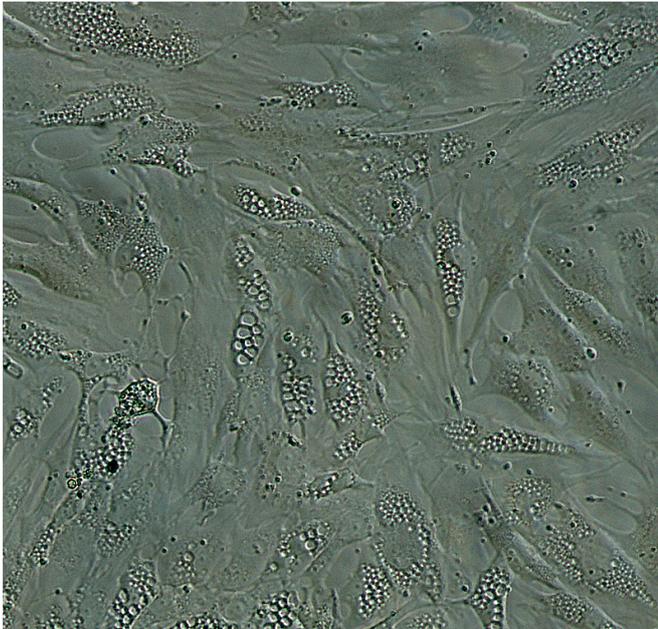


Breast cancer has a higher incidence in obese women as fat facilitates cancer stem cell expansion

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Microscope view of immature adipocytes.

An international team of researchers, with the participation of the University of Granada (UGR), has revealed new data on why breast cancer has a higher incidence and is more aggressive in obese people. The reason is that peritumoral fat (the fat around the tumor) facilitates the expansion and invasion of cancer stem cells (CSCs), which are responsible of the onset and growth of the tumor.

CSCs are found in tumors in a very small proportion, and their main characteristic is that they are responsible for metastasis originating in parts of the body far from the original tumor. Conventional chemotherapy and radiotherapy treatments are not capable of eliminating said CSCs, and often, after the initial response to the treatment, many cancer patients suffer a relapse.

Mechanisms yet to be clarified

The consequences of the obesity epidemic on cancer morbidity and mortality are very serious. It is estimated that up to 20 percent of cancer-related deaths may be attributable to obesity.

Obese women have a greater risk of suffering breast cancer after menopause, and they have a worse progression of the disease no matter their age, but the mechanisms by which obesity contributes to the development and progression of cancer aren't clear yet. Obesity-related fat causes local inflammation and prevents adipocytes (the cells forming fat) from maturing.

For this research, carried out in mice and published in the renowned *Cancer Research* magazine, researchers assessed the effects of coculturing adipocytes with [breast cancer cells](#) on tumor aggressivity, capacity of local invasion and metastatic potential of said tumor.

The results show that the interaction between [tumor cells](#) and immature adipocytes near the tumor during the first stages of breast cancer increased the secretion of cytokines (proinflammatory proteins).

"These cytokines cause a greater expansion of highly metastatic CSCs", UGR professor and co-author Juan Antonio Marchal Corrales explains.

Preclinical rationale

In addition, the researchers have described the mechanism by which this process takes place and its relation to the activation of the SRC Kinase protein. This protein induces the activation of the Sox2 transcription factor (essential to maintain stem cells characteristics) and of a small RNA

molecule called miRNA-302b.

Marchal says, "The prolonged co-culture of tumor cells with immature adipocytes or cytokines increased the proportion of CSCs (which had the ability to form new tumors), the presence of tumor cells in blood, and the metastatic potential after its implementation in mice. And last, we found that SRC-Kinase-inhibiting drugs decrease the production of cytokines and CSCs".

These findings reveal new insights underlying increased [breast cancer mortality](#) in obese individuals and provide a novel preclinical rationale to test the efficacy of SRC inhibitors for [breast cancer](#) treatment.

More information: M. Picon-Ruiz et al.

Interactions between Adipocytes and Breast Cancer Cells Stimulate Cytokine Production and Drive Src/Sox2/miR-302b-Mediated Malignant Progression, *Cancer Research* (2016). DOI: [10.1158/0008-5472.CAN-15-0927](https://doi.org/10.1158/0008-5472.CAN-15-0927)

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