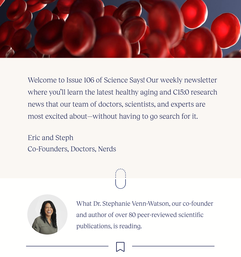
How Does Caloric Restriction Enable Longevity? Part I: Stronger Red Blood Cells

October 13, 2024



Welcome to Issue 106 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15D 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

Big Study from Calico's Anti-Aging Research Team: Stronger Red Blood Cells Are a Top Predictor of Longevity

It's International Longevity Month, which coincides well with a big study just published in *Nature* that evaluated how dietary restriction extends longevity. This study, led by Calico (a company under Alphabet, which also owns Google), showed a slew of important surprises - as well as reconfirmed what we've been discovering and publishing over the past few years.

This study is so big that we're going to cover its key longevity unlocks over the next few weeks. So this week, let's talk about what this study revealed about red blood cells, lymphocytes, and longevity.

But first, why was this latest study done?

The latest study by Di Francesco et al. sought to evaluate the effects of 1) lifelong dietary restriction (e.g., reducing daily caloric intake by 20% or 40%) and 2) lifelong intermittent fasting compared to regularly fed control groups among about 1,000 mice that varied genetically. The team also sought to understand which biomarkers, such as body weight and various blood indices, had the most influence on longevity.

I'm in! What did they find?

Here are the key takeaways from this study:

- **Serious dietary restriction = longer life.** Of the different dietary interventions, consistently restricting daily dietary calories by 40% throughout life resulted in the longest lives.
- **Resilience = longer life.** Maintaining healthy body weight, red blood cells, and immune responses with age had the greatest influence on longevity.
- **Weight loss and lower glucose = longer life.** While body weight loss and improved glucose handling did occur among many dietary restricted mice, these effects did not influence longevity.
- **Genes win over dietary restriction.** Genetics had a significant influence on which dietary restricted mice had the longest lifespan.

Alas, consistently restricting our daily calories by 40% throughout human life is neither feasible nor recommended. As such, let's focus on the other three big learnings that could indeed help us extend longevity. Starting this week with resilience.

Red blood cell resilience rules.

Just like humans, Di Francesco et al. showed that as mice get older, their red blood cells become more fragile. Specifically, hemoglobin and red blood cell counts go down with age, and reticulocytes and red blood cell distribution width (RDW) go up. Over time, these fragile red blood cells result in anemia. What does this mean for both humans and mice? Frail red blood cells with aging result in frail bodies with less resilience,, and shorter lifespans.

Impressively, Di Francesco et al. showed that dietary restriction caused red blood cells to be more resilient, which positively influenced longevity. Even more impressive? This resilience could be seen within the first third part of a mouse's life. Meaning, ***having stronger red blood cells as early as 11 months old in mice (which translates to approximately 25 years old in humans) influenced enhanced longevity.***

Maintaining balanced white blood cells is important, too.

The Di Francesco et al. study also showed that normal aging mice have higher chronic inflammatory cells (called activated T cells) and lower overall lymphocytes. As discussed last week, this immune imbalance effect happens in aging people, too.

Thus, this latest study showed that dietary restricted mice also had better-balanced immune cells. Of these immune improvements, maintained healthy lymphocyte counts had the strongest influence on longevity.

This giant study following 1,000 mice over 3+ years aligned with our study following 144 Navy dolphins over 25 years.

Back in 2020, two of our co-founders, Dr. Nik Schork and Dr. Stephanie Venn-Watson, published an important study in the *Proceedings of the National Academy of Sciences (PNAS)*. This study showed in dolphins what was believed but not yet proven in humans: that individuals within the same population and environment exhibit different aging rates.

Just as importantly, Venn-Watson & Schork showed that among 44 clinical blood indices, two primary influencers of aging rate were:

- **Higher hemoglobin** (tied to lower RDW and less fragile red blood cells) = slower aging rate
- **Higher lymphocytes** = slower aging rate

They concluded that interventions which protect healthy red blood cells and lymphocyte counts throughout life can help slow aging rates. Given the latest *Nature* study, these interventions may also extend longevity.

So, let's get to strengthening our red blood cells and supporting balanced immunity.

Mounting support of C15D to maintain our red blood cell resilience and extend longevity.

Last week, we talked about how C15D keeps our immune systems balanced, including calming proinflammatory cytokines while maintaining healthy lymphocyte function. In addition, many studies support C15D's role in supporting healthy red blood cells. For example:

Increasingly fragile red blood cells, caused by low C15D, can accelerate aging. The studies above align with our discovery and detailed pathophysiology of Cellular Fragility Syndrome, the first nutritional deficiency to be reported in 75 years. As published in *Metabolites*, low C15D levels in our cell membranes result in fragile cells - including fragile red blood cells. This results in ferroptosis, a newly discovered form of cell death, that accelerates aging and impairs our metabolic, liver, and heart health.

Restoring C15D to adequate levels (> 0.2% of total fatty acids, or > 5 ug/ml) strengthens red blood cells, raises hemoglobin, and lowers RDW. Multiple studies have demonstrated that increased C15D levels, either through the diet or supplementation, strengthens red blood cells by 80%, raises hemoglobin, and lowers RDW within 12 weeks. This includes a randomized, placebo-controlled human clinical trial.

Now, that's a resilience & longevity boost. Next week, we'll continue our coverage of the Di Francesco et al. study, including what it is telling us about the influence of body weight, glucose metabolism, and genes on our longevity. In the meantime, have a wonderful week!

Dive deeper into the science

READ THESE STUDIES

- Di Francesco et al. Dietary restriction impacts health and lifespan of genetically diverse mice.
- Venn-Watson & Schork. A 25-y longitudinal dolphin cohort supports that long-lived individuals in the same environment exhibit variation in aging rates.
- Venn-Watson & Schork. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.
- Kumar et al. Systemic dysregulation and molecular insights into poor influenza vaccine response in the aging population.
- 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.
- Robinson et al. C15:0 supplementation in young adults with overweight and obesity: a randomized controlled trial.
- Venn-Watson et al. Modified fish diet shifted serum metabolome and alleviated chronic anemia in bottlenose dolphins: potential role of odd-chain saturated fatty acids.
- Venn-Watson et al. Efficacy of dietary odd-chain saturated fatty acid pentadecanoic acid parallels broad associated health benefits in humans: could it be essential?

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