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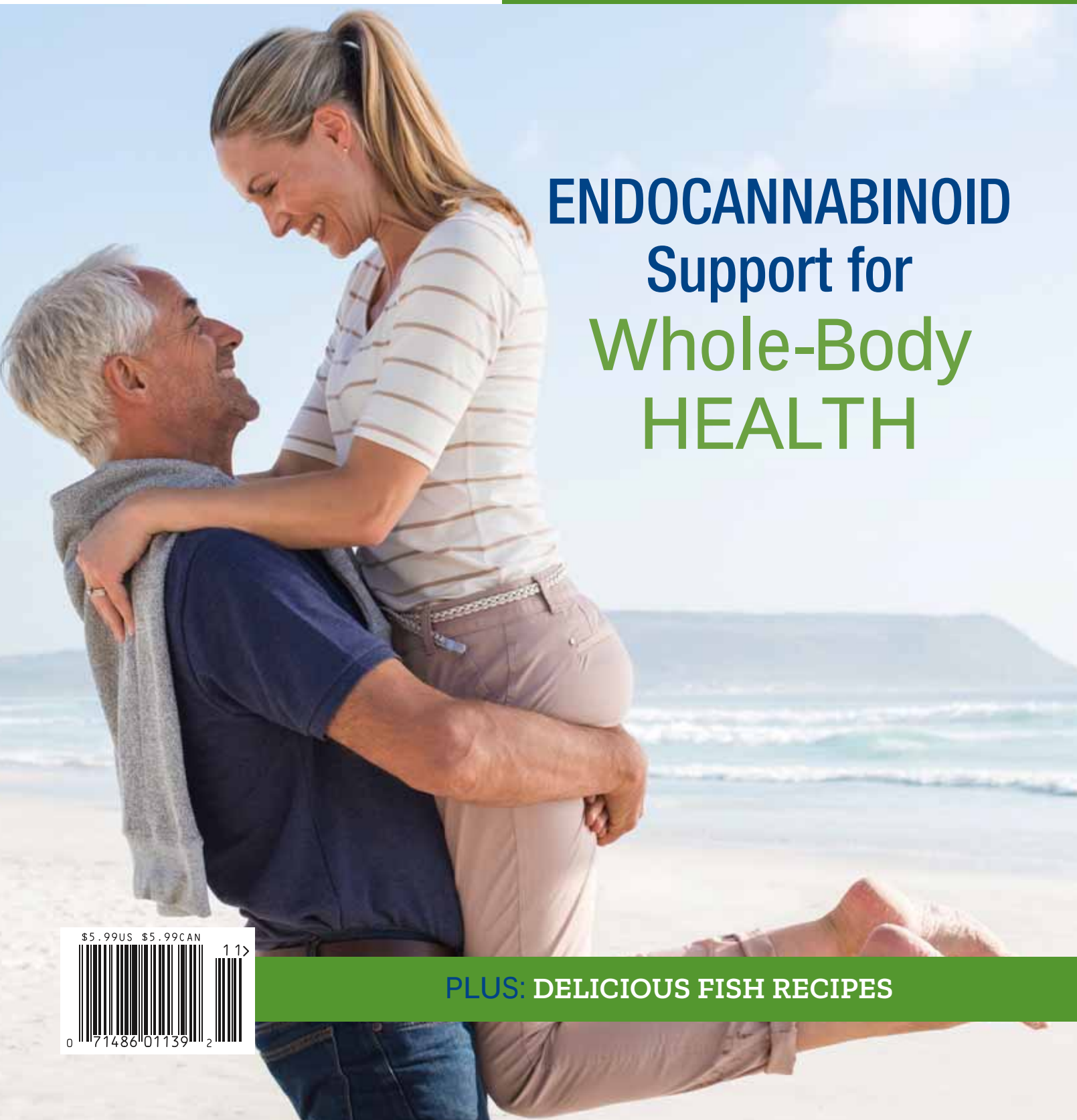

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Richard Black, DO, is a dedicated nuclear medicine physician practicing as an independent contractor out of Cleveland, Ohio. Dr. Black is board certified in internal medicine and nuclear medicine, and is licensed to practice medicine in multiple states throughout the United States.

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Aubrey de Grey, PhD, is a biomedical gerontologist and Editor-in-Chief of Rejuvenation Research, the world's highest-impact, peer-reviewed journal focused on intervention in aging. He received his BA and PhD from the University of Cambridge in 1985 and 2000 respectively. Dr. de Grey is a Fellow of both the Gerontological Society of America and the American Aging Association and sits on the editorial and scientific advisory boards of numerous journals and organizations.

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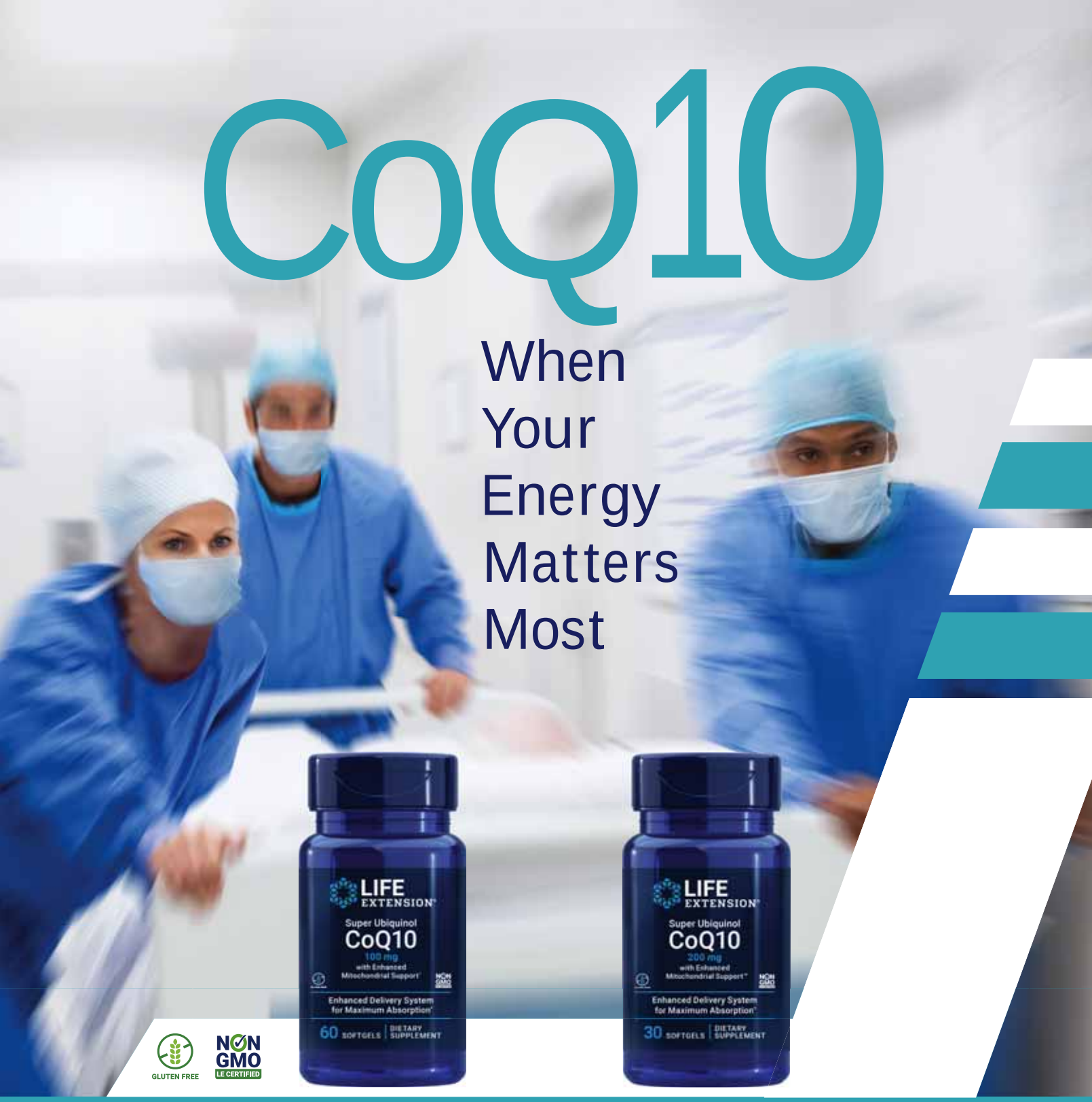

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Add Five More Years with One Therapy

WILLIAM FALOON

My 40-year quest to persuade supporters to keep their blood pressure in lower ranges continues to fail!

I'll never forget a call I received from a dedicated **Life Extension®** supporter in the 1980s who had suffered an ischemic **stroke**.

He was fortunate to fully recover.

My first question was about his **blood pressure**. It was elevated.

This supporter recalled our warning to keep blood pressure below **120/80 mmHg**. He nonetheless thought that his healthy diet and supplements protected against the effects of **hypertension**.

I instantly responded that we never implied that *anything* could protect the brain against the destructive impact of **high blood pressure**.

Despite my many articles and live presentations, I continue to interact with readers of this magazine who don't **optimize** their blood pressure.

One study shows total **life expectancy** is **five years *longer*** in people with blood pressure below **120/80** mmHg compared to people at **140/90** mmHg and above.[1]

More recent data confirm the magnitude of **heart attacks** and **strokes** occurring in those who fail to target **systolic** blood pressure below **120-130** mmHg.

This editorial describes the lost **life years** that have occurred because of this single health issue and discusses how easy it is to take corrective actions.

Each time your **heart beats**, it generates **systolic pressure** that enables oxygenated blood to circulate throughout your body.

Normal aging usually results in elevation of systolic **blood pressure** that **damages** arteries and delicate capillary beds.

Excess systolic blood pressure causes or contributes to:[2-5]

- Coronary artery disease
- Aortic valve stenosis
- Cerebral vascular disease
- Kidney failure
- Retinopathy and other eye disorders
- Dementia

Blood pressure is increasing worldwide due to ever-growing numbers of **overweight** and **obese** individuals.

If effective medications were not available, I would not be as adamant in urging *everyone* to achieve **optimal** blood pressure readings.

To use a simple analogy, imagine the sprinkler head on your garden hose is turned to the "off" position.

Would your vinyl hose remain intact longer if there were a small amount of water **pressure** coming from the spigot or if the spigot were turned all the way up, meaning your vinyl hose would have to contain high water **pressure**?

I hope the answer is obvious, i.e., lower pressure inflicts less damage!

The Framingham Heart Study

You may recall reading about the **Framingham Heart Study** but may not realize its significance.

Prior to Framingham, there were no strong and reliable data about heart attack and stroke prevention. This meant that doctors lacked the necessary evidence to optimally reduce the heart attack and stroke risk.

Findings from **Framingham** have averted hundreds of millions of cardiovascular events, yet the majority of the public overlooks these remarkable data sets.

Elevated **blood pressure** is a *major* modifiable risk factor for **cardiovascular disease** and mortality.[6,7]

According to a 2002 *World Health Organization* report, suboptimal blood pressure (defined as systolic blood pressure over **115 mmHg**) was estimated to be responsible for **62%** of cerebrovascular disease and **49%** of coronary heart disease.[8]

The relationship between blood pressure and cardiovascular disease is well established.[9]

These data are consistent with our longstanding definition of **optimal** blood pressure of **115/75 mmHg**.

Based on this, when **systolic blood pressure** is over **115 mmHg**, this means it is **suboptimal**. Typical aging people often have systolic readings far above **140 mmHg**.

Older people with preexisting vascular disease or circulatory deficits, however, often need *higher* **systolic** pressure (around **130** to **140 mmHg**) to ensure adequate circulation to their brain and kidneys.[10]

The irony of this is that **hypertension** in *early* life damages capillary beds that then require *higher*-than-optimal **systolic** pressure to obtain adequate blood flow to critical organs (e.g. brain, kidneys).

Such *higher* systolic pressure—despite being necessary in these types of cases—also inflicts more vascular damage.

Impact of Blood Pressure on Lifespans

Although many past studies have attempted to estimate the impact of **hypertension** on **heart attack** and **stroke** risk, relatively few studies have looked at the impact of blood pressure on **life expectancy**.

In addition, the life expectancy effects of elevated blood pressure in people without cardiovascular disease was not well-studied in the past.

One of the first studies to estimate the relative impact of different blood pressure ranges/targets upon life expectancy used data from the **Framingham Heart Study**.[1]

The participants in this study were allocated in the following blood pressure groups:

- Group **1**: Blood pressure below **120/80 mmHg**
- Group **2**: Systolic blood pressure between **120-139 mmHg**
- Group **3**: Blood pressure over **140/90 mmHg**

Average follow up was **27.5 years**, which is an impressive amount of time for human studies.

There was an overall increase in risk of **heart attacks** and **strokes** in Group **2** (systolic blood pressure between **120-139 mmHg** and Group **3** (blood pressure over **140/90 mmHg**) compared to Group **1**.

Significant increases in mortality (deaths) were observed in **Group 3** (systolic over **140 mmHg**), but not **Group 1** and **2**.

This is somewhat encouraging for those who require a *higher* systolic pressure of around **130 mmHg** as there was not a significant overall mortality increase.

The **life expectancy** differences between **Group 1** (below **120/80 mmHg**), **Group 2** (systolic **120-139 mmHg**) and **Group 3** (systolic over **140 mmHg**), however, were substantial.

Compared to **Group 1** (below **120/80 mmHg**), **Group 3** (over **140/90 mmHg**) had a decrease in total **life expectancy** of about **five years**.

Group 2 (systolic pressure between **120-139 mmHg**) had a decrease in total **life expectancy** that was about half as much as **Group 3** (over **140 mmHg**).

These observational data reveal the long-term **damage** inflicted by the *higher* blood pressure seen in **Group 2** and **Group 3** compared to **Group 1** (systolic blood pressure below **120 mmHg**).

A conclusion by the authors of this observational study is that **blood pressure control** should be initiated as soon as age 40.[1]

We at **Life Extension** have urged this for people of all ages (especially overweight and obese individuals) since elevated blood pressure in early life can inflict irreversible circulatory damage.

Confirmatory Results From 2017 and 2019 Studies

The study I just described was published in **2005** using **Framingham** data that were **observational** and had limitations.

More recent tightly **controlled** studies validate the risks of **suboptimal** blood pressure control.

Findings published in **2017** led to massive changes in conventional guidelines. These new recommendations target **systolic** pressure below **120 mmHg** in most people. This study was widely publicized and showed a **25%** reduction in risk of **cardiovascular events** when **systolic** blood pressure is targeted below **120 mmHg**.[11]

Studies presented at the **American Heart Association's** annual meeting in **November 2019** clarified some of these findings and suggest that **additional years of life** can be added with aggressive blood pressure control.[11]

According to the president of the American Heart Association:[11]

*"... this analysis suggests that a 50-year-old person with systolic pressure under **120 mmHg** could expect to live almost **3 years longer.**"*

By age **65**, the lifespan increase in response to **systolic** pressure targeted below 120 was **more than a year**. The lifespan increase dropped to **10 months** when optimal blood pressure control was not initiated until age **80**.[11]

To put the findings in terms of their real-world significance, data from the **Centers for Disease Control and Prevention** show that nearly **1,300 Americans** die **each day** with **high blood pressure** as a primary or contributing cause.[12]

This prompted our **Life Extension®** scientific team to estimate how many Americans may have needlessly died of hypertensive-related disorders since **1980** when ***LifeExtension®*** started publishing a health newsletter.

Unprecedented Human Carnage

Beginning around **1980**, blood pressure levels and cardiovascular risks began to show that **low normal** was better.

In **2003** the cumulative data suggested that blood pressure guidelines needed to be lowered.

It was not until **2017** that **Life Extension's** suggestions dating back to the early **1980s**—(that optimal blood pressure is below **120/80 mmHg**)—were formally implemented in standard clinical practice.[13]

To roughly estimate how many lost American "life years" occurred because of this delay in lowering blood pressure guidelines, **Life Extension**'s scientific staff amalgamated relevant published data beginning in the year 1980.

Here is the Executive Summary of our findings:

*"On the basis of the available scientific evidence, we can roughly estimate **years of life lost attributable to hypertension.** From the data we were able to collect and analyze, we estimate that approximately **37,712,740 years of life may have been lost between 1980 and 2014** due to hypertension as an underlying cause in adults aged 45 to 85+ years."*

In case the number is confusing, assume that each person who died from **less-than-optimal** blood pressure between 1980 and 2014 lost on average five years of life. This prompts us to estimate that roughly **37 million** years of life were needlessly lost from **hypertensive-related** causes during this 34-year period (1980-2014).

If you cut our estimate by **80%**, it still comes to over **seven million** years of life lost due to hypertension.

Findings from the studies described in this editorial provide stark evidence of why you need to look beyond conventional medicine guidelines when seeking to extend your healthy longevity.

And what I like so much nowadays is that you can type into Google or www.pubmed.gov search terms like "**hypertension and mortality risk**" and read the scientific reports yourself.

Refocusing Priorities

In today's soundbite media world, a catastrophic event involving the death of as little as ONE person generates headline news.

Meanwhile, over **1,600** American **cancer** patients perish every day and even more suffer and die from **cardiovascular** disorders.[14,15]

My perturbation about excess media coverage of these rare catastrophic occurrences is that it distracts from what needs to be done to address the **5,000** Americans dying each day from degenerative diseases of aging.

A Solution to the Hypertension Crisis

The prevalence and severity of today's hypertension crisis cannot be overstated. Too many people over ages 65 and 75 have dangerously elevated systolic blood pressure.

Yet **drugs** that can safely drop blood pressure into safer ranges are grossly underutilized.

At-home blood pressure monitors are accurate and inexpensive. They allow for far more careful and precise monitoring of blood pressure than visiting a doctor several times a year.

That's because blood pressure readings vary dramatically in response to a range of factors such as time of day or night, stress levels, and various other routine circumstances. By checking one's blood pressure at home, one can identify when systolic "spikes" are occurring and adjust their anti-hypertensive drug intake, in consultation with a medical professional.

Physician Assistants and Nurse Practitioners

More physician assistants and nurse practitioners should be on the front lines in curbing the epidemic of hypertension plaguing older and overweight individuals.

Under this scenario, you would bring a history of your at-home blood pressure readings to a physician's assistant or nurse practitioner, who can then prescribe low doses of drugs like telmisartan, an angiotensin receptor blocker (ARB) drug, a beta-blocker like carvedilol, and/or a diuretic.

Following the advice of this medical professional, you would begin taking the prescribed low doses of these drugs and continue monitoring your blood pressure.

If this approach failed to lower your blood pressure to optimal levels (**115/75 mmHg**), your medical professional could adjust the dose of anti-hypertensive medication.

Under this scenario, those who don't like going to doctors could monitor themselves, keeping records of blood pressure readings at various times of the day and bring the reports to a physician assistant or nurse practitioner so that other low-dose anti-hypertensive drugs could be tried, and thus achieve improved blood pressure control.

This could also be accomplished via convenient telemedicine conferences with the medical professional. The net effect would reduce medical outlays and improve patient outcomes.

Contrast the cost-effective scenario I propose to one in which people have an annual exam, one blood pressure reading, are prescribed one dose of one drug and then wait another 3-12 months to reevaluate.

Empowering patients to take control of their own blood pressure could spare millions of Americans each year from the multitude of diseases that hypertension silently inflicts.

Easy Ways to Lower Blood Pressure

The risks posed by even modest blood pressure spikes were long ago quantified. Yet too many aging and obese Americans have dangerously high **blood pressure**.

Nutrients (like garlic,[16-19] melatonin,[20-22] and fish oil[23-25]) can lower systolic pressure a few points, but most **hypertensives** need to either lose weight and/or take **drugs**, some that have **side benefits**.

A common drug class used to reduce blood pressure are **beta-blockers**. The beta-blocker drug **carvedilol** has been associated with lower cancer risk in some studies.[26-29]

A drug called **telmisartan** is a different class of medication that has been shown to improve **endothelial function**, in addition to reducing stubbornly high blood pressure.[30-33]

Please initiate measures to bring your blood pressure into optimal ranges.

I hope to reach a point where no supporter suffers a **hypertensive-related** disorder that was easily preventable.

For longer life,

William Faloon, Co-Founder
Life Extension Buyers Club

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CAUTION: If taken in high doses, magnesium may have a laxative effect. If this occurs, divide dosing, reduce intake, or discontinue product.

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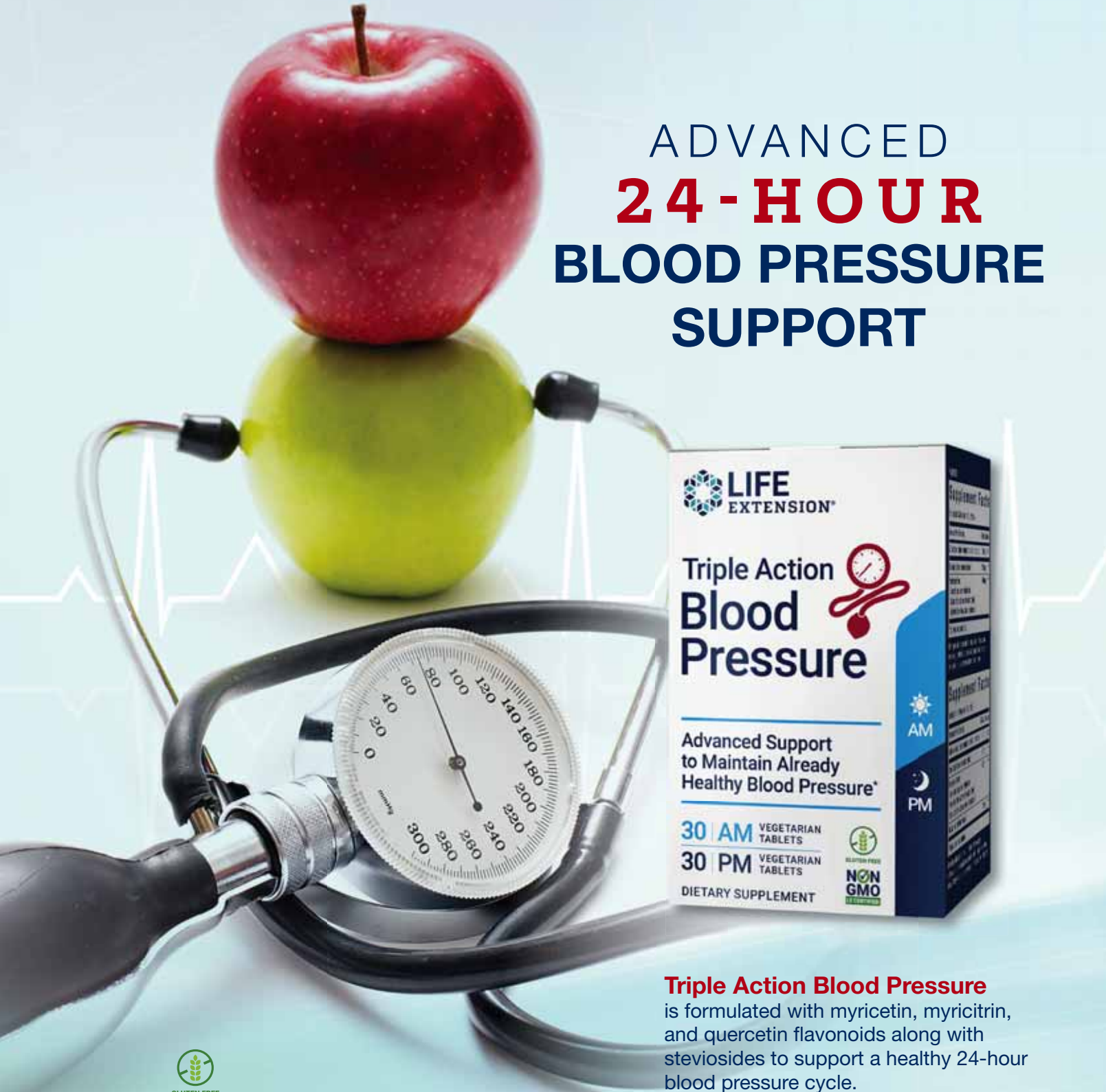

Triple Action Blood Pressure is formulated with myricetin, myricitrin, and quercetin flavonoids along with steviosides to support a healthy 24-hour blood pressure cycle.

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CAUTION: Consult your healthcare provider before use if you are taking medication or are being treated for a medical condition. Do not use if under the age of 18, pregnant, lactating, or trying to become pregnant. After taking the PM tablet, do not attempt to drive or operate heavy machinery and use caution if combining with alcohol. This product is not intended to replace anti-hypertensive medications your doctor may have prescribed.

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In the News

Glucosamine Supplementation Linked to Lower Mortality Risk

There was a lower risk of death from cardiovascular disease, cancer, respiratory disease, digestive diseases, or any cause, among individuals who supplemented with **glucosamine**, in comparison with those who didn't, a study published in *Annals of the Rheumatic Diseases* found.*

Researchers looked at 495,077 participants enrolled in the UK Biobank study. During a median of 8.9 years, 19,882 deaths occurred, which included 3,802 deaths from cardiovascular disease, 8,090 from cancer, 3,380 from respiratory disease and 1,061 from digestive disease.

Regular use of glucosamine supplements was reported by **19.1%** of the participants at baseline.

Those individuals who regularly supplemented with glucosamine, compared to those who didn't, had:

- **27%** lower risk of death from respiratory disease,
- **26%** lower risk of dying from digestive disease,
- **18%** lower risk of death from cardiovascular disease,
- **6%** lower risk of dying from cancer, and
- **15%** lower risk of death from any cause.

Editor's Note: Glucosamine is a nutritional supplement used in the management of arthritis and joint pain. These newly identified benefits are being studied now to ascertain if supplementing with **500-1500 mg** a day of **glucosamine** might be an effective way to reduce the risk of age-related disorders and all-cause mortality.

* *Ann Rheum Dis.* 2020 Jun;79(6):829-836.

Eating Less Salt Helps Support Healthy Immune Function

One simple way to help maintain healthy immune function is to lower salt intake, according to a study published in *Science Translational Medicine.**

Researchers studied the effects of a high-salt diet in mice and humans. Mice infected with listeria that received a high-salt diet had 100 to 1,000 times more of the bacteria in their spleens and livers than animals that consumed normal diets.

In humans who consumed an extra **six grams** of salt per day, immune cells in the blood known as granulocytes were less effective against bacteria, and levels of glucocorticoids increased.

When a high amount of salt is consumed, it is filtered by the kidneys, whose sodium chloride sensor activates salt excretion in the urine. This sensor is also responsible for the accumulation of glucocorticoids that inhibit the function of granulocytes that primarily attack bacteria. When granulocyte function is impaired, infections are more severe.

Editor's Note: Additionally, according to the World Health Organization, "*Salt intake of less than **five grams** per day for adults helps to reduce blood pressure and risk of cardiovascular disease, stroke, and coronary heart attack*."

* *Sci Transl Med.* 2020 Mar 25;12(536).

Reduced Heart Failure with Higher Magnesium Intake

Research findings published in the *Journal of the American Heart Association* show a lower risk of heart failure among participants in the Women's Health Initiative (WHI) who had a greater intake of magnesium, compared to those whose intake was low.*

The study evaluated data from 97,725 postmenopausal women who were free of heart failure on enrollment. Questionnaires completed by the participants after enrolling were evaluated for magnesium intake from food and supplements. During a median follow-up period of 8.1 years, 2,153 hospitalizations for heart failure occurred.

Compared to the top **25%** of magnesium consumers, who ingested an average of **461 mg** per day, women whose intake was among the lowest **25%** at **207.5 mg** per day had a **26%** greater adjusted risk of heart failure.

When magnesium from food alone was analyzed, the risk of heart failure for those consuming the least amount was **32%** higher than the group with the greatest consumption.

Editor's Note: "Women represent a large proportion of the growing heart failure epidemic, yet data are lacking regarding optimal dietary and lifestyle prevention strategies for them," the authors stated.

* *J Am Heart Assoc*. 2020 Apr 7;9(7):e013570.

Metformin Use Associated with Improved Postoperative Survival Among Diabetics

A lower risk of readmission or mortality following surgery was found among patients who were using the antidiabetic prescription medication metformin, research reported in *JAMA Surgery* revealed.*

The study included 10,088 diabetics who were hospitalized for major surgery between January 2010 and January 2016. There were 5,962 individuals who had a prescription for metformin during 180 days prior to their surgery, who were matched with 5,460 people who did not have a prescription.

Having a prescription for metformin was associated with a **28%** lower 90-day postoperative mortality risk compared to the risk experienced by those who were not using the drug.

Metformin was also associated with a lower 30-day and 90-day postoperative risk of readmission, indicating fewer postoperative complications.

It was further determined that metformin was associated with a **22%** increase in five-year survival in comparison with not having been prescribed the drug.

Editor's Note: Preoperative inflammation, as determined by the ratio of white blood cells known as neutrophils to leukocytes, was significantly lower among metformin-treated patients, which may be one mechanism through which the drug confers its protective effects.

* *JAMA Surg*. 2020 Apr 8;155(6):e200416.

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$^{\Delta}$ 3-O-acetyl-II-ketoB-boswellic acid.

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Are You *Resolving* INFLAMMATION?

BY CHANCELLOR FALOON

Chronic inflammation is connected to degenerative aging.

This has prompted scientists to coin the term **"inflammaging"** to describe this destructive process.[1]

Recent discoveries shed light on our understanding of **inflammaging**.[2]

Research shows that ***resolution*** of inflammation may be as important as ***inhibition*** of inflammation in the fight against age-related disorders.

The field of **inflammation resolution** is generating increasing interest.

This led scientists to identify compounds that help **resolve** inflammation. They are named:

Specialized pro-resolving mediators (SPMs)

Increasing **SPM levels** in preclinical models yields compelling findings.[3]

Clinical trials are currently recruiting participants and publishing results.[4]

How SPMs Resolve Inflammation

Specialized pro-resolving mediators are extracted from polyunsaturated fatty acids, predominantly found in **fish**.[3]

In response to certain conditions, such as **inflammation**, small amounts of omega-3 fatty acids are converted to even more beneficial compounds: **SPMs**.[3]

Chronic inflammatory conditions such as **inflammaging**, have been associated with lower concentrations of SPMs in the body.[5]

SPMs resolve inflammation by **three mechanisms**:[6-8]

- *Removing* dead and dying cells through a process in which **macrophage** immune cells engulf and digest dying or dead cells. This helps clean up the aftermath of inflammatory cascades.
- *Restoring* inflammation balance by decreasing **pro-inflammatory** mediators, while increasing compounds that have **anti-inflammatory** activity.
- *Renewing* damaged tissue by promoting cellular **regeneration**.

These benefits promise to help prevent many chronic aging disorders including deposition of plaque in the arteries (**atherosclerosis**).[9]

Inflamed Arteries

Inflammation is a key player in the development of heart disease.

Atherosclerosis is partially driven by an *imbalance* between pro-inflammatory and **inflammation-resolving** mechanisms in the artery inner walls.[9]

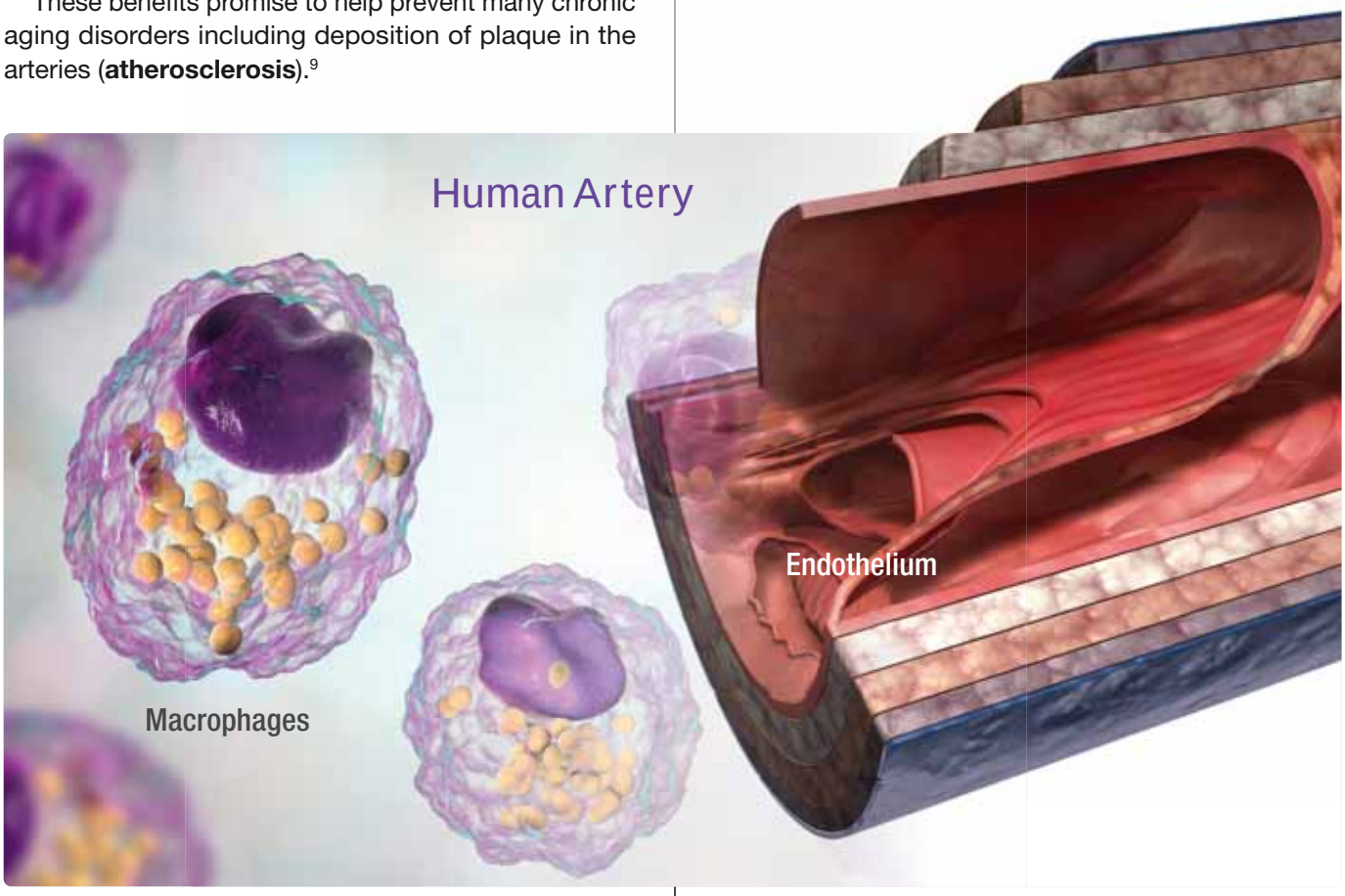
Atherosclerosis can begin when **LDL cholesterol** (the "bad" cholesterol) particles get trapped inside the endothelium (lining of the arteries).

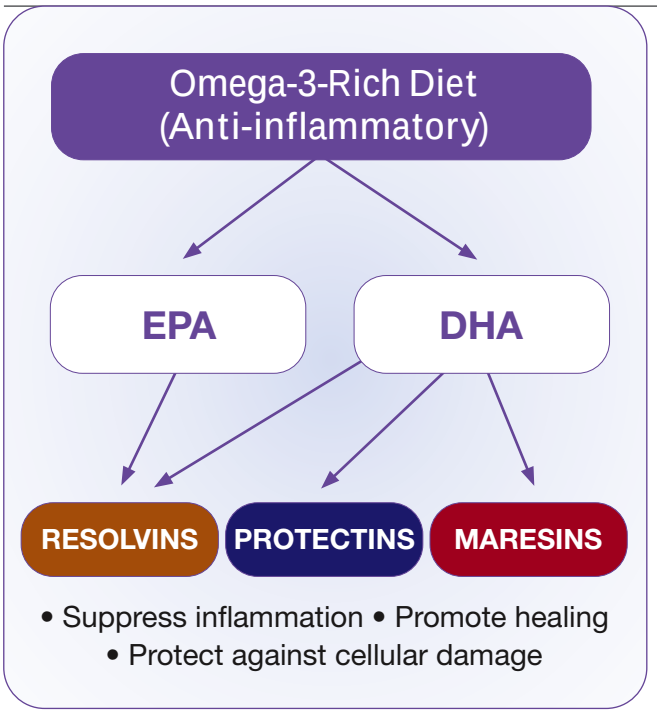
Macrophages enter the **endothelium** to clear out these oxidized LDL particles. If there is a lack of **pro-resolving mediators**, these macrophages will change into **foam cells**.[9]

This is a dangerous state that generally results in the **foam cells** dying and releasing their contents, creating an even *greater* **pro-inflammatory** environment.[9]

SPMs come into play here by initiating the *removal* of dead cells and foam cells through a process called **efferocytosis**.

If these cells are *not* removed, they contribute to plaque progression, which leads to atherosclerosis that endangers the heart, kidneys, and brain.[9,10]





How SPMs Differ from Omega-3s

The process of converting omega-3 fatty acids into SPMs requires several steps in the body.

When one eats cold water fish or takes fish oil supplements, tiny amounts may be converted to **pro-resolving mediators** (SPMs).

To meaningfully resolve **inflammaging,** *higher* amounts of standardized **SPMs** are often required beyond what can be obtained with fish oil.

Preclinical Research on SPM Precursors

In preclinical studies, SPMs *and* SPM precursors have been shown to have a variety of biological benefits.

A clinical trial of a combination of omega-3 fatty acids and SPMs demonstrates powerful effects on a range of immune, inflammatory, and blood-clotting indices.

Studies in mice have demonstrated impressive **resolution** benefits in a variety of disease models using the SPM precursor **18-HEPE**.

SPM precursors enable formation of **specialized pro-resolving mediators** (SPMs) in the body.

One study involved a rodent model that mimics some of the complications related to **cardiovascular disease**. Following surgery, researchers injected mice with the SPM precursor **18-HEPE** every three days.[12]

The mice that received **18-HEPE** were significantly shielded from damaging complications brought on by the surgical procedure.

Another study used a mouse model of **melanoma** metastasis. Researchers pretreated mouse **melanoma** cells with the SPM precursor **18-HEPE** while controls were not treated.

Healthy mice were then administered the SPM precursor 18-HEPE-treated **melanoma** cells and received additional 18-HEPE injections every other day. The SPM precursor-treated mice had significantly *less* formation of tumor colonies compared to controls.[13]

Another group of researchers found that treatment with the SPM precursor **17-HDHA** was able to *reverse* pain behavior in two rat models of osteoarthritis.[14]

The Science Behind Specialized Pro-Resolving Mediators (SPMs)

SPM *precursors* are predominantly derived from the omega-3 fatty acids EPA and DHA.

But obtaining meaningful potencies of SPMs requires a series of complex metabolic processes that are often lacking in aging individuals.

The omega-3 fatty acid precursors needed to produce SPMs in the body include:[11]

- **18-HEPE**
(18-hydroxyeicosapentaenoic acid)
- **17-HDHA**
(17-hydroxydocosahexaenoic acid)
- **14-HDHA**
(14-hydroxydocosahexaenoic acid).

These precursors listed above are then *converted* into the following specialized pro-resolving mediators (SPMs):

- **Resolvins**
- **Protectins**
- **Maresins**

These make up the bulk of the SPMs that target inflammation through the three steps of removing, restoring and renewing.

New Human Trial of SPM Precursors

A human trial of SPM precursors was published in **January 2020** and showed remarkable results.

In this study, 22 healthy volunteers aged 19 to 37 were randomized. One group received an enriched fish oil supplement containing omega-3 PUFAs *plus* a combination of SPM precursors, including **18-HEPE**, **17-HDHA,** and **14-HDHA**. The other group received a **placebo**.[18]

Researchers separated the participants into different dosing groups and performed a series of tests. They were able to conclude that the **SPM precursors**:

- Significantly increased cell surface proteins involved in *reversing* **inflammation** and **platelet aggregation** (which leads to harmful clotting) caused by the addition of a pro-inflammatory stimulus in the drawn blood of the patients.
- Increased clearance of *Staphylococcus aureus* and *E. coli*, by immune cells, which was highest at the final measurement, after 24 hours.
- Decreased **platelet activation**, a central part of the process that leads to a blood clot, in association with an increased level of **resolvins**.
- Increased the expression of genes linked to immune responses, recruitment of immune cells that fight infection and other diseases, and cellular metabolism in peripheral blood cells.

Omega-3s Help Resolve Inflammation

Because the original sources of SPMs are primarily the **omega-3 fatty acids** EPA and DHA, increasing the intake of these healthy fats will assist in resolving inflammation.[19-21]

In a recent clinical trial, researchers showed that in response to a pro-inflammatory stimulus, **EPA** and **DHA** intake leads to the formation of more SPMs.[21]

For five months, participants were given either EPA and DHA or a placebo daily, before receiving a **pro-inflammatory stimulus**. Blood was collected daily for five days after receiving the stimulus.

By the fifth day, the group that received the EPA and DHA had ***229% higher*** SPM levels than the placebo group. The levels of systemic inflammation, as measured by **C-reactive protein**, were significantly lower in the EPA/DHA treatment group compared to placebo.

The researchers repeated this testing using slight variations with their methods. Results consistently showed that EPA and DHA intake *increases* the level of SPMs in response to a pro-inflammatory stimulus.

This is great news for those who eat lots of **cold-water fish** and/or take high-potency **fish oil** supplements. Those with potential **inflammaging** issues may want to add a supplement providing **standardized** potencies of:

- **Resolvins**
- **Protectins**
- **Maresins**

WHAT YOU NEED TO KNOW

SPM Precursors + Omega-3s Resolve Inflammation

- **Chronic inflammation** is a major risk factor in aging, age-related disease, and degenerative disorders.
- Scientists have identified compounds that *resolve* inflammation, called **specialized pro-resolving mediators (SPMs).**
- SPMs are mostly derived from the **omega-3 fatty acids** EPA and DHA, which are primarily found in fish. A recent clinical trial showed that supplementation with a marine oil enriched with SPM precursors increases SPM levels and helps resolve inflammation.
- Another clinical trial showed that supplementation with omega-3s also increased SPMs in the body and helped lower levels of the inflammatory marker C-reactive protein.

Preclinical Research on SPMs

Preclinical data demonstrate promising results from the *direct* use of **specialized pro-resolving mediators (SPMs).**

In one study, researchers tested the effects of an **SPM resolvin** on mice that had obesity-associated **osteoarthritis.** The treatment was injected into the animals' joints. The results showed a significant *reduction* in pro-inflammatory macrophage infiltration into the soft tissue surrounding the joints (**synovium**), reduced severity of synovium inflammation, and prevention of cartilage degradation.[15]

A review of preclinical studies concluded that SPMs may be an effective treatment for gum disease (**periodontitis**). These studies showed that topical application of a **resolvin** and a **lipoxin** (an omega-6-derived SPM) to inflamed periodontal tissue results in a significant prevention of tooth loss compared to the control group.[16]

A mouse study showed that injections with the SPM **maresin** reduced inflammation-induced **neuropathic pain.**[17]

Summary

Chronic inflammation is so strongly correlated with age that scientists describe it as **inflammaging**.[1]

For decades, researchers have been studying how to better inhibit inflammation. They are now also beginning to understand the importance of **resolving** inflammation.

An abundance of preclinical data has demonstrated substantial potential benefits of having higher levels of **specialized pro-resolving mediators** (**SPMs**) or SPM precursors.

Polyunsaturated fatty acids, particularly the **omega-3** class, can be made into **SPMs** in your body. However, taking **SPM precursors** directly may be more effective.

Those concerned about chronic inflammation and persistently elevated inflammatory markers (like C-reactive protein and interleukin-6) may want to add a **multi-SPM** formula to their intake of omega-3 fatty acids.

Several clinical trials on SPM precursors are underway, with some completed and some still recruiting participants.[4]

Life Extension® is also now recruiting generally healthy people for a clinical trial. If you are in the Fort Lauderdale area and are interested in participating, please call **1-866-517-4536**.

If you have any questions on the scientific content of this article, please call a **Life Extension**® Wellness Specialist at 1-866-864-3027.

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Weight Loss Increases SPMs

In a recent study, researchers discovered that weight loss leads to a significant *increase* in the formation of SPMs.[22]

The researchers selected 42 patients with metabolic syndrome and took blood samples of their neutrophils, which are a short-lived type of white blood cell that eliminates pathogens.[23] The researchers then stimulated the neutrophils and measured the release of SPMs to use for comparison after the intervention.

Patients were randomly selected to go through either a weight loss program (treatment) or a weight stabilization program (control).

After 16 weeks, the researchers again took blood samples of their neutrophils and provided stimulation to measure the amount of SPM release.

At the end of the trial, the SPM release from the neutrophils of the patients in the control group was unchanged compared to baseline.

The weight loss group had significantly *elevated* SPM release compared to baseline. Compared to the control group, weight loss led to a 2-fold increase the release of the SPM E-series resolvin.

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BEYOND CBD: Plant-Based Endocannabinoid Support

BY PAUL JOHNSON

Scientists have discovered that the **endocannabinoid system** influences the balance and function of almost ***all*** bodily systems.

The endocannabinoid system plays an important role in **brain function**, influencing mood, learning and memory, pain control, sleep, appetite, and more.

But as we age, the endocannabinoid system becomes less active.[1,2] That can lead to accelerated aging and increased susceptibility to disease.[1]

Research has shown that the endocannabinoid system plays a profound role throughout the rest of the body, affecting everything from bone strength to fat and glucose metabolism.[2]

In the past years CBD (cannabidiol) products have become increasingly popular, ranging from a variety of formulations from oils to cosmetics.

This comes from the fact that CBD interacts with and supports the endocannabinoid system.

The problem is that there are many unanswered questions about the quality and efficacy of the CBD-containing products purchased commercially.

For those who want to improve their internal endocannabinoid functions, scientists have identified **four plant compounds** that favorably influence the endocannabinoid system in ***multiple ways***.

What Is the Endocannabinoid System?

Like hormones and nerve cells, the endocannabinoid system is a ***cellular communication system***, allowing various cells to send *signals* to others.

It helps to regulate and maintain the optimal function of many bodily systems.

It also helps maintain **homeostasis**, stability in response to changes in the environment, throughout the body.

The endocannabinoid system is active in most tissues. It has been identified in brain, bone, muscle, liver, and fat tissue, immune cells, and more.[1-3]

It's made up of three parts:

- Signaling molecules called **endocannabinoids**,
- **Receptors** found throughout the body, to which the endocannabinoids bind to transmit a signal, and
- **Enzymes** which break down the endocannabinoids once their work is done.

Two of the best-known endocannabinoids are **anandamide** (**AEA**) and **2-arachidonoyl glycerol** (**2-AG**). They interact with receptors throughout the body.

The name "endocannabinoid" comes from the fact that plant-based **cannabinoid** compounds, such as those found in cannabis, influence **cannabinoid** receptors on cell membranes. "**Endo**" refers to something formed *within* the body.

Unlike cannabinoids from cannabis, **endocannabinoids** do *not* have psychoactive effects. But they have a profound impact on the brain and body.

The Endocannabinoid System and the Brain

In the brain, the endocannabinoid system has been shown to be **neuroprotective**,[1] shielding brain cells against damage and age-related changes.

As a result, it is a promising research target in the battle to help protect against cognitive decline and diseases such as Alzheimer's and Parkinson's disease.[1]

Its effects in the brain also relate to many essential quality-of-life factors: mood, pain perception, cognition and memory, appetite regulation, and sleep.[2,4]

On a cellular level, scientists have found that the endocannabinoid system protects the brain by:[1]

- **Regulating brain "helper" cells**. The **glial cells** in the brain are support cells that are vital to normal brain function. The endocannabinoid system maintains their function, supporting brain cells, preventing inflammation, and guarding against neurodegeneration.

- **Promoting formation of new neurons**. As we age, our ability to form new nerve cells declines. This is a major contributor to cognitive and functional decline. The endocannabinoid system *increases* neurogenesis, helping to maintain learning and memory.

- **Boosting synaptic plasticity.** The ability of our synapses, where neurons communicate, to adapt to new information also diminishes in old age. By strengthening this ability, known as synaptic plasticity, the endocannabinoid system can help prevent cognitive decline.

- **Increasing brain-derived neurotrophic factor**. This protein supports the survival, growth, and health of neurons, which helps prevent neurological diseases, including Parkinson's and Alzheimer's.

Body-Wide Effects

Beyond the brain, the endocannabinoid system has a wide range of effects. It has been found to regulate: [2]

- Bone remodeling, in which old bone tissue is replaced by strong, new bone,
- Gastrointestinal function,
- Fat metabolism in both the liver and in fatty tissues,
- Muscle metabolism, and
- Immune cell function.

WHAT YOU NEED TO KNOW

Strengthening the Endocannabinoid System

- The **endocannabinoid system** is a signaling system that operates throughout the body, from brain to bone.
- It helps regulate and bring balance to a wide range of bodily functions, which can slow the aging process and reduce risk for chronic disease.
- Researchers have discovered four compounds that influence endo-cannabinoid system function: **oleoylethanolamide (OEA), biochanin A, guineensine**, and **beta-caryophyllene.**

How the Endocannabinoid System Works

After discovering how diverse the effects of the endocannabinoid system are, scientists investigated *how* it works. They found that it contributes to all of the following:[1]

- **Cellular "housekeeping."** Cannabinoids induce **autophagy**, when cells clear away damaged proteins and other compounds to make room for new, healthy cellular components.
- **Regulation and protection of mitochondria**. Mitochondria are the "powerhouses" of the cells. The endocannabinoid system helps regulate their normal activity and protect them from damage.
- **Modulating signaling and communication pathways**. Cell-to-cell interactions throughout the body rely in part on endocannabinoid signaling. These relationships have diverse effects, including impacts on sleep-wake cycles, pain perception, mood, learning, and memory.

All of these pathways are critical in slowing the aging process and maintaining normal tissue function in various organs.

Supporting Endocannabinoid Function

Scientists have discovered that there are ways to influence the function of the endocannabinoid system—*without* resorting to use of **CBD** (cannabidiol), **THC** (tetrahydrocannabinol), or other potentially psychoactive cannabinoids from cannabis.

The following compounds have been found to influence the activity of the ***endocannabinoid system*** through distinct but complementary effects.

Oleoylethanolamide (OEA)

Oleoylethanolamide is a fatty acid that is naturally produced in the body.

It is similar in structure to one of the endocannabinoid compounds.

Oleoylethanolamide's (OEA) activity to suppress inflammation and regulate metabolism and appetite is mediated through the activity of **endocannabinoid** receptors but without binding to them.[5-7]

OEA has also been found to have neuroprotective effects and to provide support against obesity and associated metabolic abnormalities.[6-8]

Biochanin A

Biochanin A is a plant flavone found in clover, peanuts, chickpeas, and soy.[9]

Research has found that biochanin A inhibits one of the enzymes in the endocannabinoid system called **fatty acid amide hydrolase**.[10,11] This enzyme breaks down the endocannabinoid anandamide into inactive products.

By *blocking* the activity of the enzyme, biochanin A may help to support *higher* levels of anandamide.[12]

Anandamide acts as a natural pain reliever in the body, so biochanin A may be useful in treating chronic pain and other conditions.[11]

Anandamide, through its function as a critical molecule in the endocannabinoid system, is also believed to play important roles in regulating motivation, pleasure, and mood.[3,4,13]

Guineensine

A compound isolated from black pepper, **guineensine** boosts levels of both anandamide and 2-AG.[14,15] It works by blocking the reuptake of these endocannabinoids after their release by cells.[16]

As a result, levels of anandamide and 2-AG remain *higher* in the body for *longer*. Together with biochanin A's ability to block anandamide's breakdown, this further boosts the beneficial effects of these endocannabinoids.

Beta-Caryophyllene

Beta-caryophyllene is found in many plants, including rosemary, clove, and black pepper.[14]

Scientists have discovered that this compound directly activates one of the most important endocannabinoid *receptors*, known as **CB2**, mimicking the activity of some endocannabinoids.[14]

These CB2 receptors are found throughout the body. Their activation by beta-caryophyllene has been demonstrated to:

- Reduce inflammation in brain cells,[17]
- In an animal model, improve insulin function blood glucose control, lipids, and vascular inflammation,[18]
- Protect against age-related cognitive decline and reduce levels of an age-related proinflammatory cytokine,[19] and
- Inhibit breast cancer cell growth.[20]

Summary

In the last few decades, scientists have discovered that the **endocannabinoid system** influences the balance and function of almost all bodily systems.

In the brain, it has important beneficial effects on mood, cognition, sleep, and more.

Throughout the body, it helps maintain tissue health, prevent age-related loss of function, and lower risk for disease.

Scientists have identified four plant-based compounds that influence the function of the endocannabinoid system: oleoylethanolamide (OEA), biochanin A, guineensine, and beta-caryophyllene.

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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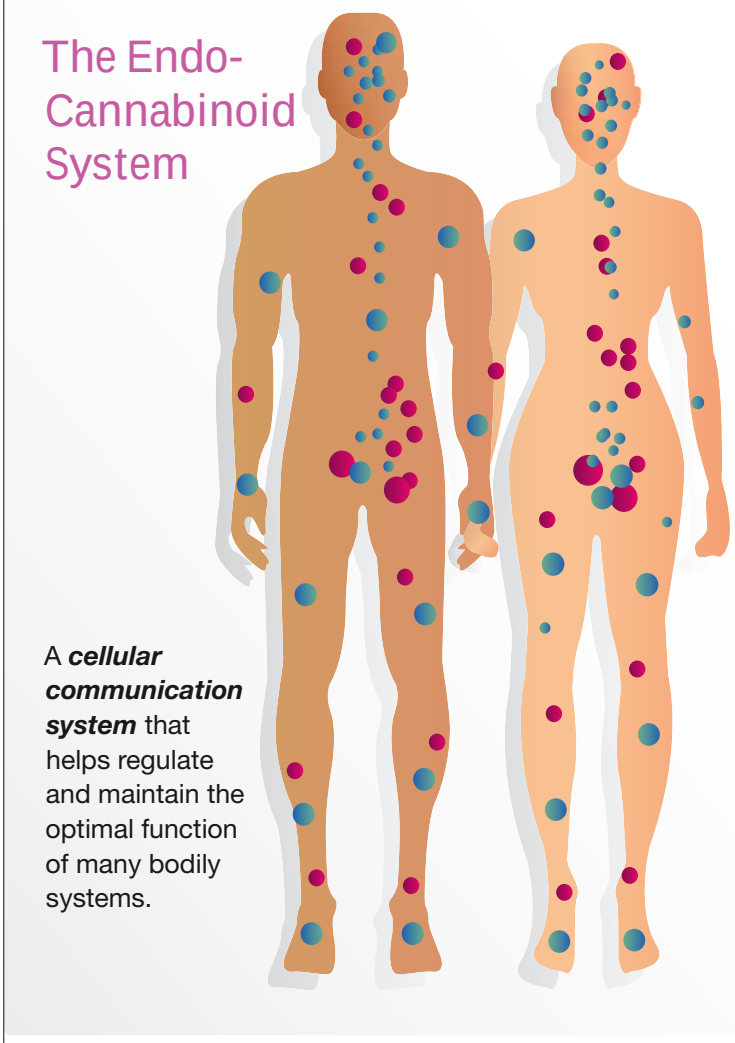

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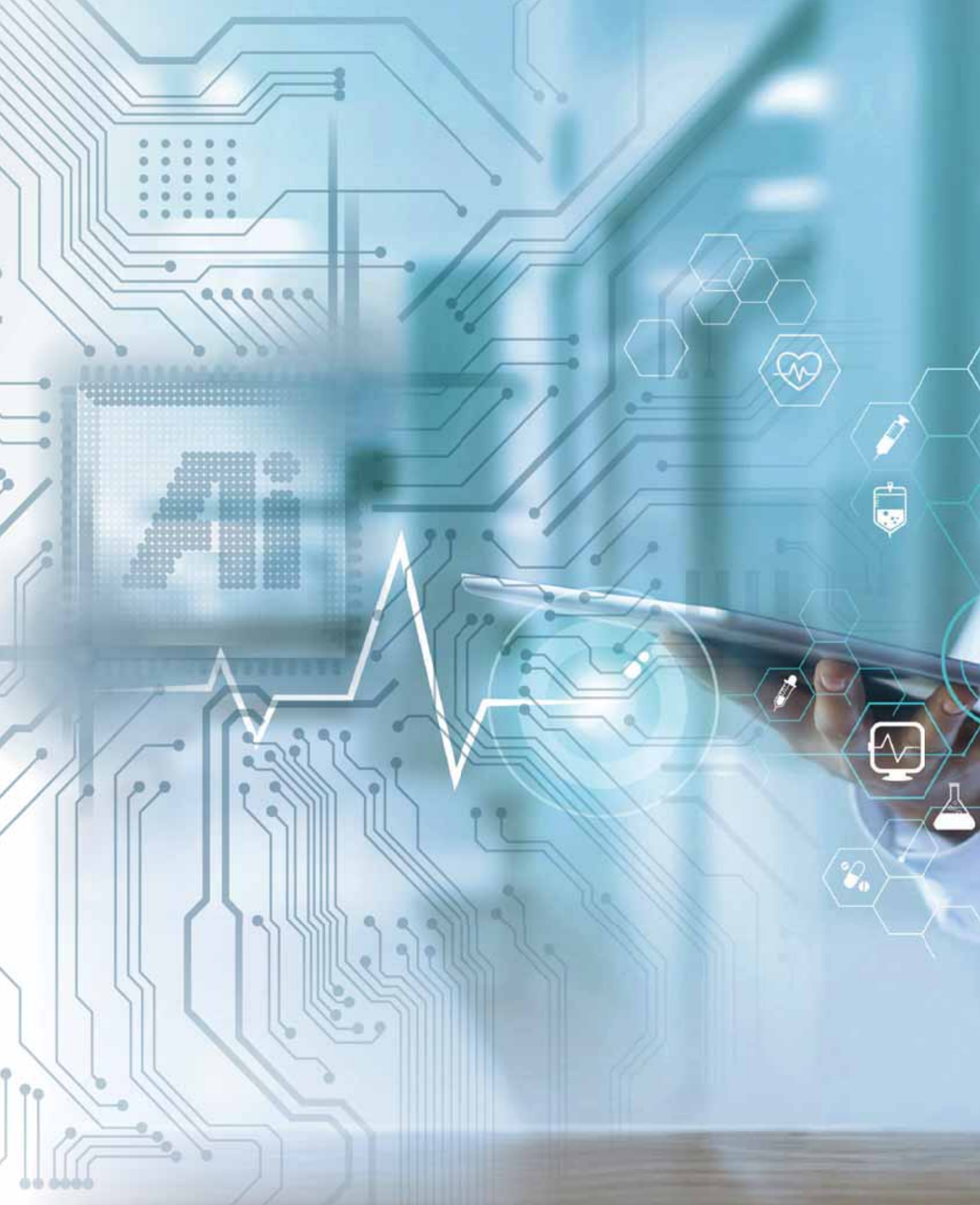

ARTIFICIAL INTELLIGENCE Identifies Longevity Pathways

BY CELIA STANTON

The drug **metformin,** prescribed to control blood sugar, has been shown to modulate many anti-aging pathways.[1-5]

In one animal study, metformin treatment led to a ***14% extension of lifespan*** when treatment was begun early in life. Another rodent study with long-term metformin treatment also extended life.[6,7]

These data applied to humans would equate to prolonging an average human life from roughly **79** years to **90** years.

A **metformin** study in the *C. elegans* model of aging led to a remarkable **33%** lifespan extension.[8]

A 2014 **human** study found that **type II diabetics** treated with **metformin** live ***longer*** than non-diabetics (who did not take metformin).[9]

Diabetics usually die sooner than non-diabetics, making this study showing **diabetics** taking **metformin** live longer than **non-diabetics** remarkable.

Seeking a metformin alternative, scientists used **artificial intelligence (A.I.)** technology to conduct a vast search for **plant-based** nutrients that mimic metformin's effects.

They were able to identify **three compounds** that modulate many of the same **pro-longevity** pathways as metformin:[1]

- **Withaferin A**
- **Ginsenoside Rg3**
- **Gamma-linolenic acid**

These three compounds, when ***highly*** concentrated, function in overlapping and distinct ways to promote expression of longevity pathways.

Metformin Extends Lifespan

Metformin was first inspired by a nutrient found in a flowering plant known as **French lilac**.[3]

It lowers **glucose** levels via several mechanisms.

Much of metformin's ability to improve insulin sensitivity is due to increasing a cellular enzyme called **AMPK**, considered a master regulator of cell metabolism.[3]

Increasing AMPK activity is an important target for **anti-aging** interventions.[2]

This ability of metformin to prevent age-related disease has been observed in humans.[10-13]

Based on its ability to extend life, a large, multi-site ($70 million) **human** trial is underway to ascertain if metformin can treat aging itself, just like chronic disease.[14]

How Metformin Fights Aging

Inspired by metformin's remarkable longevity benefits, scientists set out to find alternatives in botanical compounds.[1]

Their first step was to identify precisely *how* metformin extends life. Several studies of metformin have shown that it affects cellular pathways tied to aging, including:[2,4,15-21]

- Stimulating **AMPK**, which helps balance **mTOR** and improves cellular metabolism and energy production,
- Decreasing levels of **IGF-1**, a hormone that has been found to be lowest in people who live exceptionally long lives, and
- Activating **SIRT1**, which regulates cellular health and is considered a longevity enzyme.

Through these effects and others, metformin can protect cells and tissues from the ravages of time that would otherwise lead to degeneration, dysfunction, and disease.

As a result of all these actions, metformin:[2]

- Improves metabolic health, maintaining insulin sensitivity, improving glucose control, and reducing production of potentially toxic byproducts of metabolism,
- Protects cellular structures from damage and degradation, including maintaining healthy proteins and DNA,
- Promotes cellular "housekeeping" (known as **autophagy**), which rids the body of old, damaged structures and rejuvenates it with healthy replacements, and
- Reduces harmful chronic inflammation and cellular senescence, which rob tissues of their function.

Using A.I. to Find Alternatives

The next step was to compare metformin's actions with those of hundreds of **plant-based** compounds and see where the effects overlap.

In all, scientists identified **871** compounds that mimic metformin's actions.

WHAT YOU NEED TO KNOW

Compounds Mimic Metformin's Life-Extending Properties

- **Metformin** is a prescription drug used to treat patients with type II diabetes.
- In addition to aiding in the control of blood sugar, metformin has been found to have several **anti-aging** properties, extending lifespan and healthspan in animal models and humans.
- Inspired by metformin, scientists used advanced **artificial intelligence** technology to investigate and identify plant-based nutrients that mimic the properties of the drug.
- The scientists found three compounds that have both overlapping and distinct properties closely resembling those of metformin: **withaferin A, ginsenoside Rg3,** and **gamma-linolenic acid.**
- A *combination* of all three nutrients acts on similar health- and longevity-promoting pathways as metformin.

Sifting through this vast network of nutrients and their widespread interconnections would be practically impossible if it weren't for the speed of **artificial intelligence** to explore these data.

Using **deep-learning A.I.**, researchers found nutrients that regulate the ***same longevity pathways*** that metformin does. The artificial intelligence network was able to learn from these data and identify specific nutrients that most closely mimic the effects of metformin.[1]

A Three-Nutrient Combination

The results of the A.I. study revealed **three nutrients** that, taken together, would affect most of the same **longevity pathways** as metformin.

Some of the effects of these compounds overlap, bolstering the anti-aging impact compared to any one alone.

However, each one of the three compounds also confers unique and distinct benefits that sets it apart from the others.

Withaferin A

Withaferin A is an ingredient derived from **ashwagandha**, a plant that has been used for centuries in traditional Indian medicine to relieve stress, increase energy, and boost concentration.

Like metformin, withaferin A *increases* **AMPK** signaling and *inhibits* **mTOR**.[22,23]

As a result, **withaferin A** has been shown to have beneficial effects on metabolism. In animal models, it blocked formation of new fat tissue, leading to weight loss, and improved insulin sensitivity and glucose control.[24,25]

Preclinical and animal models have demonstrated that **withaferin A** can also help maintain healthy protein synthesis inside cells, helping to shield them from some types of degeneration that occur with advancing age and disease.[26-29]

Ginsenoside Rg3

The **ginsenosides** are a group of compounds isolated from **Panax ginseng** (Asian ginseng), another plant widely used in traditional herbal medicine for a very wide range of indications.

Ginsenoside Rg3 activates AMPK, like metformin does.[30-33] In addition, in cell and animal models it has shown potent activity to help promote the resolution of **chronic inflammation**.[34,35]

Practically *all* age-related diseases, from cardiovascular disease to cancer, have **inflammation** as a major contributing factor. Resolving chronic inflammation is one of the most promising potential ways to lower risk of disease and extend lifespan.

Like **withaferin A**, but through different mechanisms, **ginsenoside Rg3** also prevented the degeneration of critical cellular structures like the mitochondria and cellular membranes in rodent models.[36,37]

Even more impressive, it has been shown to activate **SIRT1** in a rat study.[38] The **sirtuins**, and SIRT1 in particular, are signaling proteins that shield cells from age-related damage and dysfunction. Activation of **SIRT1** has been shown in countless models to extend lifespan.[39]

Gamma-Linolenic Acid

A fatty acid found in various plants, **gamma-linolenic acid (GLA)** can be isolated from **borage seed oil**, among other sources.

Gamma-linolenic acid has been shown in clinical trials to effectively treat inflammatory conditions.[40-42]

In one, it significantly improved quality of life in patients with **rheumatoid arthritis**, reducing the swelling, stiffness, and pain in joints that is caused by chronic autoimmune inflammation.[42]

Summary

Metformin is a prescription medication which has been shown in animals and humans to improve longevity via several well-established mechanisms.

Scientists have used deep-learning **artificial intelligence** technology to scour the natural world for nutrients that have similar life-extending properties as metformin.

This extensive search revealed three ingredients with combined effects closely resembling those of metformin: **withaferin A**, **ginsenoside Rg3**, and **gamma-linolenic acid**.

These three compounds, when provided in sufficient potencies, work in overlapping and distinct ways to promote the expression of life- and health-extending pathways in much the same way as **metformin**.

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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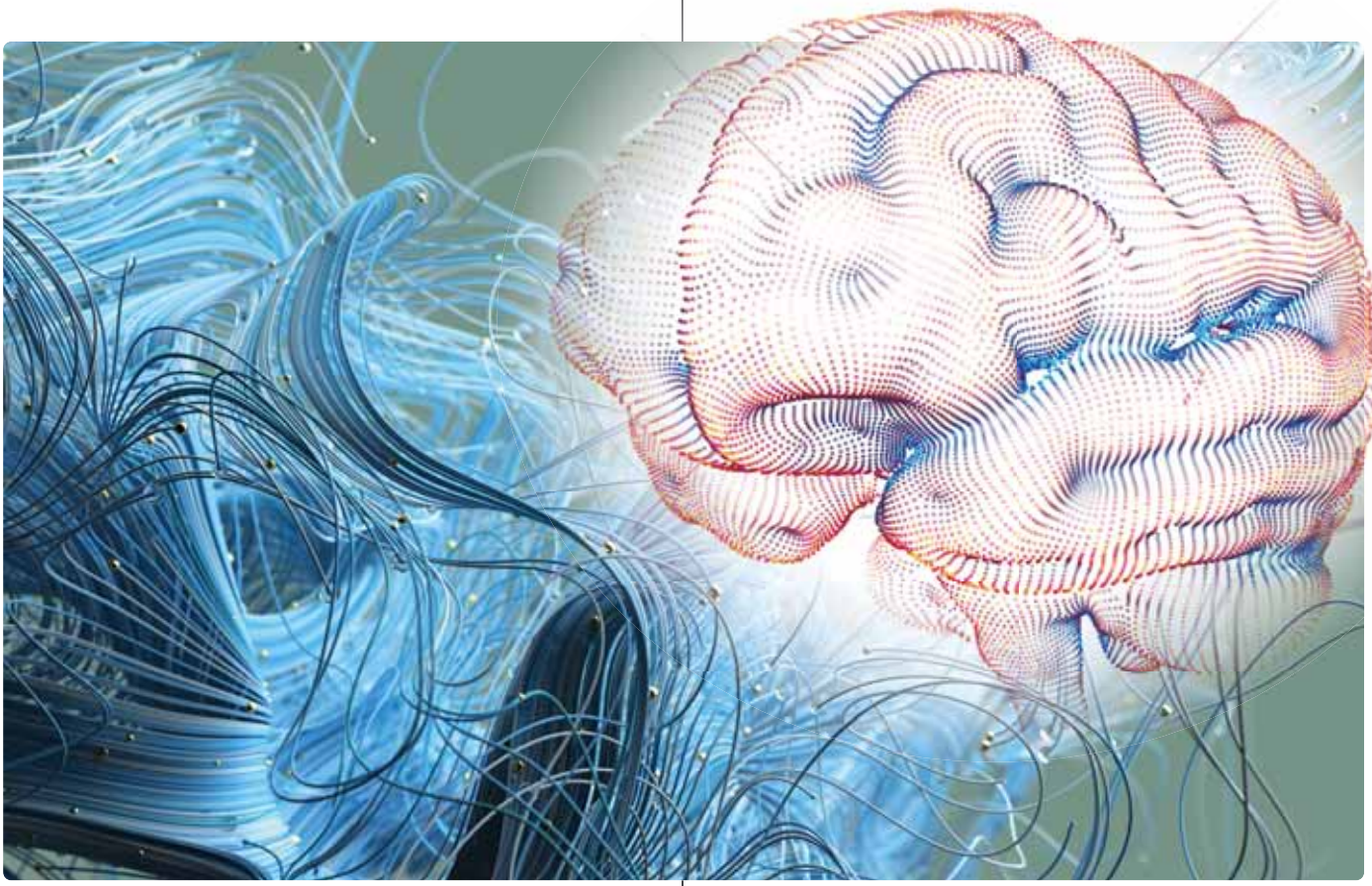

Life Got You Down for the Count?

Are you experiencing general fatigue? Do you lack motivation? Well, it's time to get up off the mat and fight back!

What you're feeling may be the result of declining NAD+ levels, a coenzyme found in every cell in your body. NAD+ facilitates ATP production, which your body uses for fuel.

Life Extension®'s best-selling NAD+ Cell Regenerator™ can help maintain the youthful levels of NAD+ you need to thrive.

NAD+ Cell Regenerator™ and Resveratrol

Item #02348 • 30 veg. caps.

1 bottle *

NAD+ Cell Regenerator™

Item #02344 • 30 veg. caps.

1 bottle *

* For pricing available to readers of this magazine, call 1-800-544-4440 or visit LifeExtension.com/NAD

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NIAGEN® is a registered trademark of ChromaDex, Inc., Patents see: **www.ChromaDexPatents.com**

For full product description and to order **NAD+ Cell Regenerator™** or **NAD+ Cell Regenerator™ and Resveratrol**, call **1-800-544-4440** or visit **www.LifeExtension.com**

TRIPLE ACTION SENOLYTIC FORMULA

COMBAT SENESCENT CELLS AND AGING

SCIENCE OF SENOLYTICS!

Senolytic compounds selectively help target senescent cells in the body.

Laboratory studies show evidence of **systemic rejuvenation** when the **senescent cell** burden is reduced.*

ONCE-WEEKLY SENOLYTIC FORMULA

Senolytic Activator provides a highly ***absorbable*** form of **quercetin phytosome**, black tea **theaflavins**, and now with **apigenin** designed to enhance the body's ability to manage **senescent cells**.

The suggested dose is to take two capsules of **Senolytic Activator** just ***once weekly***.

* *Aging Cell.* 2015 Aug;14(4):644-58.

GLUTEN FREE

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Item #02301 • 24 vegetarian capsules

1 box **$18**

4 boxes $16 each

(Each box lasts three months.)

For full product description and to order **Senolytic Activator**, call 1-800-544-4440 or visit www.LifeExtension.com

Fight Back Against Aging with

LONGEVITY A.I.™

Modulate Aging and Longevity Pathways

GLUTEN FREE

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Item #02133 • 30 softgels

1 bottle **$36.75** • 4 bottles $34 each

Geroprotect® Longevity A.I.™ has been formulated using cutting-edge, artificial intelligence (AI) technology to *modulate* ***anti-aging pathways*** favorably affected by a **calorie-restriction mimetic**.

One daily **Longevity A.I.™** softgel contains highly-concentrated **Withaferin A**, **Ginsenoside Rg3** and **Gamma-linolenic acid** to modulate pro-longevity pathways.

For full product description and to order **Geroprotect® Longevity A.I.™**, call 1-800-544-4440 or visit www.LifeExtension.com

Patent Pending. Developed in collaboration with Insilico Medicine, Inc.

BROAD-SPECTRUM
IMMUNE SUPPORT

Lactoferrin is a component of **whey protein** best known for its **immune benefits**.

An array of published studies describes how **lactoferrin** up-regulates innate and adaptive **immune** responses to a variety of antigens.

Item #01681 • 300 mg, 60 vegetarian capsules

1 bottle **$45** • 2 bottles **$40** each

(Two-Month Supply)

Contains milk.

Bioferrin® is a registered trademark of Glanbia.

For full product description and to order **Lactoferrin Caps**, call **1-800-544-4440** or visit **www.LifeExtension.com**

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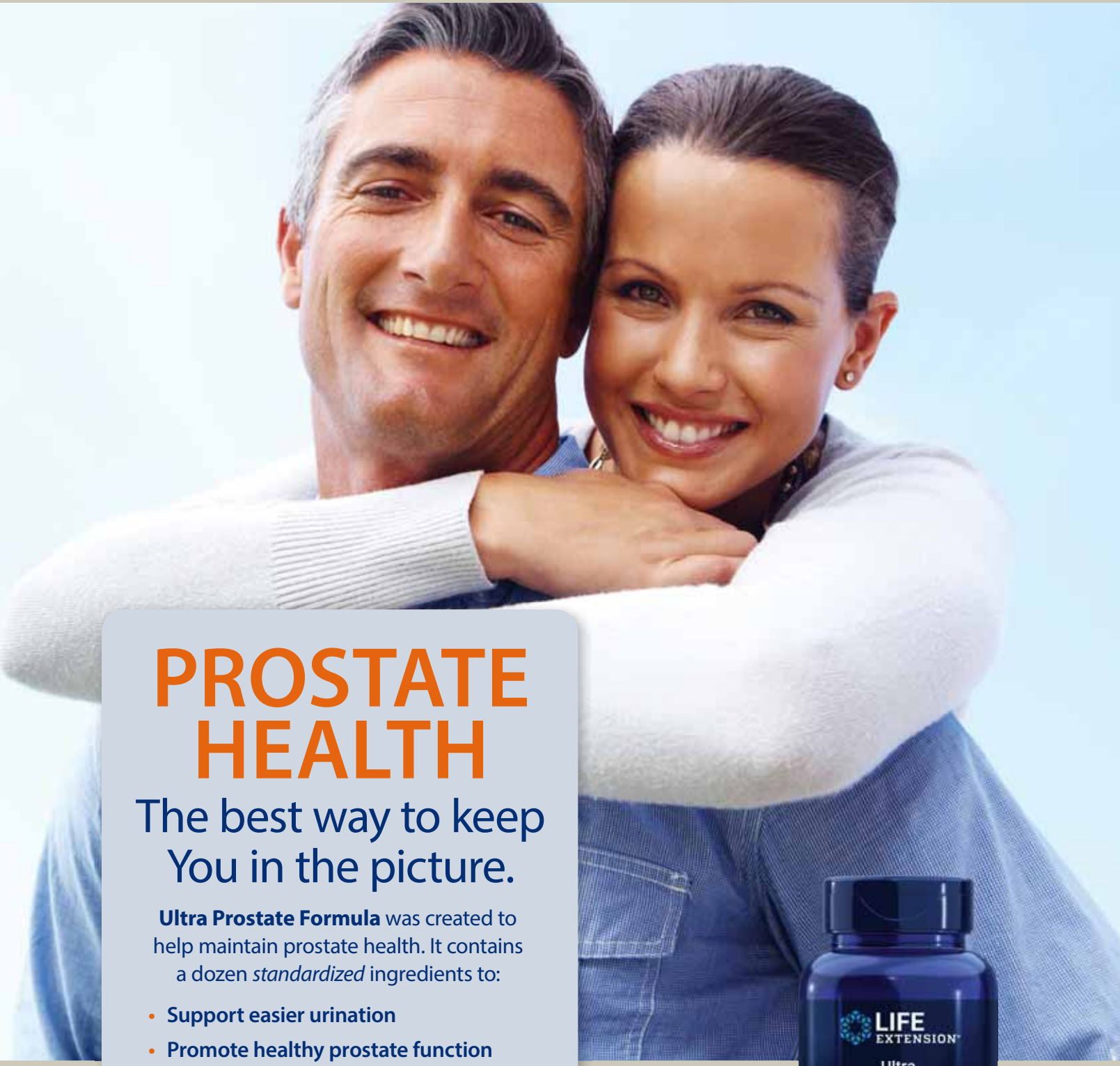

PROSTATE HEALTH

The best way to keep You in the picture.

Ultra Prostate Formula was created to help maintain prostate health. It contains a dozen *standardized* ingredients to:

- **Support easier urination**
- **Promote healthy prostate function**
- **Encourage prostate cell division**

Ultra Prostate Formula is the most comprehensive *standardized*-ingredient, prostate-health supplement.

Item #02029 • 60 softgels

1 bottle **$28.50**

4 bottles $26.25 each

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For full product description and to order **Ultra Prostate Formula**, call **1-800-544-4440** or visit **www.LifeExtension.com**

VITAMIN D'S
Winter Immune Benefits

BY JULIE MYERS

Vitamin D has shown promise against winter illness because it plays a critical role in supporting the **immune system**.

Low vitamin D levels have been associated with *higher* rates of many chronic diseases.[1-6]

This includes an *increased* risk for acute communicable diseases, including **viral infections** in **vitamin D** deficient people.[7,8]

A meta-analysis of randomized, controlled clinical trials showed a protective effect against **acute respiratory infections** with vitamin D supplementation.[9]

More than **40%** of Americans have been found to have **insufficient** blood levels of vitamin D (defined as levels between **20-30 ng/mL**).

An additional nearly **30%** of Americans have lower vitamin D levels (**below 20 ng/mL**) that qualify as **deficiency**.[10]

This factor may be especially important among adults aged 60 and over.[10]

Life Extension® supporters have long been advised of the importance of maintaining an optimal vitamin D level between **50-80 ng/mL**.

Oral intake of **vitamin D** to ensure healthy levels may help protect against winter-season conditions.

Impact on Immune Function

For the body to produce its own **vitamin D**, we need direct skin exposure to sunlight.

But we spend most of our time indoors or covered up by clothes and sunscreen. And spending more time in the sun raises the risk of skin cancer and accelerated skin aging.

The other way to get vitamin D is through diet, but most foods contain only modest amounts.

As a result, a majority of people are getting too little of this crucial vitamin.

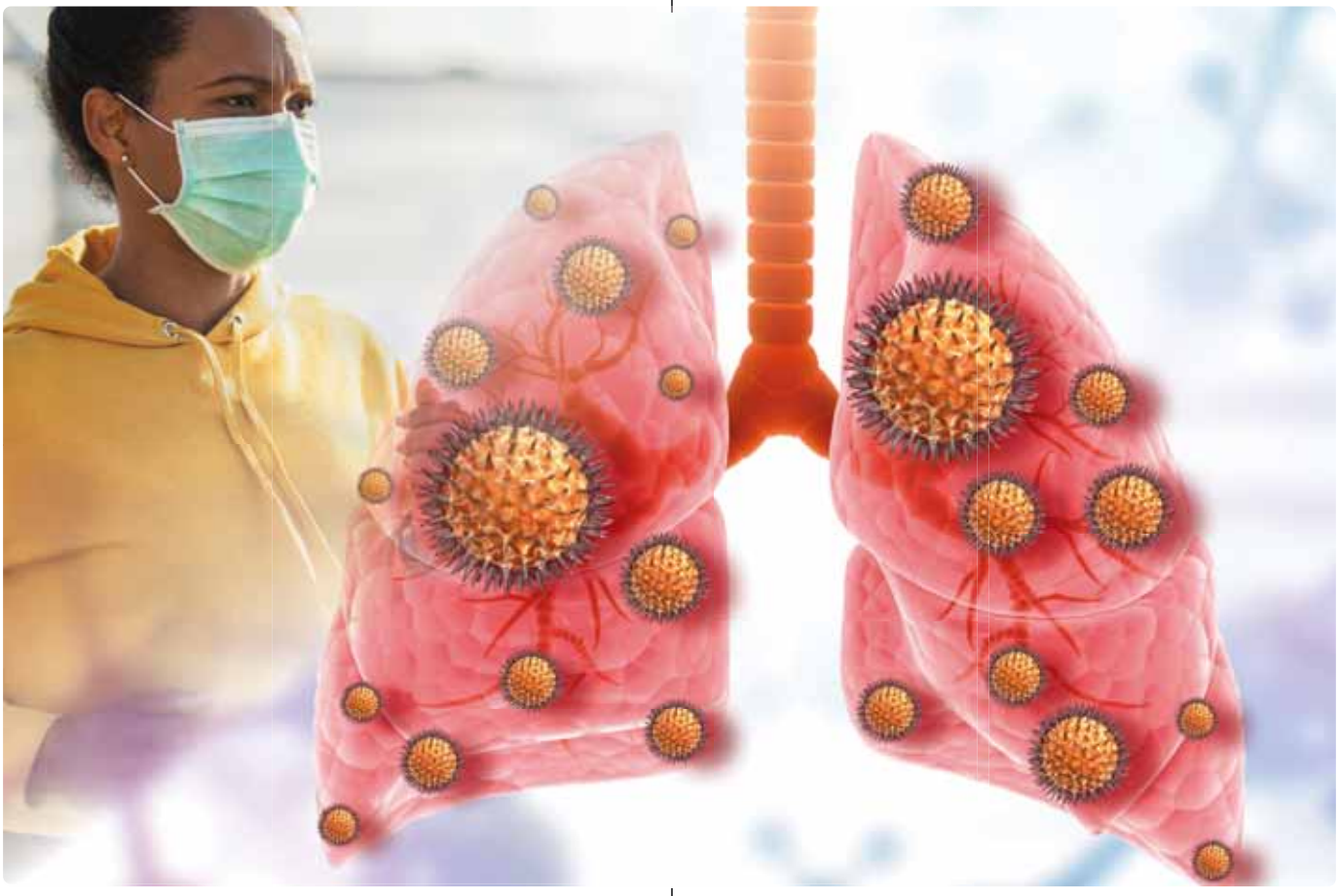
Having low levels of vitamin D is associated with a greater risk for many health problems, from cognitive decline to heart disease.[1-6]

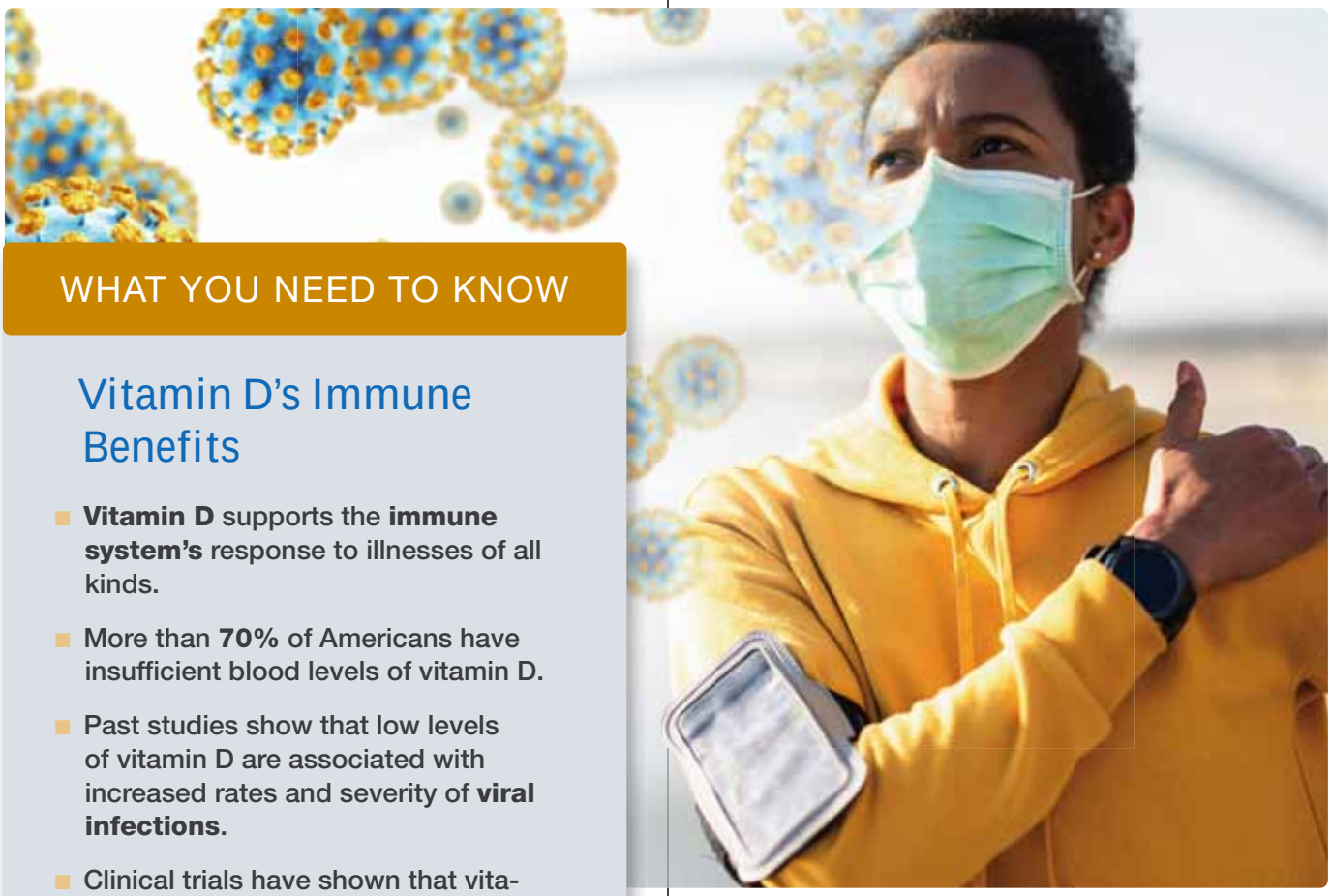
Vitamin D supports **immune health** by helping:[7,8]

- Optimize immune function that protects us from infectious disease.
- Control *overly* aggressive inflammatory immune responses, which can inflict systemic damage.

When excessive levels of immune-system proteins called **cytokines** provoke attacks on healthy tissues, the result is called a "**cytokine storm**."

This is a dangerous reaction that can lead to **acute respiratory distress syndrome** (**ARDS**), an often-fatal complication in which fluid collects in the lungs.





WHAT YOU NEED TO KNOW

Vitamin D's Immune Benefits

- **Vitamin D** supports the **immune system's** response to illnesses of all kinds.
- More than **70%** of Americans have insufficient blood levels of vitamin D.
- Past studies show that low levels of vitamin D are associated with increased rates and severity of **viral infections**.
- Clinical trials have shown that vitamin D has a protective effect against **respiratory tract infections**.

Vitamin D and Viral Illness

Viral respiratory tract infections, such as the flu, are more common during winter.

One of the reasons for this may be **seasonal variations** in our vitamin D levels. During winter, we get less sun, leading to lower vitamin D production.[11,12] That puts us at increased risk for viral infection.

Research shows that infections are *more* common and more severe in those with vitamin D *deficiency*.[12,13]

Low vitamin D is also a risk factor for more severe lung disease, including acute respiratory distress syndrome (**ARDS**).[14,15] Research suggests that those with insufficient vitamin D are at increased risk of a **cytokine storm**.[16]

This hyperproduction of inflammatory factors leads to worsening disease severity and increased risk of death. Low vitamin D levels may be associated with the dangerous inflammation that occurs in ARDS.[14,15]

Vitamin D's Protective Actions

Vitamin D contributes to many functions that help shield the body from infections and lessen their severity. Maintaining adequate levels of **vitamin D:**[14,17-20]

- Interferes with the ability of viruses to **replicate** and produce *more* viruses,
- Helps support and repair healthy cellular linings in the body, including in the airways of the **lungs**,
- Increases production of proteins that shield against **bacteria and viruses**, enhancing the ability of cells to protect themselves from infection,
- Improves the ability of **immune cells** to mount an effective attack against specific viruses, and
- Helps prevent the immune system from going overboard and producing *excessive* pro-inflammatory compounds in the lungs.

Oral Vitamin D Reduces Risk

Many studies have evaluated whether daily **oral intake** of vitamin D can reduce rates of **viral** respiratory illness.

Meta-analyses of clinical trials have shown that vitamin D has a protective effect against **respiratory tract infections**.[9,21]

The impact of vitamin D treatment is greatest in those who, to begin with, have *low* levels of vitamin D.[9]

Life Extension® supporters have long been advised of the importance of maintaining an optimal vitamin D level between **50-80 ng/mL**, and yearly blood testing.

Summary

Vitamin D supports the **immune system** in many different ways, helping to shield the respiratory tract from **viral illness**.

A large majority of adults have vitamin D levels below the optimal level.

Trials have shown that **oral vitamin D** intake modestly *decreases* rates of **viral respiratory tract** infections.•

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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Blood Testing Vitamin D Levels

There are no universal guidelines for frequency of vitamin D testing. However, given the high prevalence of vitamin D deficiency and the strong association of low vitamin D levels with several health issues, annual testing and supplementation to achieve adequate blood levels is highly recommended.

Annual blood tests can let people know whether they are taking the correct dosage to ensure optimal blood levels of vitamin D.

If you do not already maintain an optimal blood level of *25-hydroxyvitamin D* of 50 to 80 ng/mL, then take between 5,000 to 8,000 IU of vitamin D daily with meals.

HIGHER POTENCY
CARNOSINE

Carnosine is a unique dipeptide that can inhibit ***glycation*** throughout the body, thereby helping to slow normal aging processes. Suggested dose is one **500 mg** Carnosine cap taken twice daily.

Super Carnosine provides 500 mg of carnosine per capsule along with fat-soluble vitamin B1 (**benfotiamine**) to further impede glycation reactions.

Mitochondrial Energy Optimizer provides **1,000 mg** of carnosine in each four-capsule dose along with **R-lipoic acid**, **benfotiamine**, **taurine**, and **PQQ** to provide broad-spectrum support.

Item #01829 • 60 vegetarian capsules
1 bottle **$27**
4 bottles $24 each

Life Extension® was the first to introduce high-dose (**500 mg**) carnosine back in **1999**.

Item #02020 • 60 vegetarian capsules
1 bottle **$30**
4 bottles $27 each

Life Extension® carnosine is available in *three different* formulas to allow you to customize your longevity program.

***Item #01868** • 120 vegetarian capsules
1 bottle **$51**
4 bottles $45 each

Each formula provides high doses of **carnosine** to ensure **sustained** benefits.

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For full product description and to order **Mitochondrial Energy Optimizer**, **Carnosine** or **Super Carnosine**, call **1-800-544-4440** or **visit www.LifeExtension.com**

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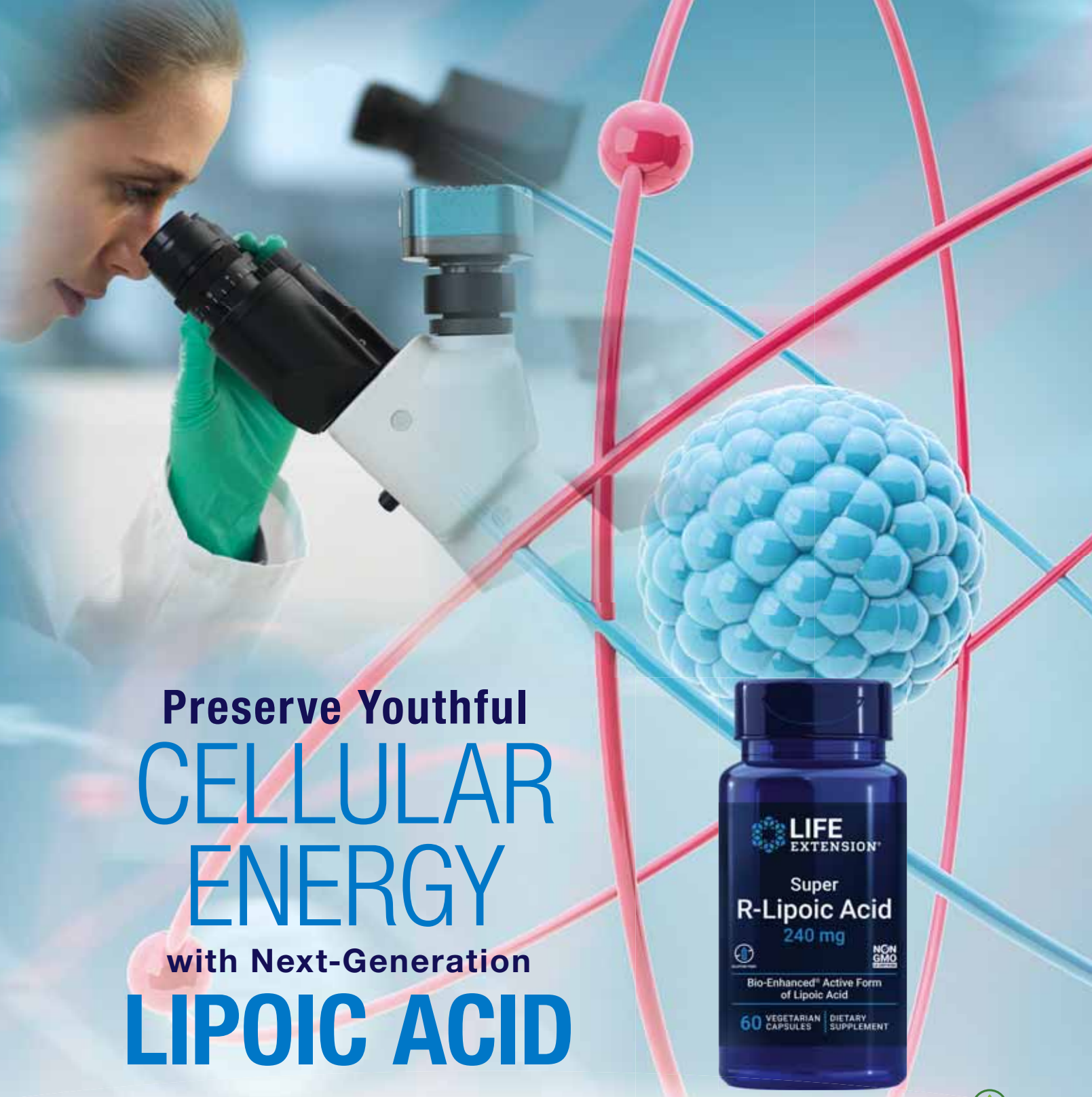

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with Next-Generation

LIPOIC ACID

Super R-Lipoic Acid is more bioavailable, stable, and potent, achieving **10-30 times** higher peak blood levels. This unique **sodium-R-lipoate** can help you reach peak plasma concentrations within just 10-20 minutes of supplementation.

For full product description and to order **Super R-Lipoic Acid**, call **1-800-544-4440** or visit **www.LifeExtension.com**

Item #01208 • 60 vegetarian capsules

1 bottle **$36.75**

4 bottles $33.75 each

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Suggested dose is one to two capsules daily.

CAUTION: If you are taking glucose-lowering medication, consult your healthcare provider before taking this product.

Bio-Enhanced® is a registered trademark of GeroNova Research, Inc.

D3

For Heart Health, Strong Bones, Skin Health, and a Vital Immune System

For full product description and to order **Vitamin D3 supplements**, call 1-800-544-4440 or visit www.LifeExtension.com

Vitamin D3 • 5,000 IU

Each tiny softgel provides **5,000 IU** of **vitamin D3** for easy swallowing.

Item #01713 • 60 softgels

1 bottle **$7.50**

4 bottles $6.50 each

Vitamin D3 • 5,000 IU with Sea-Iodine™*

For those who may be iodine-deficient. Each capsule provides **5,000 IU** of vitamin D3 + **1,000 mcg** of iodine.

Item #01758 • 60 capsules

1 bottle **$10.50**

4 bottles $9.38 each

Vitamin D3 • 7,000 IU

For individuals who need higher levels, including those who weigh over 180 pounds. Each tiny softgel provides **7,000 IU** of **vitamin D3**.

Item #01718 • 60 softgels

1 bottle **$10.50**

4 bottles $9.45 each

Vitamin D3 • 1,000 IU

Ideal for smaller individuals who also obtain **2,000-3,000 IUs** in a multi-formula. Each tiny softgel provides **1,000 IU** of **vitamin D3**.

Item #01751 • 250 softgels

1 bottle **$9.38**

4 bottles $8.44 each

CAUTION: Individuals consuming more than 50 mcg (2000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.

* If you have a thyroid condition or are taking antithyroid medications, do not use without consulting your healthcare practitioner.

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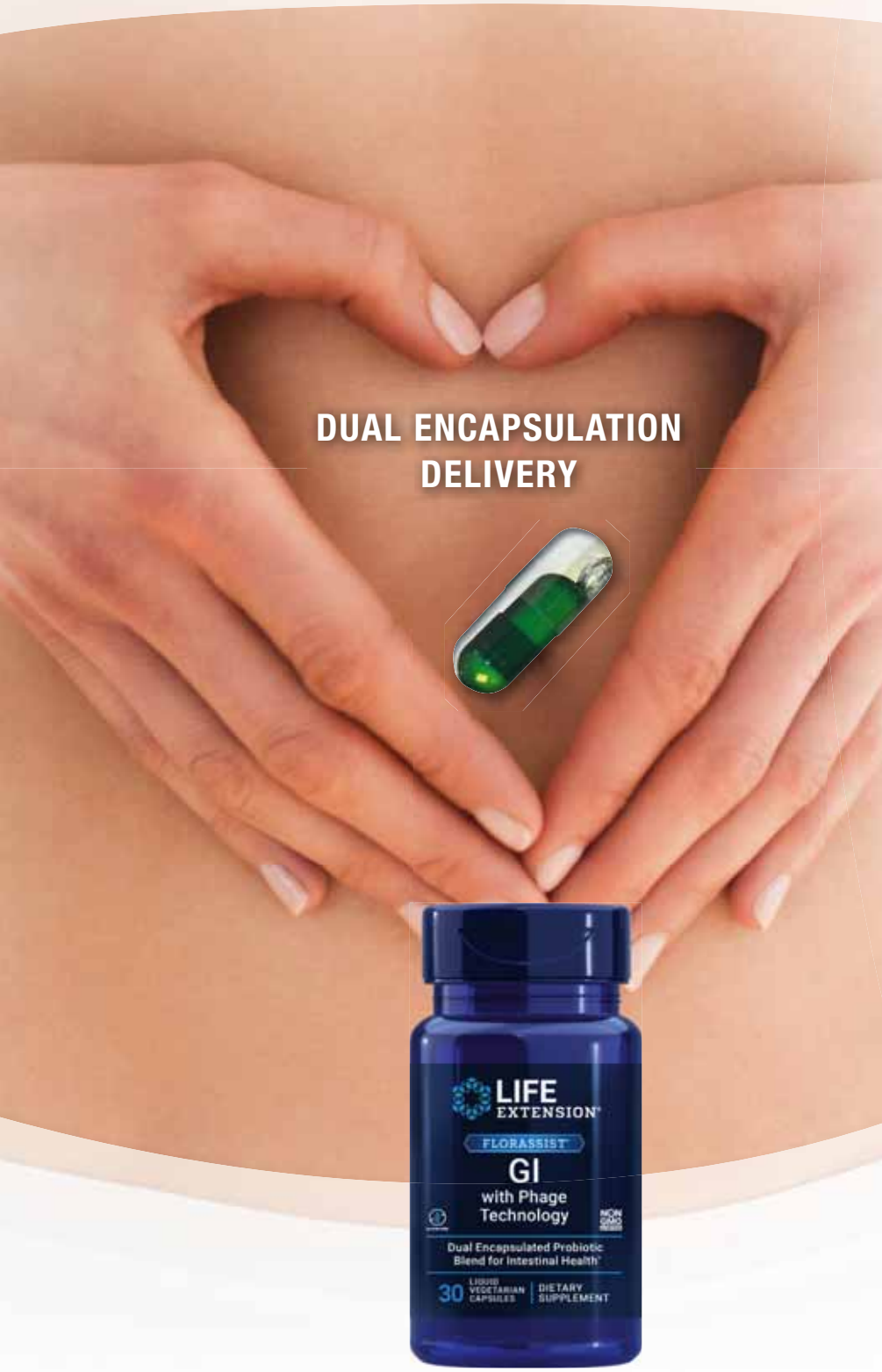
NEW PROBIOTIC BLEND FOR EVEN BETTER INTESTINAL HEALTH

FORTIFY YOUR INTESTINAL FLORA



FLORASSIST® GI with Phage Technology now provides **seven** strains of probiotics *plus* **four** types of ***phages*** in one daily **dual encapsulated** vegetarian capsule.

For full product description and to order **FLORASSIST® GI with Phage Technology**, call 1-800-544-4440 or visit www.LifeExtension.com

Item #02125 • 30 liquid vegetarian capsules

1 bottle **$24.75**

4 bottles $22.50 each

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SPECIAL **BLOOD TEST** OFFER!

VITAMIN D *plus* CBC/Chemistry *and* Lipid Panels

More than **70%** of Americans have insufficient blood levels of vitamin D, despite the ease and low cost of taking vitamin D supplements.[1]

New research daily points to the importance of maintaining optimal vitamin D levels for **healthy immunity** and full-body health.

The ***25-hydroxyvitamin D*** test assesses your vitamin D status, enabling you to increase or decrease your dose based on how close you are to achieving ***optimal*** ranges.

The **CBC/Chem/Lipid Panel** includes measurements of **cholesterol**, **glucose**, **LDL**, **HDL**, **triglycerides**, **liver/kidney function,** and blood counts including important **immune** cells.

The regular member price for the **CBC/Chem/Lipid Panel** and ***25-hydroxyvitamin D*** tests is **$82**.

For a limited time, we are offering this **CBC/Chem/Lipid Panel** plus the ***25-hydoxy-vitamin D*** blood test for only **$56** a **32%** discount off the normal price of these two tests. Sale price effective through **November 2, 2020**.

Life Extension's **CBC/Chem/Lipid Panel** plus **25-hydroxyvitamin D** includes the following tests—for just **$56**:

- **Complete Blood Count**:
  - **Red blood cell count**
  - **Hemoglobin**
  - **Hematocrit**
  - **Red blood cell indices**
  - **Mean corpuscular hemoglobin**
  - **Mean corpuscular hemoglobin concentration**
  - **Red blood cell distribution**
  - **White blood cell count**
  - **Immune cell differential count**
  - **Platelet count**
- **Fasting Glucose** (blood sugar)
- **Uric acid**
- **BUN** (blood urea nitrogen): Measures liver and kidney function
- **Creatinine**: A test used to measure kidney function
- **BUN/Creatinine Ratio**: For diagnosis of impaired renal function
- **Estimated glomerular filtration rate** (eGFR)
- **Sodium**
- **Potassium**
- **Chloride**
- **Calcium**
- **Carbon Dioxide**
- **Phosphorus**
- **Total Protein**
- **Albumin**
- **Globulin**
- **Albumin/Globulin Ratio**
- **Bilirubin**: Evaluates kidney and liver function
- **Alkaline Phosphatase**: Evaluation of liver and bone diseases
- **LDH** (lactate dehydrogenase)
- **AST** (SGOT): Evaluates liver function
- **ALT** (SGPT): Evaluates liver function
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- **Lipid Profile**: Evaluates the risk for developing atherosclerosis (arterial plaque) and coronary heart disease.
  - **Total Cholesterol**
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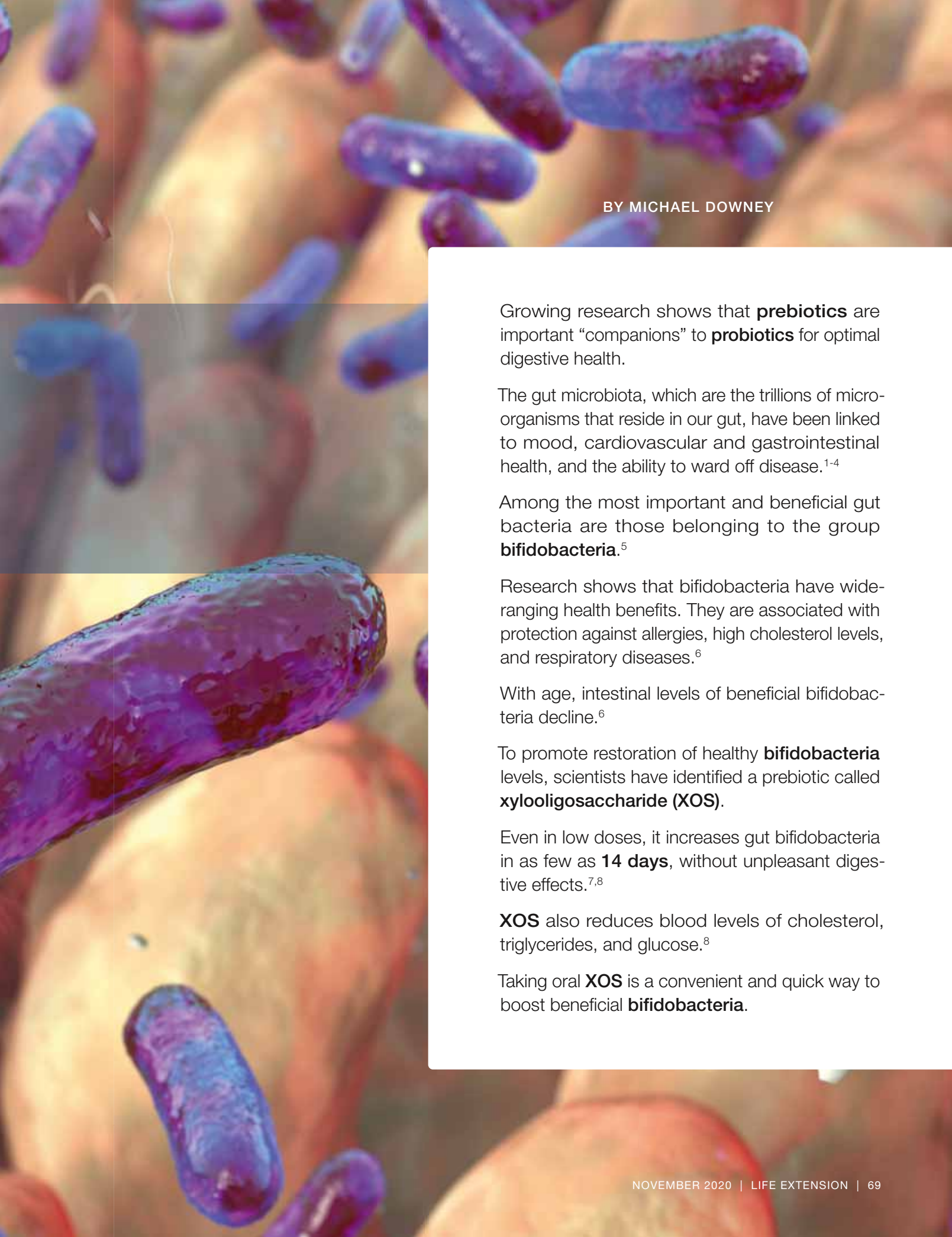
To obtain this **special CBC/Chem/Lipid Panel + Vitamin D blood panel (LC381822COMBO)** at this **low price**, call **1-800-208-3444 (24 hours a day)** or **visit www.LifeExtension.com/labspecial** to order your requisition forms. Then – at your convenience – visit a blood-drawing facility in your area.

1. Br J Nutr. 2018 Apr;119(8):928-36.

Lab tests available in the continental United States and Anchorage, AK only. Restrictions apply in NY, NJ, RI, and MA. Not available in MD..

“Feed” Your Healthy Gut Bacteria



BY MICHAEL DOWNEY

Growing research shows that **prebiotics** are important "companions" to **probiotics** for optimal digestive health.

The gut microbiota, which are the trillions of microorganisms that reside in our gut, have been linked to mood, cardiovascular and gastrointestinal health, and the ability to ward off disease.[1-4]

Among the most important and beneficial gut bacteria are those belonging to the group **bifidobacteria**.[5]

Research shows that bifidobacteria have wide-ranging health benefits. They are associated with protection against allergies, high cholesterol levels, and respiratory diseases.[6]

With age, intestinal levels of beneficial bifidobacteria decline.[6]

To promote restoration of healthy **bifidobacteria** levels, scientists have identified a prebiotic called **xylooligosaccharide (XOS)**.

Even in low doses, it increases gut bifidobacteria in as few as **14 days**, without unpleasant digestive effects.[7,8]

XOS also reduces blood levels of cholesterol, triglycerides, and glucose.[8]

Taking oral **XOS** is a convenient and quick way to boost beneficial **bifidobacteria**.

How Prebiotics Work

The trillions of microorganisms that reside in the human digestive tract—known as the gut **microbiota**—do much more than promote healthy digestion. They impact immunity, metabolism, the endocrine system, mood, and cardiovascular health.[4,9-12]

Foods that nourish and promote healthy gut flora are called ***pre*biotics**.

For a food ingredient to be classified as a prebiotic, it must:[13]

- Resist digestion,
- Be fermented by intestinal microorganisms, and
- Stimulate growth and/or activity of beneficial bacteria.

Most commercial **prebiotics** require large doses to provide optimal digestive health support. Unfortunately, this can cause excessive flatulence, bloating and general digestive discomfort.[14]

But years of research identified a prebiotic that works at extremely low doses. It's known as **XOS (xylo-oligosaccharide)**.

Even better, it specifically targets and boosts levels of **bifidobacteria**.

Bifidobacteria Decline with Age

Levels of beneficial **bifidobacteria** decline *dramatically* with age.

In early adulthood, bifidobacteria make up **30%-40%** of our gut microbiota. Those levels fall to about:[6]

- **10%** by late middle-age, and
- Less than **5%** by old age.

Replenishing intestinal bifidobacteria restores their healthful effects on the body, while leaving less room for *dangerous* bacteria to take up residence.[15]

That's where **XOS** comes in. Made from non-GMO corn cobs, this prebiotic targets bifidobacteria, *preferentially* promoting their growth.

XOS Boosts Bifidobacteria

Studies have demonstrated that **XOS** safely and significantly boosts levels of bifidobacteria.[7,8]

In one double-blind, randomized, placebo-controlled study, microbiologists and clinical researchers with the **UCLA School of Medicine** enlisted 32 healthy subjects and divided them into three groups.

Every day for eight weeks, one group took a **placebo**, the second took **1.4 grams** of XOS, and the third took **2.8 grams** of XOS.[7]

The preparation contained **70%** XOS, so that the total amount of XOS ingested in the two study groups was **1 gram** or **2 grams**, respectively.

Both treatment groups had *increases* in **bifidobacteria**, but those taking **2 grams** daily of XOS had significantly larger increases than the lower-dose group.[7]

To achieve similar increases using another common prebiotic, **FOS (fructooligosaccharides)**, you'd have to take ***10 to 20 grams***, enough to cause cramps and other digestive problems.[7]

The XOS study found no significant side effects in any of the groups.

Results in Just Two Weeks

Another team of scientists using the same doses of the *same* **XOS** preparation found that this prebiotic could significantly boost bifidobacteria levels in a much *shorter* time.[8]

The group taking **1 gram** of XOS daily saw significant increases in bifidobacteria in **28 days**.[8]

Those taking **2 grams** of XOS daily achieved significant increases in bifidobacteria in ***just 14 days***.[8]

Why bifidobacteria respond so quickly and effectively to **XOS**, and at such low doses, is still being studied.

Research shows that bifidobacteria feed on precisely the types of carbohydrates that humans cannot digest, especially the group known as **oligosaccharides**.

XOS (xylooligosaccharide) is an important example of this group.[16]

Benefits of XOS

Taking XOS and raising bifidobacteria levels results in wide-ranging health benefits.[8]

One study found that taking XOS led to gastrointestinal and metabolic improvements, including:[8]

- ***Increased fecal acidity***, which inhibits less-desirable bacteria and promotes healthy bacteria,[17]
- ***Decreased triglycerides and cholesterol*** in the blood and increased levels in feces, and
- ***Decreased blood sugar,*** protecting against type II diabetes and metabolic syndrome.

WHAT YOU NEED TO KNOW

The Benefits of a Powerful Prebiotic

- The trillions of bacteria living in the human gut have an enormous impact on our health and vulnerability to disease.
- Higher levels of bifidobacteria are associated with resistance to a wide range of age-related diseases.
- A prebiotic called **XOS (xylooligosaccharide)** has been validated in human studies to specifically target and boost bifidobacteria. It works in very **low doses**, without side effects, in as little as ***two weeks***.

A recent **2020** rat study found that **XOS** supplementation modulates gut flora and reduces colon inflammation caused by high-fat-diet-induced obesity.[18]

In addition, in treated rats XOS ***counteracted the weight gain*** induced by a high-fat diet and ***decreased inflammatory factors*** in the colon.

Summary

The trillions of organisms that reside in the human digestive tract, or the gut microbiota, are a critical factor in sustaining our resistance to disease and promoting good health.

Among the most beneficial gut bacteria are those belonging to the group **bifidobacteria**.

With age, intestinal levels of these beneficial bacteria decline.

Scientists have identified a novel **prebiotic** called **XOS (xylooligosaccharide)** that has been shown in human clinical trials to boost bifidobacteria populations in the gut in as *little as two weeks*.

Unlike other prebiotics, XOS is effective in **low doses**, without side effects.

XOS has also been shown to lower cholesterol, triglycerides, and blood sugar, risk factors for cardiovascular disease and diabetes, respectively. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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References

1. *Food Chem.* 2013;139(1-4):129-37.
2. *Panminerva Med.* 2014;56(3 Suppl 1):1-6.

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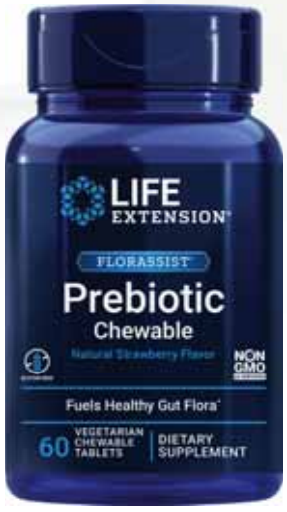

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References
1. *Front Microbiol.* 2016;7:1204.
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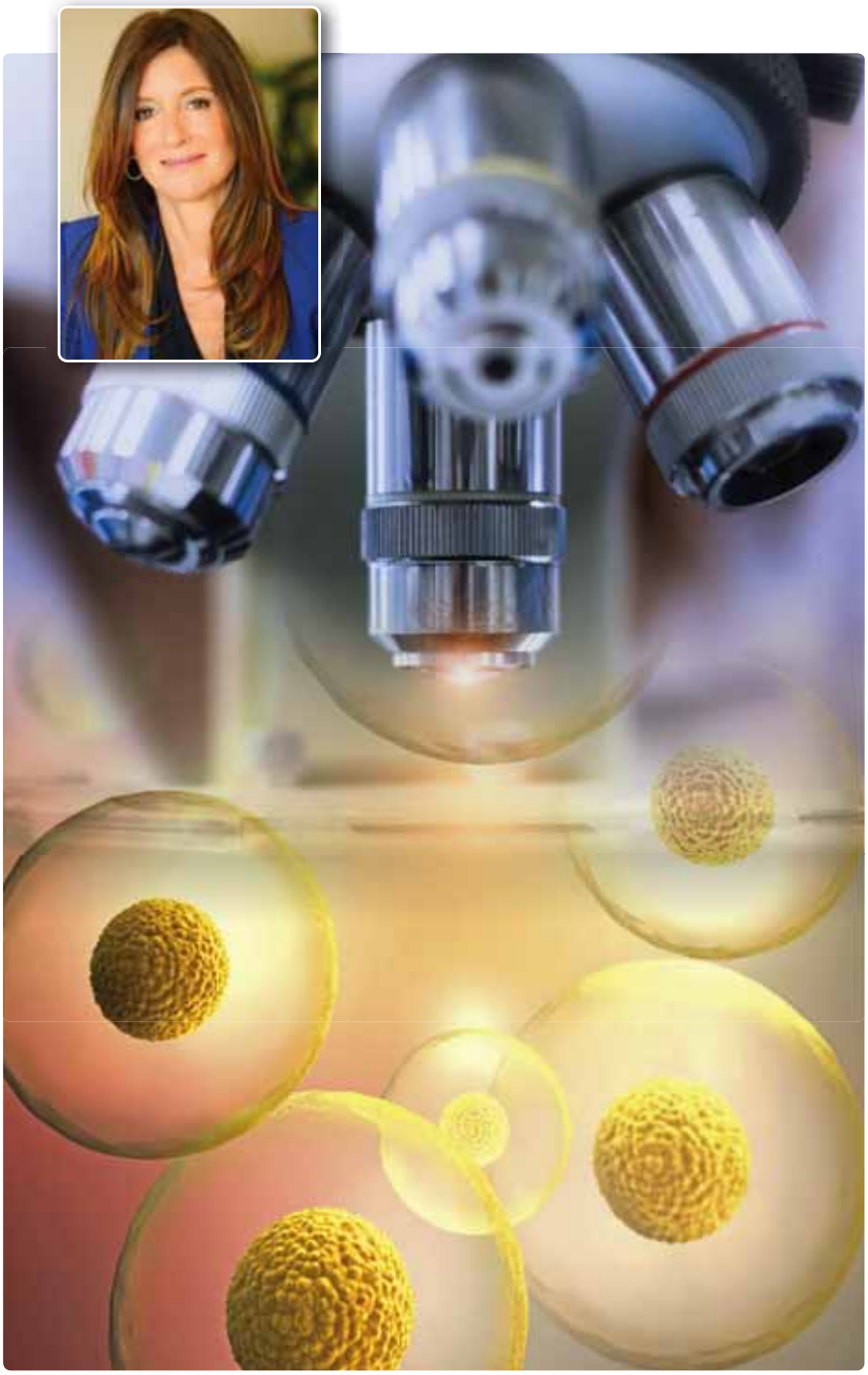
Treating Degenerative Diseases with Cell-Regenerating Exosomes

DR. LINDA MARBAN



In this interview, ***Life Extension***® talks to Dr. Linda Marban, CEO of Capricor Therapeutics.

Capricor Therapeutics is a biotechnology company focused on the discovery of cell therapies for the treatment of various diseases.

One of Capricor's areas of expertise is using specialized cells derived from the heart (cardiosphere-derived cells) to deliver regenerative factors known as **exosomes**.

Capricor is currently investigating the effects of their heart-derived cells, known as CAP-1002, to speed recovery for COVID-19 patients and restore muscle function in the fatal disease of Duchenne muscular dystrophy.

Dr. Marban discusses some of the company's current research and its potential to improve healthy **longevity** in aging people.

LE: What are cardiosphere-derived cells, also known as CAP-1002?

Dr. Marban: Our cells function as a delivery system, delivering their exosomes which help to reprogram existing cells in the body to make new proteins and reduce inflammatory consequences of diseases (which is at the root of nearly every disease). The cells that Capricor discovered are derived from the heart and possess unique properties. By isolating out these cells that help protect the heart, we are able to multiply and divide these cells and then deliver their messages of healing through the exosomes in a larger dose—essentially, taking advantage of these natural processes and expanding upon them for clinical utility.

LE: Can you describe the harvesting process and application of CAP-1002?

Dr. Marban: We take hearts that would typically be used for transplantation (and are not able to be used as such, for technical reasons) and take them back to our labs where we perform a proprietary process that includes isolating the cells, which we then put into our expansion protocol so we can have enough for dosing. We can get up to thousands of doses using large-scale manufacturing methods from a single heart using this technique and have no supply-chain issues.

LE: CAP-1002 has demonstrated favorable modulation of various inflammatory cytokines and regulation of the immune response. What diseases and other conditions can be treated by these unique cells?

Dr. Marban: There are many diseases that can be treated this way. At Capricor, we are focusing on rare diseases such as Duchenne muscular dystrophy and we focused on treating diseases of inflammation, which includes exploring the use of CAP-1002 for the treatment of COVID-19 patients.

LE: Tell us about your work using CAP-1002 on COVID-19? There is a rush to understand, treat and prevent this global pandemic. Why might CAP-1002 be beneficial?

Dr. Marban: The most important part of the cells is the immunomodulatory capability. Multiple, published, peer-reviewed studies of our cells have demonstrated favorable modulation of various inflammatory cytokines and regulation of the immune response. The current understanding of COVID-19's later stages are thought to be due to overstimulation of the immune system, which triggers a cytokine storm in which the body is overwhelmed with pro-inflammatory molecules. This immune response may become excessive and pathologic, inducing pneumonia, organ failure and death. Therefore, it can be the body's overreaction to COVID-19, rather than the virus itself, that delivers the fatal blow.

We started a small effort during the beginning of the pandemic where we treated patients with a compassionate use protocol to see if there was any potential impact on outcomes. What we found was extremely promising. Four of our patients fully recovered and are now back home contributing to and living

a full life again. We are continuing our probe into the impact of CAP-1002 to treat COVID-19 by starting a randomized, controlled clinical trial which we will be working on imminently, subject to FDA approval.

LE: CAP-1002, which are allogenic (genetically dissimilar) cardiosphere-derived cells, stimulate the immune system for cellular regeneration and are currently in clinical trials. What are your findings?

Dr. Marban: The most important finding we've made is in our Duchenne muscular dystrophy (or DMD) clinical trials. CAP-1002 is a cell that has shown to have profound immunological capabilities and leads to cellular repair. It is not functioning as a stem cell in this context. However, it triggers other cells to re-enter the cell cycle and repair damaged muscle. In DMD, the patients who have this disease do not have the gene to make a protein called dystrophin. Dystrophin is the largest protein in the body, it provides structure to cells and protects them from damage on a day-to-day basis. The most notable that are affected by this are the muscle cells. DMD is a chronic, progressive disease where boys and young men typically start showing symptoms of it around age three and their lifespan is typically limited to their 20s.

CAP-1002 has been shown to improve muscle strength and increase the ability of patients to improve movements in their arms, shoulders, and hands. These are patients who are in wheelchairs already, so they will now have better function of the muscles in their upper limbs. This will help them to drive their wheelchair, use their smartphone, and improve their quality of life in many ways.

We have also seen positive data in cardiac endpoints such as ejection fraction and volumes, which is extremely encouraging.

We are now asking the FDA to consider some type of accelerated approval for this product following its incredibly positive Phase-II data from our latest clinical trial.

LE: Can you please explain to our readers what exosome-based therapeutics are?

Dr. Marban: Exosomes are an extremely exciting and emerging class of therapeutic being explored for the treatment of a variety of different diseases. They are extremely small, single-membrane, secreted vesicles that are enriched in selected proteins, lipids, and nucleic acids. They are secreted by nearly all cell types and they are how cells communicate with each other. In other words, exosomes are the "messengers" of cells—they play a distinct role in the transmission of molecules to other cells. At Capricor, we are harnessing the power of intercellular communication and engineering exosomes into therapeutics by loading them with custom-designed nucleic acids or proteins that can direct cellular behavior and ultimately change biology.

LE: How may these nanosized particles be used to treat various diseases?

Dr. Marban: Exosomes can be used for a whole host of different diseases and biologic applications.

For example, we are now developing a potential vaccine therapy using exosomes for COVID-19. From this foundation, they can be used for other types of vaccines such as other infectious diseases or even as an immunotherapy for cancer, through targeting and killing malignant cells before they have a chance to expand and metastasize. Exosomes also can be used for genetic diseases. You can also do an array of protein replacement therapies. Essentially, anything that you want to load inside of a cell, which we've been having trouble as a field doing, can be imagined using an exosome to accomplish this, i.e. replace proteins inside cells.

LE: We are aware of your HOPE Trial and the use of cardiosphere-derived cells (CAP-1002) to treat Duchenne Muscular Dystrophy, which is nearly always fatal. We commend you for it. Projecting ahead, do you see Capricor's innovations changing medicine by treating degenerative diseases like heart failure and bone marrow disorders?

Dr. Marban: Capricor's foundational work is based on the premise of using a cell derived from cardiac tissue to treat heart disease. In fact, we have published and shown very promising data in advanced heart failure with the use of our cells. For the last few years, we have stayed focused on rare cardiac diseases such as Duchenne muscular dystrophy, but we remain open to exploring the use of our technology in other cardiac diseases.

LE: Is Capricor as optimistic as **Life Extension®** is about the potential of CAP-1002 to favorably impact human longevity? If so, in what ways will these unique cells promote human longevity?

Dr. Marban: One of the students in our lab did an interesting study a few years ago where she studied the increased longevity in rats treated with the cells. Through her research, she successfully demonstrated transfusion of blood from one of the treated rats into a rat that was untreated. We believe our cells have the potential to extend longevity of animals, but we have not yet tested this in humans. However, if you can successfully cut down the rate of heart disease and other diseases that have an effect on the human lifespan, you are indirectly addressing increasing longevity, as well.

LE: In animal studies cardiosphere-derived cells have restored certain markers of aging such as youthful gene expression, longer telomeres, increased exercise capacity and reduced inflammatory markers—all good signs to reduce the burden of aging. How soon might this be translated into human studies to reverse certain aging processes?

Dr. Marban: This is always the hard part of being a smaller biotech company. The kinds of studies that would deduce this would be large, long, and expensive. At this time, we are not using our cells for the treatment of aging, but we remain focused on treating diseases of inflammation which are indirectly related to the aging process. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

Dr. Linda Marban is the CEO of Capricor Therapeutics, and a co-founder of the company. She earned a PhD in cardiac physiology from Case Western Reserve University.

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References

1. *Anti-Aging Med.* 2011;8(2):7-14.
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Foolproof Fish

Modern Recipes for Everyone, Everywhere

BAKED HALIBUT WITH CHERRY TOMATOES AND CHICKPEAS

You don't have to live by the sea to enjoy fresh seafood for dinner. With *Foolproof Fish: Modern Recipes for Everyone, Everywhere*, by America's Test Kitchen, you can learn to cook 23 varieties of fish, plus shellfish, no matter where you live.

This versatile cookbook includes recipes for varieties of fish including salmon and catfish, tuna and bluefish, and shellfish like crab and lobster. Plus, it includes helpful substitutions in case the fish you're looking for isn't available in your area.

In addition to providing 198 tried-and-true recipes, *Foolproof Fish* covers important topics like how to properly treat a pan, how to prevent fish from breaking apart when you flip it, and to what internal temperature the fish should be cooked.

It also answers questions like which varieties work best for stews, the best way to serve various fish, and even how to prepare and crack lobster.

Fish is fresh, delicious, and a cornerstone of the Mediterranean diet—and now, *Foolproof Fish* makes preparing and serving it easier than ever.

Here, ***Life Extension***® highlights recipes from the book that feature four different types of fish. Enjoy.

—LAURIE MATHENA

Salmon, Avocado, Grapefruit, and Watercress Salad

Serves 4

Substitutions: Arctic Char or Wild Salmon

- 2 (6- to 8-ounce) skin-on salmon fillets, 1 inch thick
- 3 tablespoons plus 1 teaspoon extra-virgin olive oil, divided
- 3/4 teaspoon table salt, divided
- 1/8 teaspoon pepper
- 2 red grapefruits
- 1 small shallot, minced
- 1 teaspoon white wine vinegar
- 1 teaspoon Dijon mustard
- 4 ounces (4 cups) watercress, torn into bite-size pieces
- 1 ripe avocado, halved, pitted, and sliced 1/4-inch thick
- 1/4 cup fresh mint leaves, torn
- 1/4 cup hazelnuts, toasted, skinned, and chopped

1. Adjust oven rack to lowest position, place aluminum-foil–lined, rimmed baking sheet on rack, and heat oven to 500 degrees. Make 4 or 5 shallow slashes, about 1 inch apart, on skin side of each fillet, being careful not to cut into flesh. Pat salmon dry with paper towels, rub with 1 teaspoon oil, and sprinkle with 1/4 teaspoon salt and pepper.

2. Reduce oven temperature to 275 degrees and remove sheet from oven. Carefully place salmon skin-side down on prepared sheet. Roast until center is still translucent when checked with tip of paring knife and registers 125 degrees (for medium-rare), 8 to 12 minutes. Transfer salmon to plate. Let cool completely, about 20 minutes. Using 2 forks, flake salmon into rough 2-inch pieces, discarding skin.

3. Meanwhile, cut away peel and pith from grapefruits. Holding fruit over bowl, use paring knife to slice between membranes to release segments. Measure out 2 tablespoons grapefruit juice and transfer to separate bowl.

4. Whisk shallot, vinegar, mustard, and remaining 1/2 teaspoon salt into bowl with grapefruit juice. While whisking constantly, slowly drizzle in remaining 3 tablespoons oil until combined. Arrange watercress in even layer on serving platter. Top with salmon pieces, grapefruit segments, and avocado. Drizzle dressing over top, then sprinkle with mint and hazelnuts. Serve.

Baked Scallops with Couscous, Leeks, and Orange Vinaigrette

Serves 4

Substitutions: none

1 pound leeks, white and light green parts only, halved lengthwise, sliced thin, and washed thoroughly

1 cup Israeli couscous

5 tablespoons extra-virgin olive oil, divided, plus extra for serving

4 garlic cloves, minced

1 1/8 teaspoons table salt, divided

1/2 teaspoon pepper, divided

Pinch saffron threads (optional)

3/4 cup boiling water

1/4 cup dry white wine

1 1/2 pounds large sea scallops, tendons removed

2 tablespoons minced fresh tarragon

1 tablespoon white wine vinegar

1/2 teaspoon Dijon mustard

1/2 teaspoon grated orange zest plus 1 tablespoon juice

1. Adjust oven rack to middle position and heat oven to 450 degrees. Combine leeks, couscous, 2 tablespoons oil, garlic, 1/2 teaspoon salt, 1/4 teaspoon pepper, and saffron, if using, in bowl. Microwave, covered and stirring occasionally, until leeks are softened, about 6 minutes. Stir in boiling water and wine, then transfer mixture to 13-inch by 9-inch baking dish.

2. Pat scallops dry with paper towels and sprinkle with 1/2 teaspoon salt and remaining 1/4 teaspoon pepper. Nestle scallops into couscous mixture and cover dish tightly with aluminum foil. Bake until couscous is tender, sides of scallops are firm, and centers are opaque, 20 to 25 minutes.

3. Meanwhile, whisk tarragon, vinegar, mustard, orange zest and juice, remaining 1/8 teaspoon salt, and remaining 3 tablespoons oil in bowl.

4. Drizzle vinaigrette over scallops and serve, passing extra oil separately.

Roasted Cod with Artichokes and Sun-Dried Tomatoes

Serves 4

Substitutions: Black Sea Bass, Haddock, Hake, or Pollock

3 cups jarred whole baby artichokes packed in water, halved, rinsed, and patted dry

3/4 cup oil-packed sun-dried tomatoes, drained, 1/4 cup oil reserved, divided

3/4 teaspoon table salt, divided

1/2 teaspoon pepper, divided

1/2 cup pitted kalamata olives, chopped coarse

1 teaspoon grated lemon zest plus 1 tablespoon juice

4 (6- to 8-ounce) skinless cod fillets, 1 inch thick

2 tablespoons chopped fresh basil

1. Adjust oven rack to middle position and heat oven to 450 degrees. Toss artichokes with 2 tablespoons tomato oil, 1/4 teaspoon salt, and 1/4 teaspoon pepper in bowl, then spread into even layer in 13-inch by 9-inch baking dish. Roast artichokes until lightly browned, about 15 minutes.

2. Remove baking dish from oven and stir in olives, lemon zest, tomatoes, and 1 tablespoon tomato oil. Pat cod dry with paper towels and nestle into vegetables in dish. Brush cod with remaining 1 tablespoon tomato oil and sprinkle with remaining 1/2 teaspoon salt and 1/4 teaspoon pepper.

3. Roast until fish flakes apart when gently prodded with paring knife and registers 135 degrees, 15 to 18 minutes. Drizzle with lemon juice and sprinkle with basil. Serve.

Baked Halibut with Cherry Tomatoes and Chickpeas

Serves 4

Substitutions: Mahi-Mahi, Red Snapper, Striped Bass, or Swordfish

2 (15-ounce) cans chickpeas, rinsed

12 ounces cherry tomatoes, halved

2 shallots, minced

5 tablespoons extra-virgin olive oil, divided

1/4 cup chicken or vegetable broth

5 garlic cloves, minced

1 tablespoon grated lemon zest plus 1 tablespoon juice

2 teaspoons ground coriander, divided

2 teaspoons paprika, divided

1 teaspoon table salt, divided

1/2 teaspoon pepper

4 (6- to 8-ounce) skinless halibut fillets, 1-inch thick

1/8 teaspoon cayenne pepper

2 tablespoons chopped fresh cilantro

1. Adjust oven rack to middle position and heat oven to 400 degrees. Combine chickpeas, tomatoes, shallots, 1 tablespoon oil, broth, garlic, lemon zest and juice, 1 teaspoon coriander, 1 teaspoon paprika, 1/2 teaspoon salt, and pepper in 13-inch by 9-inch baking dish.

2. Pat halibut dry with paper towels. Combine 2 tablespoons oil, remaining 1 teaspoon coriander, remaining 1 teaspoon paprika, remaining 1/2 teaspoon salt, and cayenne in bowl. Add halibut and gently turn to coat. Nestle halibut into chickpea mixture in dish and bake until fish flakes apart when gently prodded with paring knife and registers 130 degrees, 20 to 30 minutes. Remove baking dish from oven, tent with aluminum foil, and let rest for 10 minutes.

3. Drizzle with remaining 2 tablespoons oil and sprinkle with cilantro. Serve.

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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Onions

BY LAURIE MATHENA

Chopped onions are notorious for making your eyes water. But their health benefits are nothing to cry over.

A member of the *allium* family of vegetables (which also includes garlic and leeks), onions have important **antiviral** and **immune-boosting** properties.

They are a good source of sulfur, which is important for **detoxification** and **protein synthesis**.

Onions also contain compounds that help support heart health, reduce the risk of certain cancers, and can even improve bone density.

Heart Health

Studies have shown that onions improve numerous factors associated with heart health.

Red onions in particular contain anthocyanins, which give them their deep red color. People who consume high amounts of anthocyanins have a lower risk of heart attacks.[1]

Onions also contain small amounts of a beneficial flavonoid called **quercetin**.

Animal studies have indicated that consuming onions can reduce heart disease risk factors like inflammation,[2] high triglycerides,[3] and blood clot formation.[4]

Cancer Prevention

A meta-analysis that included 16 studies and more than 13,000 people showed that compared to those with the lowest intake, people with the highest intake of onions had a reduced risk of **colorectal cancer**.[5]

Another meta-analysis showed that people who consumed the most allium vegetables (like onions and garlic) were less likely to be diagnosed with **stomach cancer**, compared to those with the lowest intake.[6]

This cancer protection is likely due to onions' **sulfur-containing compounds** (which have been shown to decrease the growth and spread of tumors in test tube studies[7]) and flavonoids like **quercetin**[8] and **fisetin**[9] (which may inhibit tumor growth).

Boost Bone Density

Consuming onions could possibly help prevent osteoporosis by decreasing bone loss and boosting bone mineral density.

In one study of perimenopausal and postmenopausal women, those who ate onions at least once a day had **greater bone density** than those who only ate them once a month or less. And compared to women who never ate onions, those who ate them most frequently decreased their risk of bone fracture.[10]

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* *Br J Pharmacol.* 2004 Mar;141(5):825-30.

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Reference: **Gerontology.* 1996;42(3):170-80.

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