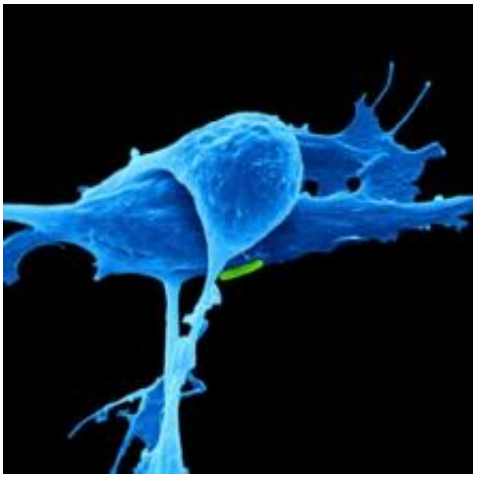
How removing a protein slows blood vessel growth in tumors

July 1 2015



Scientists from the University of Leeds and The Institute of Cancer Research, London, have discovered a new protein which triggers the growth of blood vessels in breast cancer tumours which have spread to the brain, a common location which breast cancer can spread to.

Dr Georgia Mavria's team in the School of Medicine at Leeds found that by withholding the DOCK4 protein in mouse models, a particular part of the blood vessel did not form as quickly, meaning tumours grew at a slower rate.

Dr Mavria said: "We want to understand how these tumours form and

grow, but we still need to do more research to stop these tumours growing altogether.

"The finding gives an important indicator of how the protein affects the growth of secondary breast tumours in the brain. The discovery could also enable experts to predict which patients might be at risk of their breast cancer spreading, and develop drugs to prevent the growth of secondary tumours."

Working with Professor Chris Marshall, Professor of Cell Biology at The Institute of Cancer Research, London and the late Dr Tony Pawson at the Lunenfeld-Tanenbaum Research Institute in Toronto, researchers found that a complex of two related proteins, DOCK4 and DOCK9, is critical in the formation of the lumen, the interior space of a vessel through which blood flows.

By impeding the speed at which the lumen forms, tumours are not fed as effectively by blood vessels.

Normally, when breast cancer spreads to other parts of the body, it forces new blood vessels to form to supply it with nutrients and oxygen to help it to grow, resulting in tumours that are very difficult to treat.

Professor Marshall said: "Our study reveals new insights into how the complex process of forming blood vessels is controlled. This knowledge could lead to new approaches to preventing the blood supply to tumours and metastases. If we can find new ways to reduce the blood supply to tumours, we might be able to find new ways to slow cancer growth in future."

The research, which has been published in *Nature Communications*, was funded by Breast Cancer Now, Yorkshire Cancer Research and Cancer Research UK.

Dr Matthew Lam, Senior Research Communications Officer at Breast Cancer Now, said: "These findings could one day help us better identify and treat patients that might be at risk of their breast cancer spreading to the brain, a particularly common site for metastasis.

"12,000 women have their lives cut short by breast cancer in the UK each year. An understanding of what is happening on a molecular level - such as the role played by DOCK proteins - will be essential if we are to find ways to prevent secondary tumours and finally stop women dying from the disease."

Kathryn Scott, Head of Research and Innovation at Yorkshire Cancer Research, said: "Tumours need blood vessels to grow, but these blood vessels could be the cancer's weakest link because it is believed that they are less able to become resistant to drugs than the cancer cells themselves. Targeting drugs to the blood vessels that are serving the tumour rather than the tumour itself is an exciting new area of research and we are supporting a number of projects in Yorkshire which are investigating this approach."

Dr Aine McCarthy, Science Information Officer at Cancer Research UK, said: "This research shows for the first time that a molecule called DOCK4 is a key player in tumour blood vessel development and blocking it could slow tumour growth by starving the cancer cells. But the study was carried out in mice, so more research is needed to see if drugs can be developed that target the molecule and whether this approach would be safe and effective in people with cancer."

More information: "A Rac/Cdc42 exchange factor complex promotes formation of lateral filopodia and blood vessel lumen morphogenesis", by Abraham et al, *Nature Communications*, 2015.

Provided by University of Leeds