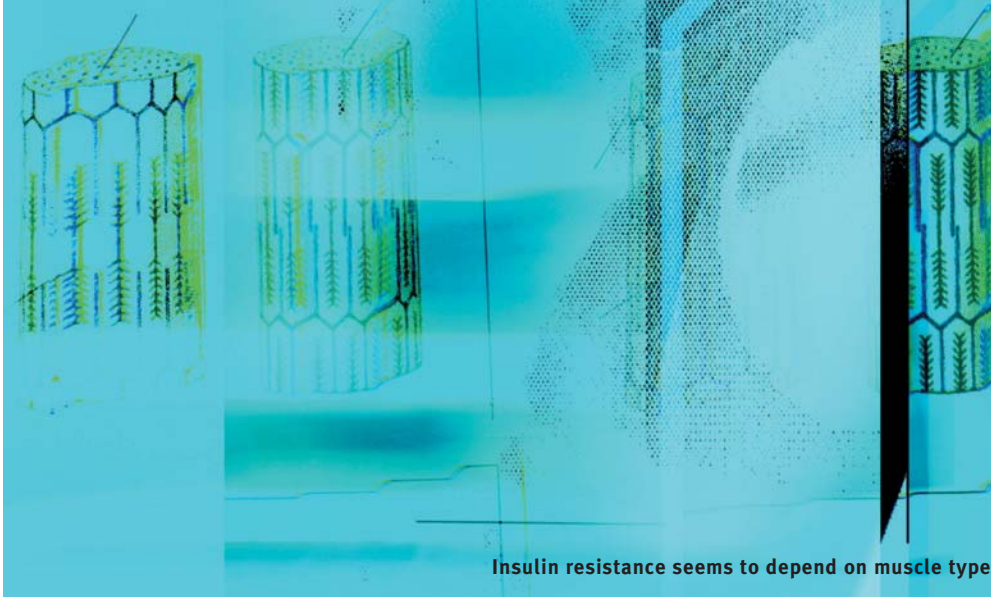
GOODPASTER ON DIGESTIVE DOMINOES

BY SARA GOUDARZI



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Insulin resistance seems to depend on muscle type

DIABETES: WHAT'S MUSCLE GOT TO DO WITH IT?

How well our skeletal muscles do their job seems to be a key factor in the development of type 2 diabetes. The specifics, however, are unclear.

Bret Goodpaster, a PhD associate professor of medicine at the University of Pittsburgh, thinks that insulin resistance depends on muscle type and its ability to accumulate potentially harmful lipids that affect sugar absorption.

We rarely think about how our bodies extract energy from food. After a meal, carbohydrates are absorbed into the bloodstream. The rest is pretty much a digestive domino effect: The pancreas secretes insulin, which attaches to cell receptors and activates other receptors to allow sugar absorption. The absorbed glucose is either oxidized or stored for later use.

At least, that's how it's supposed to work.

For about 23 million people in this country who suffer from diabetes, there's a glitch in the process. The pancreas of those with type 1 diabetes can't produce insulin. For people with type 2 diabetes—that's about 90 percent of all diagnosed diabetes cases—the pancreas secretes insulin, but it's either not enough or their bodies' cells don't respond to the hormone.

"It's not a case of insulin not being present, it's just not able to do what it needs to do to stimulate that glucose metabolism," says Goodpaster. Exactly why some people have this inability to respond to insulin has been a mystery to the scientific community, and one that Goodpaster hopes to solve.

A lifelong cyclist, Goodpaster has always been interested in exercise and human performance. He became more serious about the field when his father, at the age of 39, had quintuple coronary bypass surgery. Goodpaster was in high school at the time.

"I made the study of biology, health, disease, and exercise my passion and career," says Goodpaster.

Goodpaster has a master's degree in exercise physiology from Ohio's Kent State University and a PhD in human physiology from Ball State University, in Muncie, Ind. In addition to focusing on type 2 diabetes, he studies age-related loss of functional capacity and mobility.

Goodpaster takes advantage of novel methods, such as the acquisition of muscle and fat tissue from biopsies. By examining proteins and genes in skeletal muscle samples from human subjects, Goodpaster and his colleagues can translate findings back and forth from humans to animals and cell systems and models.

"We can literally look inside the muscle cells and see what might be some of the underlying mechanisms for this insulin resistance," he explains. "We have found that muscle cells accumulate a variety of lipids, some of which appear to be used as fuel for the muscle, whereas others appear to have a negative impact on the way the muscle effectively uses glucose."

He has recently begun to elucidate how diet and exercise seem to work at the muscle level in improving insulin resistance for type 2 diabetes.

"[We] look at accumulation of lipids in muscle to see how this might be related to this fatty acid metabolism, mitochondria function, and then, in turn, how all this potentially plays a role in the development of type 2 diabetes," he says.

Earlier this year, Goodpaster and his team convincingly showed that when older adults lose weight by dieting alone, they also lose significant amounts of muscle mass—which could affect their mobility and independence. But when they combine calorie restriction with exercise, they can nearly completely prevent that loss of muscle associated with dieting.

His group is also one of the few in the world to use positron emission tomography to look at insulin resistance in glucose metabolism of skeletal muscles. In his study, volunteers are infused with a radioactive tracer that emits positrons when glucose is metabolized; that way, researchers can pinpoint locations in the body where it's metabolizing. Physicians typically use this technology in cancer patients to determine whether a tumor is active based on how much glucose it's breaking down.

"We're essentially doing the same thing, except in fairly healthy people, looking at glucose metabolism in muscle response to insulin to see if we can get more mechanistic information about their insulin resistance," Goodpaster says.

This mechanistic information, Goodpaster hopes, will help the digestive dominoes fall into place for the 8 percent of the population suffering from type 2 diabetes. ■