Scientists make advance in cancer research

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A protein that has been at the centre of cancer drug design for the last 20 years should not be given up on according to new research from the University of East Anglia (UEA).
The most advanced version of αvβ3-integrin antagonists failed clinical trials to treat aggressive forms of brain cancer.

But research published today in the American *Heart* Association's journal *Circulation Research* shows that targeting the protein in question could still be vital in stopping the growth of tumours. Not least because the drugs targeting it cause minimal side effects compared to other drugs – which can cause bleeding in the gut and high blood pressure.

Tumours must recruit their own blood supply to grow beyond a very small size. The research team studied the cells that line blood vessels (endothelial cells) in mice, and in particular the role of a widely expressed protein called beta3-integrin.

Dr Stephen Robinson, from UEA's school of Biological Sciences, said: "This protein 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.

"The most advanced of these drugs, however, has recently failed a phase III clinical trial to treat an aggressive form of brain cancer. In line with other clinical work, patients respond to treatment for a short while but then their cancers escape the treatment.

"This research helps to explain why these very promising drugs aren't meeting with the success that was anticipated and it suggests a way forward - how to make them work better.

"We have shown how tumours continue to grow despite treatment which should block blood vessel recruitment. They modulate how they are recruiting their blood vessels by using a different pathway from the one that is being targeted. We have identified some molecular changes in endothelial cells that occur with long-term inhibition of beta3-integrin that might help the cells escape the beta3-integrin blockade.

"Our research also shows that timing is critical when targeting the protein beta3-integrin.

"Importantly, these findings have re-established the expression of beta3-integrin as a valid clinical target when treating cancer. Efforts must now be re-focused to either develop new drugs to target beta3-integrin, or figure out how to more effectively use the drugs that already exist."

'Acute Depletion of Endothelial beta3-Integrin Transiently Inhibits Tumour Growth and Angiogenesis in Mice' is published in the journal *Circulation Research*.

Provided by University of East Anglia