates double in the last thirty years.
- › Cancer Research UK supports research into all aspects of cancer through the work of more than 4,800 scientists, doctors and nurses.
- › Together with its partners and supporters, Cancer Research UK's vision is to beat cancer.
- › For further information about Cancer Research UK's work or to find out how to support the charity, please call 020 7121 6699 or visit www.cancerresearchuk.org

About the Medical Research Council (MRC)

For almost 100 years the Medical Research Council has improved the health of people in the UK and around the world by supporting the highest quality science. The MRC invests in world-class scientists. It has produced 29 Nobel Prize winners and sustains a flourishing environment for internationally recognised research. The MRC focuses on making an impact and provides the financial muscle and scientific expertise behind medical breakthroughs, including one of the first antibiotics penicillin, the structure of DNA and the lethal link between smoking and cancer. Today MRC funded scientists tackle research into the major health challenges of the 21st century. www.mrc.ac.uk

King's College London

King's College London is one of the top 25 universities in the world (*Times Higher Education* 2009) and the fourth oldest in England. A research-led university based in the heart of London, King's has more than 21,000 students from nearly 140 countries, and more than 5,700 employees. King's is in the second phase of a £1 billion redevelopment programme which is transforming its estate.

King's has an outstanding reputation for providing world-class teaching and cutting-edge research. In the 2008 Research Assessment Exercise

for British universities, 23 departments were ranked in the top quartile of British universities; over half of our academic staff work in departments that are in the top 10 per cent in the UK in their field and can thus be classed as world leading. The College is in the top seven UK universities for research earnings and has an overall annual income of nearly £450 million.

King's has a particularly distinguished reputation in the humanities, law, the sciences (including a wide range of health areas such as psychiatry, medicine and dentistry) and social sciences including international affairs. It has played a major role in many of the advances that have shaped modern life, such as the discovery of the structure of DNA and research that led to the development of radio, television, mobile phones and radar. It is the largest centre for the education of healthcare professionals in Europe; no university has more Medical Research Council Centres.

King's College London and Guy's and St Thomas', King's College Hospital and South London and Maudsley NHS Foundation Trusts are part of King's Health Partners. King's Health Partners Academic Health Sciences Centre (AHSC) is a pioneering global collaboration between one of the world's leading research-led universities and three of London's most successful NHS Foundation Trusts, including leading teaching hospitals and comprehensive mental health services. For more information, visit: www.kingshealthpartners.org .

About Breast Cancer Campaign

- › Breast Cancer Campaign aims to beat breast cancer by funding innovative world-class research to understand how breast cancer develops, leading to improved diagnosis, treatment, prevention and cure
- › Currently it supports 113 research projects, worth over £15.5 million, in 44 centres of excellence across the UK and Ireland
- › Breast cancer is the most common cancer in the UK and accounts for nearly one in three of all cancers in women
- › In the UK, nearly 46,000 new cases of breast cancer are diagnosed each year - that's 125 a day
- › For further information about Breast Cancer Campaign please call 020 7749 3705 or visit www.breastcancercampaign.org

