

Weight Loss May Change Adipose Tissue Biology, Lowering Cancer Risk

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Being overweight or having a sedentary lifestyle is associated with an increased risk of colorectal cancer, breast cancer (in postmenopausal women), and other cancers. The reasons for this are not entirely clear, but adipose tissue and physical activity are thought to influence metabolism in various ways. In obesity, adipose tissue produces greater amounts of inflammatory cytokines, which leads to a chronic state of low-grade systemic inflammation. Systemic inflammation, including elevated levels of circulating C-reactive protein, has been associated with colorectal and other cancers. It is also linked to obesity-associated insulin resistance, and is associated with several cancers, including breast, colorectal, endometrial and pancreatic cancer. Finally, adipose tissue also synthesizes estrogen, which plays a role in breast and endometrial cancers.

Past research into how changes in energy balance influence adipose tissue biology have largely been limited to studies of extreme caloric restriction. Those studies provided some evidence for an effect on inflammation, for example changes in expression of the hormone leptin, which regulates energy balance by influencing appetite and metabolism. However, it is not known how weight loss (whether by changing diet, exercise, or both) affects adipose tissue biology. Drs. Neli Ulrich, Karen Foster-Schubert, Kristin Campbell, Karen Makar, Mario Kratz, Anne McTiernan, Catherine Duggan and colleagues in the Public Health Sciences Division examined the effects after six months of diet, exercise, or both on gene expression in adipose tissue in 45 overweight or obese postmenopausal women. They also investigated whether weight loss was associated with changes in gene expression. They obtained adipose tissue samples at baseline and at six months, and investigated the expression of individual genes, as well as 15 gene sets which represent relevant metabolic pathways and which were specified *a priori*.

After six months, all three intervention groups had lost weight (diet: mean 8.8 kg, exercise: 2.5 kg, diet and exercise: 7.9 kg), with no change in controls. There was little change in the expression of the 15 pre-specified gene sets by diet or exercise groups. In contrast, when investigators examined differences by weight-change category, they observed that greater weight loss was associated with alterations in several gene-expression pathways. These included decreased expression of leptin and 17 β -hydroxysteroid dehydrogenase-1, a component of the estrogen metabolism pathway, as well as increased expression of estrogen receptor-1 and insulin-like growth factor-binding protein-3 (IGFBP-

3), another protein thought to be relevant to inflammation and the link between obesity and cancer. They also identified multiple new genes which were not hypothesized *a priori* to be associated with weight loss; their potential relationships to energy balance should be investigated further.

“We know that adipose tissue is not just a storage compartment, but can be an important player in metabolism,” according to Dr. Neli Ulrich. “This study showed that weight loss was associated with measurable changes in adipose tissue gene expression, particularly in genes encoding for adipokines, insulin signaling, and synthesis of sex hormones, and improves our understanding of the relationship between weight loss and change in expression of several genes related to cancer risk.”

“Our sample size was too small to discern different effects of a caloric-restriction program or exercise. It will be important to follow up in larger studies to understand the biologic mechanisms of these two different types of interventions on adipose tissue functioning and also to investigate other parameters, such as the influence on stromavascular cells,” Dr. Ulrich noted.

[Campbell KL, Foster-Schubert KE, Makar KW, Kratz M, Hagman D, Schur EA, Habermann N, Horton M, Abbenhardt C, Kuan LY, Xiao L, Davison J, Morgan M, Wang CY, Duggan C, McTiernan A, Ulrich CM.](#) Gene Expression Changes in Adipose Tissue with Diet- and/or Exercise-Induced Weight Loss. *Cancer Prev Res* (Phila). 2013 Mar;6(3):217-31. doi: 10.1158/1940-6207.CAPR-12-0212. Epub 2013 Jan 22.

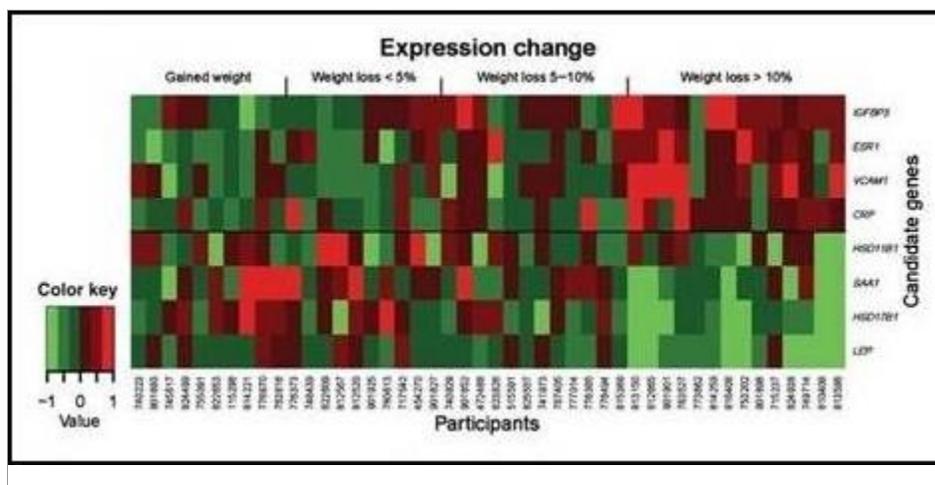


Figure modified from Campbell KL et al. *Cancer Prev Res* 2013;6:217-231

Differential gene expression, by weight change. Heat map displaying changes in expression of prespecified genes over 6 months in individuals with no weight loss, compared to those with <5%, 5–10%, and >10% weight loss. Gradients indicate the level of gene expression change over

time.
