LINUS PAULING INSTITUTE

OREGON STATE UNIVERSITY
RESEARCH NEWSLETTER

FALL–WINTER 2019

An In-depth Breakdown of the LPI Conference **LOOK INSIDE ►**

TIME FOR A GUT CHECK

THE GOMBART LAB GETS ITS HANDS DIRTY WITH THE GUT MICROBIOME

by Adrian Gombart, PhD

Adrian Gombart, PhD, professor in the Department of Biochemistry and Biophysics, has been a principal investigator in the Linus Pauling Institute since coming to Oregon State University in 2008. Typically, Dr. Gombart's research focuses on vitamin D in immune responses, but with the help of his colleague, Dr. Fred Stevens, his work took an unexpected turn to involve a compound from hops.

Scientific breakthroughs can come from the most unexpected places.

When I first arrived at the LPI, I joined the Healthy Aging Program. This was a natural fit since vitamin D is important for proper immune function in older adults.

In 2011, with the move of LPI into the Linus Pauling Science Center, conversations with my colleagues began brewing around the coffee pot in the new breakroom. As a result, my good friend, Dr. Fred Stevens, invited me to attend the informal scientific gatherings in the LPI's Cardio-Metabolic Disease group.

In these meetings, I learned about xanthohumol, a phytochemical found in the hops plant, which you have likely read about in previous LPI newsletters.

Realizing that there was significant overlap in our scientific interests and expertise, my lab started working with Dr. Stevens and Dr. Claudia Maier to determine what interactions might occur between vitamin D and xanthohumol in cells.

I can honestly say that I was amazed by the results of those studies.

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Oregon State University
Linus Pauling Institute

Richard van Breemen, PhD
Endowed Chair
and Director,
Linus Pauling Institute

FROM THE DIRECTOR

Over 50 years ago, two-time Nobel Prize winner Dr. Linus Pauling concluded that dietary supplements play a significant role in enhancing health and preventing disease. The institution that he helped establish, today known as the Linus Pauling Institute, is dedicated to making progress in this field.

A lot has happened since those days in Menlo Park, but the Linus Pauling Institute of today still keeps a focus on dietary supplements. More so now than ever before, we are focused on interdisciplinary research and educating the next generation of experts.

Most recently, researching the health effects of **botanical dietary supplements** has become essential to our mission.

One of my objectives as director of the LPI is to catalyze collaboration among our expert faculty around researching the clinical applications of botanical dietary supplements. We have chosen to focus on combating neurodegenerative diseases, like Alzheimer's, Parkinson's, or ALS, because of the increasing prevalence and enormous public healthcare burden of these conditions.

Put simply, neurodegeneration is the progressive loss of neuronal function and cognitive abilities. This often occurs in response to a stress to our nerve cells or tissues, which can come in a variety of forms. It also occurs more frequently as we grow older, since our ability to resist or recover from stress also declines.

In an effort to push back against the tide of aging in the field of neurodegeneration, we have formed a multidisciplinary team of LPI research faculty to conduct a new research project to **enhance cognitive health**. This team includes many experts in natural products and neurobiology, all dedicated to understanding how botanical dietary supplements can help improve our memory and cognitive flexibility as we age.

We know that some botanical dietary supplements can boost cognitive resilience, especially later in life. Through the application of state-of-the-art scientific methodology, including innovative pharmacology and analytical chemistry techniques, we will identify the most potent and promising of these products.

What's the scoop on curcumin?

Dr. van Breemen was recently featured in a webinar on the pharmacology of curcumin, which is one of the most abundant active constituents of turmeric. Watch it online:
http://bit.ly/LPI-Curcumin

The staff and faculty of the Linus Pauling Institute enjoying the fall colors of the OSU campus.

A comprehensive battery of tests for cognitive health and resilience will help identify the active compounds from these products with the most promise.

With this application of our expert skill sets, we can prepare biologically and chemically standardized extracts for clinical trials. Therein lies the potential for this project to help prevent or delay age-related neurodegeneration.

Among the botanicals that we will be studying are those already showing promise in cognitive health, such as **hops**, **ginkgo**, and **turmeric**. Both Dr. Stevens and I have extensively studied hops constituents, which include the compound known as xanthohumol. See the cover article by Dr. Gombart and Dr. Stevens' article on page six for more therapeutic applications of this molecule.

We hope that this project will be the first of many studies designed to elucidate the roles of botanical extracts in health. This project is just one part of the larger goal at the LPI: to push the boundaries of botanicals supplements and explore new therapeutic applications.

Enjoy this issue of the newsletter. Stay healthy and happy this winter, and you will hear from us again in the new year.

Sincerely,

Richard B. van Breemen

Have a question?

As part of the ongoing evolution of our Research Newsletter, we want to hear from our readers.

If you have questions, please send them in – we plan on addressing reader feedback in future editions.

Dr. Gombart is a principal investigator at the Linus Pauling Institute and is a professor in the Biochemistry and Biophysics department at OSU.

Vitamin D and xanthohumol can work well together — and so could their investigators! It was the start of mutually beneficial scientific partnership.

What I most appreciate about this institute and our new building are the incredible opportunities that occur when working in close proximity with colleagues with diverse scientific backgrounds and experiences. New perspectives and collaborations can take you in directions you never thought possible.

Bad Bacteria Brewing

My lab is one of several at the LPI trying to combat obesity and metabolic syndrome. Since you have heard more about this condition in previous newsletters, I will share our specific approach to tackle the health threat.

I am interested in the maintenance of gut health. Members of my lab and others have shown that poor gut health is a problem in metabolic syndrome, particularly because this condition reduces **gut barrier function** and alters the microbiome – ramping up inflammation.

The intestinal mucosa is a single layer of cells that forms a gut barrier, keeping things in our digestive tract (like bacteria) out of our bodies.

This is where xanthohumol is important. In research animals, Dr. Stevens has shown that xanthohumol is a very promising treatment for metabolic syndrome. As we try to take our work forward, I want to know if xanthohumol is doing its job through changes in the gut.

More specifically, does taking xanthohumol fix a gut microbiome that has gone bad?

Yang Zhang, a graduate student in my laboratory, is examining the changes that happen in mice that consume a high-fat diet – one of the driving forces behind metabolic syndrome. She discovered that adding xanthohumol to the diet was enough to change the composition of the gut microbiota. These changes were associated with weight loss and reversal of metabolic syndrome characteristics.

Recently published in *Molecular Nutrition and Food Research*, our study found that treatment with xanthohumol reduced dysbiosis (microbial imbalance), altered bile acid metabolism, and reduced inflammation.

In fact, some chemical derivatives of xanthohumol were just as effective as giving xanthohumol itself (For details on these derivatives, see our Fall-Winter 2018 newsletter).

Apparently xanthohumol does some good things for the gut microbiome. Now we want to find out exactly how it works.

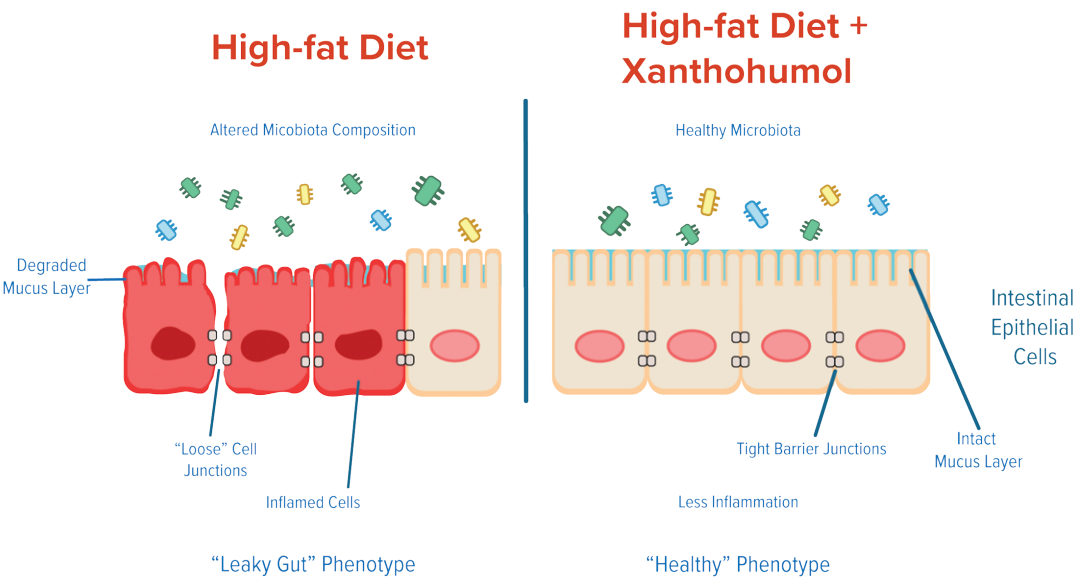
Getting Better Germs

Food that passes through the intestine feeds the microbes in our guts. When a diet is of poor quality, certain bacteria types start to take over, causing ripple effects throughout the body.

Since most animals have a thriving gut microbiome, it is not something that is easily removed. To really understand the influence of gut bacteria on metabolic syndrome, it was necessary to raise animals that had no gut bacteria at all.

These are called 'germ-free' animals. They live under very special conditions from birth to prevent any bacteria (or other microbes) from getting into their bodies from the outside. Effectively these mice live in an extraordinarily clean animal facility.

These mice are generally healthy, but they are different from their conventionally raised counterparts. Germ-free mice grow slower, gain less weight, and are less prone to obesity. They also have an underdeveloped immune system.



Xanthohumol can work in several ways to combat gut inflammation and restore a normal healthy gut. Changing gut bacteria is only one piece of this puzzle.

Current research suggests that germ-free animals do not develop metabolic syndrome. After all, no gut microbiome means nothing to spoil with a bad diet, right? Wrong.

Isabelle Logan, another graduate student in my lab, took a closer look. Working with different animal strains, she found at least one strain of germ-free mice that develops several characteristics of metabolic syndrome on a high-fat diet.

Just like their conventionally raised counterparts, the germ-free mice gain weight, are unable to clear glucose from the blood, and show elevated LDL ("bad") cholesterol.

Does this challenge the notion that bad bacteria in the gut are the cause of metabolic syndrome? Not entirely.

Although we induced something like metabolic syndrome in these animals, they did not develop all of the same characteristics. Conventionally raised mice on a high-fat diet are certainly less healthy than the germ-free mice, indicating that certain gut microbes could worsen the disease.

Maybe there is something to be said for fixing gut bacteria after all.

Since xanthohumol affects the composition of the gut bacteria and this is associated with improving metabolic syndrome, is it possible that changing the microbiome confers xanthohumol's benefits?

You will hear more from us on this topic soon. At the moment I can only say that our early results look very promising.

What about vitamin D?

In these studies, we took vitamin D out of the equation to see what xanthohumol can do alone. However, we do want to determine what vitamin D can do for immunity and gut health.

Vitamin D plays an important role in regulating the 'gut barrier,' important for keeping the contents of our digestive tract away from our tissues and bloodstream. During the development of obesity and metabolic syndrome, this barrier becomes 'leaky,' allowing increased invasion of toxins into our bodies and increasing systemic inflammation.

It is important to keep our gut barrier healthy, and we think that vitamin D is one way to do that. Maybe, along with xanthohumol, we can develop treatments that keep patients with metabolic syndrome from cascading down the path to serious chronic illness.

References

Zhang et al. *Mol. Nutr Food Res.* **(2019)** -In press. doi: 10.1002/mnfr.201900789.

Paraiso et al. *Mol Nutr Food Res.* **63 (2019)** doi: 10.1002/mnfr.201800923

Miranda et al. *Sci Rep.* **8 (2018)** doi: 10.1038/s41598-017-18992-6

The multidisciplinary xanthohumol-IBD research team. Dr. Fred Stevens is pictured in lower-left corner.

TAKING THE FIGHT AGAINST IBD TO THE NEXT LEVEL

SEED FUNDING SPARKS A COLLABORATIVE RESEARCH STUDY ON INFLAMMATORY BOWEL DISEASE

In the Stevens laboratory and other laboratories at the LPI, studies on xanthohumol have been a big success. Using the momentum generated by small grants, Dr. Fred Stevens leveraged this work to obtain a new federal grant on inflammatory bowel diseases that involves multiple research centers in the Pacific Northwest.

IBD is an umbrella term that describes many disorders of the digestive tract. These include the more well-known conditions like Crohn's disease and ulcerative colitis.

Cases of inflammatory bowel disease (also known as **IBD**) are on the rise. According to the Centers for Disease Control and Prevention, over three million people in the US have been diagnosed with this condition, part of a trend of increased prevalence worldwide.

One thing that inflammatory bowel diseases have in common – as the name suggests – is chronic inflammation. Unfortunately, the root cause of IBD is unclear, making current therapies very limited.

Treatment often includes steroids and other anti-inflammatory drugs that have terrible side effects. Indeed, many of these therapies do not address the changes in the gut bacteria that can worsen the effects of IBD over time.

Dr. Fred Stevens, principal investigator at the Linus Pauling Institute, hopes to find a better way to tackle IBD.

"I have studied the chemistry and biological activity of hop compounds for nearly 25 years," Dr. Stevens explains. "In studies conducted at the Linus Pauling Institute, we have found that xanthohumol targets a nuclear receptor protein involved in the pathogenesis of inflammatory bowel disease."

That nuclear receptor protein is the Farnesoid X Receptor (FXR for short). FXR is a one of the master control proteins in the liver, responsible for regulating bile acid, glucose, and fatty acid metabolism.

Activation of FXR in the liver can improve insulin sensitivity, lower blood lipids, and reduce inflammation.

FXR is also highly expressed in the small intestine. It is there that we can see a possible link with IBD: Patients with these diseases appear to have lower FXR activity than healthy people.

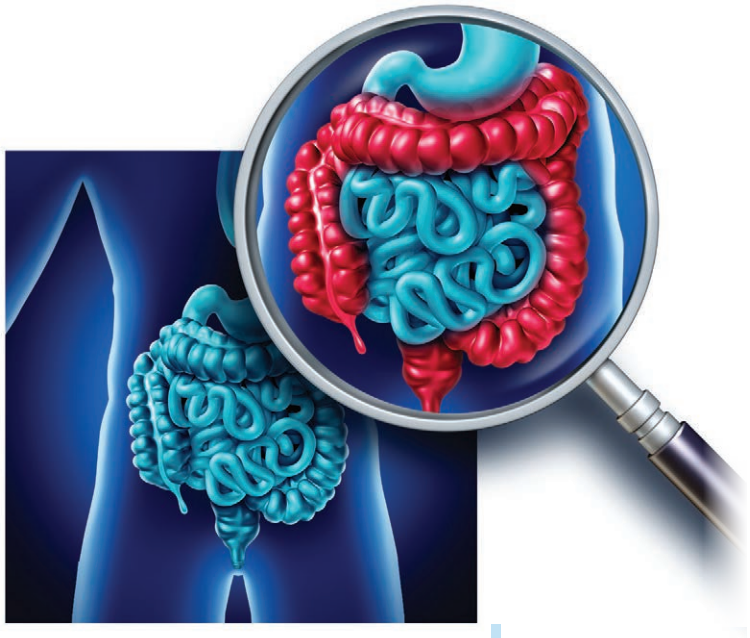
Studies in animals have suggested that xanthohumol can influence FXR. Recent cell culture studies by the Stevens lab have repeatedly demonstrated the ability of xanthohumol to stimulate FXR activity.

> "Seed funding was the only thing that made it possible for us to explore the anti-inflammatory effects of xanthohumol in inflammatory bowel disease"
>
> –Fred Stevens, PhD

Dr. Stevens' research group has also shown that xanthohumol reduces inflammation in various preclinical models of disease. For example, xanthohumol appears to influence the composition of microbe species found in the gut – a possible driving force in inflammatory response (**see cover article by Dr. Gombart**).

The combined findings gave Dr. Stevens the idea to study the effects of xanthohumol in Crohn's disease. So, he assembled a multidisciplinary team of OSU and LPI scientists with researchers from nearby research institutions. Now Dr. Stevens and his colleagues have a $1.6 million grant to continue this work.

"Seed funding was the only thing that made it possible for us to explore the anti-inflammatory effects of xanthohumol in inflammatory bowel disease," Dr. Stevens added. "That leg-up resulted in this new, four-year clinical research project."



When out of control, intestinal inflammation can lead to an increased risk of serious complications. For example, Crohn's disease can lead to an increased risk of colorectal cancer.

Currently in the process of recruiting for a human clinical trial, this project is ultimately designed to identify the effects of xanthohumol in Crohn's disease.

"We intend to identify a biological fingerprint of xanthohumol exposure in people and observe a reliable effect on inflammation in this disease," Dr. Stevens said.

"Most importantly, stakeholder companies Hopsteiner and Metagenics supported this work at the LPI," he explained. "That support brought the metabolic, biochemical, and gut microbial aspects of this project together, and was key to our success."

This team also includes other scientists from the Helfgott Research Institute at the National University of Natural Medicine and from the Pacific Northwest National Laboratory in Richland, Washington. Hopsteiner, Inc. and Metagenics, Inc. are developing a pure xanthohumol supplement suitable for human consumption.

Plant Your Own Seed – Support LPI Studies

With your support, the studies on xanthohumol have been a big success. It is a shining example of how even small donations to the LPI can be leveraged into something greater.

This large federal grant offers opportunities for LPI students and postdoctoral researchers to participate in ground-breaking studies. These experiences at LPI will help young investigators prepare for independent careers in academia, government, or industry.

Interested in living longer & feeling better?

SO ARE WE!

Here are a few ways you can support our mission:

1. Use your retirement account

Did you know that you can use retirement accounts (IRA, 401k, or similar) to make a gift while potentially avoiding unwanted taxes?

You can pass 100% of these funds to the Linus Pauling Institute **tax free**.

2. Name the Linus Pauling Institute in your estate plan

Let's chat! The OSU Foundation can help you make sure your generous contribution to the Linus Pauling Institute matches your intentions.

3. Become a monthly donor

Regular support helps us expand research efforts and **drive innovation**.

Become a monthly donor today and support our healthy aging research, life-changing clinical trials, and the training programs for next generation of scientists.

Don't wait! Contact Andrew Norwood before December 31st
to learn more about these or other ways we can support the LPI mission together!

By phone: **503.936.0086**
or by email at: **Andrew.norwood@osufoundation.org**

LPI STUDENTS

Luce Mattio

Visiting PhD Student, University of Milan

"Answering questions about life."

Luce Mattio fell in love with science at an early age. Seeing scientific discovery as a means to find answers to her many questions about the world, she pursued education in medicinal chemistry. Luce was fascinated with the study of molecular mechanisms and how the creation of new molecules could affect biological processes.

Her Master's degree work focused on the synthesis of natural compounds – producing chemicals similar to those found in the natural world. Drawn further into natural products chemistry, Luce enrolled in the doctoral program in Food Systems at the University of Milan. Her research focuses on the identification, synthesis, and biological studies of polyphenols from food or waste by-products.

For her study abroad component of her PhD program, Luce sought to work with an accomplished and respected expert in natural products chemistry. She therefore joined the laboratory of LPI investigator Dr. Fred Stevens, where she is learning various analytical and biological approaches to study bioactive molecules. After graduation, Luce would like to investigate natural products as the source of active molecules to discover new drugs.

Alan Wong

PhD Student, van Breemen Laboratory

"Exploring the wonders of nature."

Alan Wong completed his undergraduate training in geology and biochemistry at Northwestern University. As time went on, however, his passion gradually shifted from studying chemical signatures in fossils to studying plants. After an early job analyzing products for the agrochemical, food, and botanical industries, he became interested in exploring the health effects of botanical dietary supplements.

He thus joined the laboratory of Dr. Richard van Breemen, where he now focuses on connecting basic research on botanicals to their use in a clinical setting. Using some of latest mass spectrometry technologies, Alan seeks to answer previously unsolvable questions on the effects of these supplements in humans.

He is especially interested in understanding how natural products – when provided as a dietary supplement – affect hormone levels in the body. After graduation, Alan plans to take scientific tools like mass spectrometry into a clinical setting. His hope is to use these cutting-edge techniques to develop powerful bioassays that will help advance the treatment of disease.

Every student and postdoctoral trainee who studies with us furthers the impact of the Linus Pauling Institute on a global scale. If you are interested in contributing to a student's success, please contact the LPI or the OSU Foundation today to explore your options.

FOUR QUESTIONS WITH MARET TRABER

Dr. Maret Traber is one of the world's foremost authorities on vitamin E – in fact, at the LPI we call her the 'Goddess of Vitamin E.'

The world is desperately in need for a more detailed look at vitamin E in people – a goal that Dr. Traber has been reaching for since the 1980s. Recently, along with her collaborators at the NIH, she established a new method for measuring vitamin E absorption.

Her study, published in the *American Journal of Clinical Nutrition* in November, takes a giant leap forward in accomplishing that goal. What she and her colleagues found was amazing, and had far greater consequences than they initially expected.

This is an amazing study with intricate data sets in people. Before we get into the nuances, let's start with something simple: What is one thing everybody should know about your study?

"I think you can boil everything down to one magic number. All the detailed measurements, all of the logistics of getting people to eat vitamin E in very defined ways, and all of the complicated statistics say one thing: you absorb a little over half (55%) of the vitamin E from food that you eat, no matter how you choose to eat it.

This study is the very first time that vitamin E absorption has been accurately measured. We need this number to estimate how much vitamin E you need to eat every day – and it is critically important for **redefining the dietary requirements** for this vitamin in the United States."

In the year 2000, Dr. Traber was a member of the committee that set the dietary reference intakes for vitamin E.

Typically when people think of eating something that dissolves in fat, like vitamin E, you need to eat fat with it – at least to absorb it properly. Your study challenges this idea?

"Based on our previous studies, we thought the same way: you need fat in a meal to absorb vitamin E. So we started with that question: how much fat do you need?

We started the study with people eating lots of fat. The volunteers drank a beverage that was **40% fat**. When these people drank the vitamin E, everything was going according to plan. As we expected, vitamin E appeared in the blood, and over time distributed through the body.

"I call that a shake," quips Traber, "But my collaborator calls it a 'defined liquid meal.'"

We repeated the trial, this time with no fat. We expected a big change in the rate of absorption. But it turns out there was no change at all – vitamin E absorption was the same as the previous trial.

Suddenly this simple test was giving us a surprising and unexpected answer. How can these people be absorbing the same amount whether it was eaten with any amount of fat? We know from previous studies that people who can't absorb fat can't absorb vitamin E.

Something more complex than fat absorption had to be involved here."

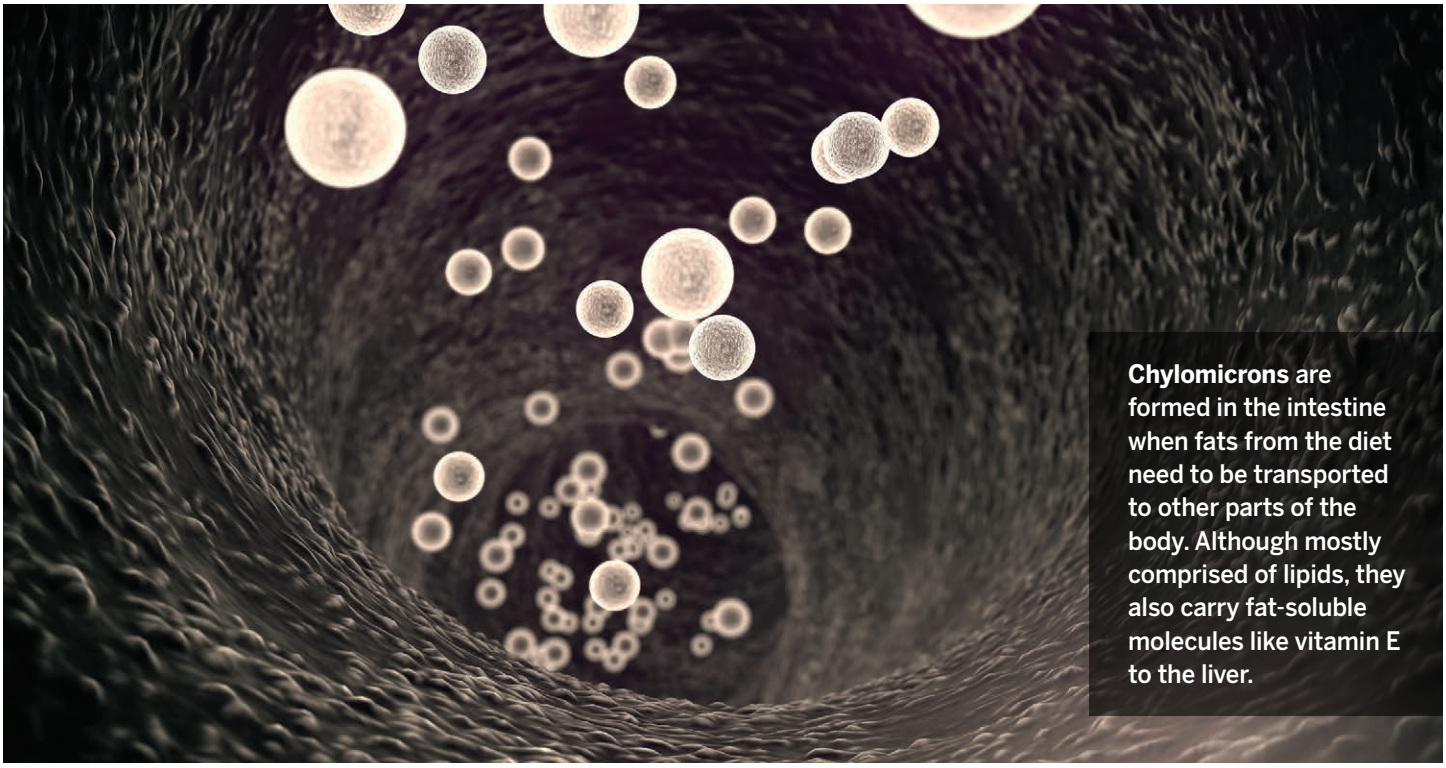
You really had no idea what was going on? I am guessing there were some fundamental doubts about your study design. What was the next step?

"My colleagues at the NIH started asking tough questions. They noted that it took a long time (9+ hours) after the person consumed vitamin E for it to show up in the blood. I had seen this in many, many studies before this one, so it was not a surprise to me.

However, my collaborators expected it to be absorbed in about three hours. Essentially, they came to me and asked: 'What's wrong with your vitamin?'

As we started to re-examine everything, we thought about the influence of food. Even though we had controlled the amount of fat and vitamin E in their lunches, it was still possible that eating was aiding vitamin E absorption.

In the end, the participants repeated the trial but this time ate nothing after breakfast – they were fasting all day long."



Chylomicrons are formed in the intestine when fats from the diet need to be transported to other parts of the body. Although mostly comprised of lipids, they also carry fat-soluble molecules like vitamin E to the liver.

"It did turn out to be a problem, but not in the way anyone expected. You see, during this fasting period very little vitamin E appeared in the blood – it trickled into the bloodstream very slowly.

Now comes the real kicker: When the participants ate their evening meal, the vitamin E was dumped into the plasma all at once. When we calculated how much the participants absorbed, we saw the same answer – high fat, no fat, or fasting made no difference.

It took us a long time to understand what was going on. Our best understanding is that vitamin E is being absorbed into the intestinal cells and is 'held' in fat droplets. There it waits, with small amounts of it being released with **chylomicrons** into the blood.

It is almost as if the intestine is metering how much fat is getting in the circulation so it does not overwhelm the liver – leaving the liver to deal with it at a reasonable pace. When you eat again, however, that all goes out the window and it needs to clear out the fat and vitamin E to make room for the next meal.

It is exciting that this work uncovered the idea that the intestine is far smarter than we used to think and dedicated to a specific role in the body."

Is this phenomenon specific to vitamin E?

"Definitely not. In an editorial to our article, Emmanuelle Reboul, a nutritionist from Aix-Marseille Université, reviewed how beta-carotene, a plant source of vitamin A, behaves in a similar fashion.

Our study is the first time this phenomenon was characterized for vitamin E. It's hard to say right now how important this process will be to understanding the absorption other fat-soluble compounds.

After this study, we finally understand why **all eight forms of vitamin E** that plants make get absorbed, even though the liver chooses to retain only one of them: alpha-tocopherol. The other forms are excreted."

Plants make alpha, beta, gamma, and delta forms of both tocopherols and tocotrienols, all of which are considered part of the 'vitamin E family.'

This interview with Dr. Traber covered so much more than we can summarize here. For example, did you know that vitamin E can easily cross in to HDL ("good") cholesterol after being absorbed? Dr. Traber and her collaborators watched it happen.

If you want to see more from this conversation, then join us online at: **http://blogs.oregonstate.edu/linuspaulinginstitute**

Or if you want to read the full study, go to: **http://bit.ly/Traber2019**

LPI 10th INTERNATIONAL CONFERENCE

In August 2019, the Linus Pauling Institute held its 10th International Conference "Botanicals, Bioactives, and Redox Mechanisms" in Corvallis, Oregon. In total, 161 people attended the conference, hailing from 55 different institutions and nine different countries. By all measures, from the scientific sessions to the public open house, it was a huge success. For a complete conference program, see: lpi.oregonstate.edu/conference

LPIIC 2019

For LPIIC 2019, the conference chairs were Dr. Richard van Breemen, Director of the Linus Pauling Institute, and Dr. Maria Clara Franco, from the Biochemistry and Biophysics department at Oregon State University.

The purpose of this conference was unique: to bring professionals working in the fields of dietary supplements and/or redox biology together with world-renown experts on the treatment of chronic disease (in particular, neurodegenerative disease and cancer).

In only a few other places in the world has such a fusion of research scientists, clinicians, and industry representatives existed, with the sole purpose of finding new ways of working together.

The conference was divided into three days of scientific presentations, each with dedicated themes for the individual sessions. On the final day, an open house featured various scientific departments at Oregon State University. This public event culminated in a keynote presentation by Nobel Laureate, Dr. Louis J. Ignarro.

Conference organizers Jen Stotts, Dr. Alexander Michels, and Caitlyn Reilley

SCIENTIFIC SESSIONS

Day One: Botanical Dietary Supplements

This day began with presentations from **Dr. Wendy Weber** from the National Institutes of Health and **Dr. Chongwoo Yu** from the Food and Drug Administration. They both spoke about how botanical supplements are viewed at the level of the federal government, including how studies on them are considered for federal funding.

Other highlights from these sessions included talks from **Dr. Paula Brown** and **Dr. Stefan Gafner**. They both exposed an important issue concerning botanicals: identification. In short, it is often difficult to know if a botanical supplement is authentic, and there are many ways that suppliers can fool existing testing procedures.

Lastly, a series of provocative presentations highlighted the therapeutic uses of botanicals. **Dr. Edward Kennelly** summarized his two decades of research on black cohosh – a supplement that is frequently adulterated – and demonstrated that the reported mechanism of action of this plant in women's health is not correct and is need of revision.

Dr. Fred Stevens gave an overview of his recent work with xanthohumol in metabolic syndrome and inflammatory bowel disease (**see page 6 for more**).

Also, **Dr. Tom Kensler** gave a spectacular update on the use of broccoli-based interventions in the detoxification of air pollutants. For instance, giving sulforaphane (a compound from cruciferous vegetables) may be a practical strategy to deal with the health risks of poor air quality.

Day Two: Neurodegeneration and an Update on Vitamins

This day began with a symposium sponsored by the International Society for Neurochemistry, chaired by **Dr. Alvaro Estevez**. This session delved into uncovering new targets for treatment of neurodegenerative conditions like Alzheimer's disease and multiple sclerosis.

Particularly fascinating were talks by **Drs. Larry Sherman**, **Jeremy Spencer**, and **Tilman Grune**, which revealed the beneficial effects of polyphenols (with an emphasis on flavonoids) on cognitive function. Later, **Dr. Lee Martin** presented on appropriate cell models to study human neurodegenerative disease.

The day also included an update on vitamin research. This session began with **Dr. Douglas Feinstein** speaking about vitamin K deficiency and how it can impact the proper function of the nervous system.

For an update on vitamin C, **Dr. Jens Lykkesfeldt** explored the effects of this vitamin on gene expression. **Dr. Fiona Harrison** addressed the vital role that vitamin C plays in the recovery from sepsis.

Dr. Adrian Gombart spoke about the results of a small clinical trial of multivitamin supplementation and immune function.

Dr. Maret Traber presented the details about her work on vitamin E absorption in human participants (**see page 10**).

Conference chair Dr. Maria Clara Franco

Drs. Maret Traber and Richard Bruno

Drs. Jens Lykkesfeldt and Fiona Harrison

Want More?

LPIIC2019 featured cutting-edge research from around the world. Much of the data at the meeting was preliminary and could not be shared widely.

If you want more details on any study mentioned here, please let us know and we will do our best to keep you informed.

Dr. Alvaro Estevez and LPI graduate fellow, Isabelle Logan

SCIENTIFIC SESSIONS (CONTINUED)

Dr. Enrique Cadenas

Day Three: Redox Biology
Redox biology is the interplay of oxidants and antioxidants in the body, and understanding how this affects health. These sessions specifically focused on the impact of redox biology on neurodegenerative diseases and cancer.

Drs. Enrique Cadenas and **Allan Butterfield** started the day with discussions about redox biology in Alzheimer's disease. Neurodegeneration is one area where the production of oxidants leads to lasting damage – and represents a large opportunity for future therapy.

Drs. Nadine Hempel, **Rebecca Oberley-Deegan**, and **Douglas Spitz** each spoke of ways to exploit the vulnerabilities of cancer cells, especially in their ability to fend off oxidative damage.

Dr. Spitz gave a fascinating update on the use of high-dose, intravenous ascorbic acid in the treatment of cancer. In a 21st century update on Pauling's work, he demonstrated how high doses of vitamin C can turn from antioxidant to pro-oxidant, creating reactive oxygen molecules that can damage (and possibly kill) cancer cells.

Drs. Douglas Spitz (seated) and Allan Butterfield

A SESSION FOR THE PUBLIC, FEATURING NOBEL LAUREATE DR. LOUIS J. IGNARRO

As Dr. Linus Pauling was a strong advocate for bringing science to a general audience, we dedicate a portion of every LPI conference to public outreach. This year, we were honored to welcome Nobel Laureate Dr. Louis J. Ignarro as our keynote speaker for this session, which was preceded by an open house that highlighted various research programs at Oregon State University.

In his presentation, Dr. Ignarro highlighted his early life as a driving force in his career. Like Dr. Pauling, he had a hungry mind that was constantly exploring questions about the world he lived in. Also like Dr. Pauling, he was fascinated by chemistry from a young age.

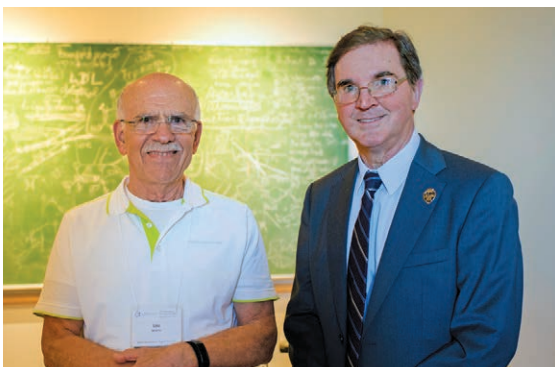
This hunger for science served him well. Indeed, when he questioned why his high school did not have a functioning chemistry lab, his instructor brought in a friend – Dr. Linus Pauling – to help set one up.

Ignarro credits this meeting with Dr. Pauling early in his formative years as contributing to his later career success in chemistry.

Dr. Ignarro delved into his studies surrounding nitric oxide, for which he was awarded the 1998 Nobel Prize in Physiology or Medicine. Dr. Ignarro and his collaborators found that the body can produce nitric oxide that causes blood vessels to relax.

Dr. Ignarro shared with us his fascinating (and often humorous) journey through the sciences. His discoveries are implicated in many different aspects of health and disease, especially concerning heart and arterial health.

For a greater perspective on redox biology, vascular function, and heart disease, we encourage you to view the videos of Dr. Ignarro's lecture on our YouTube channel: **http://bit.ly/LPIVideos**



LPI Director Dr. Richard van Breemen and Dr. Louis Ignarro visiting the OSU Library's Special Collections and Archives

Top 5 Takeaways from LPIIC 2019

1. Authenticity of botanical supplements is a big problem.

Identification, potency, and purity of botanicals plague research scientists, clinicians, government agencies, and consumers alike. Suppliers often do not take time and effort to identify their products correctly, or they try to sell inferior products. This needs to be fixed.

2. Botanicals are a promising field for therapeutics.

The science behind **botanical supplements** is advancing dramatically. Look for breakthroughs in neurodegenerative disease and cancer soon. However, many products are very potent (and potentially dangerous), so the how, when, and why to use botanicals will be important questions to address in the near future.

3. Many plants naturally contain chemicals that may protect the nervous system.

We are learning much more than ever before about the benefits of phytochemicals on the brain and nervous system. Phytochemicals are non-nutrient compounds from plants, but they may trigger cellular repair mechanisms and promote cell growth that may help **slow neurodegenerative diseases**.

4. Redox biology is a normal part of life (but also disease).

Our everyday life involves the movement of electrons in our body. This is the field of **redox biology**: understanding what electron reactions are normal and what parts can lead to disease and dysfunction. Knowing the difference between these states informs what roles antioxidants (and other redox-active compounds) can have in human health.

5. Cancer has redox vulnerabilities.

Cancer cells maintain a delicate balance. In order to push their ability to divide and grow to the limit, these cells sacrifice part of their natural defenses to oxidants. Therapies like high-dose, **intravenous vitamin C** take advantage of that vulnerability, and might just be a promising treatment in combination with certain redox-active chemotherapies.

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