An Emerging Healthy Heart-C15:0-Gut Axis, Part I

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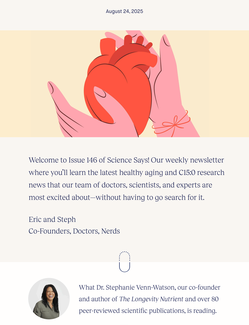

Welcome to Issue 146 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 research news that our team of doctors, scientists, and experts are most excited about—without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

A Prospective Look at C15:0, Heart & Gut Health, Part I

This year's big science story is emerging as The Year of Heart & Gut Health for C15:0. This week, we're covering a just-published prospective study by Xiao et al. that focused on circulating levels of C15:0 and the likelihood of maintaining our cardiovascular health over time. That also had a surprising link to gut health. Let's dive in.

I'm into keeping my heart healthy. Tell me more.

The studies supporting C15:0 + heart health have been mounting:

- A few weeks back, we covered a randomized cross-over clinical trial by Arghavani et al. that showed when people increased C15:0 in their diet, their C15:0 levels increased, too. And **as their C15:0 levels increased, aortic stiffness decreased** within 12 weeks.
- Then, Chen et al. and Huang et al. showed in adults and kids, respectively, that **higher C15:0 levels = healthier blood pressure.**
- Last year, a randomized and controlled clinical trial by Chooi et al. demonstrated that **daily C15:0 supplementation lowered LDL-cholesterol.**
- And over the past decade, meta-analyses of prospective cohort studies have repeatedly shown that **people with higher C15:0 levels have better long-term heart health.**

In the latest study by Xiao et al., 1,211 adults (mean age of 58 years old) were followed over 6 years to see if C15:0 levels predicted the ability to protect arterial health.

Got it. What did they find?

There were a few key findings:

- **This study re-reconfirmed baseline population C15:0 levels.** This study divided the study population into those who had the lowest to highest C15:0 levels, by quartiles. Among the 1,211 participants in this study, the lowest quartile had C15:0 levels of 0.1% of total fatty acids. The middle two quartiles had C15:0 levels of 0.2%, and the highest quartile had C15:0 levels of 0.4%. As shared in our *Metabolites* paper, C15:0 levels ≥ 0.2% are needed to not be C15:0 deficient and maintain our baseline health. Higher C15:0 levels (aka 0.4-0.6%) are considered optimal levels, especially as it relates to heart health and longevity.
- **How much dairy a person ate determined their total odd-chain saturated fatty acid levels (C15:0-C17:0).** This finding was consistent with many other studies, including Chooi et al.'s controlled clinical trial, showing that the more C15:0 we ingest, the higher our C15:0 levels.
- **People who had the highest quartile of circulating C15:0 levels (aka, 0.4%) had the healthiest long-term arterial health - even after 6 years.** Conversely, those who had the lowest quartile C15:0 levels (0.1%), had the greatest risk of developing cholesterol plaques in their carotid arteries.

Paired with the other large prospective studies above and two clinical trials, these studies increasingly support that C15:0 is good for our cardiovascular health - by lowering LDL cholesterol, decreasing arterial stiffness, and keeping our arteries clean, clear, and functioning.

So, where does the gut come into the story?

Right. In addition to the above findings, Xiao et al. also showed that the higher a person's C15:0 levels, the more diverse their gut microbiome and the higher their levels of certain types of good microbes - especially *Christensenellaceae* R-7 group. We'll cover the gut side of C15:0's health benefits next week.

How C15:0 Supports our Cardiovascular Health

You know we love going cellular. So, beyond the studies above, there are core ways C15:0 supports our cellular health - which translates to whole-body health, including our hearts. This includes the following:

- C15:0 lowers 18+ proinflammatory cytokines, including key cytokines in human vascular cell systems.
- C15:0 activates AMPK, which can help lower LDL cholesterol levels.
- C15:0 strengthens cell membranes to protect our cells (including our heart and vascular cells) against lipid peroxidation.
- C15:0 reverses ferroptosis, a new form of cell death that impairs iron metabolism and cardiovascular function.

All to explain why we should be taking this growing C15:0 science to heart. Next week, we'll cover what the Xiao et al. study had to say about C15:0 and gut health. In the meantime, have a wonderful week, everyone!

Dive deeper into the science

READ THESE STUDIES

- Arghavani et al. Impact of dairy intake on circulating fatty acids and associations with blood pressure: a randomized crossover trial.
- Chen et al. Associations between serum pentadecanoic acid (C15:0) and blood pressure: a cross-sectional analysis of NHANES data.
- Huang et al. Associations of erythrocyte membrane fatty acids with blood pressure in children.
- Chooi et al. Effect of An Asian-Adapted Mediterranean Diet and Pentadecanoic Acid on Liver Health: The TANGO Randomized Controlled Trial.
- Li et al. Saturated Fatty Acid Biomarkers and Heart Health: A Meta-Analysis of Prospective Studies. Frontiers in Nutrition 9, 963471 (2022).
- Trieu, K. et al. Biomarkers of dairy fat intake and heart health: A cohort study, systematic review, and meta-analysis. PLoS Med 18.e1003763 (2021).
- Xiao et al. Plasma biomarkers of dairy intake and gut microbiome, and their association with incident carotid plaque: a prospective cohort study.
- Venn-Watson et al. The Cellular Stability Hypothesis: Evidence of Ferroptosis and Accelerated Aging-Associated Diseases as Newly Identified Nutritional Pentadecanoic Acid (C15:0) Deficiency Syndrome.
- Venn-Watson et al. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.
- Fu, W.G. et al. Pentadecanoic acid promotes basal and insulin-stimulated glucose uptake in C2C12 myotubes.

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