

Study indicates vitamin A plays key role in the human body

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In a recently-published study mapping the structure and function of the so-called "orphan" nuclear receptor TR4, Van Andel Research Institute (VARI) investigators suggest that Vitamin A may play a more direct role than was previously known in certain physiological functions including sperm cell formation and the development of the central nervous system.

Scientists had previously determined that Vitamin A derivatives such as retinal and the retinoic acids are involved in physiological functions in the human body. But there has been little direct evidence to show that Vitamin A, or retinol, the most common dietary form of the vitamin and the parental compound of the retinoid group, is directly involved in nuclear receptor signaling pathways – a process which activates genes in the human body.

"Our study found that Vitamin A itself is active for activating nuclear receptor TR4," said VARI Research Scientist Edward Zhou, Ph.D. "Because TR4 plays roles in sperm cell production, lipid and lipoprotein regulation, the development of the [central nervous system](#), and the regulation of hemoglobin production in the embryo, we can imagine that [Vitamin A](#) may play more important roles in human physiology than was previously believed."

The study, published in the *Journal of Biological Chemistry*, was named by the journal as a "Paper of the Week," indicating that the study is in the top 1 percent of published papers in terms of significance and overall importance. About 50 to 100 such studies are selected from the more

than 6,600 published by the journal each year.

[Nuclear receptors](#) activate genes in important biological processes in the human body. Orphan nuclear receptors are a group of nuclear receptors whose ligands, or the substance to which receptors bind, have not yet been identified, and whose physiological functions have not been very well investigated.

"Recent evidence has shown that orphan nuclear receptors are required for many essential [physiological functions](#) in the human body, and can be used to help discover drug targets for human diseases," said Zhou.

"Additionally, the identification of ligands for nuclear receptors usually leads to the discovery of new types of therapeutic drugs for human diseases. A very successful example is PPARs (peroxisome proliferator-activated receptors), whose ligands are used for the treatment of diabetes."

Dr. Zhou and his colleagues in VARI's Laboratory of Structural Sciences, under the direction of VARI Center for Structural Biology and Drug Discovery Director H. Eric Xu, Ph.D., used X-ray crystallography to determine the structure of TR4's ligand binding domain. They also identified small molecules involved in TR4 transcription – the synthesis of RNA using DNA as the blueprint – that could serve as potential drug targets.

Provided by Van Andel Research Institute

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