



Experimental drug may work in many cancers

Scientists have shown that a new class of cancer drugs called PARP inhibitors, currently being tested in clinical trials to treat breast and ovarian cancer could have dramatic results when used to treat other solid tumours, according to work presented at the NCRI Cancer Conference today (Wednesday).

The research groups based at the University of Oxford and University of Toronto tested in the laboratory in mice the effects of PARP inhibitor on tumour cells exposed to different levels of oxygen.

During the growth of a tumour, areas of low oxygen occur in cells because the blood vessels supplying the tumour with oxygen are often weak, twisted and inefficient - the most aggressive tumours often have the lowest oxygen levels.

They found that cancer cells with low oxygen levels are sensitive to PARP inhibitors - an experimental group of cancer drugs. The research suggests the drug could be a powerful therapy used on its own or alongside radiotherapy and chemotherapy to treat the most tenacious tumours across all cancer types - not just breast and ovarian cancer as was previously thought.

Dr Ester Hammond, one of the lead authors based at the University of Oxford said: "These results are very exciting. We have discovered that the tumour cells which are most resistant to conventional therapies respond well to PARP inhibitors.

"At the moment PARP inhibitors are being used in trials to treat patients with breast and ovarian cancer caused by faults in their BRCA1 gene - but we have shown in the laboratory that the drug could be effective for treatment of any tumour with reasonably low levels of oxygen - especially the most aggressive tumours."

PARP inhibitors block PARP, a protein which is part of DNA's 'emergency repair kit' in cells - it prevents mistakes being passed on to daughter cells when cells grow and divide. An alternative 'repair kit' is also controlled by the BRCA1 gene - which is often damaged in breast cancer cells. When both copies of the BRCA1 gene are damaged, the cells rely on the PARP pathway to repair cell damage.

The PARP repair kit alone isn't fully effective so mistakes are replicated when the cell divides and grows - leading to cancer.

But, by blocking PARP the cell is no longer able to 'muddle on' - it can no longer repair any damage. The cell cannot replicate and it dies.

Healthy cells are unaffected if PARP is blocked because they either contain one or two working BRCA1 genes which do an effective repair job.*

Dr Lesley Walker, Cancer Research UK's director of cancer information said: "It is very encouraging to see promising new cancer treatments like PARP inhibitors

coming out of clinical trials and our drug development programmes. And it's really exciting that new research like this shows that the drug could work in many cancers - particularly some of those which are most difficult to treat."

"Cancer Research UK has funded research into PARP inhibitors and their potential use in the clinic since the 1990s, and as part of our focus we are funding a separate PARP inhibitor trial in seven UK centers, of treatment for women with advanced breast or ovarian cancer caused by BRCA1 or BRCA2 gene faults."

ENDS

For media enquiries please contact Emma Rigby on 0121 335 8401 or, out-of-hours, the duty press officer on 07050 264 059

Read the abstract of this talk on the NCRI Cancer Conference website: http://www.ncri.org.uk/ncriconference/programme/speakerAbstracts/2009Para_Este_%20Hammond.asp

You can find all the abstracts here: http://www.ncri.org.uk/ncriconference/programme/Prog_Glance.asp

***The research done in collaboration with Professors Bristow and Helleday showed that low oxygen levels in tumour cells shuts down the BRCA1 repair toolkit. So if scientists also block the PARP emergency repair kit, the cell can not repair any damage and dies - preventing cancer development."**

Oxford University's Medical Sciences Division

Oxford University's Medical Sciences Division is one of the largest biomedical research centres in Europe. It represents almost one-third of Oxford University's income and expenditure, and two-thirds of its external research income. Oxford's world-renowned global health programme is a leader in the fight against infectious diseases (such as malaria, HIV/AIDS, tuberculosis and avian flu) and other prevalent diseases (such as cancer, stroke, heart disease and diabetes). Key to its success is a long-standing network of dedicated Wellcome Trust-funded research units in Asia (Thailand, Laos and Vietnam) and Kenya, and work at the MRC Unit in The Gambia. Long-term studies of patients around the world are supported by basic science at Oxford and have led to many exciting developments, including potential vaccines for tuberculosis, malaria and HIV, which are in clinical trials.

Cancer Research UK

- Cancer Research UK is the world's leading charity dedicated to beating cancer through research.

www.ncri.org.uk/ncriconference

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- 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.uk

About the NCRI Cancer Conference

The National Cancer Research Institute (NCRI) Cancer Conference is the UK's major forum for showcasing the best British and international cancer research. The Conference offers unique opportunities for networking and sharing knowledge by bringing together world leading experts from all cancer research disciplines. The fifth annual NCRI Cancer Conference is taking place from the 4-7 October 2009 at the International Convention Centre in Birmingham.

For more information visit www.ncri.org.uk/ncriconference

About the NCRI

The National Cancer Research Institute (NCRI) was established in April 2001. It is a UK-wide partnership between the government, charity and industry which promotes co-operation in cancer research among the 21 **member organisations** for the benefit of **patients**, the public and the scientific community.

For more information visit www.ncri.org.uk

NCRI members are: the Association of the British Pharmaceutical Industry (ABPI); Association for International Cancer Research; Biotechnology and Biological Sciences Research Council; Breakthrough Breast Cancer; Breast Cancer Campaign; Cancer Research UK; CHILDREN with LEUKAEMIA, Department of Health; Economic and Social Research Council; Leukaemia Research; Ludwig Institute for Cancer Research; Macmillan Cancer Support; Marie Curie Cancer Care; Medical Research Council; Northern Ireland Health and Social Care (Research & Development Office); Roy Castle Lung Cancer Foundation; Scottish Government Health Directorates (Chief Scientist Office); Tenovus; Welsh Assembly Government (Wales Office of Research and Development for Health & Social Care); The Wellcome Trust; and Yorkshire Cancer Research.

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