Breast cancer drug could hold the key to fighting other tumours

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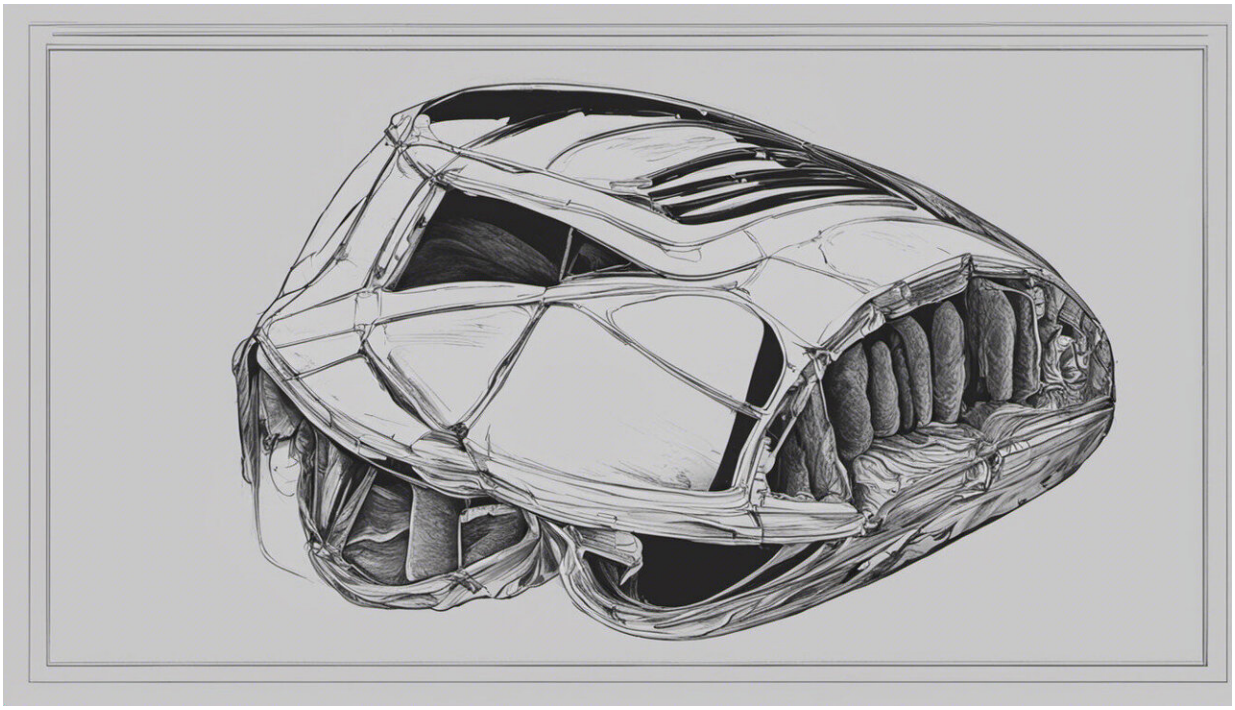

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New research out of the United Kingdom is showing that a common drug used in the fight against breast cancer could also be employed in the fight against other tumours. The drug in question is geldanamycin, and has made a name for itself for its ability to attack a protein associated with the spread of breast cancer. More recently, however, a laboratory-

based study has discovered that it can also degrade a different protein that triggers blood vessel growth. These results were published in the journal *PLOS ONE*.

According to Dr Sreenivasan Ponnambalam, reader in human disease biology in the University of Leeds' Faculty of Biological Sciences, one of the major challenges facing medical practitioners in the battle against cancer is stopping unwanted blood vessel growth. He went on to explain the significance of their results: 'This is potentially very significant because tumours secrete substances that stimulate blood vessels to develop around them, forming networks that supply nutrients and provide pathways for spread around the body.'

Dr Ponnambalam further noted, 'This is one of the big problems in cancer: how can we stop the tumour growing and spreading through these blood vessel networks?'

Geldanamycin is not the only drug currently available that tries to stop this type of growth; there are other drugs available, but they have certain risks associated with them. One type tries to attack directly the membrane protein VEGFR2, which is essential for new blood vessel growth. However, that approach carries the risk of serious side-effects because proteins in the membrane walls of blood vessels do important work such as controlling blood pressure.

The importance of their finding is that geldanamycin on the other hand offers a novel and potentially safer solution because it suppresses the protein indirectly. The new study, which was based on experiments with human cells and different animal models, discovered that geldanamycin indirectly triggered the clearance of the VEGFR2 protein by activating a cellular quality control system that breaks down many proteins. That quality control system already degrades VEGFR2 relatively slowly but the drug accelerates the process, preventing activation of the protein and

inappropriate new blood vessel formation.

'With conventional treatments, we have been trying to deal with the situation after the switch has been thrown. What this drug does is destroy the key part of the switch before that switch is thrown,' Dr Ponnambalam said. 'Geldanamycin and chemical derivatives have been under intensive study in the laboratory and in clinical trials for the past 20 years. The cost to the NHS or patients could be relatively low compared to the expensive existing anti-cancer drugs, which are still under patent,' Dr Ponnambalam added.

With such benefits, the team is eager to continue their research which was supported by the Wellcome Trust, the British Heart Foundation, a BBSRC-CASE PhD Studentship Award, and a University of Leeds ORSAS Tetley & Lupton PhD Scholarship.

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