San Francisco, CA - New data presented last week at EPI|NPAM 2010, the Cardiovascular Disease Epidemiology and Prevention and Nutrition, Physical Activity, and Metabolism 2010 Conference, provided some early evidence that the secret to weight loss might lie in DNA and that the best way to shed excessive pounds is to diet according to genotype [1].

Researchers are cautious, of course, but the latest study showed that when individuals were assigned to different diets—including the low-carbohydrate Atkins diet and low-fat Ornish diet—based on their genotype, they lost significantly more weight than those assigned to a diet unsuited to their genetics.

"Say you and your wife went on the Atkins diet, and you both think you followed it religiously, but you lost 13 pounds and she lost nothing and is angry because she followed the same diet. Well, she might have a different genotype," senior investigator Dr Christopher Gardner (Stanford University, CA) told heartwire. "She isn't genetically predisposed to do well on a low-carbohydrate Atkins diet."

Lead investigator on the study was Dr Mindy Dopler Nelson (Stanford University).

From A to Z to DNA

Dr Christopher Gardner

The new data are derived from a study the group previously conducted in 311 overweight women who were randomized to four popular diets: the very-low-carbohydrate Atkins diet, the low-carbohydrate Zone diet, the very-low-fat Ornish diet, and the low-fat LEARN diet. In that trial, known as the Atkins-Traditional-Ornish-Zone (A TO Z) study, which was previously reported by heartwire, women assigned to the Atkins diet had a modest benefit relative to the other diets, but overall results were disappointing in that the women, on average, lost only about 10 pounds.

"Within every diet group, though, some of the women lost more than 30 pounds and kept it off for over a year," said Gardner. "And some of the women gained more than 10 pounds. Within every diet, the range is at least 40 to 50 pounds. Between the different diets, the weight loss difference was just a few pounds, yet within the group, the difference is much larger. This is actually much more interesting than the difference between groups. How can the responses to the same diet be so different?"

With these data, the researchers were approached by Interleukin Genetics (Waltham, MA), asking them if they could obtain the DNA of the study participants. The company had previously identified three genes—ABP2, ADRB2, and PPAR-gamma—that could predict weight loss. These genes were shown to predict weight loss in three different studies, were biologically plausible, and were shown to have gene-diet interaction, said Gardner.

The researchers obtained DNA from 138 women and analyzed the weight loss according to genotype and diet in 133 participants. Among those participants who completed the 12-month study, researchers observed a significant interaction between diet assignment and weight loss after taking genotype pattern into consideration.

Women assigned to a genotype-appropriate diet lost 5.3% of their body weight compared with just 2.3% among those not matched to genotype (p=0.005). Within the Atkins group, for example, those appropriately assigned by genotype lost approximately 12 pounds compared with 2 pounds for those who lacked the low-carbohydrate genotype. In the Ornish group, similar reductions in weight were observed among those appropriately assigned by genotype.

Gardner said the proportion of individuals who were genetically predisposed to the low-fat or low-carbohydrate diets is roughly 50-50, so a significant number of people will fall into each category. He stressed, however, that all individuals assigned to the diet groups were instructed to make healthy, wholesome food choices.

"If they were on low-carbohydrate and high-fat, they weren't told to eat butter and whipped cream but to eat nuts, seeds, and fatty fish," he said. "If they were on the low-fat diet, they weren't told to just eat low-fat Snackwell cookies but to eat veggies, whole grains, and beans. I get worried when people just say low-carbohydrate or low-fat because they don't really understand what that means. This is what really undermines the whole public-health low-fat message."

Part of the whole nutrition puzzle

Commenting on the results of the study for heartwire, Dr Lawrence J Appel (Johns Hopkins University, Baltimore, MD) said there is interest in the genetic underpinnings of nutrition, but these provocative findings need to be replicated by other researchers. He stressed, however, that the environment is key in reducing obesity worldwide.

"This is an area of burgeoning interest," said Appel, "but the obesity epidemic occurred pretty quickly, over the past 10 or 20 years, and our genetic pool did not change in the same period. Our obesity epidemic is an environmental problem. Given the environment, genes might influence the response to the environment, but are the genes causal? No. It's likely that the environment has a dominant impact."

Gardner agrees, telling heartwire that the genetic predisposition to do well on certain diets, but not on others, will not put an end to the obesity epidemic, but that the findings could be helpful in fighting the battle of the bulge. The results are retrospective and need to be interpreted cautiously, but his group is planning to conduct a larger prospective study that assigns individuals to the different diets based on genotype.

"The results don't explain the whole nutrition puzzle, but it explains a large enough chunk to be of interest," he said.

Gardner and Nelson have no financial stake in Interleukin Genetics or the genetic test the company manufactures. Three other authors of the paper, Drs Prakash Prabhakar, Venkateswarlu Kondragunta, and Kenneth Kornman, are employees of Interleukin Genetics