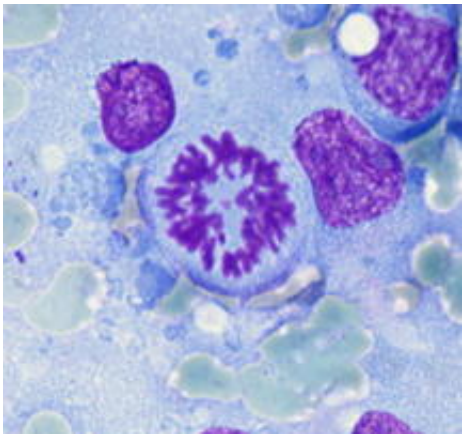
Study points to way of improving chemotherapy response

September 2 2011



Paclitaxel blocks cancer growth by stopping cells separating into two new cells.

(Medical Xpress) -- Blocking key proteins could improve response to a common chemotherapy drug, suggests an Oxford University-led study which used cancer cells grown in the lab.

The research offers several new targets for developing future drugs to boost the success rate of the tumour-shrinking drug paclitaxel (Taxol).

Paclitaxel is a chemotherapy drug commonly used to treat breast and ovarian cancer, but some tumours can become resistant over time and start growing again. The drug blocks the growth of cancer by interfering with microtubules – structures that help chromosomes to separate during cell division.

The international team of researchers found that blocking certain proteins stabilised the microtubules and made ovarian cancer cells more sensitive to paclitaxel. The findings are published in the journal *Cancer Research*.

Lead researcher Dr Ahmed Ahmed of the University of Oxford said: 'Our work provides further evidence for the important link between the stability of microtubules, the backbone of the cell, and sensitivity to paclitaxel.

'And because the proteins we've identified share the same target as paclitaxel, it raises the prospect of developing more specific drugs that sensitise cancer cells to paclitaxel without damaging the surrounding tissues.'

Previous research by Dr Ahmed and colleagues in the Nuffield Department of Obstetrics and Gynaecology found that the loss of a protein called TGFBI – which sends messages that stabilise the microtubules – caused paclitaxel to fail.

So to test the theory that microtubule stability may be essential for paclitaxel response, the researchers systematically blocked other signalling proteins in ovarian cancer cells growing in the lab, to see which might alter paclitaxel response.

Dr Robert Bast of the University of Texas MD Anderson Cancer Centre, who was also involved in the work, said: 'Our study has revealed several new proteins involved in microtubule stability that could be potential targets for drugs to improve the sensitivity of cancer cells to paclitaxel, without damaging healthy cells.'

The research was funded by Cancer Research UK, the University of Oxford, the Camilla Samuel Fund, and the MD Anderson Cancer

Center.

Dr Julie Sharp, senior science information manager at Cancer Research UK, said: ‘Overcoming drug resistance is a key challenge for our researchers. Unravelling the genetic basis of cancer to find out what determines whether a patient will respond to treatment will help us take a more targeted approach to tackle this problem. This approach could lead to fewer side effects and provide a lifeline for patients who have stopped responding to conventional treatments.’

Provided by Oxford University