Cell's 'power plant' genes raise vision disorder risk

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Genetic variation in the DNA of mitochondria – the "power plants" of cells – contributes to a person's risk of developing age-related macular degeneration (AMD), Vanderbilt investigators report May 7 in the journal *PLoS ONE*.

The study is the first to examine the mitochondrial genome for changes associated with AMD, the leading cause of blindness in Caucasians over age 50.

"Most people don't realize that we have two genomes," said lead author Jeff Canter, M.D., M.P.H., an investigator in the Center for Human Genetics Research. "We have the nuclear genome – the "human genome" – that makes the cover of all the magazines, and then we also have this tiny genome in mitochondria in every cell."

Canter teamed with Jonathan Haines, Ph.D., and Paul Sternberg, M.D., experts in AMD genetics and treatment, to examine whether a particular variation in the mitochondrial genome is associated with the disease. The genetic change occurs in about 10 percent of Caucasians, referred to as mitochondrial haplogroup T.

"We suspect that this variant will be one of a small group of important genetic variations that underlie AMD," Canter said. "By knowing this, we have a better chance of predicting accurately who will get the disease."

AMD affects as many as 10 million people in the United States, robbing them of the sharp central vision necessary for everyday activities like reading, driving, watching television, and identifying faces. The toll of the disease is expected to mount as the U.S. population ages.

The genetics of AMD has been a “hot” area lately, Canter said. Haines led a team that identified a variant in the Complement Factor H (CFH) gene as accounting for up to 43 percent of AMD. Variations in ApoE2 and a gene called LOC387715 on chromosome 10 have also been linked to the disease, and Haines and colleagues demonstrated an interaction between the chromosome 10 gene and smoking in raising AMD risk.

The current study also examined variation in these nuclear genes in 280 cases and 280 age-matched controls, and demonstrated that the mitochondrial genome variation was independent of the known nuclear factors.

“We’re at the stage where we can use genetic information to predict who is likely to develop AMD well before they actually develop it,” said Haines, director of the Center for Human Genetics Research. “Now we can conduct trials of preventive treatments – something’s that never been possible before.”

Sternberg, G.W. Hale Professor and Chairman of the Vanderbilt Eye Institute, is leading a trial to test preventive measures in AMD.

Variation in the mitochondrial genome reflects human migrations and different environmental exposures. Changes in the mitochondrial DNA can alter the efficiency of energy generation and lead to over-production of “reactive oxygen species” – free radicals that can damage the cell.

“By identifying genetic changes associated with the mitochondria, our results lend additional confirmatory evidence for the role of oxidative

stress in AMD," Sternberg said. "This supports study of interventions that attempt to bolster our antioxidant defenses."

"I can see a day when physicians order genotyping on patients at a certain age to determine risk for AMD and put things in place – dietary changes, antioxidants, increased screening – that could prevent the disease," Canter added. "This would be truly personalized medicine."

Canter emphasized that variation in the mitochondrial genome has been linked to a wide variety of diseases including neurodegenerative diseases like Parkinson's and Alzheimer's as well as breast cancer and trauma survival.

"It's important to realize that there's another genome in the mitochondria, and even though there are not many genes there, they're important," Canter said.

Source: Vanderbilt University