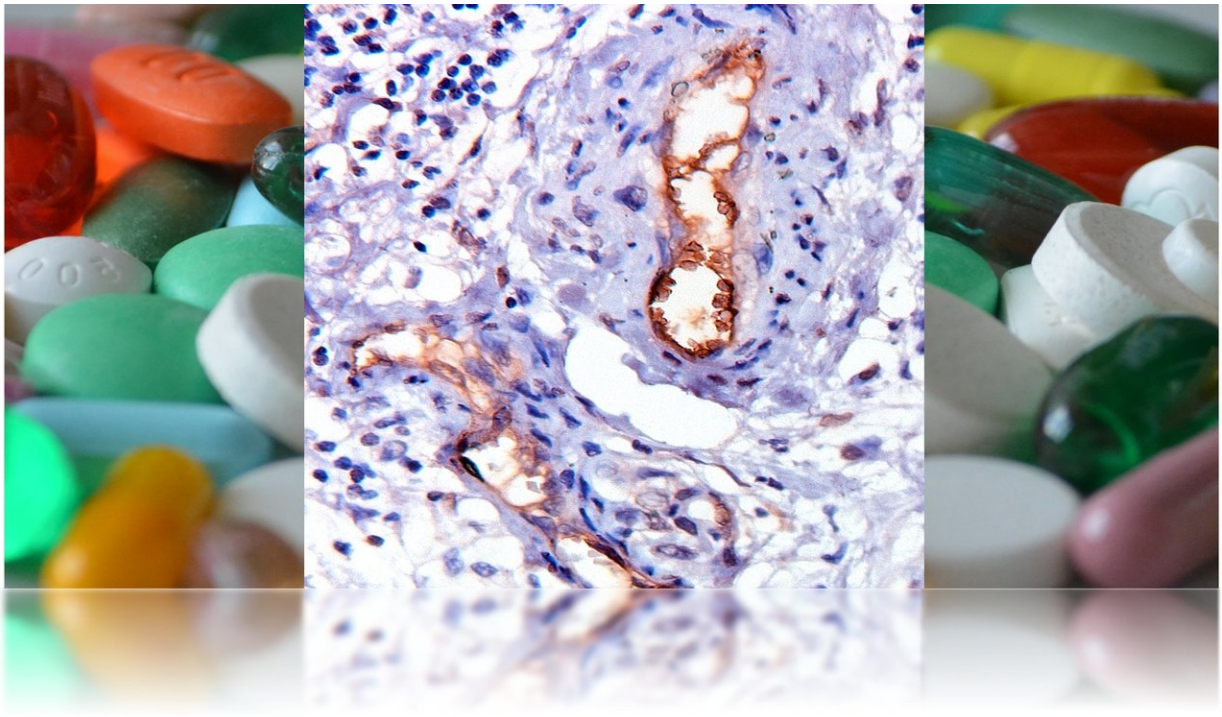
A new way to cut the power of tumors

December 20 2018



Immunohistochemical staining for the insulin receptor (INSR) in a microscopic section of human stomach cancer. A clear overexpression of this receptor

(brown) is seen in the tumor tissue, while this is absent in non-cancerous stomach tissues. Credit: Université de Genève

Instead of tackling tumors head-on, an international team of researchers from the University of Geneva (UNIGE) and the Amsterdam UMC, location VUmc in Amsterdam has chosen to regulate their vascularization by intervening with cellular receptor that is overexpressed specifically in tumor blood vessels. By acting on the development of the blood vessels within the tumor, scientists hope to modulate vasculature and deliver the treatments extremely accurately, and even if necessary to cut nutrient supply to the tumor. These findings are published in the *British Journal of Cancer*.

The Swiss and Dutch researchers have studied the mechanisms underlying the growth of new blood vessels inside tumors. In doing this, they stumbled on the overexpression of the receptor that normally serves as the receptor for insulin in the vasculature within the tumor. This finding may pave the way for developing a targeted treatment for cancer. "From a genomic screen, we have discovered the role of this receptor, called the insulin receptor (INSR), mainly represented by the shorter oncofetal and non-metabolic isoform A(INSR-A), in the process of blood vessel formation. A molecule specifically targeting this receptor may allow us to modulate tumor growth or even completely block it," says Patrycja Nowak-Sliwinska, assistant professor in the School of Pharmaceutical Sciences of the Faculty of Sciences of UNIGE and first author of the study.

After many years of investigations, the researchers were able to confirm this discovery in both in vitro and in vivo experiments. They now hope to develop a specific molecule, with the help of an industrial partner.

Comparisons on eleven tumor types

One of the strengths of this research is its ability to precisely target the tumor endothelium, the innermost layer of blood vessels in contact with the blood, while sparing healthy cells. To ensure this, the researchers compared healthy and diseased tissue sections for 11 types of tumors, including kidney, colon and breast tumors. The importance of insulin receptors as a target for cancer treatment highlighted by this research also lies in the indirect approach of the disease.

"When cancer cells are attacked directly, failure is common, as each procedure can lead to a change in the tumor's behavior. They are genetically unstable and may mutate into drug-resistant variants. We need to outsmart cancer cells," said Arjan W. Griffioen, the head of Angiogenesis Laboratory at the Amsterdam UMC. By intervening with endothelial cells and targeting the vascularization for which they are responsible, researchers avoid frontal attack on the tumor. "We do not act directly on cancer, but we found the valve that regulates the vascularization of cancer cells," conclude the researchers.

More information: Patrycja Nowak-Sliwinska et al. Oncofoetal insulin receptor isoform A marks the tumour endothelium; an underestimated pathway during tumour angiogenesis and angiostatic treatment, *British Journal of Cancer* (2018). DOI: 10.1038/s41416-018-0347-8

Provided by University of Geneva