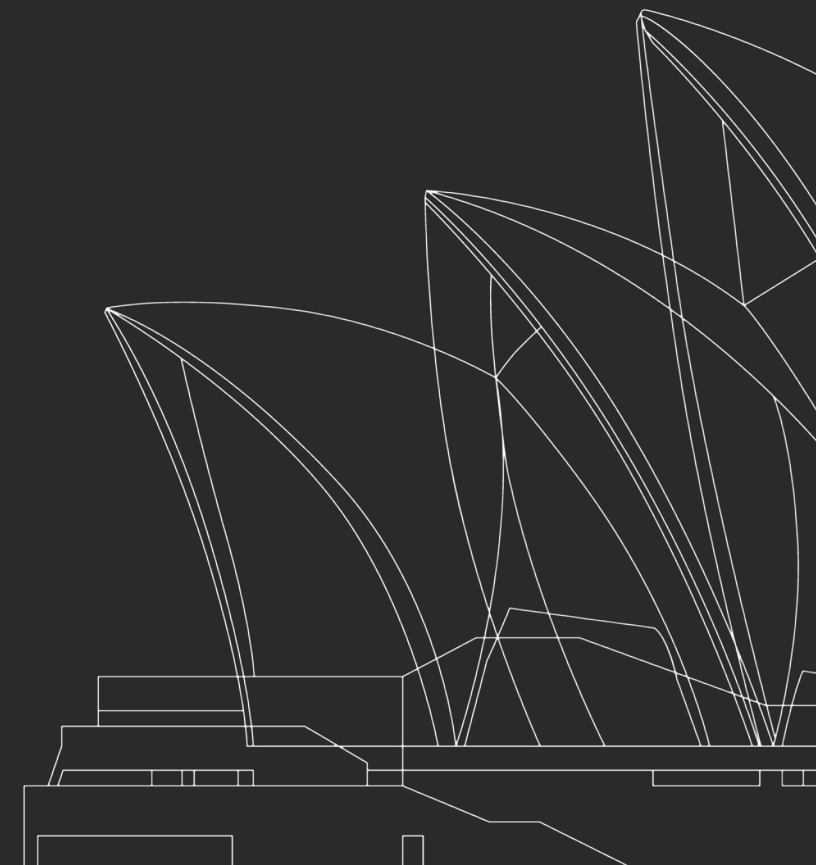


IADSA

International Alliance of Dietary/
Food Supplement Associations

HORIZON SCANNING

2019



AMINO ACIDS



IASDA Annual Week
Sydney, Australia
April 12, 2019

Horizon Scanning: Amino Acids

Kyowa Hakko Bio Co., Ltd.
Karen E. Todd, RD
Yoko Kawada, PharmD

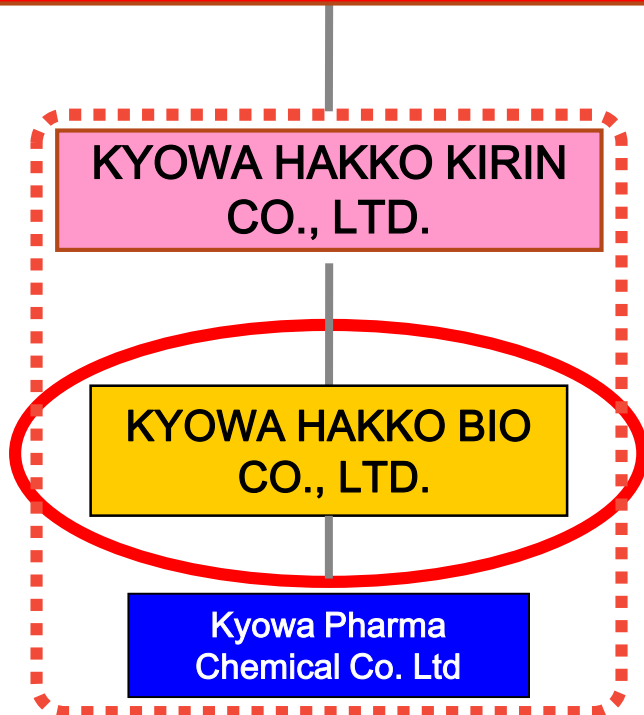
Company Overview



Date of incorporation	February 23, 1907
Number of Group companies	281
Number of employees	40,097

KIRIN Kirin Holdings

Kirin Holdings Company, Ltd.



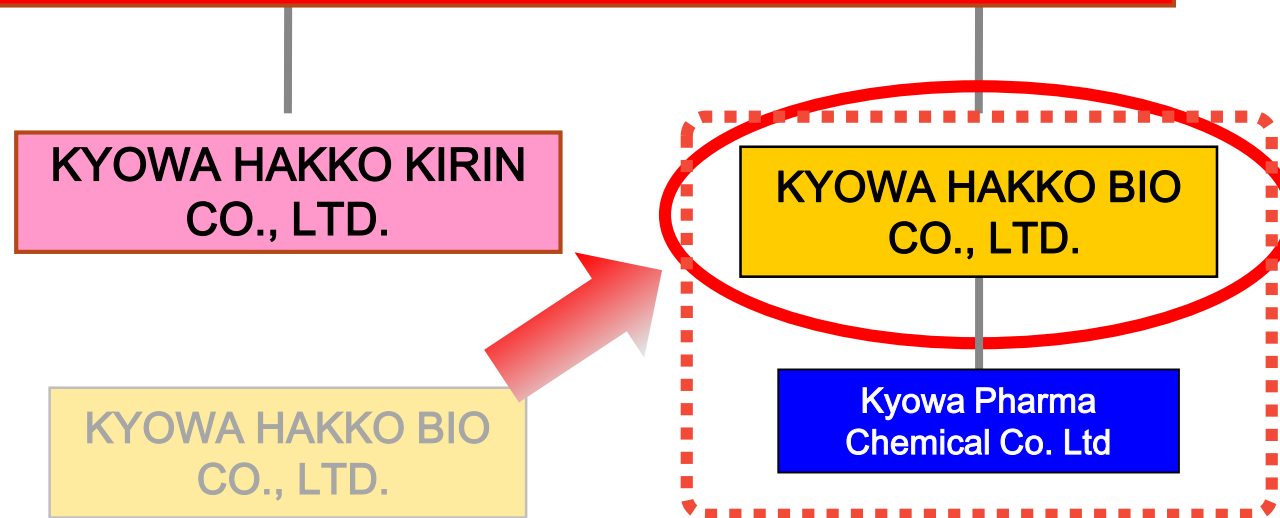
Company Overview



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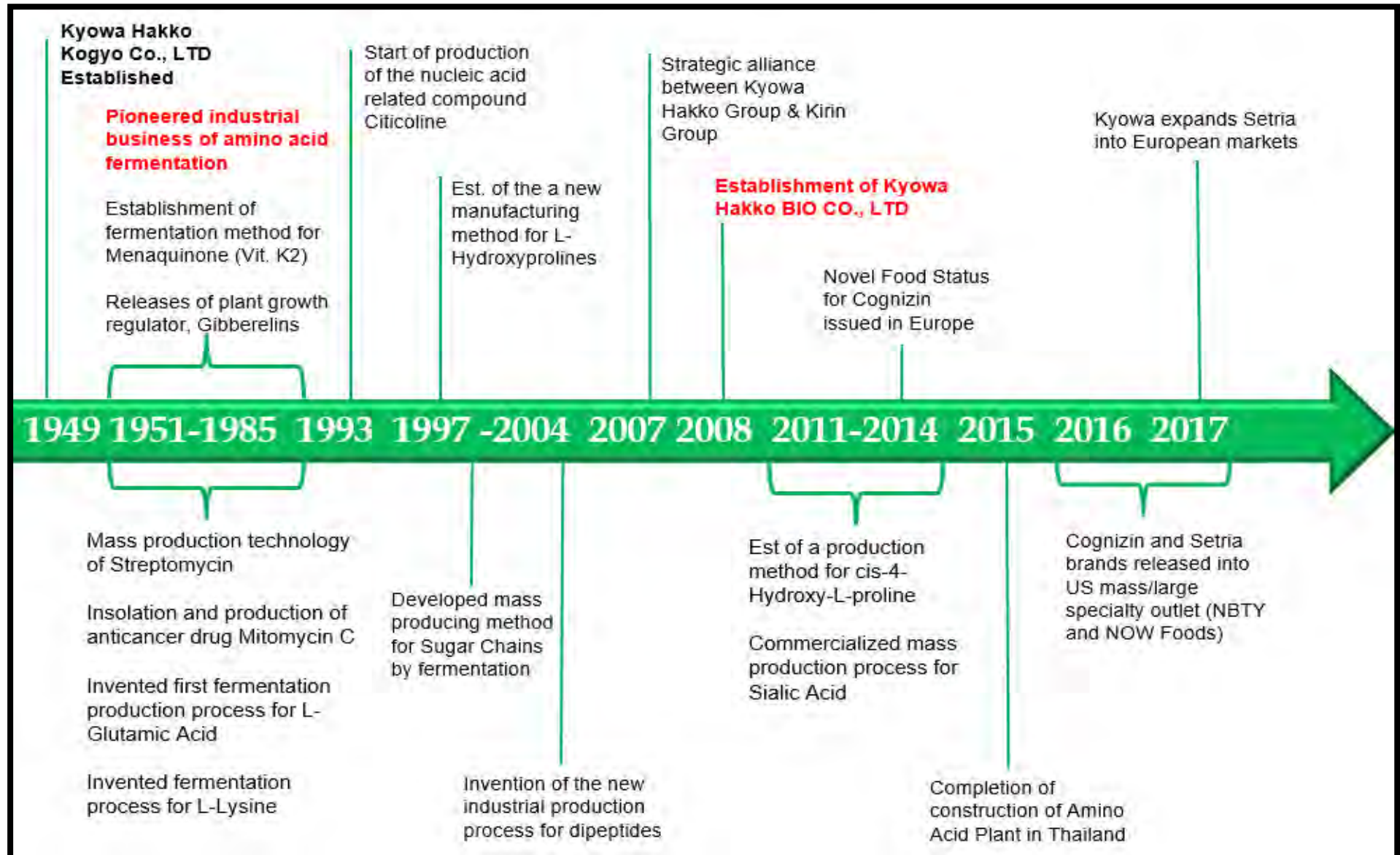
KIRIN Kirin Holdings

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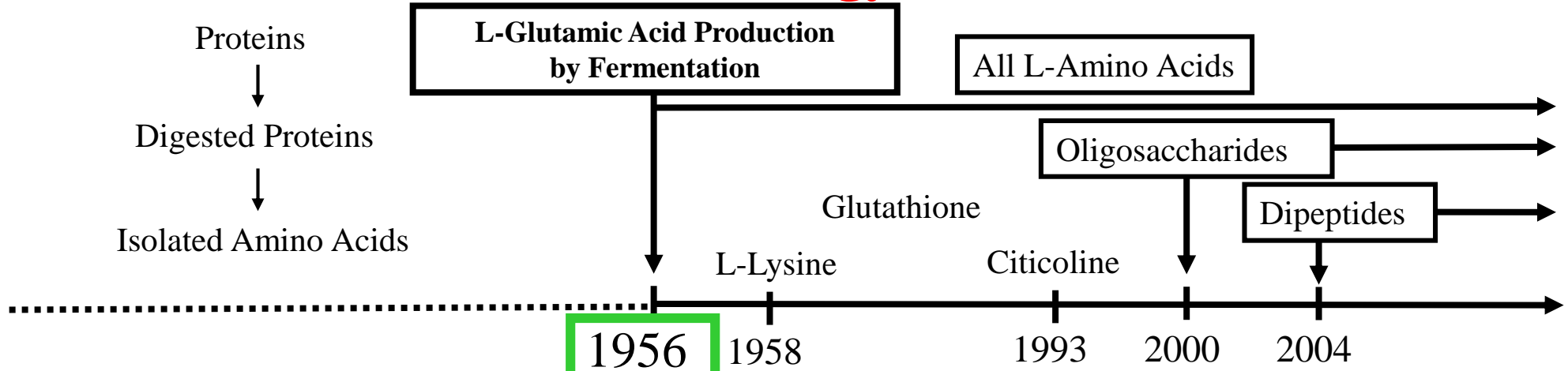


On April 24th, 2019, Kirin Holdings is planned to acquire 95 % of KHB share, in order to strengthen “Health and Well-being” business.

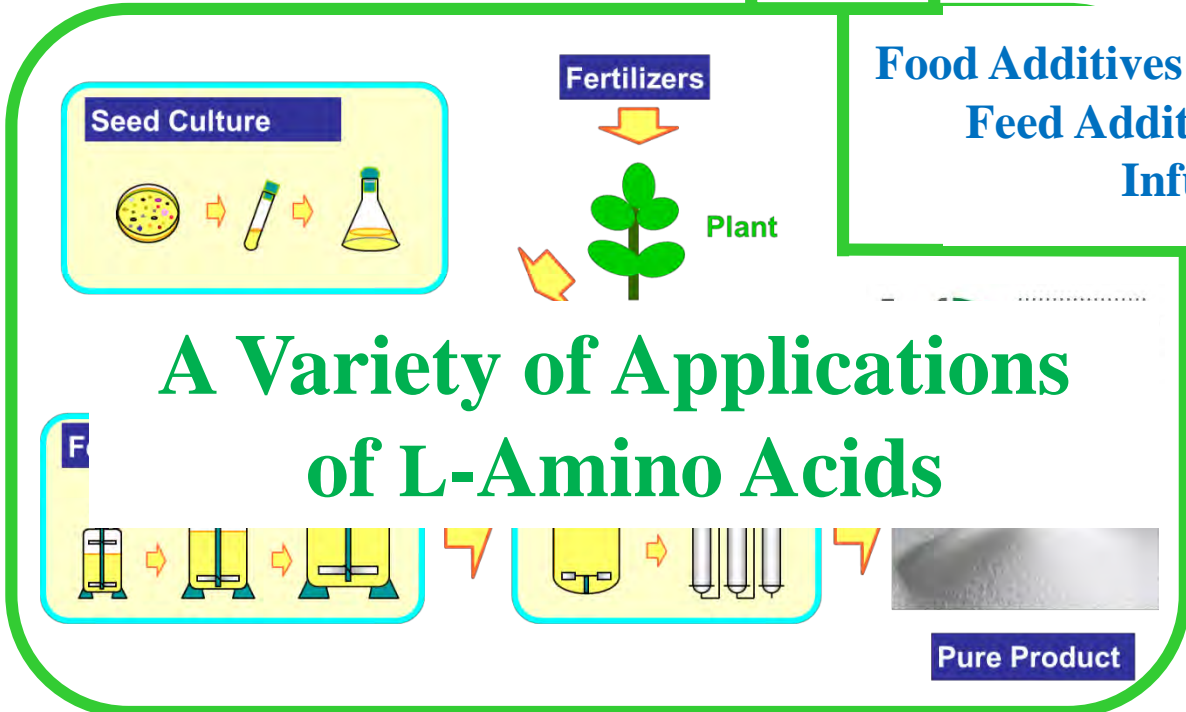
Kyowa Hakko Timeline



Based on Fermentation Technology



A Variety of Applications of L-Amino Acids



The diagram shows the production process: Seed Culture (petri dish, test tube, flask) → Plant (with Fertilizers) → Pure Product (via industrial machinery).

- Food Additives
- Feed Additives
- Infusions
- Health Foods
- Infant Formula
- Sports Nutrition
- Dietary Supplements
- Drugs
- Cosmetics
- Cell Culture Media

Table of contents

- What are amino acids?
- Functions of Amino acids
 - ① Basic nutrition
 - ② Sensory function (Flavor and taste)
 - ③ Bioregulation
- Various functions of amino acids
- Role of amino acids in society in the future

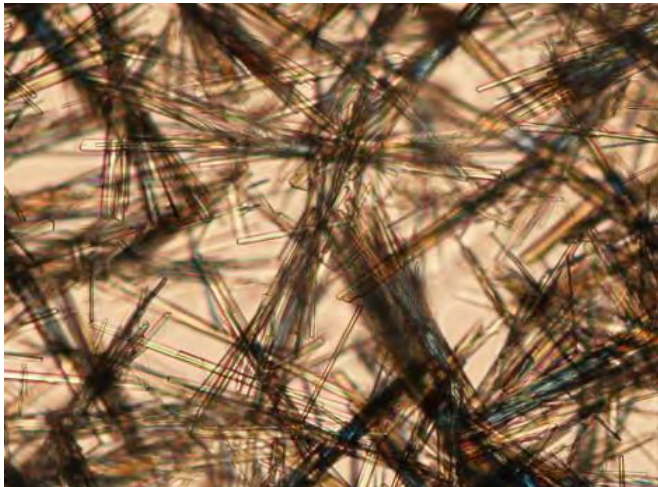
What are amino acids?



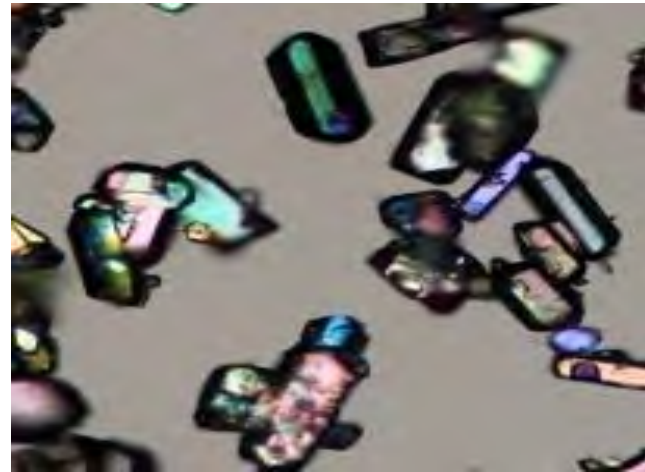
Arginine



Glutamine



Alanine



Aspartic acid

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Amino acids as nutrients

Essential components that support our daily activities



Seasonings

② Sensory Function



Stress



③ Bioregulation function



Metabolic Syndrome

Amino acid



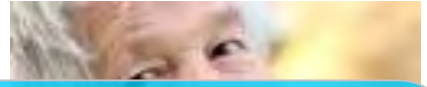
Basic nutrition

① Basic nutritional function



Body

Medical food



① Amino acids as basic nutrients

Amino acids works as building blocks of proteins.

Proteins Create the Body

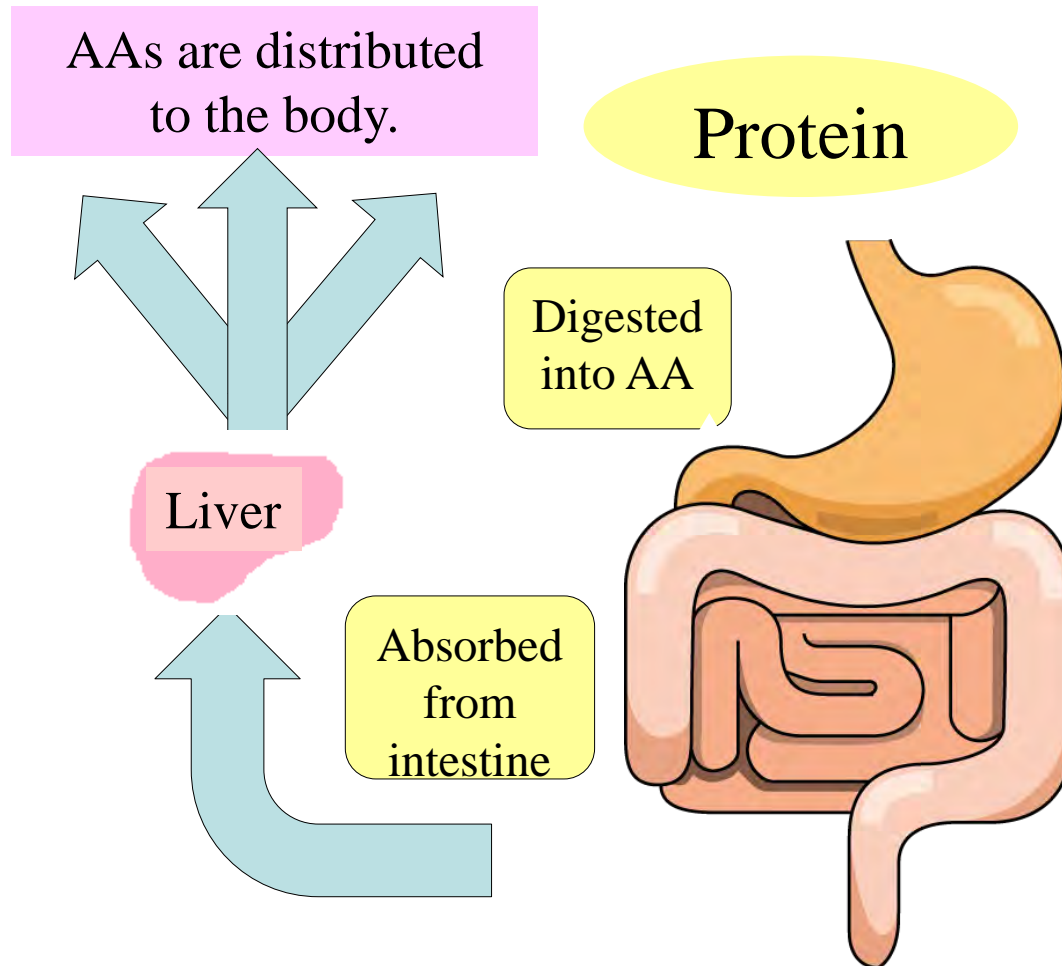


Raw materials are
amino acids!

All over
the bodies

- Brain
- Hair
- Eyes
- Nails
- Skin
- Bones
- Muscles
- Blood

About 20% of the body is made of amino acids.



Proteins are broken down into amino acids that are absorbed in the digestive tract

20 amino acids that make up proteins

Glycine

Serine

Asparagine

Nonessential amino acid

Alanine

Arginine

Aspartic acid

Tyrosine

Proline

Glutamine

Valine

Leucine

Glutamic acid

Lysine

Essential amino acid

Tryptophan

Threonine

Cysteine

Methionine

Histidine

Phenylalanine

② Sensory functions

Amino acids greatly affect taste

- Glutamic acid, an ingredient that imparts a umami taste
- Ingredients that confer bitterness... BCAA, methionine
- Ingredients that confer sweetness... alanine, glycine

e.g., shrimp/crab sweetness → glycine

Sea urchin bitterness to methionine

Tomato flavor, sourness → glutamic acid, aspartic acid



By ripening and fermentation, enhancement of umami taste
→ Proteins are degraded and amino acids are increased.

③ Amino acids as bioregulatory functions

- Improvement in liver function, anti-fatigue effect, ornithine
- Vascular and blood flow improvement... citrulline
- Relax... GABA, theanine
- Energy production... creatine

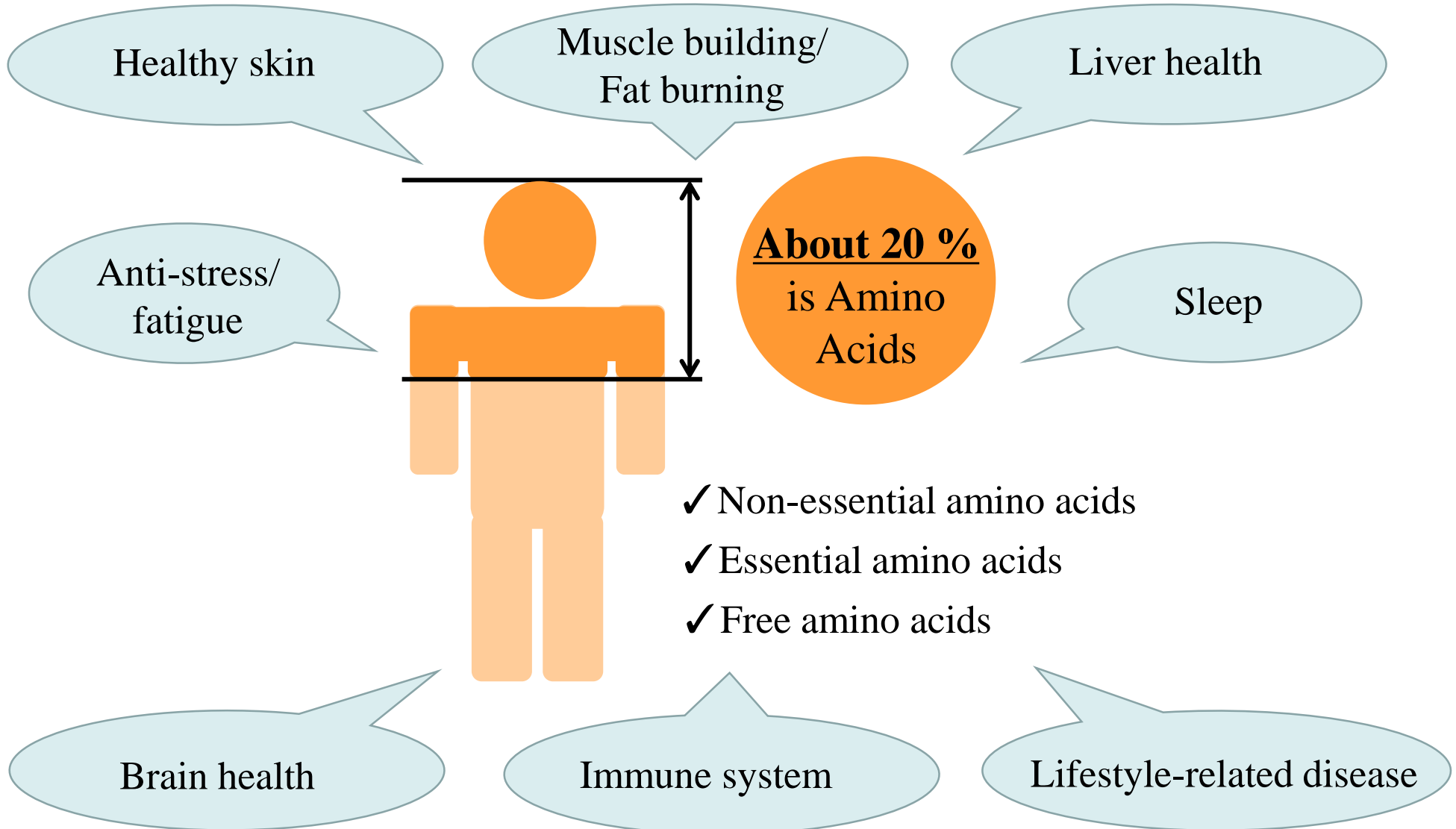
Free amino acid

Not a Raw Material for Protein but Acts Alone in the Body

Table of contents

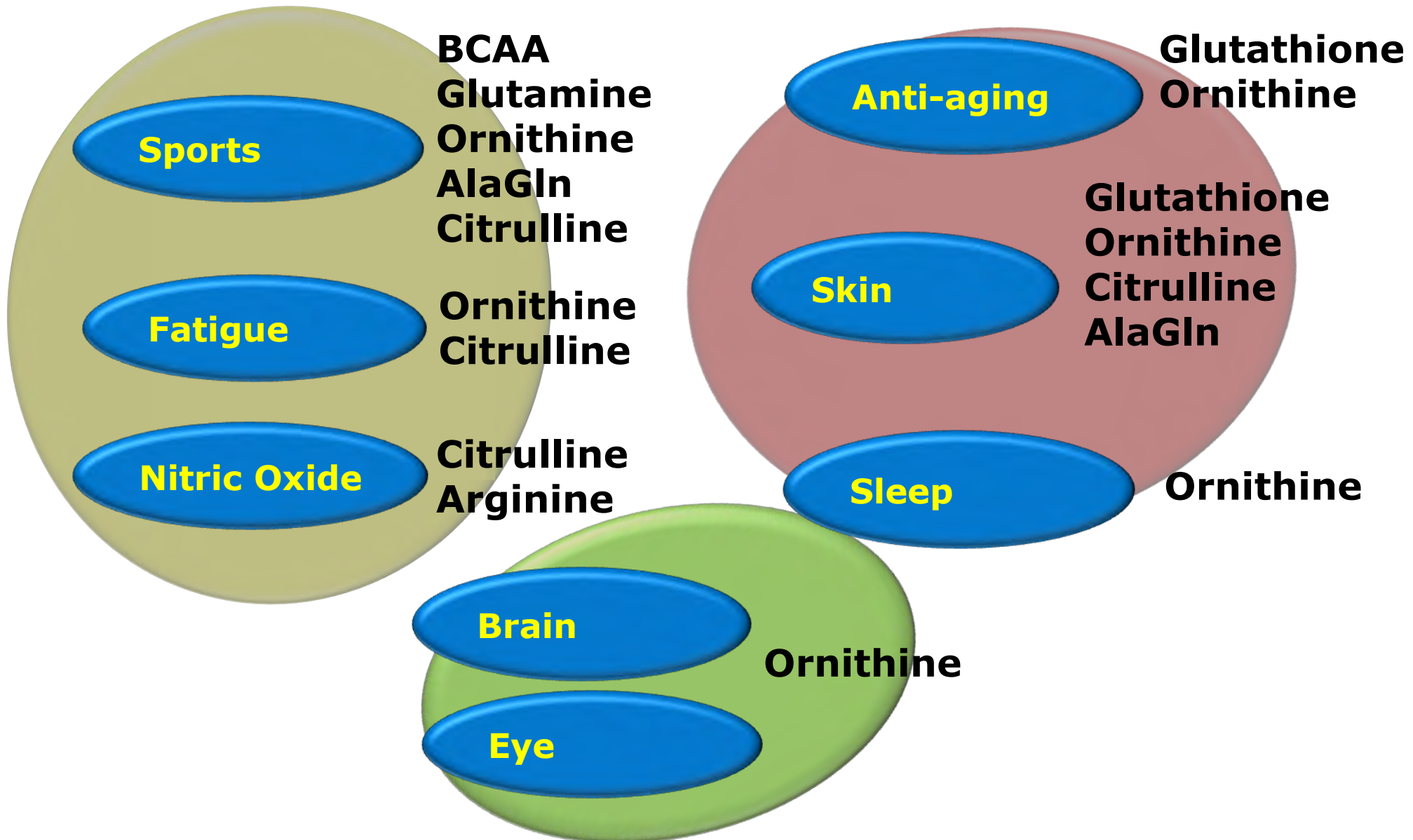
- **What are amino acids?**
- **Nutrition and amino acids**
 - ① Basic nutrition and amino acids
 - ② Flavor and amino acids
 - ③ Bioregulation and amino acids
- **Various functions of amino acids**
- **Role of amino acids in society in the future**

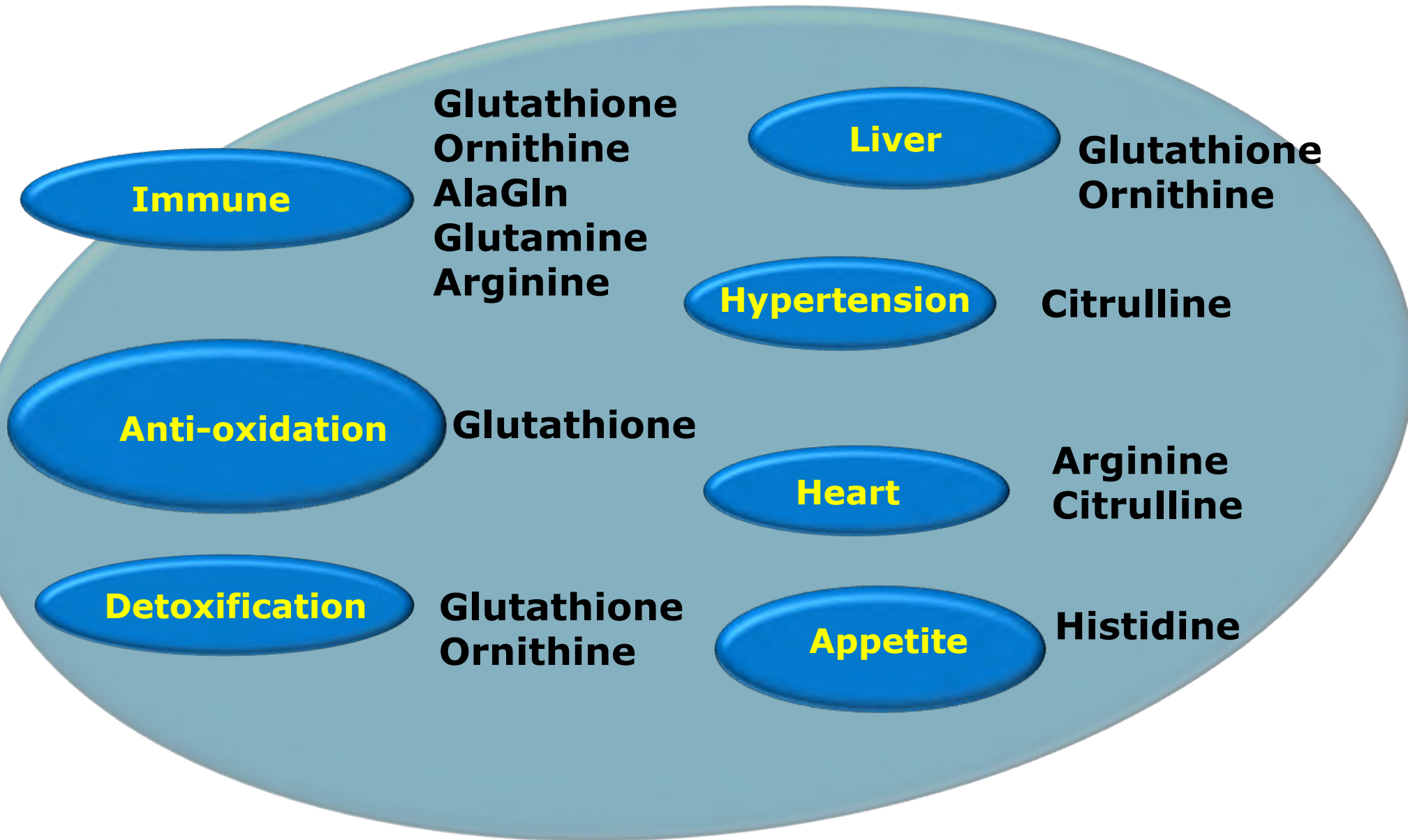
What are Amino Acids?



Various functions of amino acids

- **Muscle and amino acids**
- **Diet and amino acids**
- **Blood vessels, blood flow,
and amino acids**
- **Liver and amino acids**

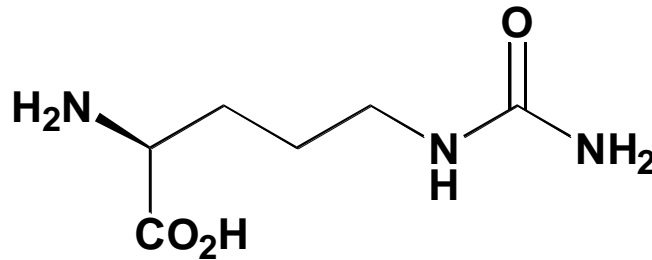




L-Citrulline is a non-protein amino acid

Structure of L-Citrulline

Molecular formula $C_6H_{13}N_3O_3$
FW 175.19



Scientific name: L-2-amino-5-ureidovaleric acid
CAS No. 372-75-8

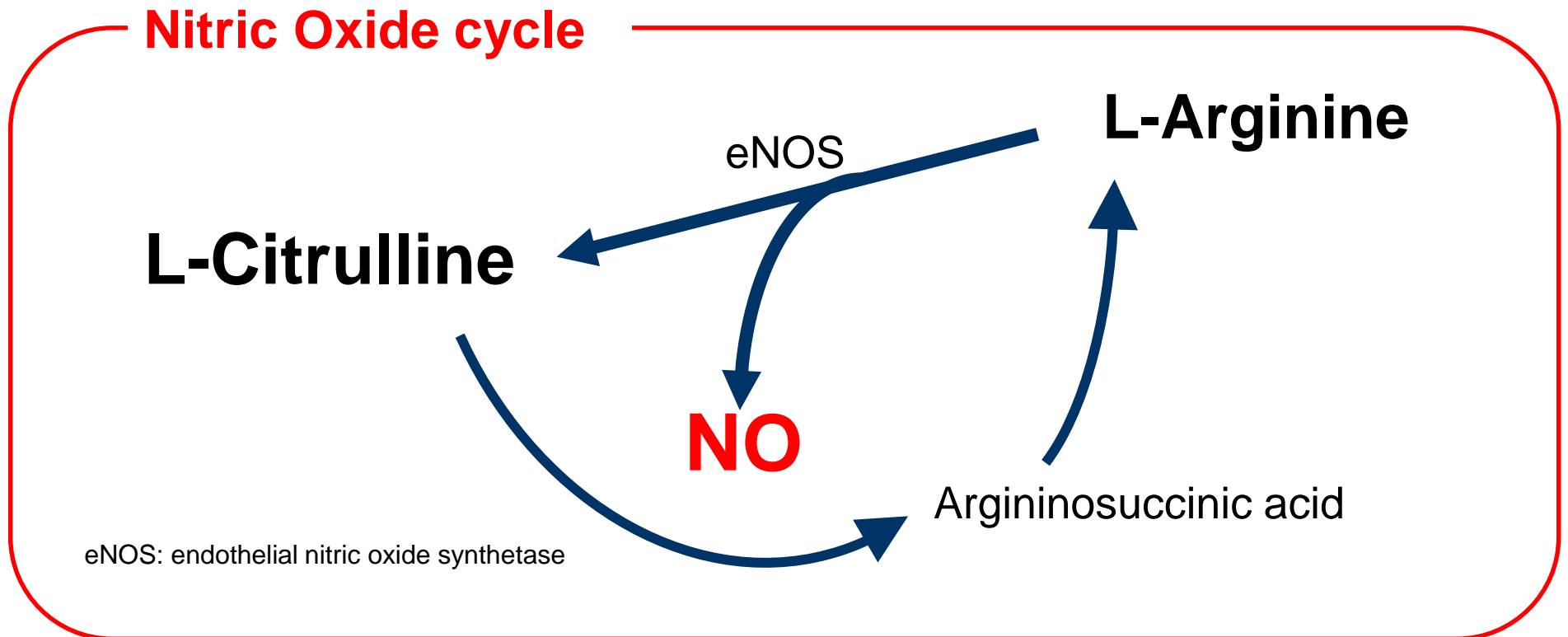


Name is derived from *Citrullus*, watermelon in Latin word.

KYOWA's L-Citrulline is produced by fermentation method with high quality.

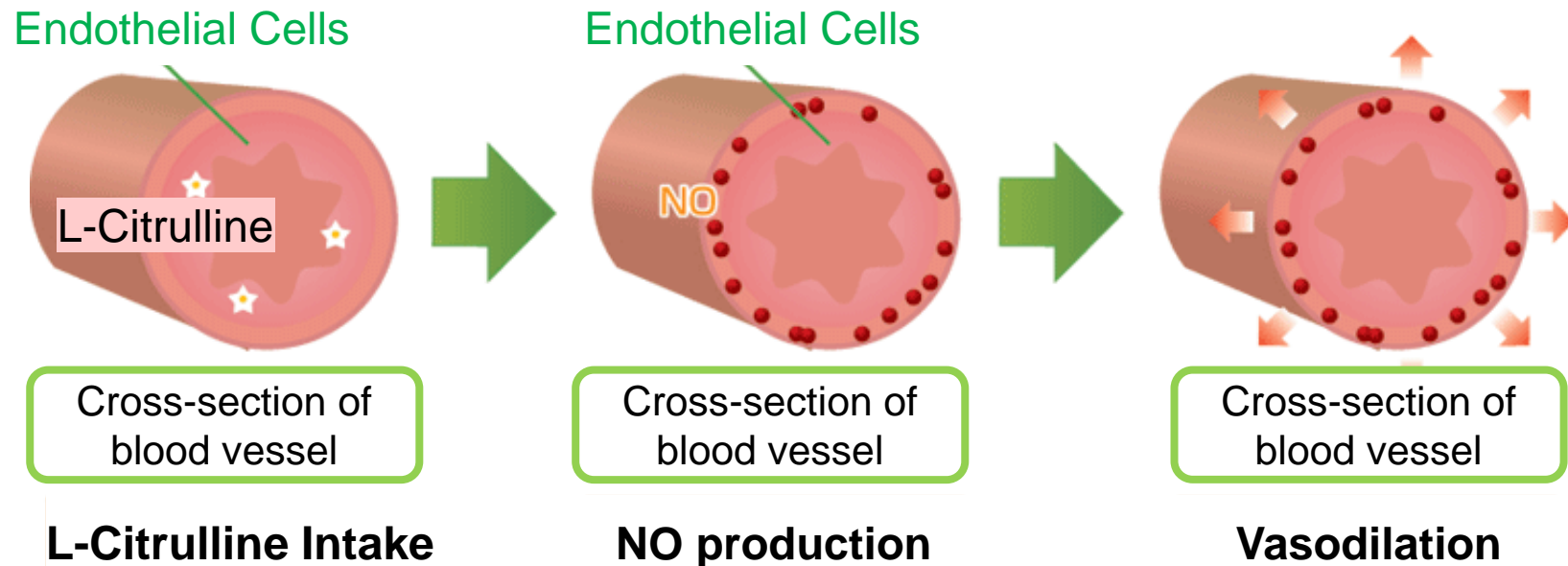
Nitric Oxide is produced from Amino Acids in NO cycle

Conversion from L-Arginine to L-Citrulline produces NO in NO cycle



What is Nitric Oxide ?

- ✓ Is naturally produced in our body
- ✓ Works as signaling molecule in many physiological processes
- ✓ Contributes to increase blood flow and lower blood pressure through vasodilation.



Improves exercise performance

Design: Double-blind randomized placebo-controlled 2-way crossover study

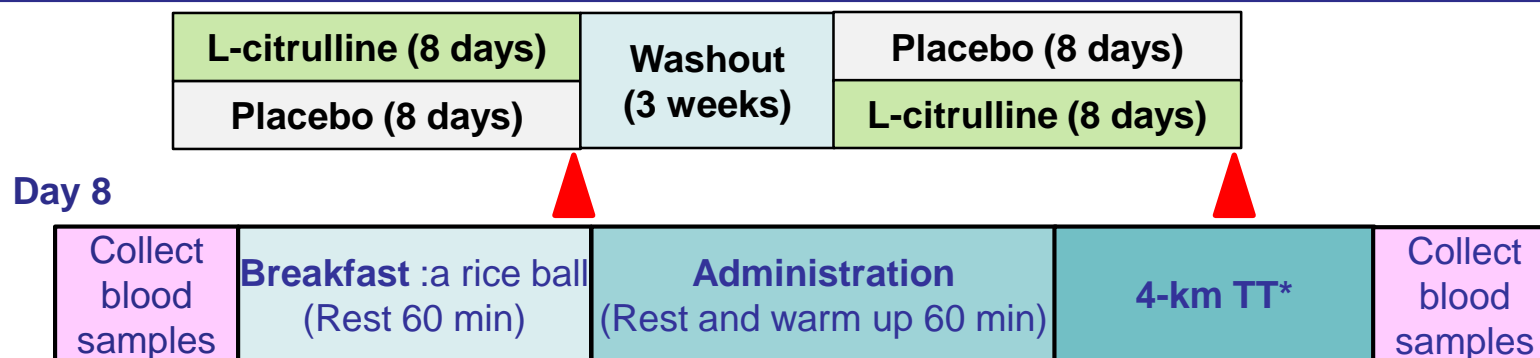
Subjects: Twenty-two trained healthy Japanese

(mean age 29 ± 8.4 years, body mass index 24 ± 3.3 kg/m²)

Samples: 2.4 g of L-citrulline or placebo

Administration term: 8 days

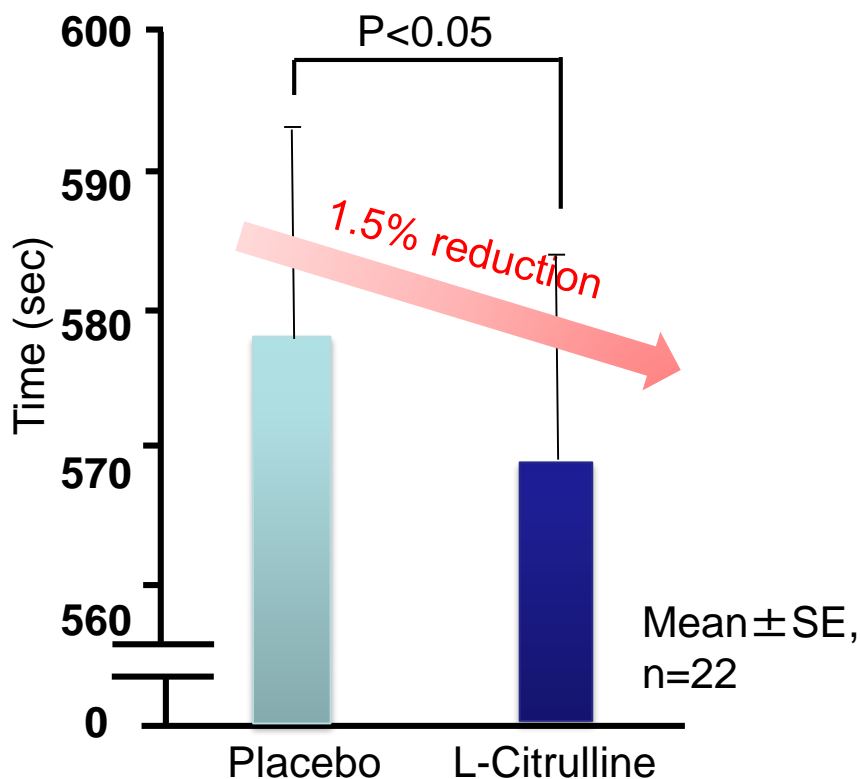
Measurement: Cycling time trial completion times, power output (PO), Oxygen utilization rate (PO/VO₂), plasma nitrite and nitrate (NO_x), visual analog scale (VAS) scores



*4-km TT: 4-km cycling time trial by cycle ergometer

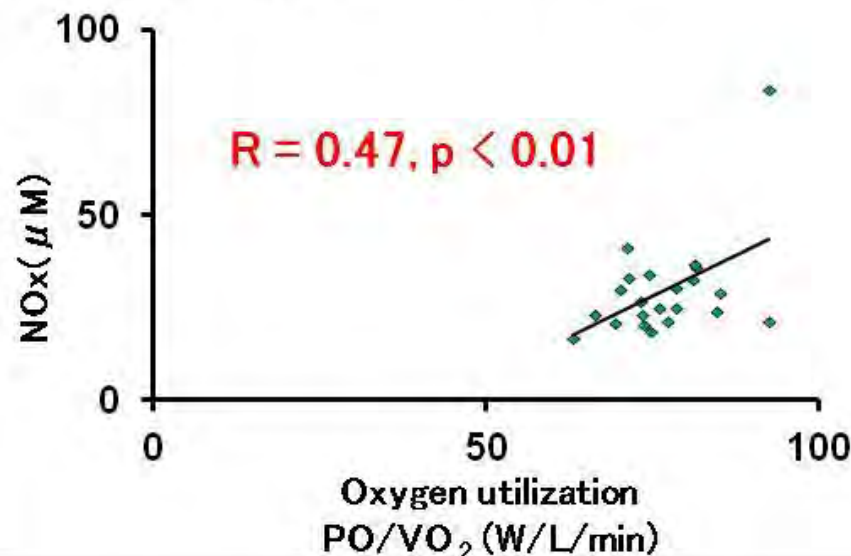
【Result 1】

Completion times of the 4 km TT



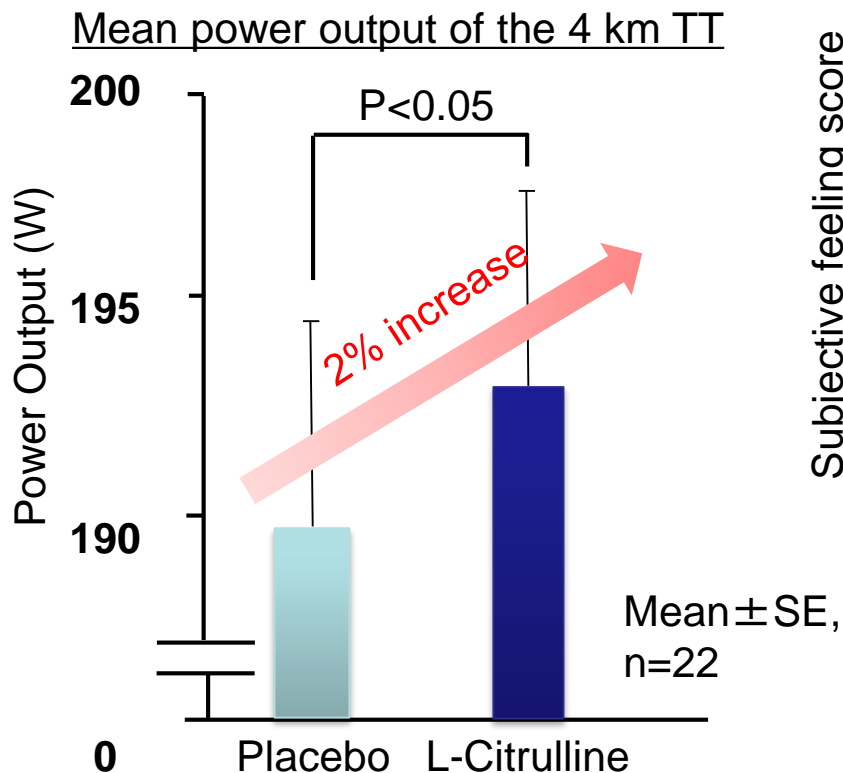
In-house data Correlation between plasma NOx and oxygen utilization rate in the L-citrulline group

*No significant correlation in Placebo group (R=0.30, p=0.17)

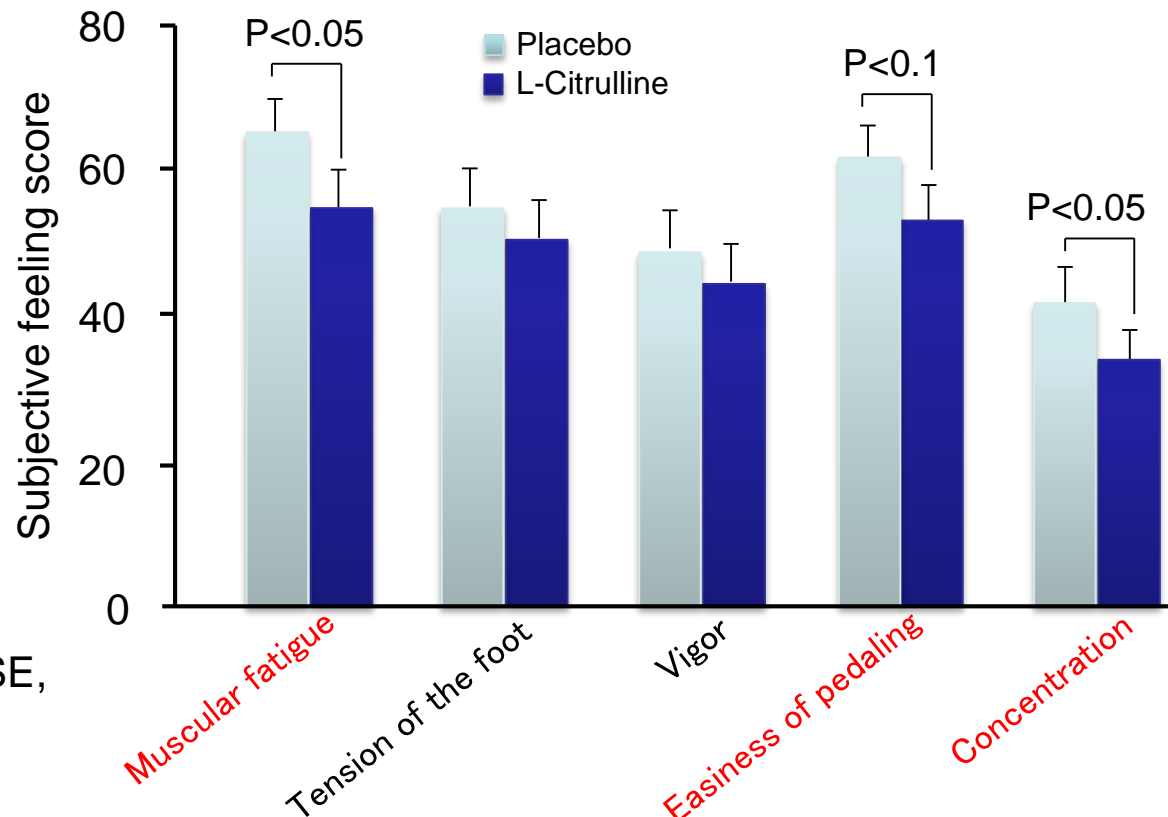


- Significantly reduced completion time compared with placebo
- A positive correlation between NOx levels and Oxygen utilization rate was observed

【Result 2】



Subjective feelings immediately after exercise(VAS)

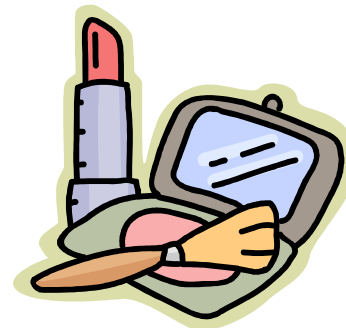
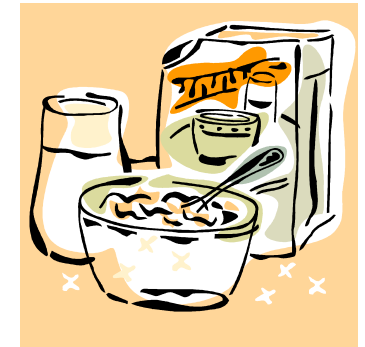
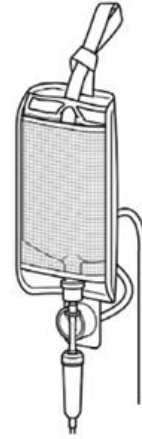


- Significant Increased mean power output compared with placebo
- VAS : Significant improved [Muscle fatigue][Cibcebration] and trend improved [Easiness of pedaling] compared with placebo

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- Infusion
- Medicine
- Medical Food
- Food & Beverages
- Flavor(s)
- Sports Nutrition
- Dietary Supplement
- Cosmetics & Toiletry
- Industrial, and etc.



Old Thinking - Treat Disease: Drugs

New Thinking - Prevent Disease: Diet

Given the future aging society,

The role of diet may increase even more

Thank you!



NOTE Intention

Although this document is based on academic data,
Please observe the relevant laws and regulations such as the Health
Promotion Law and the Pharmaceutical Affairs Law with regard to the
wording of amino acids used in consumer products presented here.

OMEGA 3

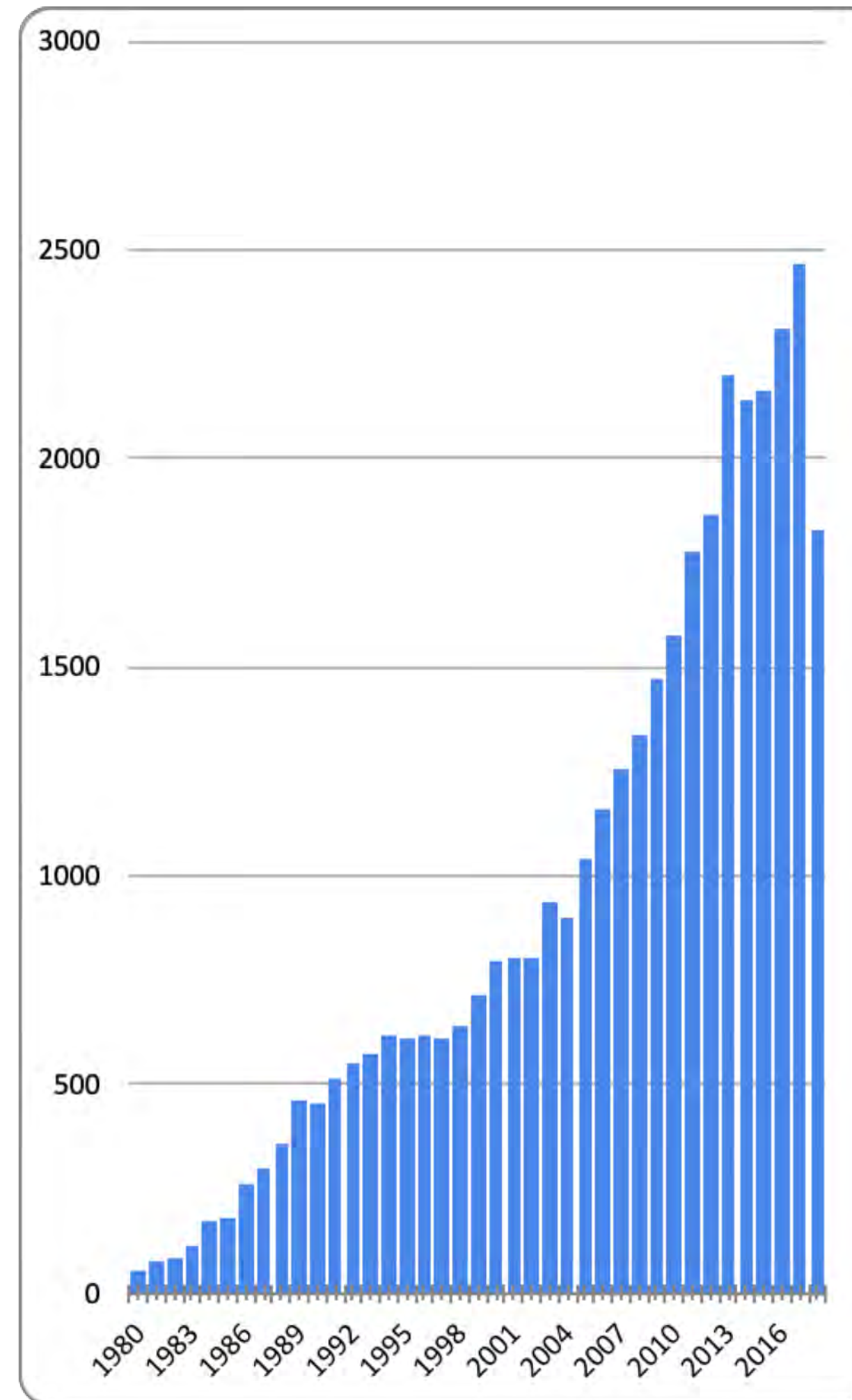


“The Heart of the Omega-3 Industry”

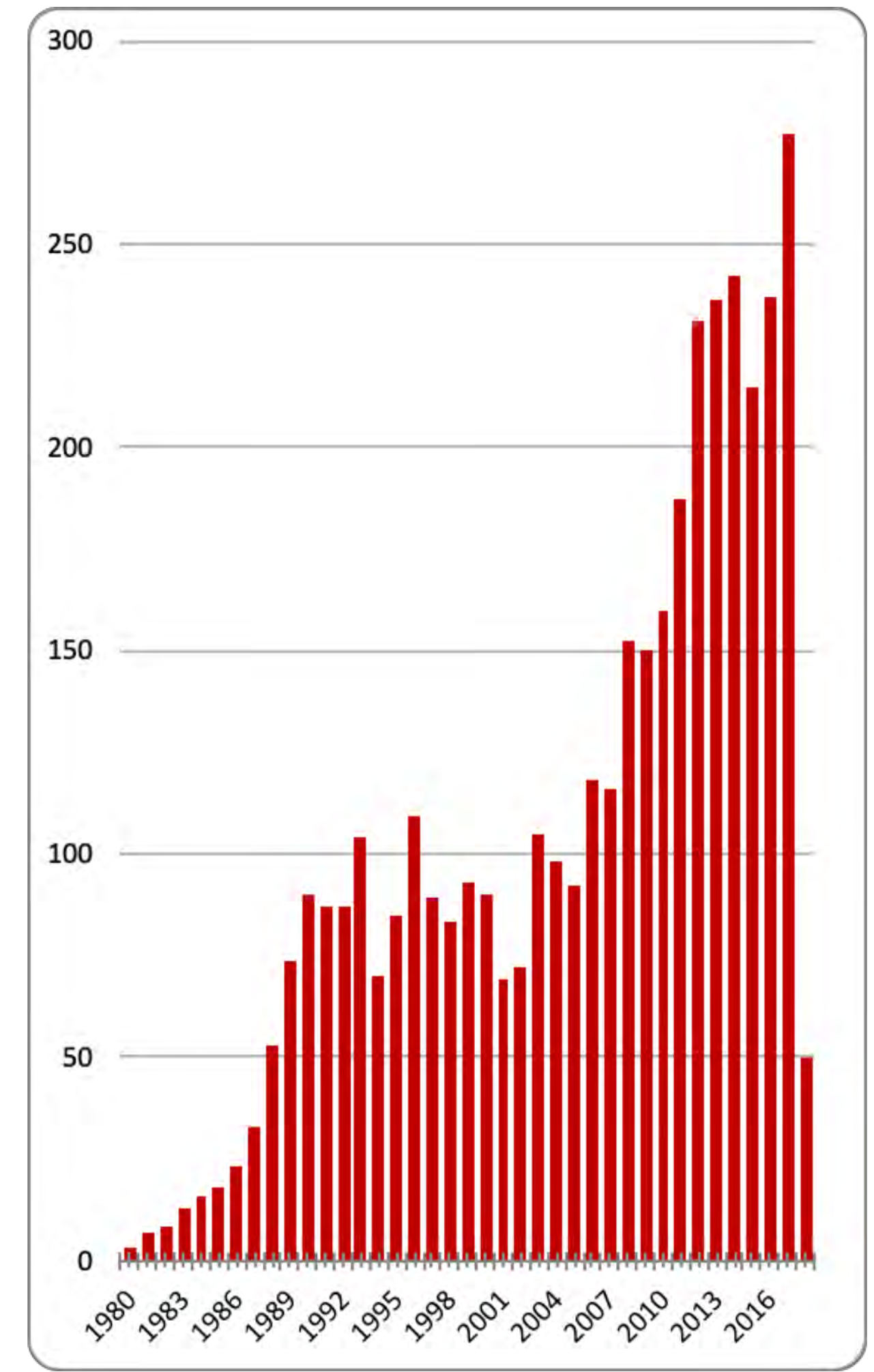
- 200 member companies throughout omega-3 supply chain
- Promote consumption of EPA and DHA globally
- Members adhere to quality standard as condition of membership

Describe the category in 1-3 words

- **Scientifically-based**
- Global (in terms of sources and markets)
- Confusing at the consumer level



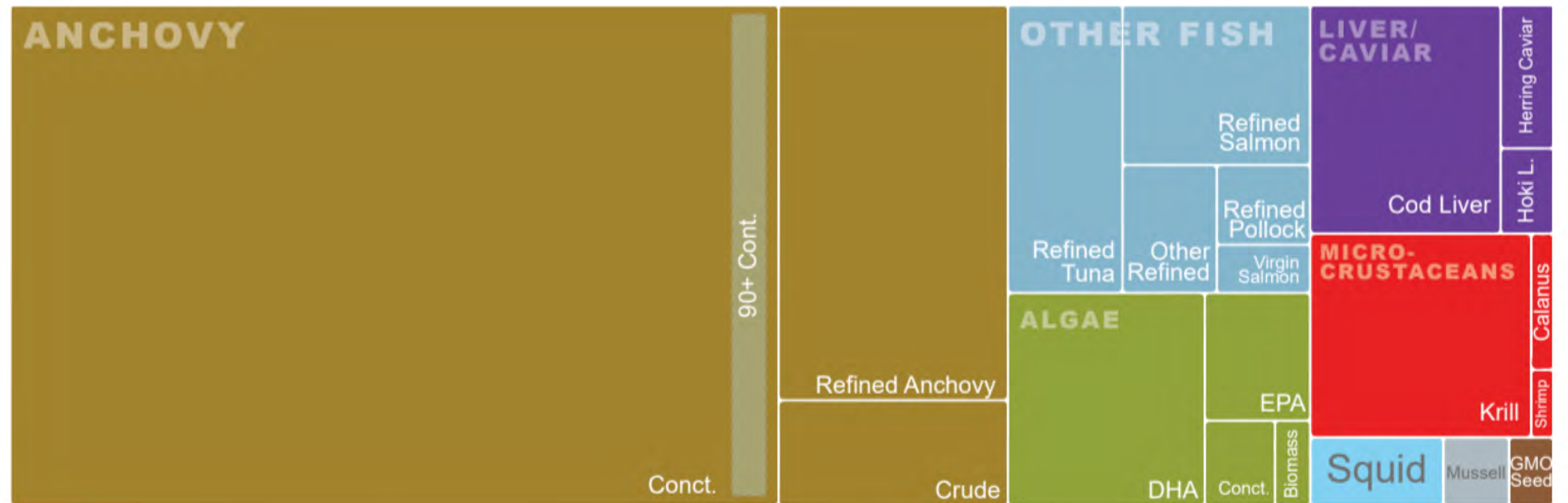
37,000 published papers



4000 clinical trials in humans

Describe the category in 1-3 words

- Scientifically-based
- **Global (in terms of sources and markets)**
- Confusing at the consumer level



GOED Member Product Sources in 2018, by Proportion

Describe the category in 1-3 words

- Scientifically-based
- Global (in terms of sources and markets)
- **Confusing at the consumer level**

US Media Headlines: VITAL Study

Fish Oil and Vitamin D Supplements May Not Help Prevent Heart Attacks and Cancer, Study Says

≡ TIME

Vitamin D and Fish Oils Are Ineffective for Preventing Cancer and Heart Disease

The New York Times

Health & Science
Fish-oil drugs protect heart health, two studies say

The Washington Post
Democracy Dies in Darkness

Vitamin D And Fish Oil Supplements Mostly Disappoint In Long-Awaited Research Results

n p r

Eating more fish or taking omega-3 fish oil supplements can cut heart attack risk, studies find

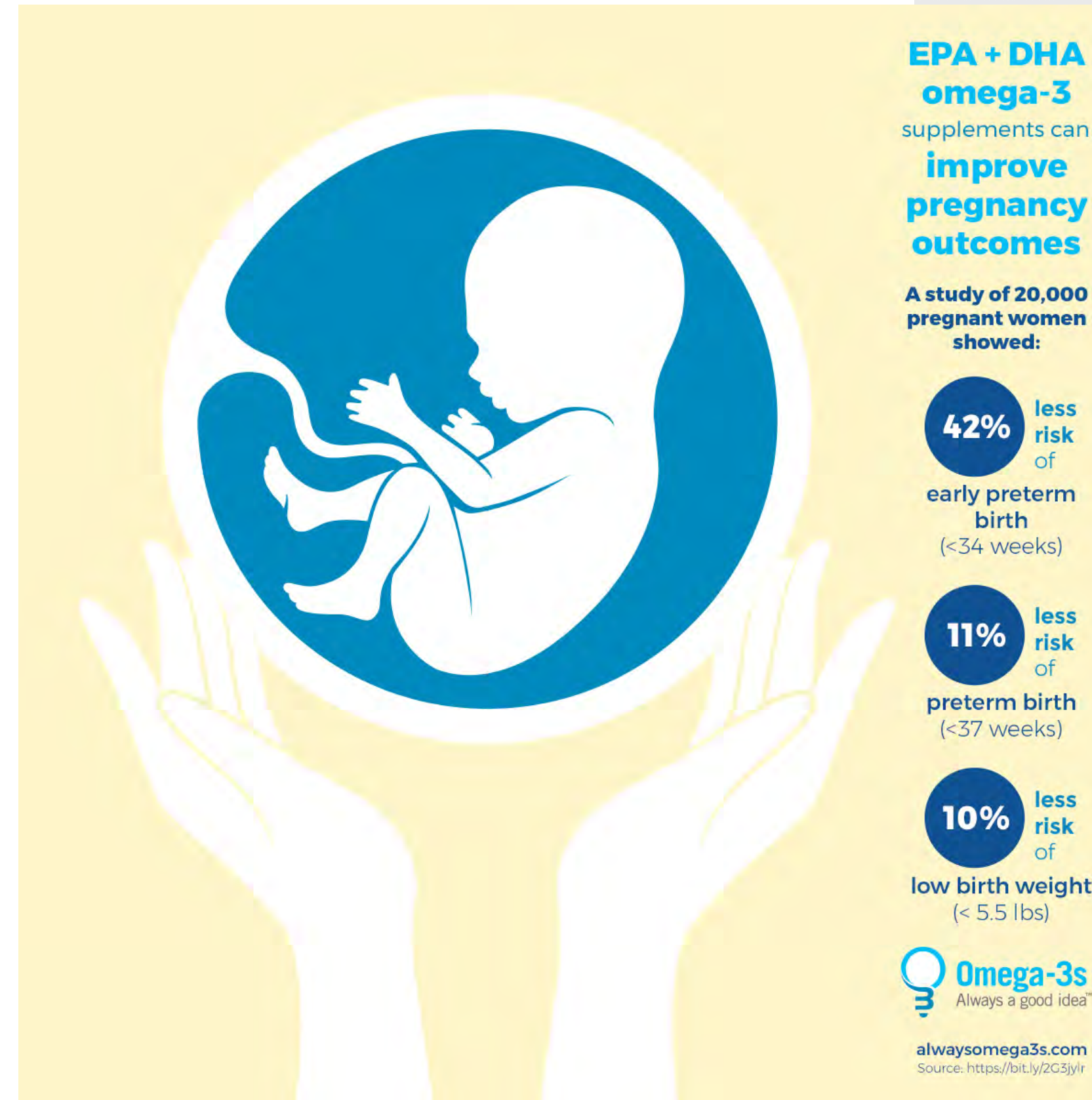
© CBS NEWS

Fish oil cuts heart attack risk, vitamin D lowers odds of cancer death

REUTERS

Developments in the past few years

- Evolution of the science
 - Three large-scale human clinical trials published last year
 - ASCEND, VITAL and REDUCE-IT
 - Solidified science around several cardiovascular outcomes
- Definitive paper on omega-3s reducing the risk of pre-term birth



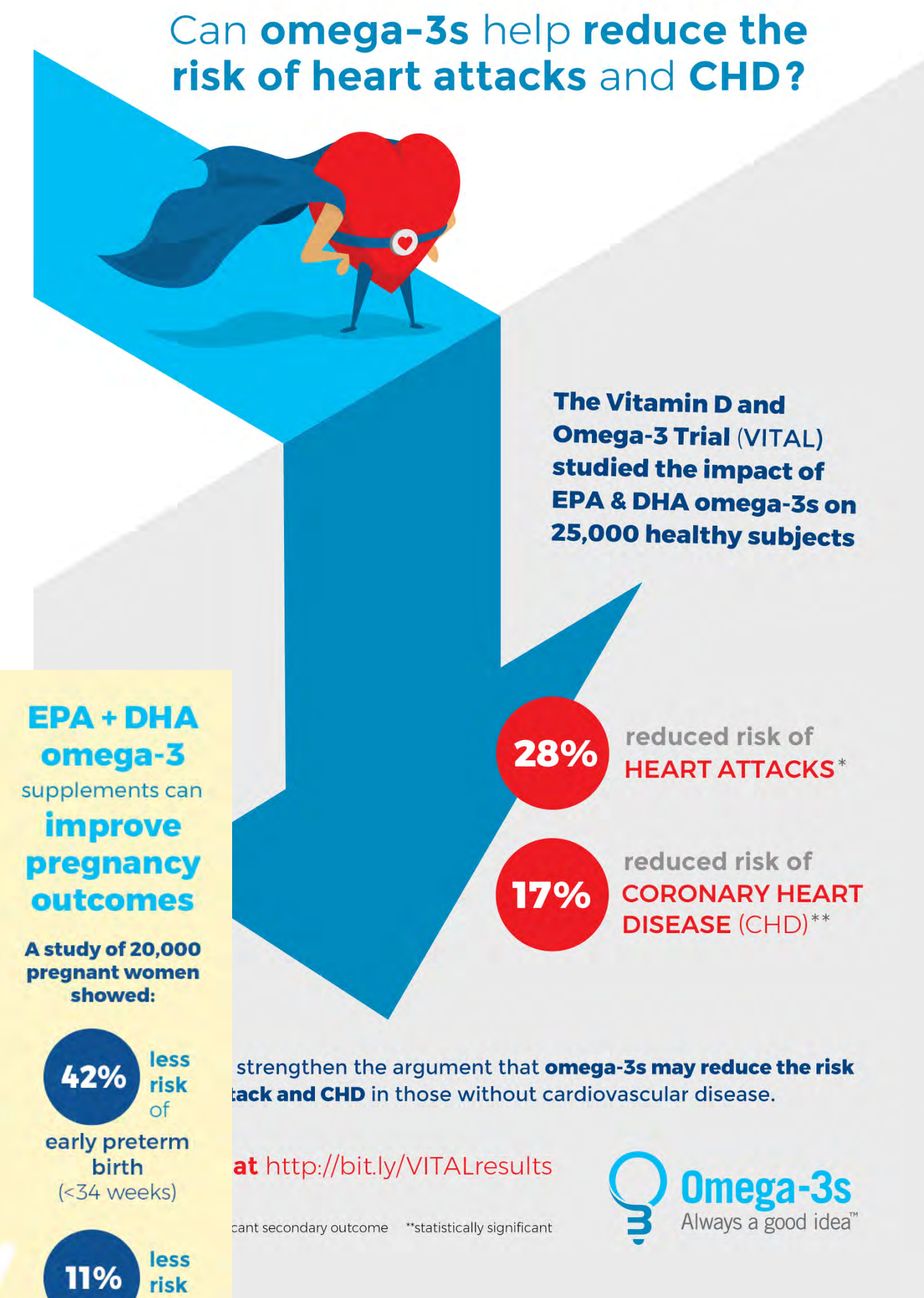
EPA + DHA omega-3 supplements can improve pregnancy outcomes

A study of 20,000 pregnant women showed:

- 42% less risk of early preterm birth (<34 weeks)
- 11% less risk of preterm birth (<37 weeks)
- 10% less risk of low birth weight (< 5.5 lbs)

Omega-3s
Always a good idea™

alwaysomega3s.com
Source: <https://bit.ly/2G3jYlr>



Can **omega-3s** help reduce the risk of heart attacks and **CHD**?

The **Vitamin D and Omega-3 Trial (VITAL)** studied the impact of EPA & DHA omega-3s on 25,000 healthy subjects

- 28% reduced risk of **HEART ATTACKS***
- 17% reduced risk of **CORONARY HEART DISEASE (CHD)****

strengthen the argument that **omega-3s may reduce the risk of heart attack and CHD** in those without cardiovascular disease.

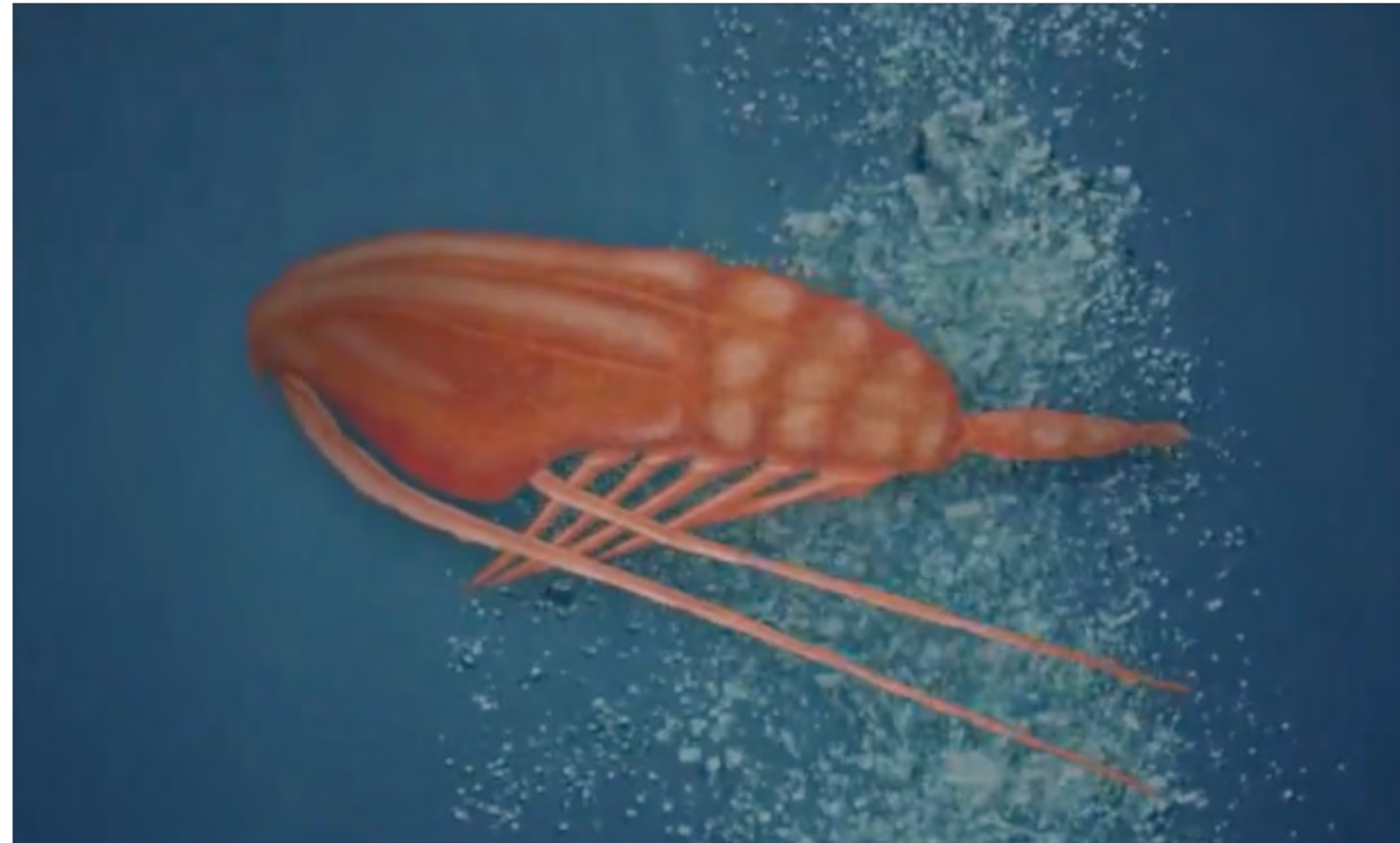
at <http://bit.ly/VITALresults>

†non-significant secondary outcome **statistically significant

Omega-3s
Always a good idea™

Developments in the past few years

- Evolution of product sources and forms



What are three major barriers?

- Resistance at the Codex level for an NRV, as well as no recommended intakes in US and Canada
- Negative consumer media headlines around neutral science
- Design of scientific studies not supportive of positive outcomes
 - Not taking into consideration pharmaceutical interventions
 - No measurement of baseline omega-3 levels
 - Study not significantly powered to achieve stated result

Is the category recognized in policy?

Depends on the geography

- No DRI in US, Canada
- Recommended intakes from many individual scientific bodies or government organizations
- No Codex NRV

- Retracted intake in some areas
 - I.e., Japan eliminated recommendation for EPA/DHA intake for cardiovascular health

Are there initiatives to promote the category?



研究显示，DHA
还对人生命后期的记忆力和认知有积极的影响

Share our omega-3 infographics

Learn why omega-3s are so important for you and your friends.



Tweet This
Share on twitter.
Click to tweet »

Omega-3s and Heart Health

YOU NEED MORE OMEGA-3S

EPA & DHA are the most important omega-3s in your diet.

YOU SHOULD KNOW:

In the United States, men only get 50% and women only get 40% of the omega-3s they need daily.

YOU SHOULD CARE BECAUSE:

EPA & DHA omega-3s have been shown to support normal triglyceride and blood pressure, and they may also reduce the risk of cardiovascular disease.

HOW THEY HELP YOUR HEART:

EPA & DHA omega-3s have been shown to support normal triglyceride and blood pressure, and they may also reduce the risk of cardiovascular disease.

There are more than 37,000 published studies on omega-3s, making them some of the most studied nutrients in the world.

EPA & DHA are the most important omega-3s in your diet - and you can get them from a variety of sources, including seafood, fortified foods, and dietary supplements.

Omega-3s and CHD

EPA AND DHA OMEGA-3S MAY LOWER YOUR RISK OF CORONARY HEART DISEASE

Coronary Heart Disease (CHD) kills **370,000+** people in the U.S. each year and **7 million+** worldwide.

Studies show that getting enough EPA and DHA omega-3s can benefit heart health. EPA and DHA can help maintain:

- Healthy triglyceride levels
- Healthy blood pressure

A recent study published in *Mayo Clinic Proceedings* found that EPA and DHA consumption may reduce the risk of CHD, particularly in higher risk populations.

- 16%** in those with high triglycerides
- 14%** in those with high LDL cholesterol

Expert global scientific organizations recommend **250-500mg** of EPA and DHA per day for adults.

- There are 3 ways to add more EPA and DHA to your diet.
- Eat fatty fish, like salmon, tuna or sardines.
- Take an omega-3 supplement.
- Consume foods fortified with EPA and DHA.

Explore by condition



Heart Health



Brain Health



Eye Health



Are you getting enough omega-3s?

Omega-3s and Brain Health

YOUR BRAIN NEEDS OMEGA-3S

Your brain needs omega-3s throughout your life.

EPA & DHA omega-3s are the most important omega-3 fatty acids in the diet to support brain health.

Consumption of fatty fish per week or a 3-fatty supplement can literally "light" up the brain.

EPA & DHA omega-3s are the most important omega-3 fatty acids in the diet to support brain health.

Consumption of fatty fish per week or a 3-fatty supplement can literally "light" up the brain.

Omega-3s and Eye Health

nutrition FOR EYE HEALTH

3 EYE HEALTH stats

- 88%** of Americans do not get enough omega-3 fatty acids to support eye health.
- 14%** of Americans do not get enough omega-3 fatty acids to support eye health.
- 78%** of Americans do not get enough omega-3 fatty acids to support eye health.

3 COMMON myths + facts

omega 3s FOR EYE HEALTH

Research shows that consuming EPA and DHA omega-3s may help support eye health.

Most health professionals recommend adults get Omega-3s from EPA and DHA sources for general health and wellbeing. There are three ways to get enough Omega-3s: Eat fatty fish, like salmon or sardines. Take an omega-3 supplement. Consume foods fortified with EPA and DHA.

RESEARCH-BACKED REASONS TO RECOMMEND OMEGA-3S

EPA and DHA omega-3s are backed by decades of research showcasing their benefits for the heart, brain, eye, and prenatal health. Omega-3s aren't just beneficial - they're vitally important for every cell in the body. This site provides important information you need to educate your patients about the benefits of EPA and DHA omega-3s.



Heart



Brain



Eye

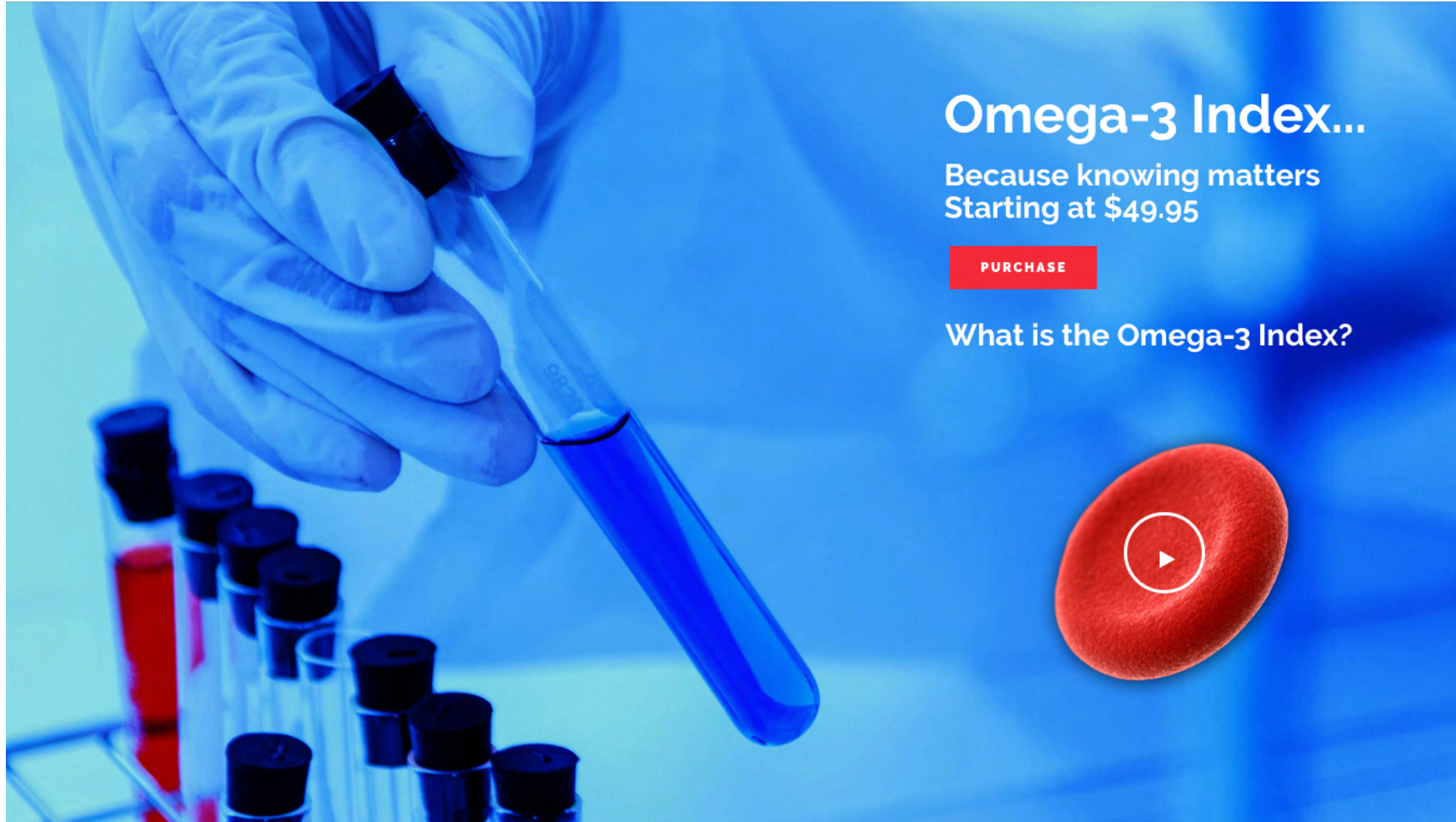


Prenatal and Infant

For consumers: alwaysoomega3s.com
For practitioners: fatsoflife.com



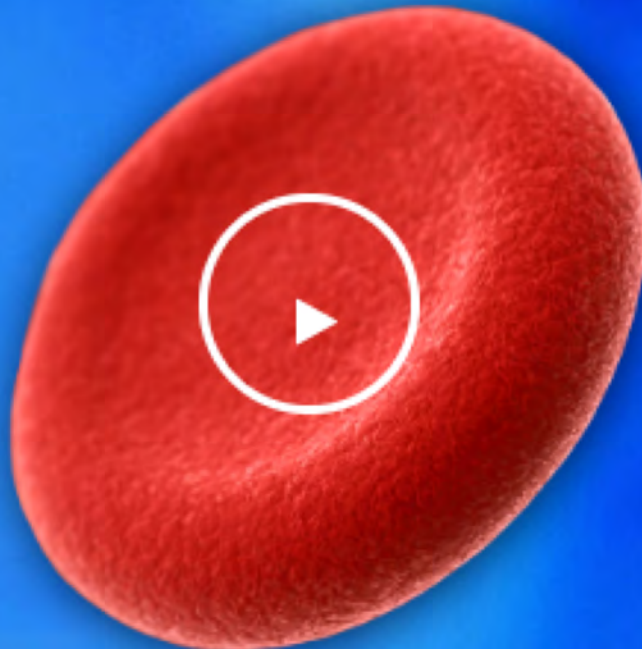
Are there initiatives to promote the category?



Omega-3 Index...
Because knowing matters
Starting at \$49.95

[PURCHASE](#)

What is the Omega-3 Index?



How is the market evolving?

- **New developments in sources (algae, calanus, green shelled mussel)**
- New product forms (gummies, fish oil/olive oil combination)
- Rapid growth in China and Asia Pacific region



How is the market evolving?

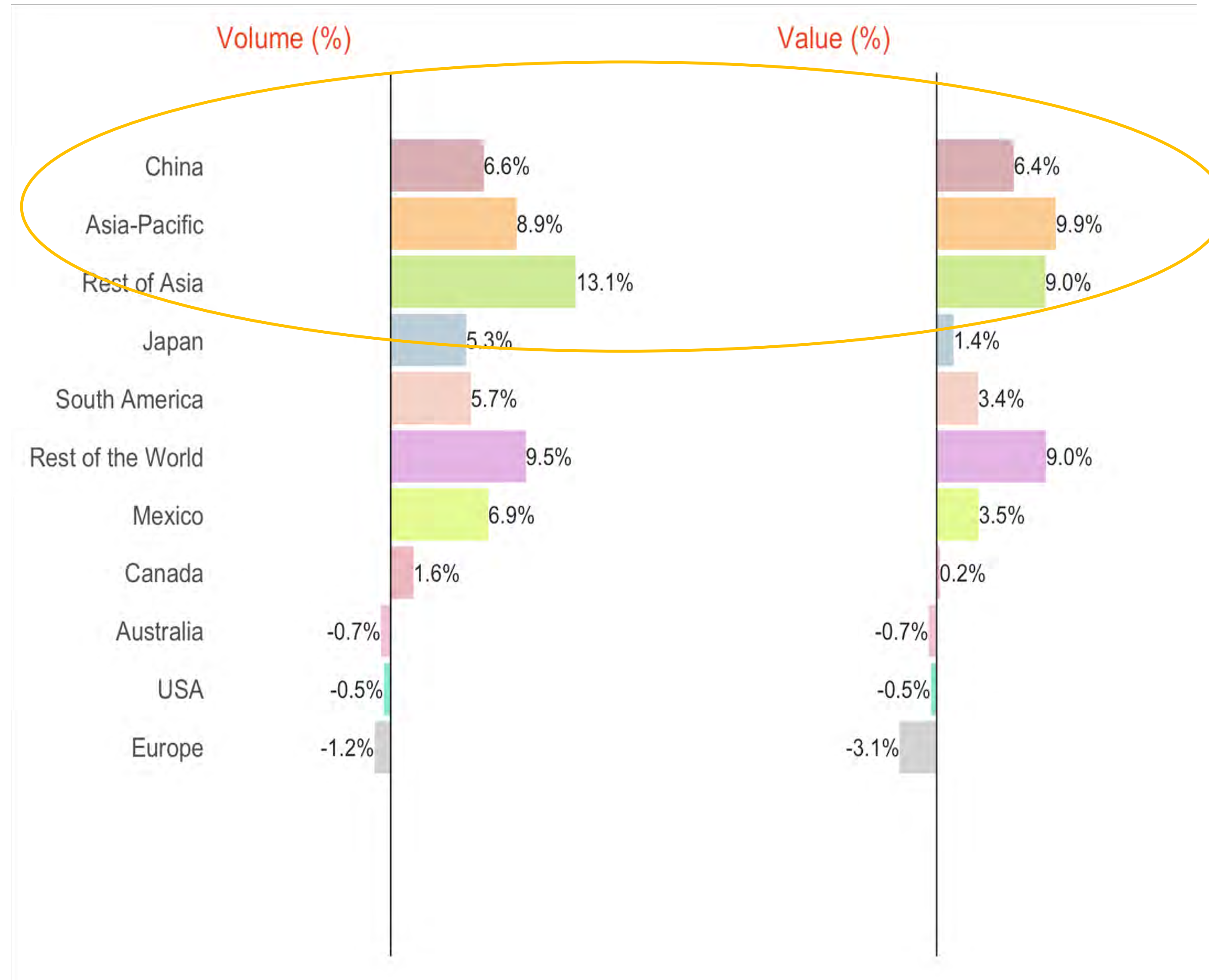
- New developments in sources (algae, calanus, green shelled mussel)
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- Rapid growth in China and Asia Pacific region



How is the market evolving?

- New developments in sources (algae, calanus, green shelled mussel)
- New product forms (gummies, fish oil/olive oil combination)
- **Rapid growth in China and Asia Pacific region**

Growth Rates by Percent Change from 2016 to 2017



Science: what are the game changers?

STUDY	DATE PUBLISHED	OUTCOME
Cochrane Review	July 2018	Negative
ASCEND	August 2018	Mixed
VITAL	November 2018	Mixed but more positive than expected
REDUCE-IT	November 2018	Positive

Take home message:

The science is much better than what you read in the popular press.

VITAMINS & MINERALS

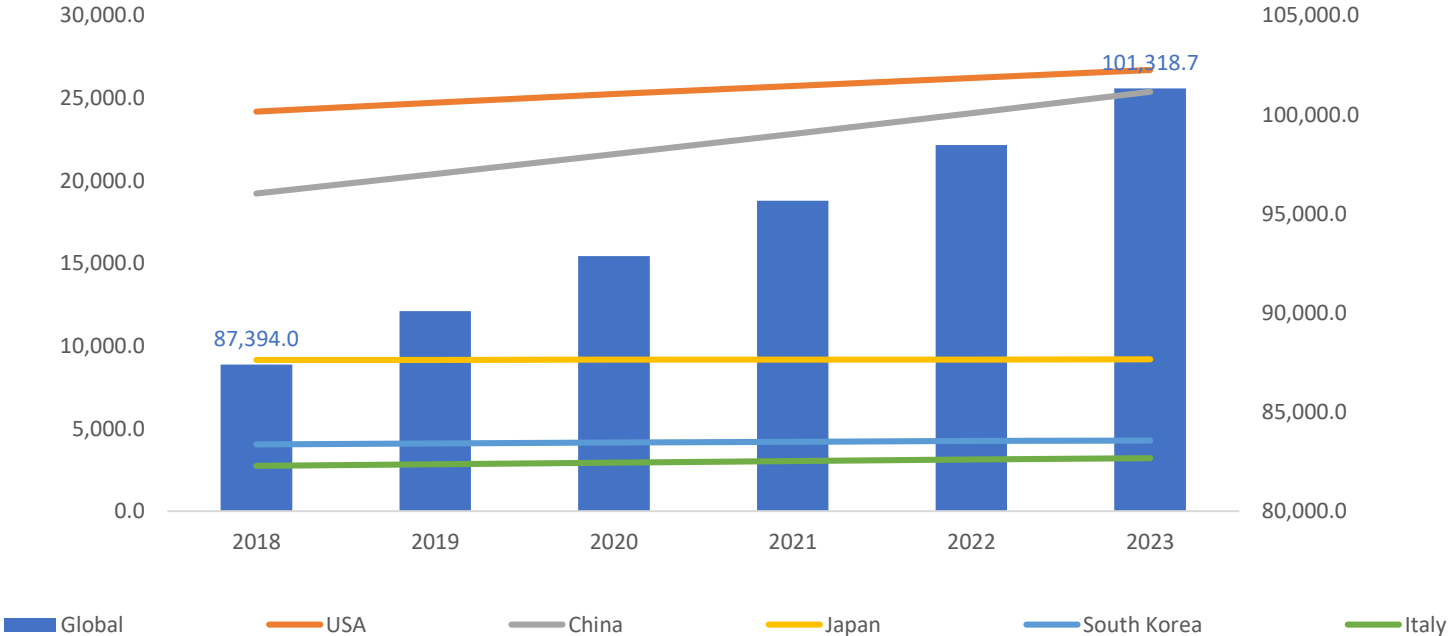
Dietary Supplements A Vitamin & Mineral perspective

***Consumer insight-driven solutions
Inspiring people to better he***

**Gerhard Gans,
DSM, VP RA/QM**

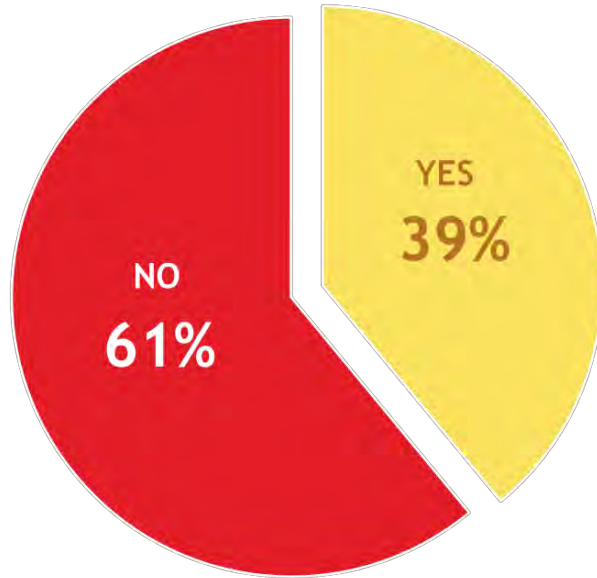


Global VDS Market Size



Such a simple solution, yet...

Q. Do you currently take dietary supplements? *



There are two overarching Themes



MORE ENGAGING

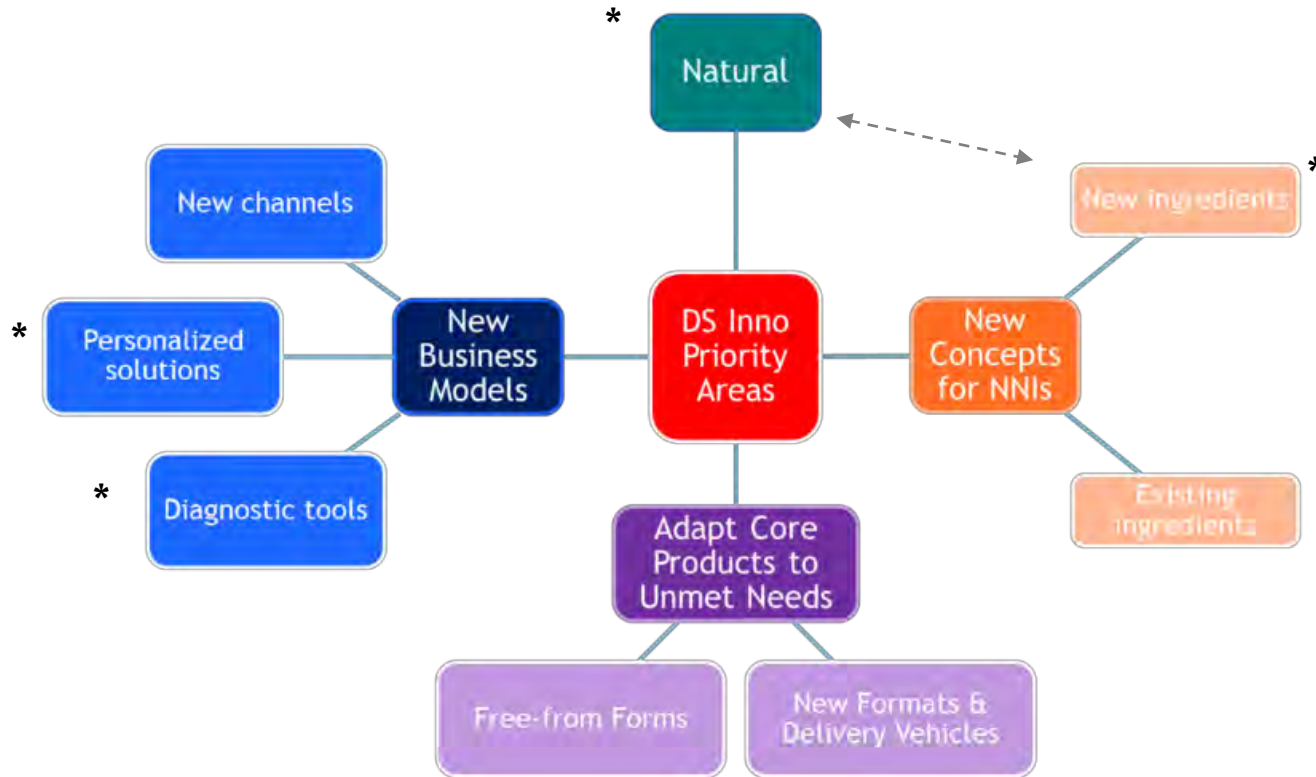
How can new science and technology create contact points to the consumer



THE RIGHT SUPPLEMENTS

What attributes of an ingredient can make a difference in the consumer's perception

INNOVATION FOR THE FUTURE – FOCUS AREAS





MORE ENGAGING

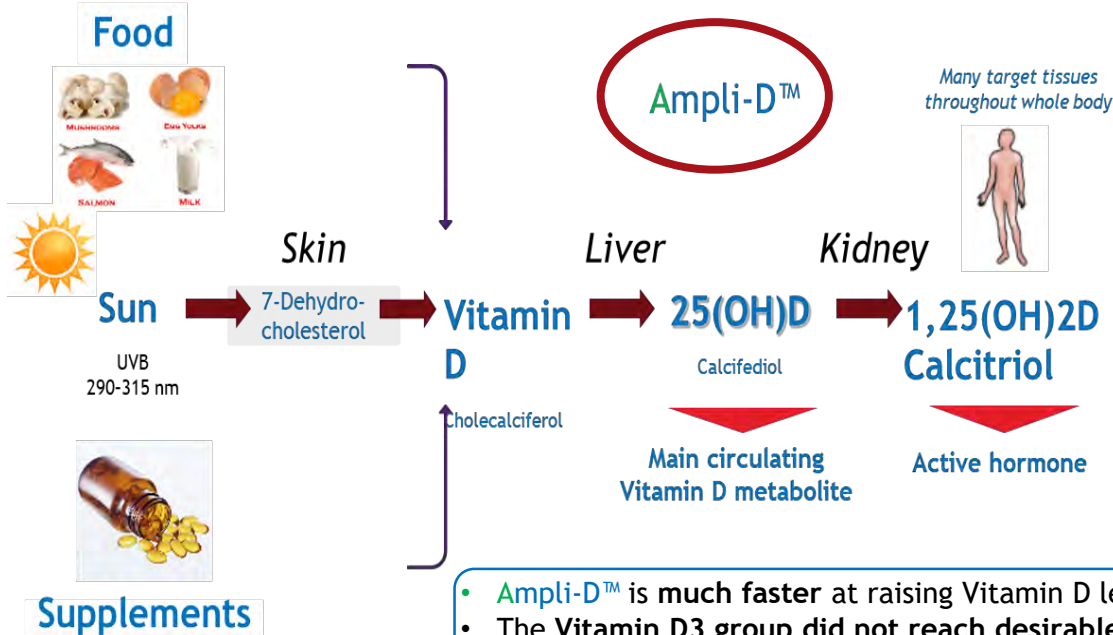
*Measuring your
personal nutrient status*



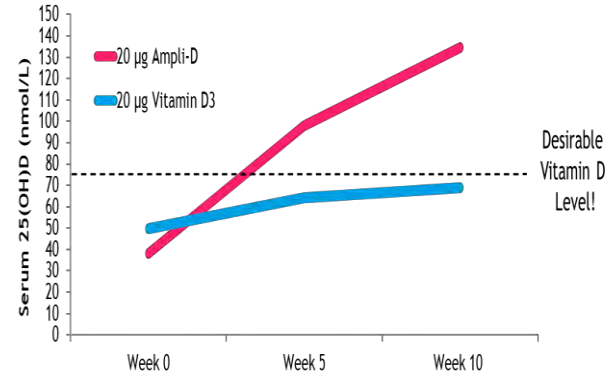


THE RIGHT SUPPLEMENTS

Example: Introducing Ampli-D™ The Naturally Active Form of Vitamin D!



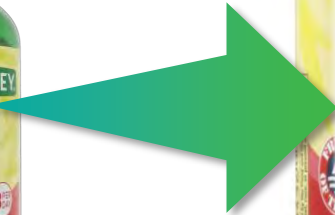
Ampli-D™ 10-Week Bioequivalence Study: Randomized, Double-Blind, Placebo-Controlled Trial



- **Ampli-D™ is much faster at raising Vitamin D levels than Vitamin D!**
- **The Vitamin D3 group did not reach desirable Vit. D blood level, even with 20mcg over 10 weeks**
- **The Ampli-D group easily reach the desired levels in about 3 weeks!**



THE RIGHT SUPPLEMENTS



Conclusions

DS is a growing consumer segment

New science can provide new talking points for the consumer

New analytical techniques (non-invasive spot testing or big data analysis) will create new consumer needs

“side factors” like sustainability will create differentiation and fulfill specific customer expectations



**KEEP
CALM**

AND

**TAKE YOUR
SUPPLEMENTS**

