

Four genes indentified that influence levels of 'bad' cholesterol

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Scientists at the Texas Biomedical Research Institute in San Antonio have identified four genes in baboons that influence levels of "bad" cholesterol. This discovery could lead to the development of new drugs to reduce the risk of heart disease.

"Our findings are important because they provide new targets for the development of [novel drugs](#) to reduce heart disease risk in humans," said Laura Cox, Ph.D., a Texas Biomed geneticist. "Since these genes have previously been associated with cancer, our findings suggest that genetic causes of heart disease may overlap with causes of some [types of cancer](#) ." The new study, funded by the National Institutes of Health (NIH), is published online and will appear in the July print issue of the *Journal of Lipid Research*.

Texas Biomed scientists screened their baboon colony of 1,500 animals to find three half-siblings with low levels of [low density lipoprotein](#) (LDL), or "bad," cholesterol, and three half-siblings with high levels of LDL. In the study, these animals were fed a high-cholesterol, high-fat diet for seven weeks. Scientists then used gene [array technology](#) and high throughput sequencers to home in on the genes expressed in the two groups and differentiate those in the low LDL groups from those in the high LDL group. They discovered that four genes (named TENC1, ERBB3, ACVR1B, and DGKA) influence LDL levels. Interestingly, these four genes are part of a signaling pathway important for [cell survival](#) and disruption of this pathway promotes some types of cancer.

It is well-known that a high level of LDL is a major risk factor for heart disease. Despite concerted efforts for the past 25 years to manage [cholesterol levels](#) through changes in lifestyle and treatment with medications, heart disease remains the leading cause of death and mortality in the United States and around the world. It will account for one out of four U.S. deaths in 2013, according to the [American Heart Association](#).

Heart disease is a complex disorder thought to be a result of interactions between genetic and environmental factors, which occur primarily through diet. To understand why humans have different levels of LDL and thus variation in risk for heart disease, the genetic factors causing these differences need to be understood.

However, these studies are difficult to do in humans because it's practically impossible to control what people eat. Instead, Texas Biomed scientists are using baboons, which are similar to humans in their physiology and genetics, to identify genes that influence [heart disease risk](#).

The new research also suggests that knowing many of the genes responsible for heart disease may be necessary to devise effective treatments. For example, several genes may need to be targeted at once to control risk.

The next step in this research is to find the mechanism by which these genes influence LDL cholesterol. "That starts to give us the specific targets for new therapies." Cox said. If all goes well, this information may be available within two years.

More information: The paper can be found at:
<http://www.jlr.org/content/early/2013/05/06/jlr.M032649.full.pdf+html>.

Provided by Texas Biomedical Research Institute

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