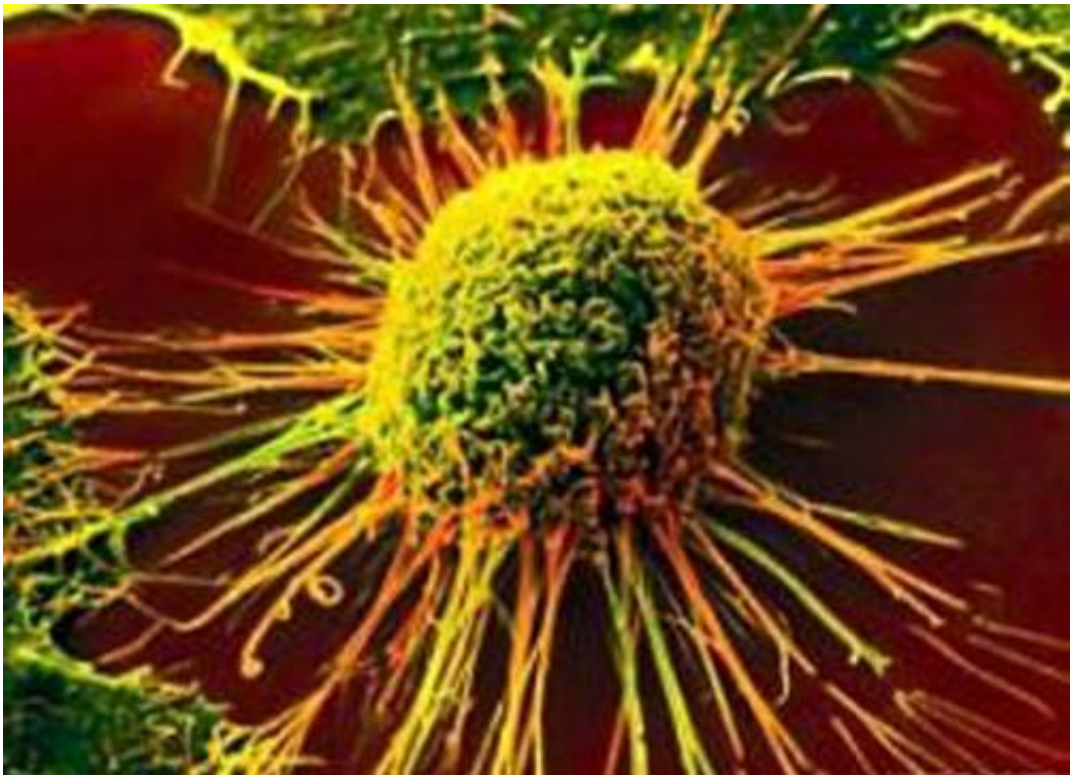
Cancer thwarts treatment by 'stealing' blood vessels

April 7 2016



Cancers can resist treatment by 'stealing' blood vessels from nearby tissues, a new study shows.

The important new study is the first to show that tumours can become resistant to drugs over time by learning to steal normal blood vessels

from surrounding tissue - a process that researchers call vessel co-option.

The process of new blood vessel growth - angiogenesis - is important for cancers to grow, and several anti-angiogenic drugs have been developed to combat it. However, cancers often become resistant to these drugs, through mechanisms which until now were poorly understood.

The study, from researchers at The Institute of Cancer Research, London, and Sunnybrook Research Institute, University of Toronto, shows it could be possible to treat cancers by designing new therapies that block both vessel co-option and angiogenesis. These may be more effective than existing treatments, which only block angiogenesis.

The research is published today (Thursday) in the *Journal of the National Cancer Institute*, and was funded by organisations including the Canadian Institutes for Health Research, Worldwide Cancer Research, Canadian Liver Cancer Foundation and Breast Cancer Now.

In the study, scientists used mice to examine how a type of liver cancer called hepatocellular carcinoma can become resistant to an anti-angiogenic drug called sorafenib.

They discovered that tumours which responded to treatment initially relied mainly on growing their own blood vessels, but developed resistance to treatment by actively stealing the normal pre-existing blood vessels of the liver instead.

The researchers believe their study may have implications not only for the treatment of liver cancer, but also for other cancer types including metastatic breast cancer and metastatic bowel cancer. Scientists at The Institute of Cancer Research are currently investigating the implications of this research for these other cancer types.

Interestingly, the researchers also found that the switch to vessel co-option was reversible. On stopping treatment, the tumours switched back to using angiogenesis - providing a potential explanation as to why some patients can respond again to the same anti-angiogenic drug after they have a 'treatment holiday.'

Because there are no existing drugs that target vessel co-option, the researchers also carried out experiments to identify how vessel co-option works. They discovered that the cancer cells increase their ability to move when they co-opt vessels, suggesting that targeting cancer cell movement might be used to block vessel co-option.

Study co-leader Dr Andrew Reynolds, Leader of the Tumour Biology team at The Institute of Cancer Research, London, said:

"Our study is the first to show that cancers can adapt to treatment by actively co-opting blood vessels from nearby tissues as a mechanism of drug resistance.

"In the future, we hope our results will lead to the development of new drug types that target vessel co-option. We believe that drugs which are designed to target vessel co-option could be particularly effective when used alongside existing therapies that block new blood vessel growth.

"Although the current study was focused on liver cancer in mice, we are also currently investigating whether our results are relevant for patients affected by breast and bowel cancer. Our research also emphasises the importance of further studies to better understand the process of vessel co-option, which seems to play an important role in tumour growth but has been relatively under-studied."

Study co-leader Professor Robert Kerbel and lead author Elizabeth Kuczynski from the Sunnybrook Research Institute, University of

Toronto, said:

"This work has been a multinational and multi-disciplinary collaboration. By working with Dr Reynolds in the UK and Dr Vermeulen in Belgium, as well Dr Yousef and Dr Foster in Toronto, we combined expertise in molecular and cellular biology, pathology and imaging in order to address a key question in the field. As a result, we have obtained important information which should eventually lead to improved anti-cancer therapies for patients in the future."

Katie Goates, Senior Research Communications Officer at Breast Cancer Now, said:

"This new insight into how cancers could be commandeering nearby blood vessels to resist treatments may be significant for a number of disease areas. We hope that this knowledge can now be harnessed and applied to help slow the spread of breast cancer.

"Ultimately, if we can stop breast cancers spreading in the first place - where they become incurable - we'll finally be able to stop women losing their lives to this dreadful disease."

More information: *Journal of the National Cancer Institute*, dx.doi.org/10.1093/jnci/djw030

Provided by Institute of Cancer Research