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New link between cholesterol and hyperuricemia offers potential as therapeutic target

A new link between a high cholesterol condition and an excess blood uric acid level has been identified by an international collaboration among Nara Medical University, RIKEN, and the University of Houston. A cholesterol metabolite, known as 27HC (27-hydroxycholesterol), was found to increase the expression of uric acid transporter that facilitates reabsorption, and may prove to be a promising drug target (Figure 1).

The new study, conducted by a team of researchers from Nara Medical University led by senior author Dr. Eiichiro Mori, Associate Professor and chair of the Department of Future Basic Medicine, University of Houston led by co-senior author Dr. Michihisa Umetani, Assistant Professor of the Center for Nuclear Receptors and Cell Signaling, and RIKEN Center for Biosystems Dynamics Research led by Dr. Minoru Takasato, Team Leader of Laboratory for Human Organogenesis, was recently published in *The FASEB Journal*.

Elevated levels of blood uric acid, or hyperuricemia, lead to various diseases such as gout, renal diseases, and cardiovascular diseases. Most uric acid is excreted in the urine, while some portion of uric acid is reabsorbed from urine to blood to maintain a proper level of blood uric acid through uric acid reabsorption transporters. The correlation between hyperuricemia and metabolic diseases, such as obesity and high cholesterol conditions, is well known. However, the mechanisms driving the impact of cholesterol on uric acid transporters were unknown.

Using human cells, animal models, and human kidney organoids generated from induced pluripotent stem (iPS) cells, the researchers found that 27HC promotes the expression of URAT1 (also known as SLC22A12), which plays an important role in the reabsorption process, via estrogen receptors in the kidney (Figure 2). Their results indicate that elevated levels of 27HC in a high cholesterol condition can increase uric acid reabsorption, which in turn increases blood uric acid levels. These findings shed new light on a novel treatment option for hyperuricemia-related diseases by targeting 27HC.

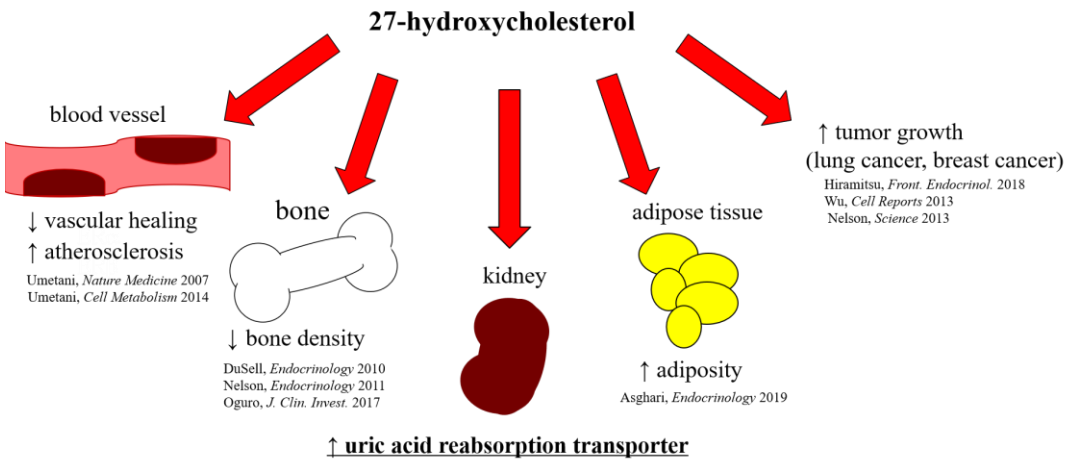

Figure 1. The effects of 27-hydroxycholesterol in various tissues discovered by this group.

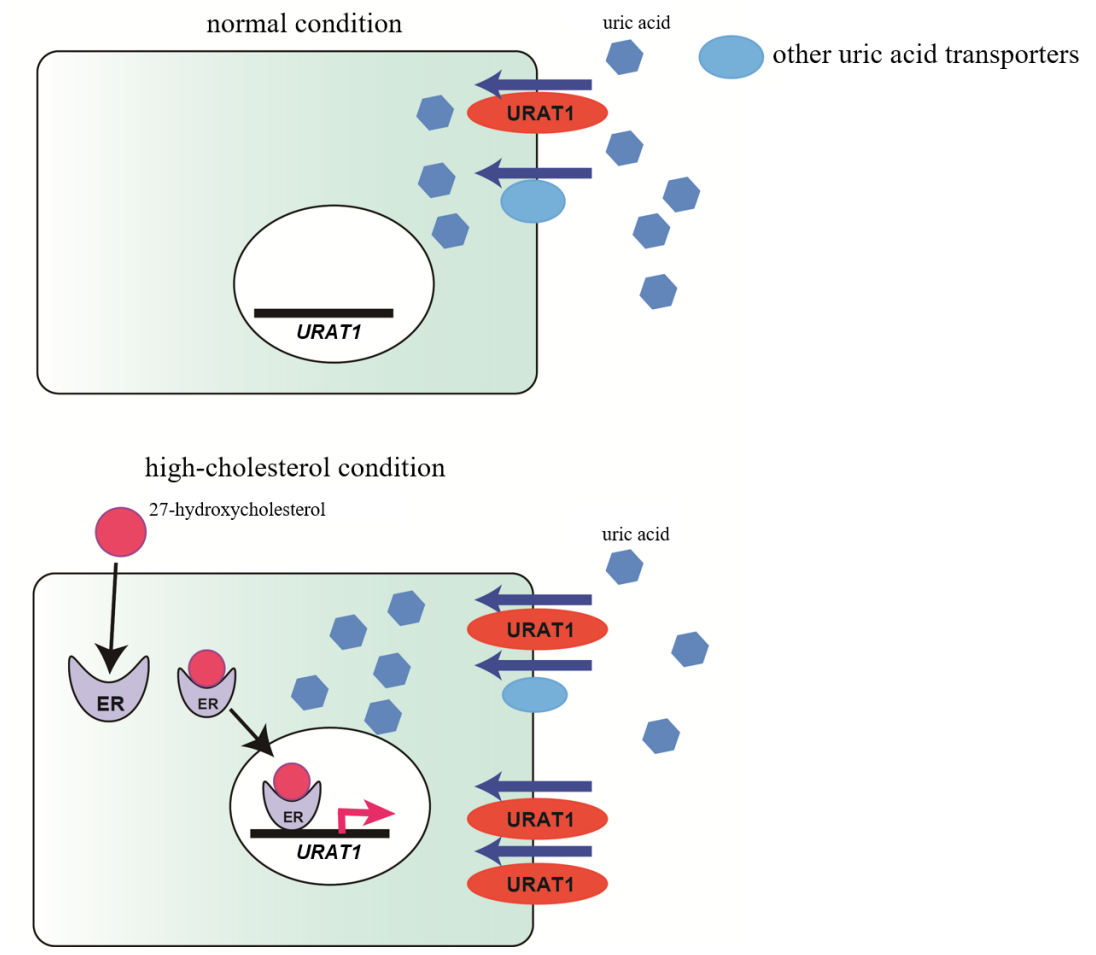

Figure 2. 27HC binds to estrogen receptors (ER) and induces URAT1/*SLC22A12* expression.

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