Blood protein EPO involved in origin and spread of cancer

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Researchers at the Swedish medical university Karolinska Institutet have demonstrated that a growth hormone, PDGF-BB, and the blood protein EPO are involved in the development of cancer tumours and that they combine to help the tumours proliferate in the body. These new preclinical findings offer new potential for inhibiting tumour growth and bypassing problems of resistance that exist with many drugs in current use. The results are published in the scientific journal *Nature Medicine*.

Angiogenesis is the formation of new blood vessels from pre-existing ones, and is one of the most important research fields in the treatment of such diverse conditions as cancer, metastases, obesity, heart disease, stroke, diabetes and chronic inflammation. The process is also important in healthy individuals for wound healing, the menstrual cycle and other normal processes. Professor Yihai Cao and his team are researching into angiogenesis and its links to cancer and other diseases, and in the present study show the significant role played by a growth factor, PDGF-BB.

"It's a member of the PDGF family and significantly contributes to blood vessel development, which is one of the characteristic signs of cancer, says Professor Yihai Cao. Our preclinical findings suggest that PDGF-BB causes systemic effects in the body, which is to say that rather than being active locally it goes into the blood and interferes with the function of several organs so that the entire body is affected."

Their studies are carried out on mice, and in the present study they were able to show that when the growth factor PDGF-BB binds to its

receptors, it stimulates the blood protein EPO (Erythropoietin), which, in turn, controls the production of red blood cells, that provide more oxygen for tumor growth and metastasis.

"EPO has several functions," says Professor Yihai Cao. "It produces more blood and stimulates angiogenesis, and we have revealed the underlying mechanism. It also stimulates tumour angiogenesis by directly stimulating the proliferation, migration and growth of endothelial cells and their ability to form the so-called epithelial tube. PDGF-BB promotes the stimulation of extramedullary haematopoiesis, enlargement of the liver and spleen, which increases oxygen perfusion and protection against anaemia." The introduction of PDGF-BB in mice thus boosts erythropoietin production and the haematopoietic parameters. In addition, EPO may directly act on tumor cells to promote their growth and metastasis.

"We believe that the increase in EPO might be responsible for tumoural resistance to anti-angiogenetic drugs, which only target PDGF ligands. The combination of drugs targeted at both PDGF and EPO has potential superior therapeutic benefits and might circumvent today's serious resistance problems," says Professor Yihai Cao, adding that they will continue to study mouse models and explore opportunities for clinical studies on patients.

More information: "PDGF-BB modulates hematopoiesis and tumor angiogenesis by inducing erythropoietin production in stromal cells", Yuan Xue, Sharon Lim, Yunlong Yang, Zongwei Wang, Lasse Dahl Ejby Jensen, Eva–Maria Hedlund, Patrik Andersson, Masakiyo Sasahara, Ola Larsson, Dagmar Galter, Renhai Cao, Kayoko Hosaka & Yihai Cao, *Nature Medicine* AOP 4 December 2011.