HEALTH

Gene study: People who eat less can live longer

WASHINGTON (AP) — Genes that play a key role in aging tend to stay vigorous in response to a low-calorie diet, says a study that may help explain why animals that eat less often live longer.

Tomas A. Prolla and Richard Weindruch, both of the University of Wisconsin, Madison, said their genetic analysis of mice showed that genes that normally deteriorate with age tended to continue functioning in a youthful way when the mice were underfed.

They said the study, to be published in the journal *Science* on Friday, may explain why a reduced-calorie diet can cause mice to live up to 50 percent longer.

Weindruch said it is not scientifically appropriate yet to recommend that people of normal weight go on calorie-restricted diets in order to prolong life, but he added: "This line of research bears watching."

He also said the research could lead to drugs that would help slow the aging process in humans, although there have been no definitive studies proving that a reduced-calorie diet in humans will extend life.

What is clear, Weindruch said, is that obesity damages health and that one reason for this might be changes in genes linked to aging.

There have been studies in monkeys that show a low calorie diet does lower blood pressure and raise levels of "good" cholesterol, both signs of improved health that suggest a longer life. Those studies, however, did not examine the fundamental genetic changes that occur as a part of the aging process.

Reduced-calorie diet can cause mice to live up to 50 percent longer.

"This study is quite important because it breaks new ground in giving us an understanding of what happens to gene expression with age," said Dr. Raj Sohal, a professor of biological sciences at Southern Methodist University. Although the study was with mice, he said it suggests that "if you overeat, you are accelerating the aging process."

"This study has analyzed more genes with regard to aging than all previous studies combined," said Prolla. He said 5 to 10 percent of the entire mouse genome was examined.

In the Wisconsin laboratory study, the researchers fed one group of mice a regular diet while restricting by 24 percent the calories in the food given to another group. The diets all contained healthful levels of vitamins, minerals and proteins. Only the calories were reduced. This creates a condition of undernutrition, but not malnutrition, Weindruch said.

After 30 months, muscles were taken from the animals and the activity of 6,347 genes was analyzed.

"We chose muscle for analysis because it is an important target for the effects of aging," Weindruch said. "Muscle is lost routinely with old age and contributes to physical frailty."

The researchers found that more than 100 genes either increased or decreased their activity with age. "At the molecular level, normal aging looks like a state of chronic injury in muscle," said Prolla.

However, for mice fed the restricted diet, about 84 percent of the genetic alterations associated with aging were completely or partially suppressed.

"At the molecular level," the study found, "calorie-restricted mice appear to be biologically younger than animals receiving the control diet."

"This clearly suggests that the reduction of calorie intake not only increases lifespan in mice, but seems to affect a broad spectrum of age-associated changes at the gene expression level," said Weindruch. He said these genetic changes clearly play a role in extending life in those animals.

Many of the genes affected by aging are those that help the body rid itself of oxygen radicals, chemicals produced during the process of metabolizing calories in cells. Oxygen radicals are known to be damaging to DNA, the body's genetic material.

Mice fed the full-calorie diet tended to lose the benefit of these oxygen radical control genes with age. The genes continued to work vigorously, however, in mice fed the calorie restricted genes.

Though the study evaluated muscles, Weindruch said that similar molecular effects may occur in the brain and in the heart, both of which tend to show the effects of the aging process.