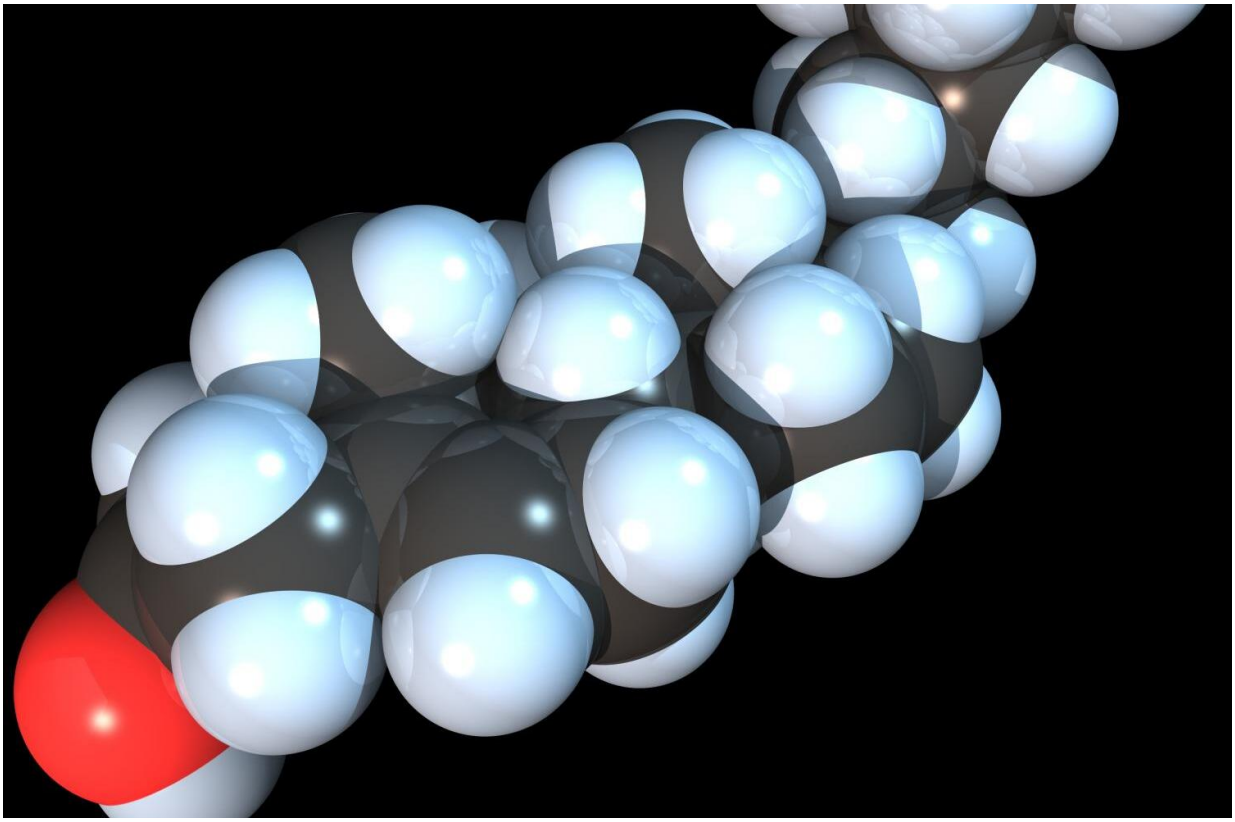
MedicalXpress

Researchers determine 3-D atomic structure of cholesterol transporter

May 26 2016



Space-filling model of the Cholesterol molecule. Credit: RedAndr/Wikipedia

Using X-ray crystallography, UT Southwestern Medical Center researchers have determined the 3-D atomic structure of a human sterol transporter that helps maintain cholesterol balance.

"Determining the structure of this protein complex helps us to understand the mechanism by which the two component proteins work together to clear sterols from the body," said Dr. Daniel Rosenbaum, Assistant Professor of Biophysics and Biochemistry at UT Southwestern and a corresponding author of the study, which was published today in *Nature*. "This knowledge, in turn, could lead to finding highly targeted therapies to treat or prevent diseases related to sterol imbalance."

Cholesterol is an essential component of cell membranes. Two ATP binding cassette (ABC) half transporters, ABCG5 and ABCG8, form a complex that transports sterols across membranes.

Specifically, the ABCG5/ABCG8 complex is involved in excretion of sterols from the liver and the intestines. Disruption by mutations in either protein can lead to the disorder sitosterolemia. Patients with sitosterolemia have elevated levels of cholesterol and other sterols in their tissues and blood, which can cause heart attacks at an early age, Dr. Rosenbaum said.

Under normal conditions, animals maintain sterol balance by limiting dietary sterol uptake from the gut and promoting sterol secretion from the liver into the bile, added Dr. Rosenbaum, a Eugene McDermott Scholar in Medical Research.

Dr. Helen Hobbs, a Howard Hughes Medical Institute (HHMI) Investigator and Director of the Eugene McDermott Center for Human Growth and Development as well as a recent recipient of the $3 million Breakthrough Prize in Life Sciences for her work on cholesterol genetics, is the study's other corresponding author. Additionally, Dr. Hobbs is Chief of Clinical Genetics, Professor of Internal Medicine and Molecular Genetics, and holds the Eugene McDermott Distinguished Chair for the Study of Human Growth and Development, the Philip O'Bryan Montgomery, Jr., M.D. Distinguished Chair in Developmental

Biology, and the 1995 Dallas Heart Ball Chair in Cardiology Research.

Lead author Dr. Jyh-Yeuan "Eric" Lee, a research scientist in the McDermott Center, said humans have 48 ABC transporters that are classified into seven subfamilies, called A to G.

"The structure we deduced for the ABCG5/ABCG8 complex represents a new type of ABC transporter architecture, and is the first mammalian ABC transporter to be crystallized in a lipid bilayer and solved to atomic resolution," Dr. Lee said.

In addition, Dr. Rosenbaum said, the study data could provide insight into the structural elucidation of other ABC transporters, most of which remain uncharacterized.

Provided by UT Southwestern Medical Center