Gene silencing paves way to new treatments for breast cancer

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(Medical Xpress) -- Cancer Research UK scientists have discovered that switching off a gene called CERT makes breast cancer cells more sensitive to a range of drugs. The research is published in the *Journal of Pathology*.

Their research could also lead to new tests to help doctors determine which breast cancer patients will benefit from chemotherapy by measuring levels of the CERT protein. The study showed that low levels of this protein are associated with a better outcome in women treated with chemotherapy. If confirmed in larger studies it could save women from unnecessary treatment.

By switching off the CERT gene the researchers improved the effects of a range of drugs called taxols (such as paclitaxel) on breast cancer cells. They found that particular cancer cells became more susceptible to a form of cell death called autophagy – where the cell eats itself. This approach specifically targeted polyploid cancer cells, those that contain too many chromosomes.

Polyploid cells can lead to chromosomal instability, where cells contain more or fewer than the usual 46 chromosomes. Cancers with chromosomal instability are linked to poor survival because they become even more damaged. This generates differences from one cancer cell to the next that may enable the cancer to resist drug treatment.

Dr Charles Swanton, head of translational research at Cancer Research

UK's London Research Institute, said: "These results are interesting because they provide some insight into new ways of specifically targeting cancer cells before they develop chromosomal instability – a state where the tumour develops a range of characteristics that can lead to drug resistance. We are now trying to exploit this, either with existing drugs, or by developing new ones, to find a combination of drugs that promote this particular type of cell killing."

Dr Julie Sharp, senior science information manager at Cancer Research UK, said: "Understanding why treatments can stop working is vital to ensure more cancer patients survive. This research reveals how resistance to treatment in some breast cancers can arise and highlights how we might identify those women who will benefit from chemotherapy, saving many from unnecessary treatment. The researchers are now looking to confirm their findings in a larger group of women, and if we see similar results, a test for CERT levels could become routine in the clinic."

More information: Lee, A., & et al (2011). CERT depletion predicts chemotherapy benefit and mediates cytotoxic and polyploid-specific cancer cell death through autophagy induction *The Journal of Pathology* DOI: 10.1002/path.2998

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