Top 5 Scientific Discoveries of 2024: One Heck of a Year for C15:0

December 22, 2024

Welcome to Issue 114 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 over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

C15:0 For All

This was indeed a big year for C15:0 scientific discoveries. For those of you who have been reading *Science Says!* (thank you, by the way), you already knew that. In this wonderful time of the year for roundups, we'll spend this issue on the 5 biggest C15:0 scientific discoveries during 2024.

Top Discovery #5: C15:0 is Essential for All

It was back in 2020 that our co-founders first published C15:0 as an essential fatty acid - the first to be discovered in over 90 years - in *Nature's Scientific Reports*. During 2024, numerous studies from independent teams confirmed and reconfirmed that C15:0 is indeed an essential dietary nutrient that all animals - from worms to mice to humans - need to develop and stay healthy. Specifically:

- Ruan et al. showed that, absent of ALL other nutrients (be it glucose, carbohydrates, amino acids, or other fatty acids), *C15:0 by itself enabled baby worms to develop and grow as if they were fed a full nutrient diet.* By using the C. elegans worm model, this study shows that C15:0's essentiality may go back 20 million years. Dang.
- Across two back-to-back papers, Cieleski et al. *reconfirmed that C15:0 is an essential fatty acid using a gold standard nutritional deficiency study in mice* and a literature review of human studies.
- In a third study following mother-child pairs over nearly a decade, Yuan et al. continued to show that *the more C15:0 human-mom has, the better her baby's body growth and childhood cognitive development.*

Top Discovery #4: Nutritional C15:0 Deficiencies Cause Cellular Fragility Syndrome

As expected of a truly essential nutrient, we published in *Metabolites* the first nutritional deficiency syndrome to be discovered in 75 years. A culmination of the past decade of Office of Naval Research-funded studies, we detail the following pathophysiology behind Cellular Fragility Syndrome, which is caused by nutritional C15:0 deficiencies:

- When our cell membranes have low levels of sturdy C15:0 (defined as ~ 0.2% total fatty acids, ~ 5 μg/ml or ~ 20 μM), our cell membranes become fragile and undergo lipid peroxidation, including our red blood cells.
- Fragile red blood cells (detected via high RDW and declining hemoglobin) are engulfed by special cells in our liver, called Kupffer cells. Over time, this results in excess iron deposition in our liver.
- When lipid peroxidation combines with unwanted iron, the result is systemic ferroptosis - a newly discovered form of cell death that accelerates aging, as well as the onset of type 2 diabetes, heart disease, and fatty liver disease.

While Cellular Fragility Syndrome may be present in as many as 1 in 3 of us, the good news is that C15:0 supplementation successfully reversed all key components of ferroptosis - effectively treating Cellular Fragility Syndrome in relevant models.

Top Discovery #3: Two Positive Clinical Trials

During 2024, two independent, randomized, double-blinded and controlled clinical trials using pure C15:0 supplementation were published, both of which had positive results:

- In a placebo-controlled study led by UC San Diego, Robinson et al. showed that daily C15:0 supplementation effectively raised C15:0 levels. Which is great... but more importantly, *when C15:0 levels got above and beyond the threshold for nutritional C15:0 deficiency (aka > 5 μg/ml), young adults with a history of fatty liver disease experienced lower liver enzymes and higher hemoglobin within 12 weeks.* These results reconfirmed C15:0's role in improving liver and red blood cell function.
- Meanwhile, Chooi et al.'s clinical trial showed that women supplemented daily with *C15:0 had higher C15:0 levels, lower LDL-cholesterol, and an improved gut microbiome health within 12 weeks.* These benefits were above and beyond the benefits of caloric restriction and the Mediterranean diet.

Even better, both clinical trials showed that C15:0 supplementation was safe with no side effects.

Top Discovery #2: C15:0 is a Key Player in Gut Health to Support Whole Body Health

Oh so many studies are showing the importance of gut health to support our whole body health. And boy, 2024 landed a healthy handful of studies showing C15:0's important role in supporting our gut health:

- In their clinical trial, Chooi et al. showed that C15:0 supplementation increased the abundance of *Bifidobacterium adolescentis*, a good gut microbe that supports our metabolic health - and even extends longevity in multiple species.
- Singh et al. demonstrated that C15:0 supplementation helped improve the integrity of gut health lining (making it less leaky), as well as lowering inflammation to improve gut health in two mouse models.
- Similarly, Wu et al. showed that C15:0 repairs the gut barrier lining and lowers inflammation in mice, which aligned with their reports of higher C15:0 among people with optimal gut health.

Understanding that two of C15:0's primary roles are to strengthen cells and calm inflammatory responses throughout our body, its role in protecting the integrity of our gut lining and keeping it calm is not so surprising, right?

Top Discovery #1: The Longevity Nutrient.

In Copenhagen this summer, Dr. Nicholas Schork (head of NIH's prestigious Longevity Consortium) presented C15:0 as a leading geroprotector at ARDD. ARDD is the world's largest longevity therapeutics conference, where the who's who present the latest and greatest in longevity-enhancing compounds.

Since geroprotectors are molecules that slow aging and the onset of chronic conditions of aging, these are the holy grail of longevity molecules. Dr. Nik called out the following attributes of C15:0:

- C15:0 is an essential nutrient animals have evolved over millions of years to use to extend health and longevity.
- C15:0 has a core role of strengthening cell membranes, which extends lifespans across species.
- In addition, C15:0 activates AMPK, inhibits mTOR, attenuates six hallmarks of aging, and has more cell-based benefits than rapamycin, solidifying mechanisms of action that are known to slow aging and extend longevity.

Dr. Nik concludes that *the extent of research on C15:0 across large epidemiological, receptor-based, cell-based, in vivo and clinical studies, makes C15:0 the most broadly supported human geroprotector to date.*

Which is why Simon & Schuster is releasing a whole book behind the fascinating discovery and science behind C15:0, called *The Longevity Nutrient*. How about that?

A big year, indeed. Thanks to everyone for being part of our (and now the world's) journey, culminating in a need to restore and optimize C15:0 levels to help restore and optimize our health.

Have a great week, and Happy Holidays!

Dive deeper into the science

READ THESE STUDIES

- Venn-Watson et al. C15:0 as an essential fatty acid, anti-inflammatory nutrient, and PPAR activator.
- Ruan et al. C15:0 solely triggers healthy development in C. elegans.
- Cieleski et al. New insights on pentadecanoic acid with special focus on its controversial essentiality: A mini-review.
- Cieleski et al. Dietary pentadecanoic acid supplementation at weaning in essential fatty acid-deficient rats.
- Yuan et al. Associations between C15:0 and child cognitive development.
- Yuan et al. Associations of maternal consumption of dairy products during pregnancy with perinatal C15:0 biofluids.
- George et al. The fatty acid species and quantity consumed by the breastfed infant are important for growth and development.
- Venn-Watson S. The Cellular Stability Hypothesis: Evidence of Ferroptosis and Accelerated Aging-Associated Diseases as Newly Identified Nutritional Pentadecanoic Acid (C15:0) Deficiency Syndrome.
- Dixon et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death.
- Robinson et al. C15:0 supplementation in young adults with overweight and obesity: a randomized controlled trial.
- Chooi et al. Effect of Mediterranean diet and C15:0: the TANGO randomized controlled clinical trial.
- Singh et al. Effect of C15:0 supplementation on mouse models of gut health.
- Wu et al. Effect of C15:0 supplementation on mouse models of gut health.
- Venn-Watson & Schork. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.

- Nerd out on all the C15:0 science at DiscoverC15.com.