

Scientists find gene for high cholesterol in blood

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Scientists at the Southwest Foundation for Biomedical Research (SFBR) in San Antonio have found a gene that causes high levels of bad cholesterol to accumulate in the blood as a result of a high-cholesterol diet.

Researchers studied a strain of laboratory opossums developed at SFBR that has normal blood levels of "bad" low-density lipoprotein (LDL) cholesterol when fed a standard low-cholesterol diet, but extremely elevated levels of LDL cholesterol when fed a high-cholesterol diet. These high-responding opossums are used to identify the genes and the underlying mechanisms that control response to dietary cholesterol.

"This research will improve our understanding of cholesterol metabolism and may shed light on why some people have high levels of bad cholesterol in blood while others do not when they consume cholesterolenriched diets," said John L. VandeBerg, Ph.D., SFBR's chief scientific officer and senior author on the paper. Published in the October issue of the Journal of Lipid Research, the work was funded by the National Institutes of Health and the Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation.

The study involved analyzing various lipids, or fats, in blood and bile to find differences in cholesterol metabolites, sequencing <u>candidate genes</u> of interest to find mutations, and determining the impact of each mutation by <u>genetic analyses</u>. This led to the discovery that the ABCB4 gene, which encodes a protein known to transport fats from the liver into



bile to facilitate excretion of cholesterol from the body, is defective in the high responders. Malfunction of the ABCB4 protein was found to impair cholesterol excretion, causing <u>bad cholesterol</u> to accumulate in the blood when a high-cholesterol diet is consumed.

"This is the first report to show that ABCB4 has a role in controlling <u>blood</u> cholesterol levels in response to dietary cholesterol in an animal model," said VandeBerg.

The next step is to determine if any ABCB4 mutations have an effect on levels of LDL cholesterol in humans who consume a high cholesterol diet. "If we can identify early in life those people who are going to be adversely affected by consumption of high levels of cholesterol, we can encourage their parents and them to receive individually tailored counseling to establish dietary habits that protect them from cardiovascular disease," VandeBerg said.

Provided by Southwest Foundation for Biomedical Research

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