Adipose cells and breast cancer -- a dangerous combination

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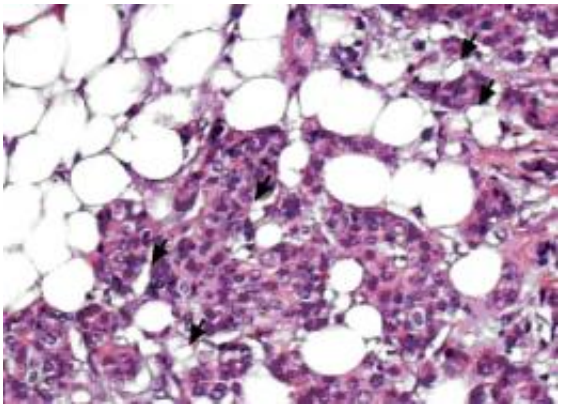

Section of tumor (mauve) in the presence of adipocytes (white discs). The arrows indicate adipocytes modified by the tumor. Credit: G. Escourrou

Apart from its direct effect on health (such as cardiovascular diseases and diabetes), obesity is increasingly suspected of playing a role in the prognosis of breast cancer and, in particular, its propensity to spread. However, no direct cause and effect relationship had been demonstrated until now. This breakthrough has finally been made through the collaborative work of two teams of researchers from Inserm, CNRS and the Université Paul Sabatier (France). Their research has made it possible to highlight, both in vitro and in vivo, the presence of adipose cells (known as adipocytes) near breast tumors. These adipocytes have specific biological characteristics. When associated with tumors, they are capable of modifying the characteristics of cancerous cells, making

them more aggressive. The results of this work are published in *Cancer Research* of 1st April 2011.

Numerous statistical studies have already established a link between obesity and the "aggressiveness" of breast cancer in women, without ever succeeding to explain this phenomenon. In order to find an explanation, the researchers studied the cross-talk between adipose cells and tumor cells.

The external part of the breast essentially contains fat tissue, mainly composed of adipose cells. Apart from storing/releasing fats, these cells are capable of secreting numerous proteins. The researchers therefore attempted to find out whether these proteins play a role in the development of breast cancers.

To do so, the teams headed by Philippe Valet at the Institut des Maladies Métaboliques et Cardiovasculaires (Inserm/Université Paul Sabatier) and Catherine Muller at the Institut de Pharmacologie et de Biologie Structurale (CNRS/Université Paul Sabatier) used an original co-culture system between mammary tumor cells and adipocytes. In the presence of tumor cells, the adipocytes exhibit a modification in the secretion of some of their proteins, including inflammatory proteins such as interleukin-6 (IL-6). Adipose cells progressively establish a real interaction with the tumor, which leads to an increase in its "colonization potential" and thus its aggressiveness.

Indeed, when injecting mice with tumor cells co-cultivated beforehand with adipocytes, the researchers observed that the tumor was more likely to form metastases. A significant factor is that these specific modifications in adipocytes have been observed in human tumors, confirming the importance of the phenomenon. In addition, the researchers observed that the adipocytes near large human tumors, with ganglionic invasion, contained more IL-6. The protein could thus play an

important role in the adipocyte-induced spread of breast cancer.

This works shows that adipocytes undoubtedly play an unexpected role in the spread of such tumors. “Our results now demonstrate how adipocytes actively participate in the progression of breast cancer, orchestrated by tumor cells. They suggest that in the case of obesity, the adipocytes associated with breast cancer could be more likely to amplify the 'aggressive' effect of tumors”, the researchers say. “This hypothesis still needs to be verified both in mice and humans.”

The study targets the development of specific strategies for overweight patients suffering from the most aggressive cancers. For example, identifying the signals supplied by the adipocytes to stimulate the invasive properties of tumor cells could represent a new lead for treating these patients.

More information: “Cancer-associated adipocytes exhibit an activated phenotype and contribute to breast cancer invasion”, Béatrice Dirat, et al. *Cancer Research*, 1st April 2011.

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