

## LAY ABSTRACT

TITLE: Individual-specific variation in the respiratory activities of HMECs and their bioenergetic response to IGF1 and TNF $\alpha$

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To proliferate and survive cancer cells find new ways to get enough nutrients and energy to meet their needs. The changes in energy production can contribute to the aggressive nature of some forms of cancer. However, it is not known whether there are differences that pre-exist to cancer development or contribute to risk. In order to assess pre-existing variations of energy production (metabolism) in normal cells, we have examined the metabolic pathways in cells of the normal milk ducts in the breast. These cells were chosen because they are the ones largely at risk for developing cancer. We looked at normal breast cells from women who have cancer and compared them to the same types of cells from women who have never had cancer. In examining how these cells make their energy we noticed an interesting difference between the cells isolated from women who have cancer and those that don't. Of those that have cancer, 89-90% did not respond to the addition of pyruvate, a metabolite responsible for providing more energy in the mitochondria (the powerhouses of cells). The lack of pyruvate affects

could be seen in cells from the breast that had cancer as well as the cells from the opposite breast that did not have cancer suggesting that it was specific to the individual not the specific breast tissue. The cells from women who did not have cancer were much more varied. Only half of the breast cells from cancer-free individuals could not respond to the pyruvate. We asked whether the cells that didn't respond were from older or heavier individuals, but these risk factors did not appear to correlate with the lack of response to pyruvate. We tested the impact of two proteins, linked to breast cancer risk, which are found circulating throughout the body. We found that exposure to both proteins could alter the energy pathways, but that one in particular, insulin like growth factor (IGF1), could alter the numbers of cells that could respond to pyruvate in this manner. Taken altogether, this study identifies a potential difference in normal breast cells between women who have developed breast cancer and those that have not. Future studies will be done to determine if this response has a causative or predictive role in breast cancer development.