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New target discovered for treatment of cancer

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Researchers at the Swedish medical university Karolinska Institutet have discovered a new way of blocking the formation of blood vessels and halting the growth of tumours in mice. A substance that exploits this mechanism could be developed into a new treatment for cancer.

For a cancer tumour to be able to grow larger than the size of a pea, the cancer cells need to stimulate the formation of new blood vessels that can supply the tumour with oxygen and nutrients, a process known as angiogenesis. A number of medicines which inhibit angiogenesis have been developed, but their effect has been limited, and there is still a major need for better medicines.

The new results concern a receptor on the surface of blood vessel cells called ALK1. When the researchers blocked ALK1 in tumours in mice, angiogenesis was inhibited and the tumours stopped growing. The ALK1 receptor is activated by a family of signalling proteins called TGF-β proteins that are very important for communication between different types of cell in a wide range of key processes in the body. The study indicates that two members of the TGF-β family (TGF-β and BMP9) work together to stimulate angiogenesis in tumours.

ALK1 was blocked partly by genetic means and partly using a pharmaceutical substance called RAP-041.

"We believe that RAP-041 could be used in combination with existing angiogenesis inhibitors to achieve the maximum effect," says associate

professor Kristian Pietras, who led the study.

Clinical studies of ACE-041, the human equivalent of RAP-041, have already been begun in the USA by the company that holds the patent on the substance. One goal of these studies is to find out which types of tumour are most sensitive to ALK1 blockade.

More information: 'Genetic and Pharmacological Targeting of Activin Receptor-like Kinase 1 Impairs Tumor Growth and Angiogenesis', Sara Cunha, Evangelia Pardali, Midory Thorikay, Charlotte Anderberg, Lukas Hawinkels, Marie-José Goumans, Jasbir Seehra, Carl-Henrik Heldin, Peterten Dijke, Kristian Pietras, *The Journal of Experimental Medicine*, online 11 January 2010.

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