



NEW YORK REGIONAL SOCIETY OF PLASTIC SURGEONS

2018 RESIDENTS' NIGHT ABSTRACT

Abstract Submission: C3 (Group 2)

Title: *Interrogating the Interactions Between Adipocytes and Breast Cancer in a Patient-Derived Tissue Engineered Platform: Implications for the safety of autologous fat transfer in the setting of breast ductal carcinoma*

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PURPOSE: Autologous fat transfer for breast reconstruction is an increasingly ubiquitous procedure, with 60% of members of the American Society of Plastic Surgeons reporting the use of fat grafting for reconstructive purposes. Despite the increasing popularity, minimal morbidity, and overall good outcomes of this procedure, many unanswered questions remain, including the safety of autologous fat transfer in the setting of breast cancer. Adipocytes have been identified as a source of exogenous lipids in other cancer cell types and may similarly provide energy to fuel malignant survival and growth in breast cancer. Indeed, obesity is a known risk factor for the development and prognosis of breast cancer. To date, clinical studies on the oncologic safety of fat transfer have produced conflicting results and pre-clinical data and models are lacking. Therefore, we have developed a novel, 3D, patient-derived tissue engineered platform to directly assess the metabolic interactions among cells of the breast cancer tumor microenvironment.

METHODS: Breast adipose tissue was acquired from patients undergoing breast reduction surgery. The tissue was enzymatically digested to retrieve adipocytes and adipose stromal cells. Polydimethylsiloxane wells were filled with patient-derived adipocytes labeled with the green fluorescent lipid dye boron-dipyrromethene (BODIPY) and adipose stromal cells encapsulated in type I collagen to mimic the breast cellular microenvironment. A monolayer of red fluorescently-labeled MDA-MB-231 and MDA-MB-468 breast cancer cells were seeded on the surface. Cultures of BC cells in non-adipocyte containing collagen matrices served as controls. Constructs were fixed at 24 and 48 hours after co-culture. Lipid transfer was observed using laser scanning confocal microscopy and analyzed using ImageJ/FIJI and Imaris.

RESULTS: Confocal microscopy revealed a dense culture of native adipocytes containing fluorescent lipid droplets in the 3D collagen culture platform. RFP-expressing breast cancer cells were found in close proximity to lipid-laden adipocytes. Lipid transfer from adipocytes to breast cancer cells was observed by the presence of small, green BODIPY-positive lipid droplets within RFP-expressing breast cancer cells (Figure 1). Breast cancer cells which were not in close proximity to adipocytes did not contain these droplets, and the control collagen disks which did not contain adipocytes or stromal cells also did not demonstrate any lipid droplets

within the breast cancer cell cytosol.

CONCLUSIONS: We have established a novel 3D platform to study the breast cancer microenvironment, and have confirmed for the first time the direct transfer of exogenous lipid from primary human breast adipocytes to breast cancer cells. Transfer of lipids directly from adipocytes to breast cancer cells can induce aberrant metabolism to fuel malignant growth and adaptive survival. Our novel platform can untangle the complex interplay within the breast cancer tumor microenvironment for high-throughput analysis and better elucidate the safety of autologous fat transfer in post-oncologic mastectomy.

Figure 1

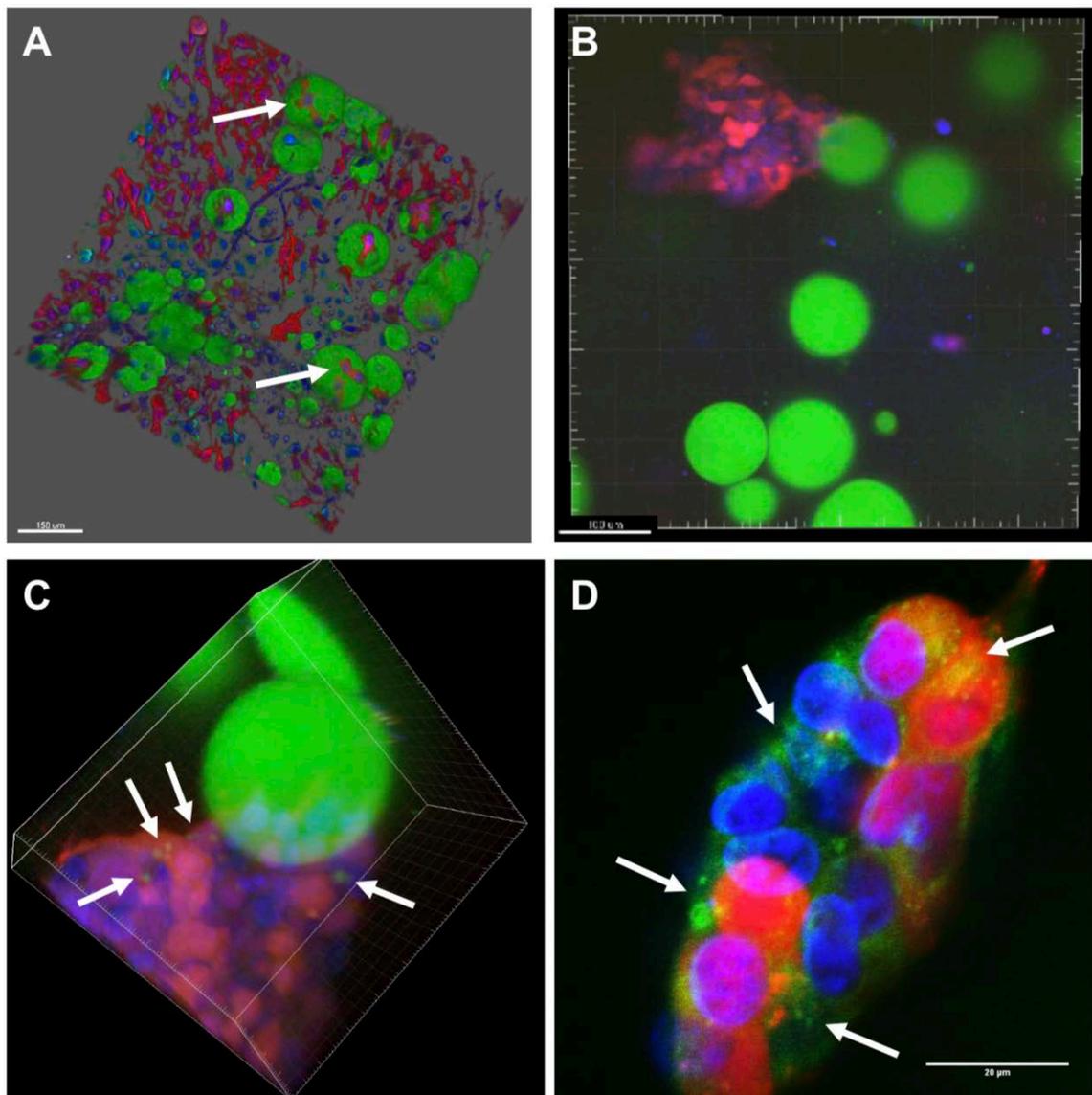


Figure 1. Breast Cancer-Adipocyte Interactions and Lipid Transfer. Confocal microscopy image demonstrating interaction between adjacent RFP-labeled breast cancer cells and BODIPY-stained adipocytes A.) at the MDA-MB-231 breast cancer cell monolayer (white arrows) and B.) between MDA-MB-468 breast cancer cells and adjacent adipocytes within the bulk. C.) Higher magnification

3D image demonstrating lipid droplet accumulation (green, with white arrows) in MDA-MB-468 breast cancer cells (red) after 24-hour incubation with adipocytes. D.) Confocal image of lipid droplet accumulation (green, with white arrows) in MDA-MB-468 breast cancer cells (red) after 48-hour incubation with adipocytes. All images are representative of multiple images taken for both MDA-MB-231 and MDA-MB-468 cells.