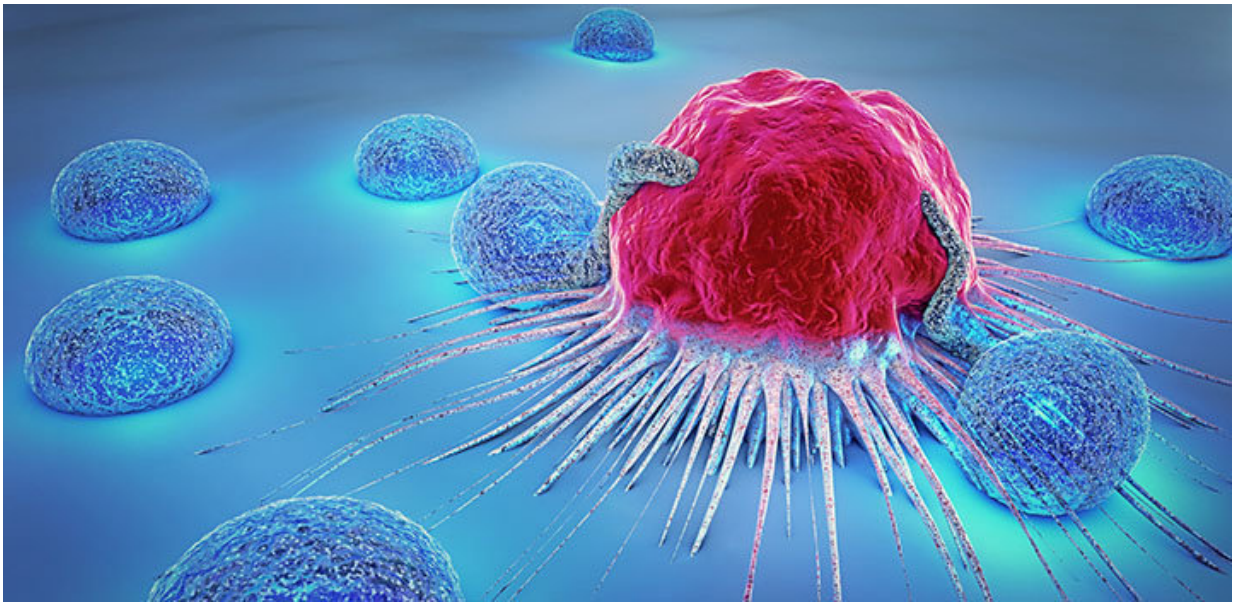
Research could help fine-tune cancer treatment

May 25 2018



Credit: University of East Anglia

Cancer therapies that cut off blood supply to a tumour could be more effective in combination with existing chemotherapeutic drugs—according to new research from the University of East Anglia.

New research published today in the journal *EMBO Reports* reveals that tumour growth is better-reduced in mice when the expression of a particular protein called Beta3-integrin is targeted in combination with

drugs that are already used in cancer patients.

It is hoped that the findings could help fine-tune treatment for cancer patients and revitalise an interest in the use of microtubule targeting agents (MTAs) which are commonly used as chemotherapies in cancer patients.

Lead researcher Dr. Stephen Robinson from UEA's School of Biological Sciences, said: "Tumours must recruit their own blood supply to grow beyond a very small size and this process is called angiogenesis.

"Anti-angiogenic drugs stop tumours from growing their own blood vessels, and this in turn can slow the growth of the cancer, or shrink it. Targeting angiogenesis is therefore seen as crucial in many anti-cancer strategies.

"However many anti-angiogenetic therapies target proteins that help the functioning of a patient's normal blood supply—and this can lead to nasty side effects including haemorrhage, strokes, high blood pressure, and fatigue."

The research team has long looked at Beta3-integrin as a better anti-angiogenic target because the protein is not expressed in normal blood vessels, but is expressed in tumour blood vessels. This reduces the potential for unwanted side effects.

Now the team has shown that targeting Beta3-integrin in combination with microtubule targeting agents, which are widely used in cancer patients, works better than targeting Beta3-integrin alone. Microtubules are protein structures in cells that help them move and divide.

Specifically, the Robinson lab looked at how Beta3-integrin and microtubules interact with one another in the cells that line blood vessels

(endothelial cells), and showed that microtubules behave differently when Beta3-integrin levels are reduced; the microtubules become more sensitive to the chemotherapies that are used to hit them.

Dr. Robinson said: "This protein, Beta3-integrin, has been the focus of drug design over the last two decades because its expression is vastly increased in endothelial cells during blood vessel recruitment to tumours.

"We found that targeting the protein Beta3-integrin in combination with the use of microtubule targeting agents (MTAs) could be a good way to stop tumours recruiting a blood supply to grow.

"This is really important because MTAs are already in clinic and commonly used as chemotherapies such as paclitaxel in cancer patients. Meanwhile Beta3-integrin inhibitors have been at the centre of cancer drug design for over 20 years and are well-tolerated in clinical trials.

"We hope that this research could revitalise interest in this sort of therapy and lead to a re-purposing of MTAs as anti-angiogenic inhibitors, in combination with targeting Beta3 integrin."

'The β3-integrin endothelial adhesome regulates microtubule dependent cell migration' is published in the journal *EMBO Reports* on May 25, 2018.

More information: Samuel J Atkinson et al, The β3-integrin endothelial adhesome regulates microtubule-dependent cell migration, *EMBO reports* (2018). DOI: 10.15252/embr.201744578

Provided by University of East Anglia