

New Pathways Explored for Diabetes, Obesity, and Inflammation

When a person has diabetes, the condition is often associated with other health problems, too. For example, diabetes has such a strong link with obesity that the term “diabesity” is often used by healthcare professionals. The excess fat that an obese person carries with them produces many inflammatory substances. The resulting inflammation in the body contributes to joint pain, sleep apnea (breathing stops for short periods of time during the night), gall bladder disease, liver injuries, as well as heart disease and damage to blood vessels. Given the strong links between diabetes, obesity, and inflammation, researchers are looking at new pathways in the body that can be targets for drug treatments. Drugs that may eventually be developed might not only assist in treating diabetes, but could also be of benefit in health conditions that involve inflammation and obesity. Four specific targets are currently being explored by researchers including adiponectin, ghrelin, resveratrol, and leptin.



Adiponectin is a protein that is produced in fat tissue. It is released into the blood stream and appears to regulate a variety of processes involved with diabetes. For example, adiponectin helps cells remove sugar from the blood, it helps the body respond better to insulin, and it blocks the liver from making sugar. Studies in people with diabetes found levels of adiponectin are often low in these patients. Small investigations have recognized that some drugs already used as treatments for diabetes may increase adiponectin levels, including glimepiride (Amaryl), pioglitazone (Actos), and rosiglitazone (Avandia). Even some blood pressure medications were found to increase adiponectin levels. Additional treatments are ongoing to investigate exactly how

FOR MORE INFORMATION

American Diabetes Association
<http://professional.diabetes.org/UserFiles/File/Make%20the%20Link%20Docs/CVD%20Toolkit/03-Taking-Care.pdf>

National Institute of Diabetes and Digestion and Kidney Disease
http://win.niddk.nih.gov/publications/health_risks.htm

National Library of Medicine
www.nlm.nih.gov/medlineplus/diabetes.html

Based on “Diabetes Mellitus, Inflammation, Obesity: Proposed Treatment Pathways for Current and Future Therapies” by Travis Sonnett, Terri Levien, Brian Gates, *The Annals of Pharmacotherapy*, April 2010, <http://dx.doi.org/10.1345/aph.1M640>. For Our Patients is provided by *The Annals* to help explain the latest research and information relating to your medications. These summaries are for informational purposes only and are not a substitute for professional advice from your personal medical provider. If you have questions about this material, you should discuss it with your physician or pharmacist. This summary may be reproduced without permission for not-for-profit educational purposes only. Any other use must be approved by the publisher. © Copyright 2010, Harvey Whitney Books Company, hwbooks.com.
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adiponectin fits into diabetes and obesity. In the future, drugs that mimic the actions of adiponectin may be developed.

Gherlin is a small protein made in the intestines, but its actions are in the brain. Specifically, gherlin stimulates appetite. As a result, higher levels of gherlin circulating in the body can cause people to eat more, gain weight, and deposit more fat cells. In addition, gherlin inhibits insulin release from the pancreas and blocks the breakdown of fat. Both of these effects can worsen diabetes problems. Some people think that gherlin may cause people to have difficulty losing weight or even be responsible for some individuals regaining weight quickly after initial weight loss. Drugs that block the actions of gherlin restore insulin function, reduce appetite and promote weight loss in rats and mice. However, studies in humans have not yet been conducted.

Resveratrol is found in peanuts, grapes, and red wine. Many people think that it is the resveratrol component of wine that explains why the French population (who often drink red wine) has a lower rate of heart disease compared to other European countries despite similar diets high in saturated fat. Specifically, resveratrol activates a protein that protects cells from oxidative stress and DNA damage. It is thought that resveratrol and related compounds protect cells from damage that occurs with aging and chronic diseases. As a result resveratrol-like compounds may prevent or protect cells from damage caused by high blood sugar levels. This could be beneficial since people

with diabetes often suffer from nerve, kidney, and retinal damage. In rats, resveratrol reduces inflammation, protects from nerve damage, and decreases nerve pain. Resveratrol is unique because it is being developed as a drug, but it is already available as a dietary supplement, and it is found in foods. Human studies with resveratrol and other related pharmaceutical compounds are currently under way.

Like adiponectin, leptin is usually made in fat cells. Fifteen years ago, researchers discovered that this protein is deficient in severely obese mice. When leptin was administered to the mice, substantial decreases in food intake and body weight were noted. Unfortunately, the same effects were not observed when the protein was given to obese people. Leptin, by itself, did not lead to weight loss in overweight individuals. It appears that obese people already have high levels of leptin in their body, but their body has become resistant to it. Recent studies have focused on ways to make the body more sensitive to the effects of leptin. In mice, giving leptin along with leptin “sensitizers”, looks promising. Time will tell whether this new approach will also work in humans.

There is much that remains to be understood about diabetes. Studies that investigate these 4 new pathways are in early stages of exploration. Further studies in both animals and humans will be needed. Perhaps someday, new drugs that target these pathways will improve current treatment options for people with diabetes and related conditions.