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Date: November 13, 2014

Source: University of Western Ontario

**Summary:** An estrogen receptor, previously shown to regulate blood pressure in women, also plays an important role in regulating LDL cholesterol levels, researchers have discovered.

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**W**hat makes some women more susceptible to heart disease than others?

To help answer that question, researchers at Western University's Robarts Research Institute have identified that an estrogen receptor, previously shown to regulate blood pressure in women, also plays an important role in regulating low-density lipoprotein (LDL) cholesterol levels. LDL, also known as bad cholesterol, drives the process that leads to heart disease.

This finding provides evidence that the hormone estrogen plays a key role in regulating two of the most common risk factors for heart disease and stroke. It may also help to explain why post-menopausal women with lower levels of estrogen are more likely to have multiple risk factors for heart disease.

Dr. Ross Feldman, a clinical pharmacologist at London Health Sciences Centre and a scientist at the Schulich School of Medicine & Dentistry's Robarts Research Institute, and his colleagues showed that the G-protein coupled estrogen receptor 30 (GPER) when activated by estrogen helps lower LDL cholesterol levels in the blood by inhibiting the protein PCSK-9.

Their findings will be published this week by the journal *Arteriosclerosis, Thrombosis and Vascular Biology*.

"This is a really important finding because there has always been some indication that estrogen was protective in lowering cholesterol, but we didn't understand how," said Dr. Feldman. "The mechanism of estrogen's effect was kind of a black box because we didn't know the receptors responsible for doing it."

The study, which looked at two populations of women in northern Alberta and London, Ontario, also found that women who carry a common gene variant for GPER have a significant increase in LDL cholesterol levels. The gene variant, found in about 20 per cent of the population, impairs the ability of GPER to function and was shown in a previous study by the same authors to be associated with significant increases in blood pressure in women.

"What we found is that women who have this same defective GPER, have higher LDL levels. That tells us that the second rate GPER is important not only for blood pressure, but for cholesterol levels as well," said Dr. Feldman. "Together, these are the two most powerful risk factors in terms of heart disease and both are adversely affected by having a second-rate GPER."

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St. Jude patient Mason, age 5

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The above story is based on materials provided by **University of Western Ontario**. Note: Materials may be edited for content and length.

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1. Y. Hussain, Q. Ding, P. W. Connelly, J. H. Brunt, M. R. Ban, A. D. McIntyre, M. W. Huff, R. Gros, R. A. Hegele, R. D. Feldman. **G-Protein Estrogen Receptor as a Regulator of Low-Density Lipoprotein Cholesterol Metabolism: Cellular and Population Genetic Studies.** *Arteriosclerosis, Thrombosis, and Vascular Biology*, 2014; DOI: 10.1161/ATVBAHA.114.304326

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