# Study reveals how genes interact with their environment to cause disease

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A UCLA study reveals how human genes interact with their environment to boost disease risk. Published in the Feb. 18 online edition of the *American Journal of Human Genetics*, the findings shed light on why the search for specific gene variants linked to human diseases can only partly explain common disorders.

"We know that genes and environmental factors influence common human diseases like heart disease, diabetes and cancer," explained principal investigator Jake Lusis, professor of medicine, human genetics and microbiology, immunology and molecular genetics at the David Geffen School of Medicine at UCLA. "Most research, however, has focused on unraveling the genetic component of disease risk while ignoring the effect of environmental stimuli. Our study examined how the molecular interaction between the two helps lead to disease."

"Smoking and high cholesterol, for example, each increase a person's risk for heart disease," he said. "But when you add them together, the total risk exceeds its parts. Their interaction creates a dangerous synergy that causes damage beyond what the two can cause independently."

Unlike earlier studies that focused on a single gene, the UCLA team scrutinized the activity of thousands of human genes both at rest and under stress. In particular, the scientists zeroed in on gene expression—the process by which a gene's DNA sequence is converted into cellular proteins.

Using arteries that surgeons had trimmed from 96 donated hearts prior to organ transplantation, Lusis and his team cultured cells from the inner lining of the blood vessels. To mimic environmental stress, the scientists exposed the cells to fats that incite inflammation and lead to atherosclerosis, or hardening of the arteries. Then they looked at the cells' genes and compared their normal expression patterns to their activity under stress.

"The genes responded differently to inflammation depending on their genetic makeup," said first author Casey Romanoski, a UCLA graduate student in human genetics. "About 35 percent of the most affected genes were influenced by the interaction between their genetic variants and the fats."

"You can't effectively study genes divorced from their environment," she added. "The missing link lies in the intersection of genes with their environment."

"Our findings demonstrate that these interactions are important in humans and should be considered in genetic research," said Lusis. "Improving our understanding of the molecular architecture of disease may one day provide us with a new tool for how we address common disorders like cancer, diabetes and heart disease."

Provided by University of California - Los Angeles