Abstract


Leptin and Adiponectin Modulate the Self-renewal of Normal Human Breast Epithelial Stem Cells.

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OBJECTIVE: Multiple mechanisms are likely to account for the link between obesity and increased risk of postmenopausal breast cancer. Two adipokines, leptin and adiponectin, are of particular interest due to their opposing biologic functions and associations with breast cancer risk. In the current study, we investigated the effects of leptin and adiponectin on normal breast epithelial stem cells.

FINDINGS: Levels of leptin in human adipose explant-derived conditioned media positively correlated with the size of the normal breast stem cell pool. In contrast, an inverse relationship was found for adiponectin. Moreover, a strong linear relationship was observed between the leptin/adiponectin ratio in adipose conditioned media and breast stem cell self-renewal. Consistent with these findings, exogenous leptin stimulated whereas adiponectin suppressed breast stem cell self-renewal. In addition to local in-breast effects, circulating factors, including leptin and adiponectin, may contribute to the link between obesity and breast cancer. Increased levels of leptin and reduced amounts of adiponectin were found in serum from obese compared with age-matched lean postmenopausal women. Interestingly, serum from obese women increased stem cell self-renewal by 30% compared with only 7% for lean control serum.

CONCLUSION: Taken together, these data suggest a plausible explanation for the obesity-driven increase in postmenopausal breast cancer risk. Leptin and adiponectin may function as both endocrine and paracrine/juxtacrine factors to modulate the size of the normal stem cell pool. Interventions that disrupt this axis and thereby normalize breast stem cell self-renewal could reduce the risk of breast cancer.

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