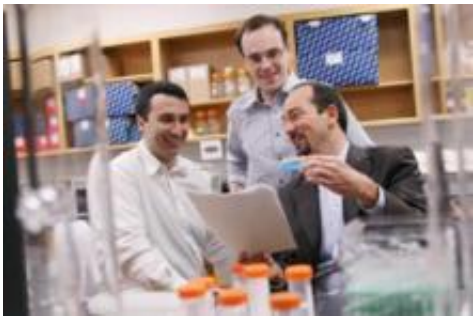
Study shows how substance in grapes may squeeze out diabetes

October 15 2009



From left: Drs. Giorgio Ramadori, Laurent Gautron and Roberto Coppari are researchers at UT Southwestern Medical Center. Credit: UT Southwestern Medical Center

A naturally produced molecule called resveratrol, found in the skin of red grapes, has been shown to lower insulin levels in mice when injected directly into the brain, even when the animals ate a high-fat diet.

The findings from a new UT Southwestern Medical Center study suggest that when acting directly on certain proteins in the brain, resveratrol may offer some protection against diabetes. Prior research has shown that the compound exerts anti-diabetic actions when given orally to animals with type 2 diabetes (non-insulin dependent diabetes mellitus), but it has been unclear which tissues in the body mediated these effects.

"Our study shows that the brain plays an important role in mediating

resveratrol's anti-diabetic actions, and it does so independent of changes in food intake and body weight," said Dr. Roberto Coppari, assistant professor of internal medicine at UT Southwestern and senior author of the study appearing online and in the December issue of Endocrinology.

"These animals were overrun with fat and many of their organs were inflamed. But when we delivered resveratrol in the brain, it alleviated inflammation in the brain," added Dr. Coppari.

Dr. Coppari emphasized that his study does not support the conclusion that consuming products made from red grapes, such as red wine, could alleviate diabetes.

"The main reason is that resveratrol does not cross the blood brain barrier efficiently," he said. "In order for the brain to accumulate the same dose of resveratrol delivered in our study, the amounts of red wine needed daily would surely cause deleterious effects, especially in the liver. Rather, our study suggests that resveratrol's analogs that selectively target the brain may help in the fight against diet-induced diabetes."

For the study, the researchers investigated what happens when resveratrol acts only in the brain. Specifically, they wanted to know whether resveratrol injected in the brain activated a group of proteins called sirtuins, which are found throughout the body and thought to underlie many of the beneficial effects of calorie restriction. Previous animal research has shown that when these proteins are activated by resveratrol, diabetes is improved. In addition, drugs activating sirtuins currently are being tested as anti-diabetic medications in human trials, Dr. Coppari said.

In one group of animals, researchers injected resveratrol directly into the brain; another group received a saline-based placebo. All the surgically treated animals consumed a high-fat diet before and after the surgery.

Dr. Coppari said the insulin levels of the animals treated with the placebo solution rose increasingly higher post-surgery. "That's a normal outcome because insulin sensitivity decreases the longer you keep an animal on a high-fat diet."

Insulin levels in the mice given resveratrol, however, actually started to drop and were halfway to normal by the end of the five-week study period, even though the animals remained on a high-fat diet.

In addition, the researchers found that resveratrol did indeed activate sirtuin proteins in the brain.

Dr. Coppari said the findings support his team's theory that the brain plays a vital role in mediating the beneficial effects of resveratrol and that manipulation of brain sirtuins also may have other beneficial outcomes. "By knowing that the central nervous system is involved, pharmaceutical companies can begin to focus on developing drugs that selectively target sirtuins in the brain," he said.

The next step, Dr. Coppari said, is to determine precisely which neurons in the brain are mediating the effects of the resveratrol.

Source: UT Southwestern Medical Center (news : web)