

Late Breaking News

Research Highlights from Penn State Researchers

Cardiolipin Remodeling by ALCAT1 Links Oxidative Stress and Mitochondrial Dysfunction to Obesity

By Jia Li, Caroline Romestaing, Xianlin Han, Yuan Li, Xinbao Hao, Yinyuan Wu, Chao Sun, Xiaolei Liu, Leonard S. Jefferson, Jingwei Xiong, Kathryn F. LaNoue, Zhijie Chang, Christopher J. Lynch, Huayan Wang, Yuguang S

Cardiolipin is a fatty molecule that is an essential part of the cellular machinery that carries out the final step in converting the food we eat into a usable source of energy for the body. This final energy-conversion process requires oxygen, and “oxidative stress” develops if the system is overloaded. Oxidative stress results in damage to the cardiolipin molecules, and can be observed in association with many metabolic diseases including diabetes and obesity. ALCAT1, an enzyme produced by cells in response to oxidative stress in conditions such as diet-induced obesity, was recently found to be involved in the production of a specific type of cardiolipin that is extremely sensitive to oxidative damage, causing the body’s energy producing components to function improperly. This damage has now also been linked to insulin resistance. The resulting damage is similar to that which is observed in type 2 diabetes. Interestingly, the damage was found to be reversed by treatment with an anti-diabetic drug that works as an insulin sensitizer. Consequently, a lack of the ALCAT1 enzyme prevented the onset of diet-induced obesity and significantly improved energy production and insulin signaling in mice. These findings identify a key role of ALCAT1 in the body’s ability to create a usable source of energy as well as one’s likelihood of developing diet-induced obesity.

Cell Metabolism, Volume 12, Issue 2, 154-165, 4 August 2010 Copyright © 2010 Elsevier Inc. All rights reserved. 10.1016/j.cmet.2010.07.003

Link to the published abstract: [//www.cell.com/cell-metabolism/abstract/S1550-4131%2810%2900235-4#Summary](http://www.cell.com/cell-metabolism/abstract/S1550-4131%2810%2900235-4#Summary)

Gastric Bypass Surgery Alters Behavioral and Neural Taste Functions for Sweet Taste in Obese Rats

By Hajnal A, Kovacs P, Ahmed TA, Meirelles K, Lynch CJ, Cooney RN.

Roux-en-Y gastric bypass surgery (GBS) is the most effective treatment for morbid obesity. GBS is a restrictive malabsorptive procedure, but many patients also report altered taste preferences. This study investigated the effects of GBS or a sham-operation (SH) on body weight, glucose tolerance, behavioral and neuronal taste functions in the obese Otsuka Long-Evans Tokushima Fatty (OLETF) rats lacking CCK-1 receptors and lean controls (LETO). OLETF-GBS rats lost body weight (-26%) and demonstrated improved glucose tolerance. They also expressed a reduction in 24-h 2-bottle preference for sucrose (0.3 and 1.0M) and decreased 10-s lick responses for sucrose (0.3M through 1.5M) compared to OLETF-SH or LETO-GBS. A similar effect was noted for other sweet compounds but not for salty, sour or bitter tastants. In lean rats, GBS did not alter responses to any stimulus tested. Extracellular recordings from 170 taste-responsive neurons of the pontine parabrachial nucleus revealed a right-ward shift in concentration-responses to oral sucrose in obese compared to lean rats (OLETF-SH vs. LETO-SH): overall increased response magnitudes (above 0.9M), and maximum responses occurring at higher concentrations (+0.46M). These effects were reversed by GBS, and neural responses in OLETF-GBS were statistically not different from those in any LETO groups. These findings confirm obesity-related alterations in taste functions and demonstrate the ability of GBS to alleviate these impairments. Furthermore, the beneficial effects of GBS appear to be independent of CCK-1 receptor signaling. An understanding of the underlying mechanisms for reduced preferences for sweet taste could help in developing less invasive treatments for obesity.

Am J Physiol Gastrointest Liver Physiol. 2010 Jul 15. [Epub ahead of print]

PMID: 20634436 link: <http://www.ncbi.nlm.nih.gov/pubmed/20634436>

Effects of Friedreich's Ataxia GAA Repeats on DNA Replication in Mammalian Cells

By Gurangad S. Chandok¹, Mayank P. Patel¹, Sergei M. Mirkin^{2,*} and Maria M. Krasilnikova¹

ABSTRACT

Friedreich's ataxia (FRDA) is a common hereditary degenerative neuro-muscular disorder caused by expansions of the (GAA)_n repeat in the first intron of the frataxin gene. The expanded repeats from parents frequently undergo further significant length changes as they are passed on to progeny. Expanded repeats also show an age dependent instability in somatic cells, albeit on a smaller scale than during intergenerational transmissions. Here we studied the effects of (GAA)_n repeats of varying lengths and orientations on the episomal DNA replication in mammalian cells. We have recently shown that the very first round of the transfected DNA replication occurs in the lack of the mature chromatin, does not depend on the episomal replication origin and initiates at multiple single-stranded regions of plasmid DNA. We now found that expanded GAA repeats severely block this first replication round post plasmid transfection, while the subsequent replication cycles are only mildly affected. The fact that GAA repeats affect various replication modes in a different way might shed light on their differential expansions characteristic for FRDA.

Nucleic Acids Research. 2012 Jan 19.

Link to full article: <http://nar.oxfordjournals.org/content/early/2012/01/18/nar.gks021.full-text-lowres.pdf>