Membrane fluidity influences sensitivity of ovarian cancer cell lines to auranofin

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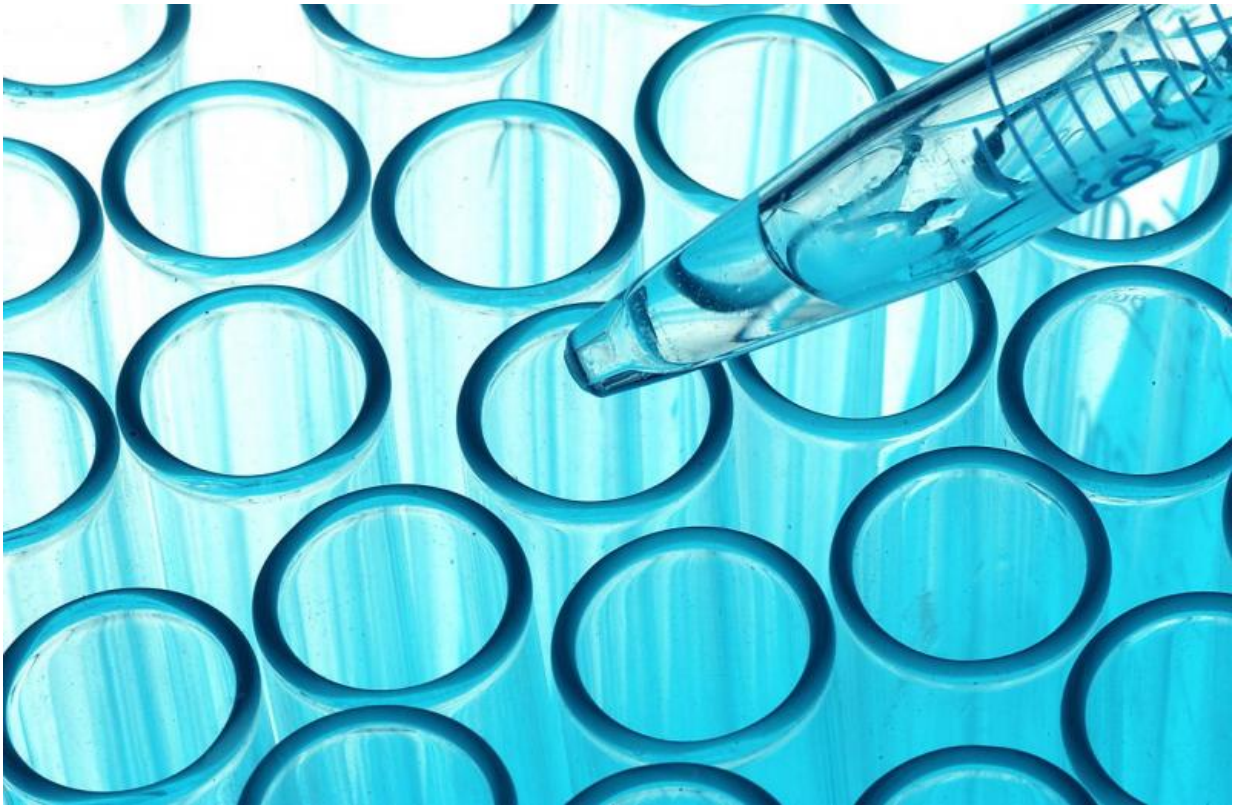

Credit: University of Plymouth

Increased fluidity in cell membranes could have a major impact on an ovarian cancer cell's sensitivity to treatment using the anti-rheumatic drug auranofin, research led by Plymouth University suggests.

Auranofin is currently undergoing trials for repurposing to treat recurrent epithelial ovarian cancer, which makes up around 90 per cent of diagnosed ovarian cancers.

A previous study, also led by Plymouth University, showed its use can reduce the survival rates of cancerous cells exhibiting depleted levels of BRCA1 gene (breast cancer 1, early onset).

Now new research, published in Mutation Research – Genetic Toxicology and Environmental Mutagenesis, has shown that increased fluidity within the cell membrane can enhance the ability of auranofin to induce increased DNA damage and cellular oxidation in these cells.

Cell membranes consist of a phospholipid bilayer, which protects a cell from its surroundings and controls the movement of substances.

Awadhesh Jha, Professor of Toxicology and Associate Head (Research) in the School of Biological Sciences, is the corresponding author of the study. He said:

"Most traditional chemotherapeutic drugs act by damaging the DNA of cells, which leads to cell death. But in order to try and build resistance to this cancer cells evolve by changing their genetic properties and cell membrane rigidity could be one of the confounding factors through which they become resistant to treatment. If a means to influence membrane fluidity could be achieved, it could enhance a drug's capability to cause DNA damage within cancer cells and significantly influence treatment outcomes."

The research was conducted by Dr Deepu Oommen and Dr Nicholas Dodd, from the Genetic Toxicology & Ecotoxicology Research Group at Plymouth University, on two common strains of ovarian cancer cell lines – IGROV1 and OVCAR5. They used cutting edge techniques to

determine DNA damage and cell death, and electron spin resonance analysis to assess cell properties.

It showed that IGROV1 cells exhibited a more fluidised membrane compared to OVCAR5, were more sensitive to auranofin induced cytotoxicity and exhibited an increased number of DNA double strand breaks upon auranofin treatment.

Previous research has shown that chemo-resistant cancer cells demonstrate greater rigidity of the cell membrane, with the current study suggesting that greater uptake of auranofin could be influenced by increased membrane fluidity.

Its authors also say further studies should now be undertaken to identify ways to exploit the fluidic nature of the cancer cells so that they can be eliminated.

Dr Dennis Yiannakis, Consultant Clinical Oncologist at Plymouth Hospitals NHS Trust, said:

"We have a successful collaboration between the University and the Hospital to carry out basic research in ovarian and lung cancer trying to improve the outcomes of treatment for these cancers. This work had been in part funded by the Magic Rainbow Appeal which is supported by local patients and their carers. The Appeal is also supported by the Plymouth and Cornwall Cancer Fund."

More information: Deepu Oommen et al. Linking genotoxicity and cytotoxicity with membrane fluidity: A comparative study in ovarian cancer cell lines following exposure to auranofin, *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* (2016). DOI: 10.1016/j.mrgentox.2016.09.003

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