New ways to treat solid tumours

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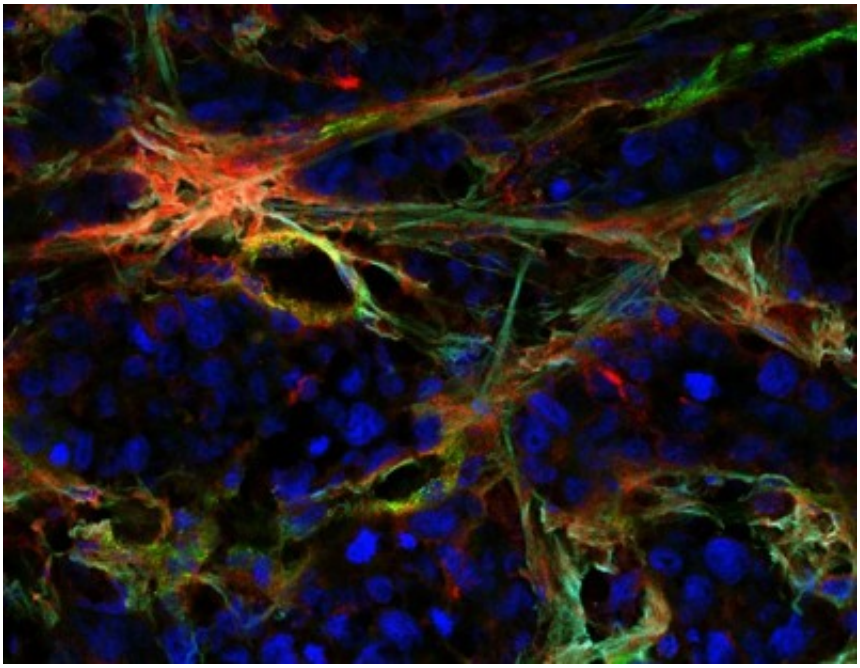

(Medical Xpress)—An international team of scientists has shown that an antibody against the protein EphA3, found in the micro-environment of solid cancers, has anti-tumour effects.

As EphA3 is present in normal organs only during embryonic development but is expressed in blood cancers and in solid tumours, this antibody-based approach may be a suitable candidate treatment for solid tumours.

The researchers from Monash University and Ludwig Cancer Research, in Australia, and KaloBios Pharmaceuticals, in the US, have had their findings published in the journal *Cancer Research*.

The team, led jointly by the late Professor Martin Lackmann, from the School of Biomedical Sciences at Monash; and Professor Andrew Scott, from Ludwig Cancer Research, has found that even if tumour cells do not have this molecule they can thrive by recruiting and taking advantage of supporting EphA3-containing cells in the tumour micro-environment.

First author, Dr Mary Vail, Monash Department of Biochemistry and Molecular Biology said: "The tumour cells send out signals to the surrounding area and say: 'We need a blood supply and a foundation upon which to spread'."

"We have shown that EphA3 expressing stromal stem cells, which are produced by the bone marrow, form cells that support and create blood vessels in tumours," Dr Vail said.

Professor Andrew Scott's team at Ludwig introduced human prostate cancer cells into a mouse model to mimic disease progression in humans. EphA3 was found in stromal cells and blood vessels surrounding the tumour.

They also observed that treatment with an antibody against EphA3 (chIIIA4) significantly slowed tumour growth. The antibody damaged tumour blood vessels and disrupted the stromal micro-environment, and cancer cells died because their 'life-support' was compromised.

"In addition, we screened various tumours from patient biopsies - sarcomas, melanomas as well as prostate, colon, breast, brain and lung cancers - and confirmed EphA3 expression on stromal cells and newly

forming blood vessels," Professor Scott said.

"Our research findings indicate that the tumour micro-environment is important, and monoclonal antibodies against EphA3 are one way to target and kill a variety of solid tumours as well as blood cancers."

Currently, KaloBios Pharmaceuticals is testing the anti-EphA3 antibody KB004 in a multi-centre Phase I/II clinical trial in Melbourne and the US in patients with EphA3 expressing blood malignancies: AML, MDS and myelofibrosis.

Dr Vail, who collaborated with her former mentor on the project for 10 years, said this research represented Martin Lackmann's life work.

"Martin was dedicated to helping people, and believed that KB004 was a promising therapeutic approach. He rightly anticipated that it would be well-tolerated in cancer patients, and through this collaborative project, his pioneering research has progressed to clinical trials and potentially new treatments for cancer patients," Dr Vail said.

The research study was funded by ARC, NHMRC and KaloBios Pharmaceuticals.

More information: *Cancer Research*. cancerres.aacrjournals.org/content/74/16/4470.full

Provided by Monash University

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