Obesity, Adipocytes, and Breast Cancer

PhD thesis - Half time review seminar

April 23\textsuperscript{th}, 2019

Conference room, Kamprad, at 1 PM

Department of Clinical Sciences Lund, Oncology

PhD student: Malin Bergqvist

Main supervisor: Ann Rosendahl, Associate professor, Lund University

Co-supervisors: Signe Borgquist, Professor, Aarhus University/Lund University
Martin Johansson, Professor, University of Gothenburg

Reviewers: Göran B Jönsson, Professor, Lund University
Anna-Maria Larsson, Oncology consultant, Lund University/SUS
Background

Obesity is a global health concern associated with increased incidence and impaired prognosis of breast cancer, where excess body fat and an altered metabolic state can lead to molecular changes favoring tumor progression. The overall project objective is to bring insights into biological processes linking these conditions with implications for breast cancer initiation and prognosis.

Method

The first study investigated the impact by normal and obesity-associated adipocytes on breast cancer cells in vitro with regards to cell morphology, proliferation and motility. The adipokine secretome was analyzed by proteome profiler array for putative biological mediators and adipokine receptor gene expression was explored in breast cancer cell lines and primary breast tumors. Study II investigated associations between the adipokine receptor Adenylate Cyclase Associated Protein 1 (CAP1) with actin regulatory properties, and body constitution among 718 women with primary invasive breast cancer in the Malmö Diet and Cancer study. Tumor-specific CAP1 levels were assessed by immunohistochemistry of tissue microarray, following thorough antibody validation. Covariation of CAP protein expression with patient-/tumor characteristics and breast cancer outcome was explored.

Preliminary results

Study I: Adipocyte-derived factors altered breast cancer cells toward a more aggressive phenotype, effects that were more pronounced when mimicking an obese state. The adipokine resistin was upregulated during obesity-associated compared with normal condition. The resistin-receptor CAP1 gene was more abundantly expressed in estrogen receptor-negative breast cancer cells and was associated with shorter overall and relapse-free survival among breast cancer patients. Study II: Patients with low tumor-specific CAP1 protein expression were older at diagnosis, displayed anthropometric measures indicative of an unhealthier physique, and more often had tumors with unfavorable characteristics. Low CAP1 levels were further associated with impaired breast-cancer specific and overall survival.

Implications

A deeper biological understanding of the effects by obesity on breast cancer progression is needed. Adipocytes stimulate both breast cancer cell proliferation and migration. The adipokine receptor CAP1 displayed a divergent role in breast cancer where high CAP1 gene expression and low tumor-specific CAP1 protein level predicted impaired breast cancer prognosis. These contrasting results warrant further investigations into the regulation of CAP1 and its role in obesity-related breast cancer.

Publications and manuscripts
