Links Between Inflammation, Breast Cancer, and Obesity

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Charlotte Kuperwasser, PhD, Tufts University School of Medicine, Boston, Massachusetts, USA, discussed the links between obesity, inflammation, and breast cancer. In 2009 to 2010, 35.7% of US adults ≥20 years were obese [National Center for Health Statistics. *Health, United States, 2011* 2012]. According to Dr. Kuperwasser, there is an important relationship between obesity and breast cancer pathogenesis that needs to be studied.

Obesity has been associated with increased inflammation. Studies have demonstrated inflammatory changes in the adipose tissue of mammary glands in obese mice fed a high-fat diet. These changes include the presence of macrophages, inflammatory cytokines, and increased neoangiogenesis. Similar changes have been observed in breast tissue from obese women. A human-in-mouse model using human stromal and epithelial mammary gland components was developed to study the development of breast cancer [Kuperwasser C et al. *Proc Natl Acad Sci* USA 2004; Proia DA, Kuperwasser *C. Nat Protoc* 2006]. The model mimics the inflammatory breast stromal changes observed in obesity with the generation of obesity-like stromal cells. Using this model, researchers have investigated the promotion of angiogenesis by macrophages in response to the obesity-like environment. In obese fat tissue, MCP-1 expression is upregulated, resulting in crown-like structures and macrophage recruitment, and increased neoangiogenesis [Arendt LM et al. Submitted]. Additional experiments with this model showed that stromal changes associated with obesity accelerated tumorigenesis, generated higher grade tumors, and increased macrophage recruitment and angiogenesis during the early growth period.

The human-in-mouse model experiments showed that macrophages were necessary for tumor progression associated with obesity. Based on these experiments, Dr. Kuperwasser and colleagues investigated whether tumor growth associated with obesity could be affected by targeting associated macrophages or inflammatory cytokines. The studies found that chemical inhibition of MCP-1 and interleukin-1b with anakinra and RS102895 reduced tumor associated macrophage recruitment to (p=0.02) and angiogenesis in (p=0.01) growing tumors when compared to vehicle. These findings have led to development of a proposed model for disrupting tumor progression in obese fat tissue.

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