Researcher pinpoints the cellular mechanism responsible for modulating the permeability of blood vessels

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Dr. Jean-Philippe Gratton, Director of the Endothelial cell biology research unit at the Institut de recherches cliniques de Montréal (IRCM), identifies a new intracellular mechanism responsible for modulating vascular permeability: the nitrosylation of beta-catenin protein by nitric oxide. This scientific breakthrough could have a possible impact on the treatment of cancerous tumours by altering the permeability of the blood vessels irrigating them. Dr. Gratton's team will publish the results of its research tomorrow in the scientific journal *Molecular Cell*.

The permeability of blood vessels is determined, in part, by the space between endothelial cells, or the cells lining the inside of all blood vessels. Increasing permeability is an essential step in angiogenesis, the process of formation of new blood vessels. Vascular endothelial growth factor (VEGF) is responsible for triggering angiogenesis, and increasing vascular permeability through the activation of the eNOS enzyme, which in turn produces nitric oxide (NO), an intracellular gas.

"We already knew that NO plays a very important role in the modulation of vascular permeability and that it could represent a target for blocking the growth of tumours," explains Dr. Gratton. "However, we ignored how it worked. We have now shown that beta-catenin is the specific protein targeted by nitrosylation - the chemical modification of proteins in endothelial cells by NO."

Nitrosylation of beta-catenin allows endothelial cells to detach from one another, thus increasing vascular permeability. This process could eventually help regenerate damaged arteries after a heart attack. On the contrary, reducing endothelial permeability in cancerous tumours could help prevent the creation of new blood vessels on which they feed, and consequently block their growth. A better understanding of NO's functions could therefore have an important impact on numerous fields of research, as this molecule is involved in many physiological and pathological processes.

"The identification of new cell mechanisms responsible for altering the permeability of blood vessels is a an important step in cancer research," says Dr. Morag Park, Scientific Director of the Canadian Institutes of Health Research's Institute of Cancer Research, "this discovery can potentially have a significant impact on how we treat certain types of tumour growth."

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