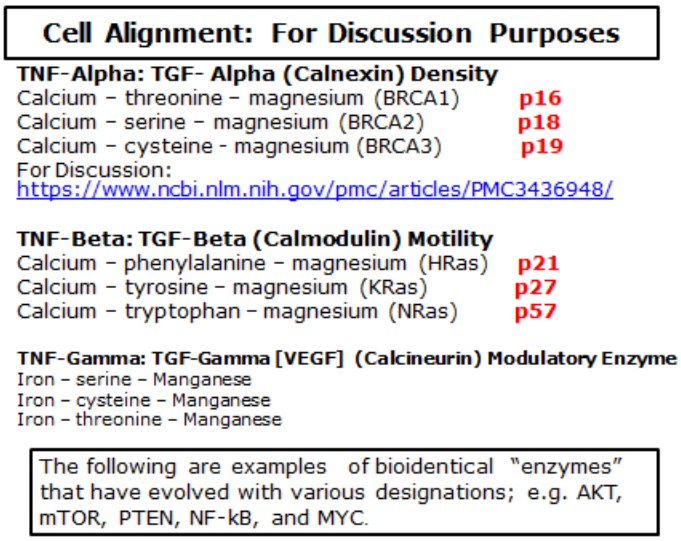
MCFIP - Numerous studies link angina pectoris to calnexin.

Refer to the following for discussion purposes with qualified computational biologists.



Many studies correlated cholesterol-27-hydroxylase (CH27H - 27HC) and cholesterol-25-hydroxylase (CH25H - 25HC) with BRCA1 and BRC2. A sizeable number of studies link angina pectoris to 27HC or calnexin.

Our computational biology modeling in conjunction with neuropeptide relationship between NPY (nitric oxide based) and PP (hydrogen sulfide based) provide verifiable support for the fact that interactions between the vasodilator nitric oxide the vasoconstrictor hydrogen sulfide can result in a spectrum of outcomes ranging from angina pectoris to a heart attack.

From the perspective of cardiometabolic disease, based on frequency, angina is a biomarker for a possible heart attack that must be addressed by a primary care physician.

https://neurosciencenews.com/obesity-molecule-14823/

The role of a single molecule in obesity

NEUROSCIENCE NEWSAUGUST 28, 2019

Summary: *A molecule called 27HC directly affects white adipose tissue and increases body fat, even if you eat a healthy diet.*

Source: *University of Houston*

A single cholesterol-derived molecule, called 27-hydroxycholesterol (27HC), lurks inside your bloodstream and will increase your body fat, even if you don't eat a diet filled with red meat and fried food. That kind of diet, however, will increase the levels of 27HC and body weight.

"We found 27HC directly affects white adipose (fat) tissue and increases body fat, even without eating the diet that increases body fat," reports University of Houston assistant professor of biology Michihisa Umetani in the journal *Endocrinology*. First author of the paper, doctoral student Arvand Asghari, adds, "But it does need some help from the diet to increase body weight because it expands the capacity of the fat already in the body."

Long term applications of the findings could lead researchers to a treatment that reduces the levels of 27HC, which could result in reduced capacity for making fat. "We hope to develop a new therapeutic approach toward modulating 27HC levels to treat cholesterol and/or estrogen receptor-mediated diseases such as cardiovascular diseases, osteoporosis, cancer and metabolic diseases," said Umetani, whose lab is part of the UH Center for Nuclear Receptors and Cell Signaling.

Prior to this research, 27HC was known as an abundant cholesterol metabolite, and Umetani's group has reported its detrimental effects on the cardiovascular system, but its impact on obesity was not well known.

Role of estrogen receptors

Obesity is one of the main risk factors influencing cardiovascular disease worldwide in both men and women and estrogen plays a role in both sexes. Menopause in females, with its accompanying decrease in estrogen, seems to hasten the increase in fat tissue because estrogen protects against adiposity and body weight gain. In men, estrogens are also synthesized locally by conversion of testosterone, so they may also play important roles in the development of fat tissues in males.

"Estrogen receptors (ERα and ERβ) are members of the nuclear receptor superfamily and are present in adipocytes," said Umetani. "Patients with a non-functional ERα are obese, and those that do not have ERα have increased fat tissue even when they eat the same amount of food, indicating that ERα is the important isoform in the regulation of adipose tissue by estrogen."

The main function of 27HC in the liver is to reduce excess cholesterol. Previously, Umetani discovered that 27HC binds to estrogen receptors and acts as an inhibitor of ER action in the vasculature. It turned out that the effects by 27HC are tissue-specific, thus 27HC is the first identified naturally-produced selective estrogen receptor modulator, or SERM.

ABOUT THIS NEUROSCIENCE RESEARCH ARTICLE

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Original Research: Closed access
"27-Hydroxycholesterol Promotes Adiposity and Mimics Adipogenic Diet-induced Inflammatory Signaling". Arvand Asghari, Tomonori Ishikawa, Shiro Hiramitsu, Wan-Ru Lee, Junko Umetani, Linh Bui, Kenneth S Korach, Michihisa Umetani.
Endocrinology. doi:10.1210/en.2019-00349

Abstract

27-Hydroxycholesterol Promotes Adiposity and Mimics Adipogenic Diet-induced Inflammatory Signaling

27-Hydroxycholesterol (27HC) is an abundant cholesterol metabolite and has detrimental effects on the cardiovascular system, while its impact on adiposity is not well known. In this study, we found that elevations in 27HC cause increased body weight gain in mice fed a high-fat/high-cholesterol diet in an estrogen receptor (ER) α-dependent manner. Regardless of diet type, body fat mass was increased by 27HC without changes in food intake or fat absorption. 27HC did not alter energy expenditure in mice fed a normal chow diet and increased visceral white adipose mass by inducing hyperplasia but not hypertrophy. While 27HC did not augment adipocyte terminal differentiation, it increased the adipose cell population that differentiates to mature adipocytes. RNA sequencing analysis revealed that 27HC treatment of mice fed a normal chow diet induces similar inflammatory gene sets as those seen after high-fat/high-cholesterol diet feeding, while there was no overlap in inflammatory gene expression among any other 27HC administration/diet change combination. Histological analysis showed that 27HC treatment increased the number of total and M1-type macrophages in white adipose tissues. Thus, 27HC promotes adiposity by directly affecting white adipose tissues and by increasing adipose inflammatory responses. Lowering serum 27HC levels may lead to an approach targeting cholesterol to prevent diet-induced obesity.