

LINUS PAULING INSTITUTE

DIGITAL DIGEST

SUMMER/FALL 2023

UPDATES FROM THE MICRONUTRIENT INFORMATION CENTER LOOK INSIDE ►

A MAN OF LEGEND

Highlights of Dr. Linus Pauling's Life as Told by Chris Petersen

On April 11, 2023, Chris Petersen from the OSU Libraries presented the webinar *Visions of Linus Pauling: Reflections on the Man and His Institute*. This engaging presentation provided a comprehensive view into the remarkable life of Dr. Linus Pauling, mirroring Petersen's latest book, *Visions of Linus Pauling*.

The article below is a brief synopsis of Petersen's presentation, touching only on Pauling's unwavering commitment to health research and the captivating history of the Linus Pauling Institute of Science and Medicine.

The full recording of the webinar and interviews with Petersen are available [on our YouTube channel](#). A condensed transcript of Petersen's presentation is available upon request.

A Pioneer in Chemistry and Molecular Biology

Dr. Linus Pauling was a talented structural chemist. He exhibited a remarkable ability to visualize the true nature of molecules and formulate hypotheses about molecular structures from experimental data.

In the first few decades of his career, Pauling meticulously deciphered the structures of dozens of small molecules using the innovative technique of X-ray crystallography. With this, he made substantial contributions to the burgeoning field of structural chemistry and deepened his understanding of atomic interactions.

In the mid-1920s, Pauling went to Europe as a Guggenheim Fellow and learned about quantum mechanics, a then emerging topic in the field of physics. As a result, Pauling was able to better understand and describe chemical bonding – that is, the way atoms join together to form molecules.

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Oregon State University
Linus Pauling Institute

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Emily Ho, PhD
Endowed Chair and Director,
Linus Pauling Institute

FROM THE DIRECTOR

Greetings from the Linus Pauling Institute, and welcome to the very first edition of the *LPI Digital Digest*!

You'll notice that the digest bears a resemblance to our *LPI Research Newsletter*. While the familiar format remains, the *Digital Digest* provides summaries of our online endeavors and outreach initiatives, rather than focusing on our published scientific work (those studies will continue to be highlighted in the newsletter).

In this inaugural issue, we're excited to bring you insights from two of our recent webinars. Check out the captivating article on the cover based on the webinar "Visions of Linus Pauling: Reflections on the Man and His Institute" all about Dr. Linus Pauling and the history of the Institute.

Also, make sure to read our article on page 7 with a follow-up from the webinar "Come Fly with Me: New Tools to Investigate Parkinson's."

Our final webinar of 2023 is tentatively scheduled for early December. I will be presenting our latest outreach endeavor: The *LPI's Top Ten* – a guide focused on essential nutrients for addressing common health concerns with a special spotlight on older adults.

As with our previous webinars, registration is required to watch it live. We'll be sure to let you know as soon as we have it scheduled so you can sign up.

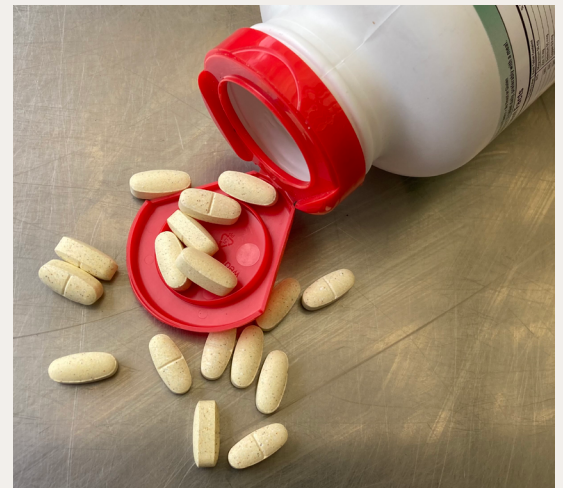
Mark your calendars, as our next edition of the *LPI Research Newsletter* is set to hit the scene in November, where we'll bring you more in-depth information about our recent scientific publications.

And one more thing: Don't miss the updates from our online Micronutrient Information Center on the next page. You can expect to see more from the MIC in the spring.

Hope you are enjoying the start of fall!

LPI IN THE NEWS

- Dr. Emily Ho is the 2023 OSU Alumni Association Distinguished Professor, as announced during [University Day at Oregon State University](#). Dr. Richard van Breemen won the OSU Impact Award for Outstanding Scholarship at the same event.
- Dr. van Breemen was also named on the [2023 Power List by The Analytical Scientist](#) for the third year in a row.
- A research team led by Drs. Fred Stevens and Adrian "Fritz" Gombart found that a compound derived from hops reduces the abundance of [a gut microbe associated with metabolic syndrome](#).
- Drs. Tory Hagen and Kathy Magnusson recently published their latest clinical trial in older men, showing that shows daily multivitamin use improves nutritional status [and helps to maintain cellular metabolic functions](#).



The Linus Pauling Institute's newest clinical trial on multivitamins will be featured in the next issue of the *LPI Research Newsletter*, coming in November 2023.

MICRONUTRIENT INFORMATION CENTER UPDATES

Choline Article

- **New Section on Inadequacy:** Most people in the United States fall short of the recommended daily intake of choline in their diets. Specific segments of the population face a higher risk of inadequate choline intake. Notably, vegetarians and vegans, as well as pregnant and lactating individuals, belong to these higher-risk groups.
- **Brain Development:** The role of supplemental choline in preventing neural tube defects during embryonic development remains uncertain; randomized controlled trials of choline supplementation during early pregnancy are needed to determine if choline is protective. However, a recent clinical trial involving maternal choline supplementation during late pregnancy demonstrated potential cognitive benefits for infants when compared to expectant mothers with lower choline intake levels, suggesting a role for choline throughout the entire pregnancy.
- **Safety Update:** Recent research has brought attention to a choline metabolite known as trimethylamine N-oxide (TMAO), indicating potential associations between high blood TMAO levels and cardiovascular disease, kidney disease, and type 2 diabetes. However, research in this area shows conflicting results. Importantly, it is worth noting that elevated circulating TMAO levels might merely serve as a biomarker of disease rather than being a direct causal factor.

The full text of the article on choline can be found online at:

lpi.pub/MIC-choline

Copper Updates

- **Revised Sections on Deficiency:** Although instances of dietary copper deficiency are relatively rare, depletion of copper reserves can arise from specific genetic conditions such as Menkes disease. Disorders linked to intestinal malabsorption (such as celiac disease, Crohn's disease, and short bowel syndrome) and prolonged use of high-dose zinc supplementation can also contribute to copper depletion.
- **Copper Excess:** Copper toxicity from dietary intake is quite rare, but it does manifest in genetically acquired copper overload disorders like Wilson's disease. Even without a genetic predisposition, prolonged consumption of high amounts of copper has the potential to induce liver damage. While numerous studies indicate that daily doses of up to 10,000 µg (10 mg) pose no risk of liver damage in generally healthy individuals, there remains concern that this intake level might result in negative health outcomes.
- **Summarizing Chronic Disease Risk:** Copper is involved in several chronic diseases, including cardiovascular disease, osteoporosis, and neurodegenerative disorders like Alzheimer's and Parkinson's disease. The update to the copper article compiles insights from observational studies and intervention trials that have contributed to our current understanding of these conditions. 🌐

The full text of the article on copper can be found online at:

lpi.pub/MIC-copper

Continued from Cover

These groundbreaking discoveries were shared through a series of scientific articles and his seminal book, *The Nature of the Chemical Bond*. But, even as Pauling's theories reshaped the global understanding of atomic bonds, he set his sights on deciphering the structures of larger and more complex molecules.

In the 1940s, Pauling was determined to unravel the intricate structures of proteins. Unlike the relatively simple molecules Pauling worked on previously, proteins contain thousands – if not tens of thousands – of atoms and determining their structures represented new levels of difficulty.

Proteins are strings of individual amino acids. With his knowledge of chemical bonds and molecular structures, Pauling realized that certain patterns were likely to develop. He proposed the groundbreaking concept that amino acids formed a coiled helical shape, which turned out to be one of the foundational components of protein structures, known as the alpha helix.

The significance of the alpha helix was immense, as it was a structural pattern that manifested in a diverse array of proteins. Armed with this innovative insight, Pauling's research into protein structure surged forward, culminating in the elucidation of the structure of hemoglobin, the iron-containing protein necessary to carry oxygen in our blood.

“Pauling did not just have an impact on molecular biology, he helped start the scientific field.”

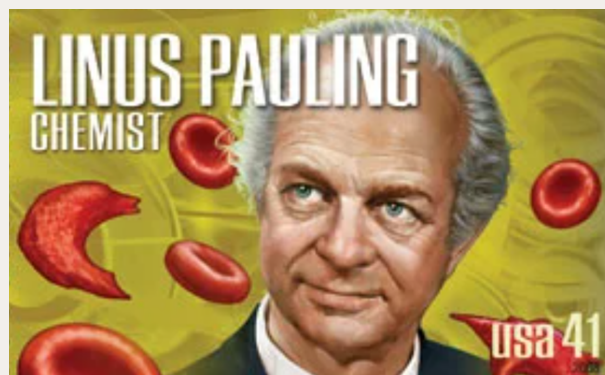
–Chris Petersen

In 1949, Pauling and his research team coined the term “molecular disease” when they characterized the amino acid structure of hemoglobin type S, the atypical form of hemoglobin that causes sickle cell disease.

At the time, proteins were the new frontier, and the importance of DNA was still shrouded in mystery. Yet, Pauling's discovery of the alpha helix heralded a new field of study – one that would be called molecular biology.

In 1954 he was honored with the Nobel Prize in Chemistry for his monumental discoveries of the intricacies of chemical bonds and the complex structures of molecules.

This accolade was remarkable in its own right, as it marked the first instance where the Nobel committee acknowledged a chemist for a complete body of work instead of a solitary eureka moment. It was very important to Pauling to be recognized in this distinguished manner.



A US Postal Service stamp issued in 2008 commemorates the career of Dr. Linus Pauling, recognizing his contributions to the field of molecular biology, his characterization of the hemoglobin protein, and the molecular basis of sickle-cell anemia.

The Origins of Orthomolecular Medicine

When Pauling was in his late thirties, he was diagnosed with Bright's disease, also known as glomerulonephritis, a serious kidney affliction. During that era, this diagnosis was akin to a death sentence because an effective treatment did not exist.

Fortunately, Pauling sought the care of Dr. Thomas Addis, a physician who proposed a unique and unconventional strategy to manage the disease. Addis recommended that Pauling restrict his protein and sodium intake.

Thanks to his wife Ava Helen and her unwavering commitment, Pauling was able to stick to this dietary protocol for years. As a result, Pauling witnessed a remarkable turnaround in his kidney health, defying the odds of the time.

Some people have speculated that this health crisis demonstrated to Pauling the power of good nutrition. However, Pauling's research would not directly focus on nutrition until the mid-1960s, when he announced that he was interested in the application of vitamin megadoses for the treatment of mental health conditions.

In 1967, he published his first treatise on “orthomolecular methods” in psychiatry, which would eventually evolve into what Pauling would term “orthomolecular medicine.” In essence, Pauling's orthomolecular medicine theory postulated that optimal health hinges on the precise deployment of the right molecules in the right amount at the right moments.

Pauling believed that mental health conditions emerged when key vitamins did not reach the brain properly. Thus, he suggested that large oral doses of vitamins might be necessary to restore balance and allow the brain to function normally.

These ideas were soon applied to vitamin C when Pauling received a letter from Dr. Irwin Stone, a biochemist who had been using vitamin C to improve his health for years. Stone's theories about vitamin C sparked curiosity within Pauling, who then embarked on a journey of personal exploration and research.

A unique aspect of human evolution is our inability to produce vitamin C, a trait that sets us apart from many other creatures. This caught Pauling's attention, prompting him to draw connections between other animals' ability to produce vitamin C and our lack thereof and laid the groundwork for the development of what we now know as the megadose theory.

Pauling's advocacy of megadoses of vitamin C soon captured public attention, particularly with the publication of his book, *Vitamin C and the Common Cold*, in the early 1970s. In the book he recommended high-dose vitamin C supplementation to prevent respiratory illnesses, sparking debate on the potential health benefits of vitamin C.

“Because we’re not able to synthesize our own internal vitamin C... Pauling believed that we were often living in a state of suboptimal health.”

–Chris Petersen

Subsequently, Pauling collaborated with Scottish physician Dr. Ewan Cameron on new publications that elevated the discourse on the role of vitamin C in cancer treatment. This work would eventually pave the way for the use of intravenous vitamin C in the treatment of cancer.

Today, Pauling's career is often distilled into his role as “the vitamin C guy.” It is remarkable that he started this quest at an age when many people think about retirement.

Indeed, he was a proponent of vitamin C and orthomolecular medicine for the last three decades of his life. However, Pauling's quest to change the way we view nutrition was not without its consequences.

A Place to Call His Own

During the late 1960s, Pauling's fascination with vitamin C grew immensely. He sought the support of Stanford University, where he was then employed, to establish a research center that would allow him to advance his vitamin-related theories. However, Stanford declined his request, prompting Pauling to make a pivotal decision to part ways with the university.

Instead, Pauling and his supporters rallied to establish their own research institution in 1973. Originally christened the Institute of Orthomolecular Medicine (see picture below), it was co-founded by Dr. Pauling, Art Robinson, and Keene Dimick.

Yet, a challenge emerged soon after its establishment: the chronic issue of securing research funding. Pauling already had a controversial reputation at the time the Institute was established. Combined with the unconventional nature of his approach to vitamin C research, the Institute struggled to obtain grants from conventional sources.

Thus, the Institute often relied heavily on private donations. This required Pauling and his team to devise innovative strategies to sustain their endeavors. One of these was rebranding the institution as the Linus Pauling Institute of Science and Medicine.

However, as public opinion of Pauling rose and fell, so did the Institute's financial support.

Examples of this are evident throughout Pauling's prolonged and highly publicized fight over vitamin C in the treatment of cancer. In 1976, Pauling and Cameron published *Cancer and Vitamin C*, suggesting that vitamin C may be an effective treatment to extend the life of cancer patients.

This was a boon for the Institute, as Pauling's supporters gave more donations to support this work. On the other hand, when more and more people turned to vitamin C as a “natural” cure for their cancers, this irritated some physicians who saw Pauling's work as professional overreach by a scientist into the field of medicine.

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The Institute of Orthomolecular Medicine was the original name for the Institute, established as a non-profit organization in May, 1973, it was located in an office building in Menlo Park, California.

In 1974, the Institute's Board of Associates officially renamed it to the Linus Pauling Institute of Science and Medicine. Due to his international fame and respect, attaching Pauling's name to the organization helped provide needed research funding.

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Under immense pressure by Pauling's supporters to explore vitamin C as a potential cancer therapy, the National Cancer Institute eventually consented to start clinical trials. When initial results were not promising, incredible debates erupted between Pauling and Dr. Charles Moertel, the lead investigator in the clinical studies at the Mayo Clinic.

In January 1985, the friction seemed to come to a head when the Mayo Clinic released the results of their second trial on vitamin C and cancer. In this report and in the publicity that followed, Moertel branded vitamin C as ineffective for cancer treatment.

The Institute was caught off guard by the report. Pauling and Cameron vehemently contested these findings, labeling the Mayo Clinic study as fraudulent and denying the assertion that Moertel had closely replicated their methodology.

By then, the damage was already done. Pauling – and by extension, the Institute – now had a tarnished reputation. Many journals and newspapers refused to publish Pauling and Cameron's rebuttals or only did so too late. As public opinion shifted, the Institute's financial standing faltered.

While some research stirred up controversy, there were other projects in the Institute that yielded financial gain. For instance, research into using vitamin C as a treatment for HIV/AIDS attracted donations, especially from the San Francisco Bay Area. Researchers at the Institute also began exploring the effect of phytic acid in cancer prevention, a program that was almost entirely supported by a philanthropist based in New York.

By 1990, however, the Institute was in a state of upheaval. Leadership changes and reorganization efforts to refocus on its orthomolecular medicine roots did little to gain new research funding. New work on vitamin C and heart disease generated some public interest but also created divisions within the Institute.

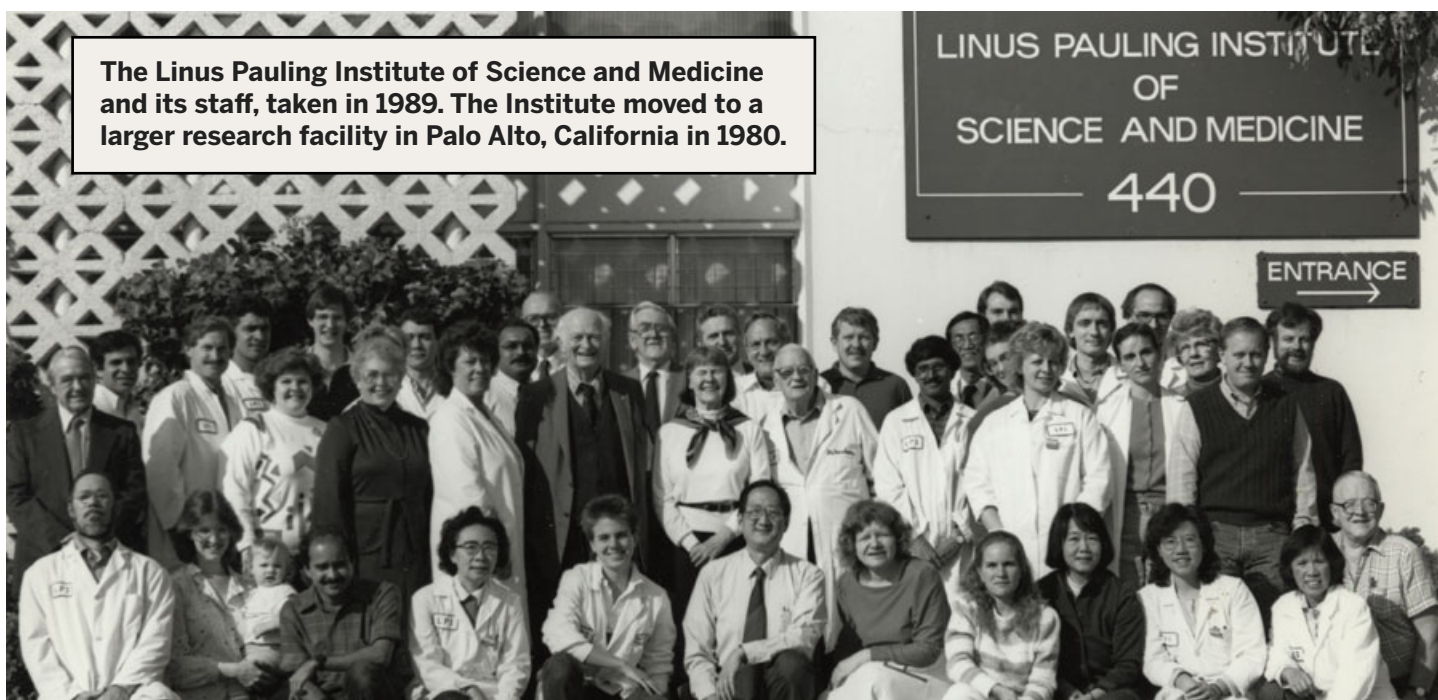
Dr. Ewan Cameron died in 1991, effectively ending the Institute's cancer research program. In the same year, a ninety-year-old Linus Pauling was diagnosed with advanced prostate cancer.

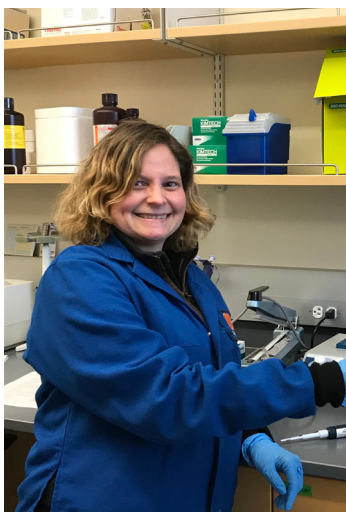
It was at that point that the daily operations of the Institute came under the care of Pauling's son, Dr. Linus Pauling Jr., and the Institute's CEO, Stephen Lawson. Many speculated that the Institute's days were over, but Lawson and Pauling Jr. were convinced that a new strategy was needed.

Although Pauling battled his cancer for three more years, his journey ended in August of 1994. After his death, Linus Jr. and Lawson exacted a plan to associate with Oregon State University.

In 1996, the Institute transitioned from California to Oregon State University and was renamed the Linus Pauling Institute, ushering in a new chapter of success. Its new director, Dr. Balz Frei, elevated the research profile of the Institute to what it is today.

Now entrusted to Dr. Emily Ho, the Institute continues the pursuit of scientific excellence that honors the Pauling legacy. 🍷





Alysia Vrailas-Mortimer
Associate Professor,
Department of Biochemistry
and Biophysics,
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**The recording for
this webinar is now
available online at**
lpi.pub/FlyWebinar2023

“COME FLY WITH ME” RECAP

On July 11, Dr. Alysia Vrailas-Mortimer presented the webinar *Come Fly with Me: New Tools to Investigate Parkinson's* that centered on her approach to researching age-related neurodegenerative diseases using fruit flies – and the new capabilities that fruit fly research affords to the Linus Pauling Institute.

Below are two key takeaways from Dr. Vrailas-Mortimer's enlightening talk. More details about the Vrailas-Mortimer laboratory can be found in the [Spring 2023 edition of the LPI Research Newsletter](#).

P38 is a protein of interest for aging.

Dr. Vrailas-Mortimer's research focus is the function of a protein called p38, a pivotal player in the aging process. When the gene encoding p38 is removed, aging markedly accelerates, resulting in a significantly reduced lifespan. Conversely, genetically engineering the flies to express extra copies of this gene triggers a remarkable 37% increase in the fly's lifespan.

Additionally, flies lacking the ability to produce p38 have impaired locomotor abilities: they move more sluggishly and struggle to regain balance upon falling. Vrailas-Mortimer explained, “Despite their young age, these flies exhibit behavior akin to advanced age.” Again, engineering the flies to make higher-than-normal amounts of p38 protein delays the onset of locomotor challenges that typically develop with aging, allowing them to function better when they get older.

Both processes appear to involve oxidative stress. Flies lacking the ability to make any p38 protein experience elevated oxidative stress throughout their bodies. The neurons involved in the development of Parkinson's disease are especially affected. In contrast, flies engineered to produce extra amounts of p38 exhibit minimal signs of oxidative stress.

“Superfruit” to the rescue?

Exposure to certain chemicals can heighten Parkinson's disease risk. Instances of this phenomenon have been observed with certain herbicides, resulting in Parkinson's cases among both humans and animals. Vrailas-Mortimer is interested in whether antioxidants could help safeguard neurons from deterioration after exposure.

To explore this in fruit flies, Vrailas-Mortimer procured dietary supplements at a local grocery store. These included a composite “superfruit” blend (rich in antioxidants from five different fruits) and pure acai berry. Ginger supplements were used as a control due to their comparatively low antioxidant content.

When flies lacking the gene to produce p38 were provided a standard diet or a diet infused with the ginger supplement, they experienced the accelerated aging process described above. Supplementation with either the “superfruit” blend or the acai supplement extended their lifespan close to that of a normal fly.

And, the “superfruit” or the acai supplements also prevented these flies from developing age-related deteriorations in locomotor activity and aided in preserving their circadian rhythm.

While these supplements showcased promising results, applying these findings to humans presents challenges. During the Q&A session, Vrailas-Mortimer acknowledged, “Clinical trials involving various antioxidant supplements have yielded limited success in Parkinson's.” Beyond dose, she emphasized that timing is also a crucial factor. “Many clinical trials recruit patients with advanced Parkinson's disease,” she explained, “And antioxidant supplementation may be less effective at later stages of the disease.” 🍌

CREATE A LEGACY OF HEALTH

WE CAN IMPROVE LIVES FOR GENERATIONS TO COME

with our research and outreach programs. Continuing the Pauling legacy, the Linus Pauling Institute seeks to discover and share the new ways that nutrition can help everyone live longer, better lives.

And you can help make that happen.

We invite you to learn more about how thoughtful planning today can help you create a sustaining legacy of health at the Linus Pauling Institute.

Start today by watching the recording of our

Create Your Legacy webinar online at

lpi.pub/Legacywebinar

Ready for the next step? [Contact us](#) to learn more.



Oregon State University
Linus Pauling Institute

LINUS PAULING INSTITUTE DIGITAL DIGEST

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