

#PeptideWC2022

MITOPHOGY AS A KEY LONGEVITY PATHWAY

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After graduating with a B.S. in biology from Binghamton University, Jen completed her dietetic internship at New York-Presbyterian Weill Cornell Medical Center and received her master's degree in Integrative and Functional Nutrition at Saybrook University.

Jen runs a holistic nutrition practice outside of New York City where she works with individuals on expanding health span and optimizing health.



Disclosure: Paid Consultant for Amazentis



Timeline Nutrition started with a simple question about the nature of cellular health



The investigation was conducted at our home lab on the campus of the Swiss Institute of Technology (EPFL)



Our findings were quite remarkable and create a new opportunity for those interested in optimizing health and promoting longevity

Our goal is to target biological pathways that prolong healthspan



Healthspan

The duration of life during which one is in good health

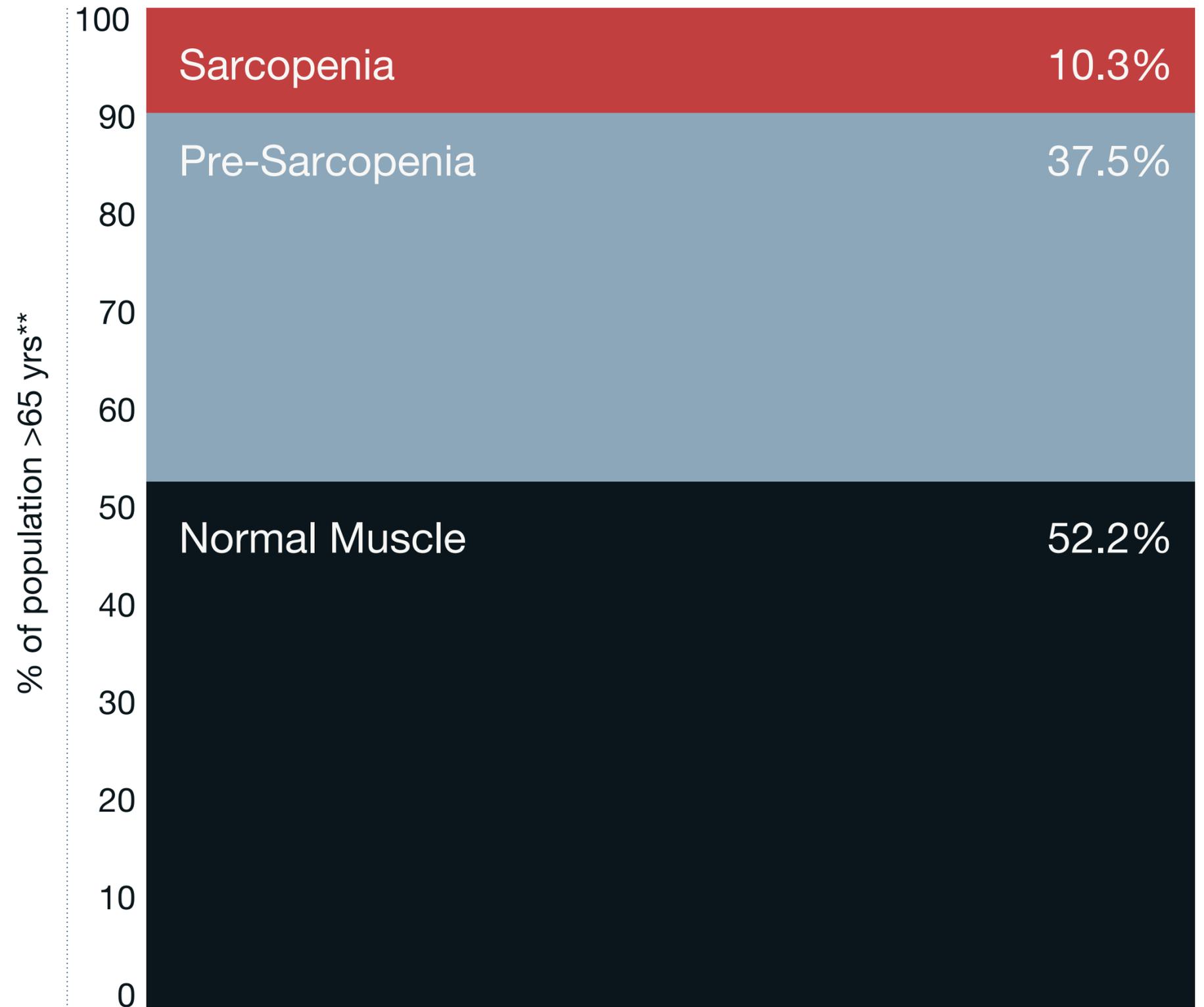
Lifespan

The duration of one's life

Age-related decline in muscle function: a tremendous unmet need

There are 56 million people 65 years and older in the US alone

Worldwide, there will be 1 billion people over 65 years old by 2030



*JAGS Vol 52, 80-85, 2004

**US Census 2014 est. in 2020

Muscle aging starts in our 30s

Hand grip strength (for e.g.) declines 10% every decade

Early intervention strategies are needed

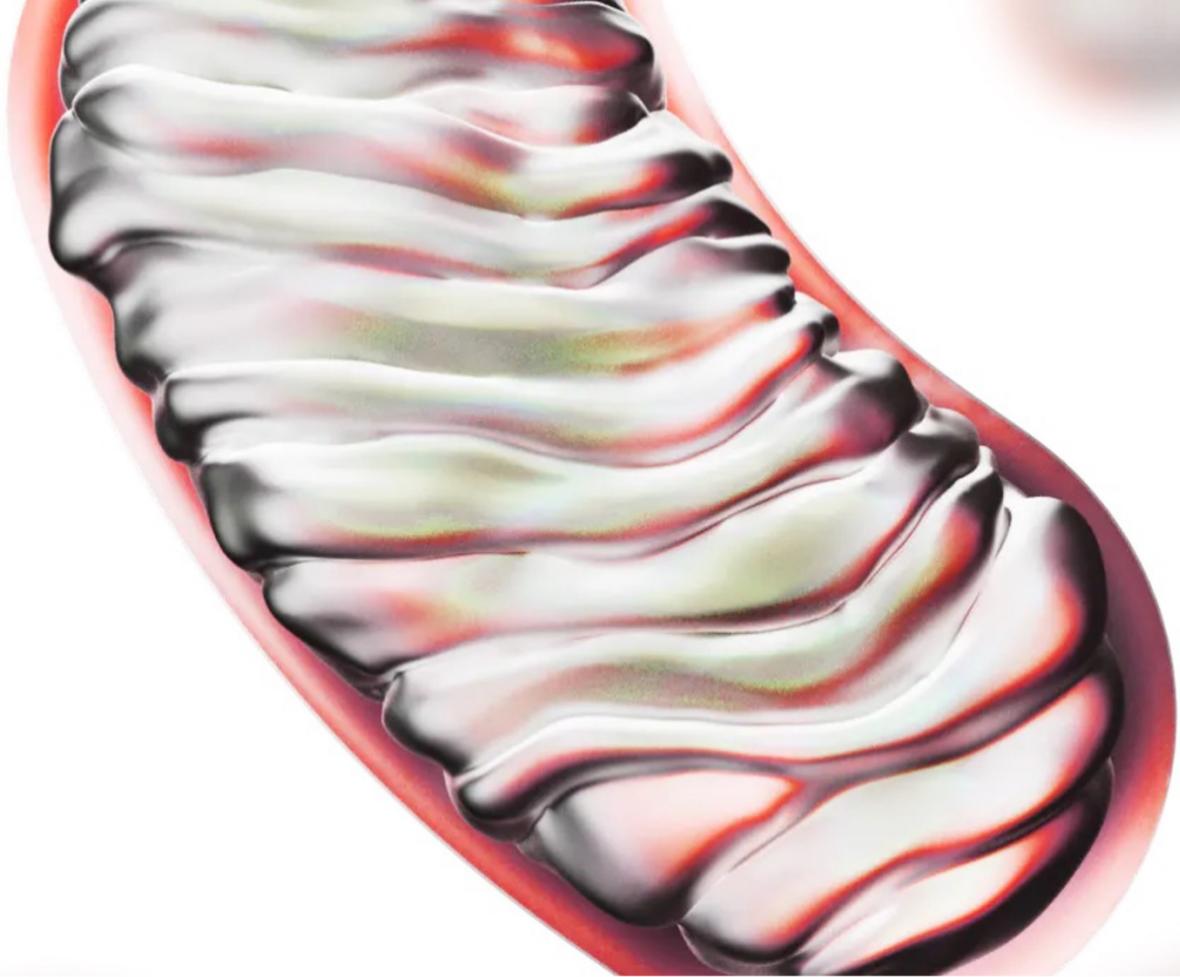


Mitochondria are the bedrock of good health

Healthy cells rely on healthy mitochondria. Their optimal function is essential particularly in heart, kidney, eye, brain and muscle function.

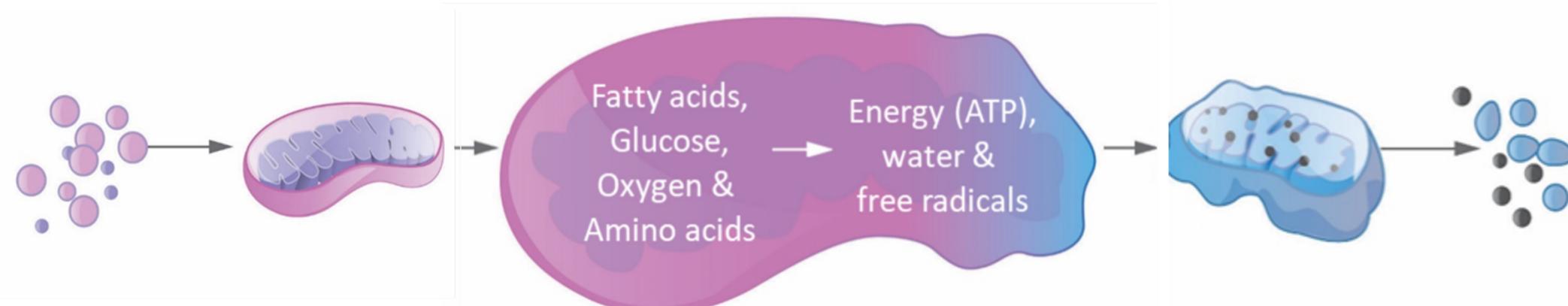
Our clinical research to date has focused on muscle health as muscle cells have a high concentration of mitochondria.





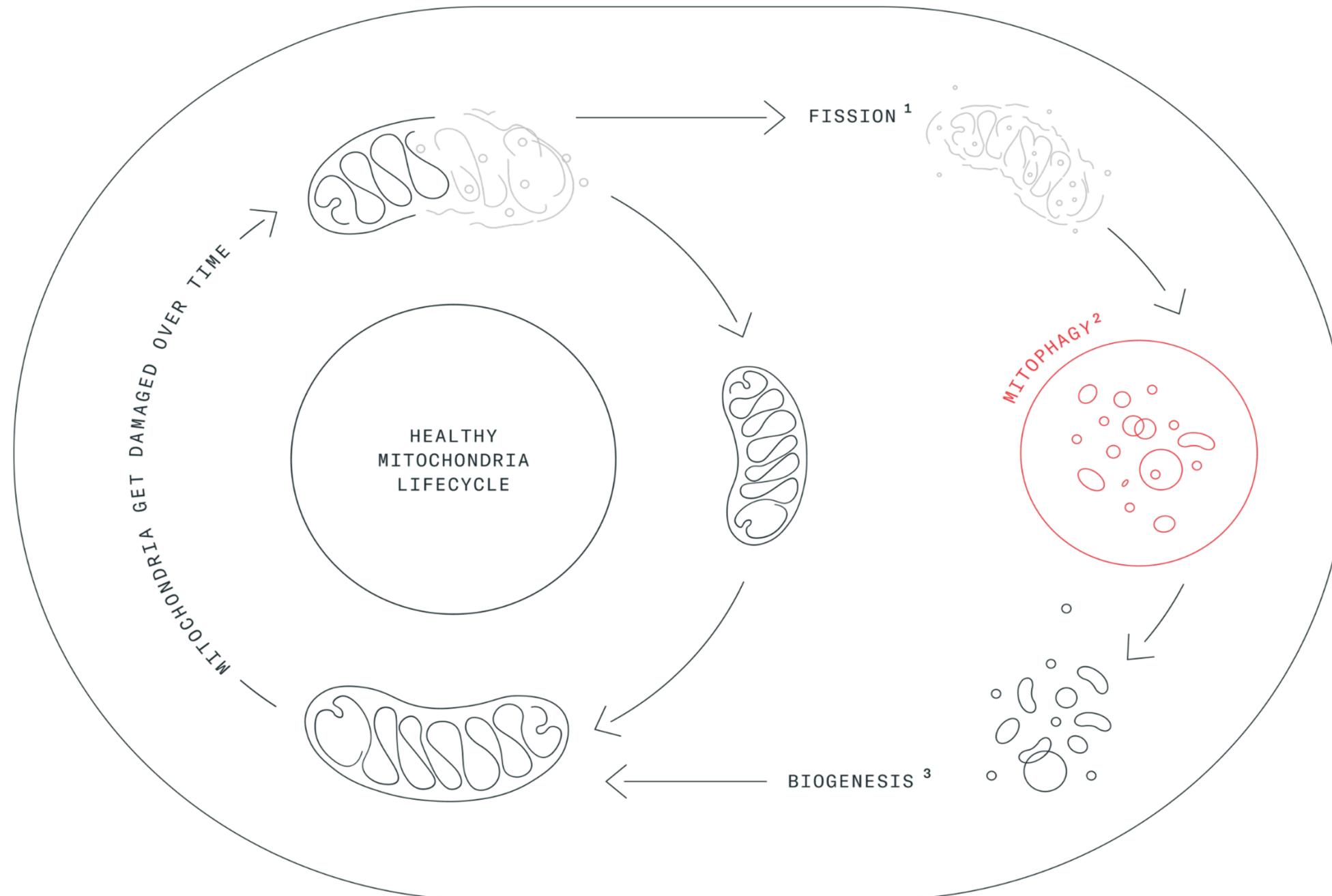
Mitochondrial damage and decline are a hallmark of aging

Activation of mitochondrial anti-aging pathway



	Biogenesis	Energy Production	Mitophagy
Pathways to Target	Creation of new mitochondria	Optimal functioning of mature mitochondria	Clearance of damaged mitochondria
Nutrition Based Bioactives	Resveratrol Urolithin A NAD+ supplementation (Vit. B3, NR, NMN)	CoQ10 L-Carnitine Creatine	Urolithin A

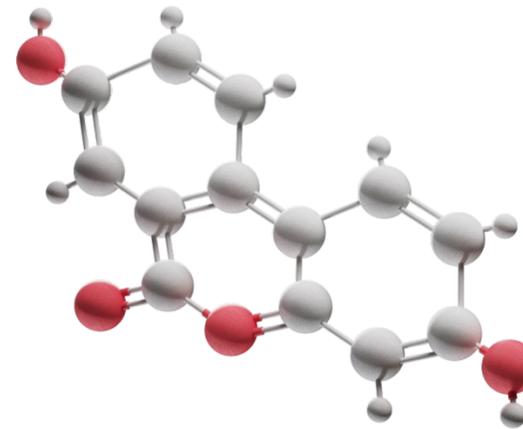
Targeting Mitophagy to Improve Mitochondrial Function



Mitophagy
The biological pathway activated with regular exercise and intermittent fasting

Urolithin A:

A naturally-occurring postbiotic produced by gut microflora



Ellagitannins

Pomegranates, berries & nuts are rich sources of compounds known as ellagitannins, a precursor to Urolithin A

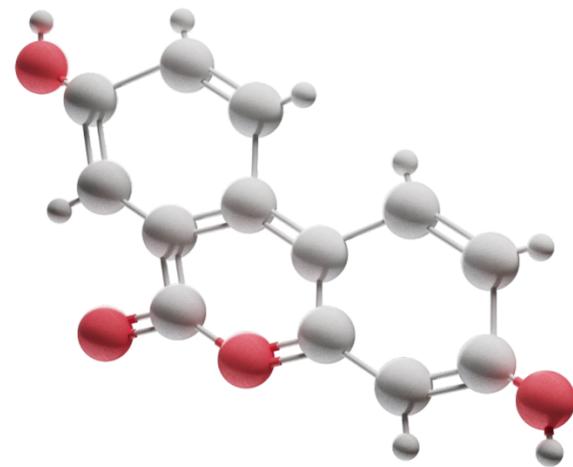
Gut transforms Ellagitannins to Urolithin A

Ellagitannins are transformed by the gut microbiome into metabolites, including Urolithins. Only 30-40% people produce Urolithin A and at variable quantities.

Triggers Mitophagy

This is the process by which dysfunctional mitochondria are recycled and repackaged into new, healthy mitochondria.

Building on a decade of work on mitophagy modulation



Timeline focuses on the discovery of natural compounds that boost mitophagy.



Urolithin A

Shown to extend lifespans in worms by 45%



Shown to improve endurance in aged mice by 57%



Shown to significantly improve mitochondrial health and muscle strength vs placebo and endurance in human clinical trials

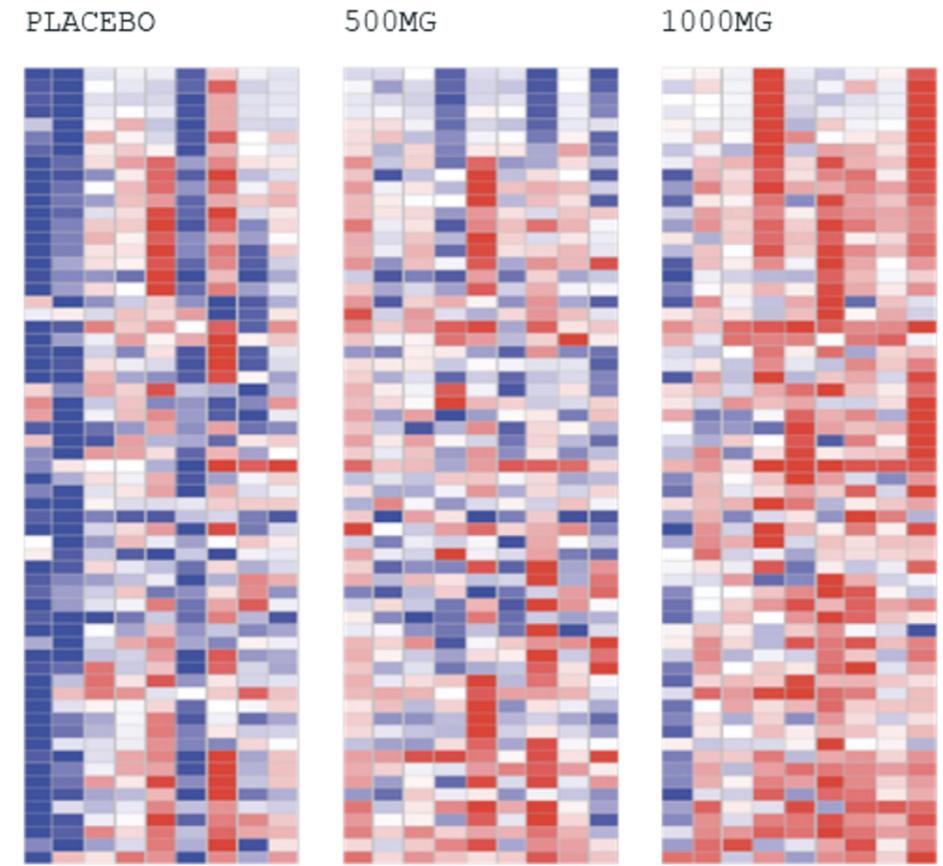


Timeline commercializes Urolithin A as a postbiotic

RCT Trial 1: Mitopure was safe and statistically improved mitochondrial health in skeletal muscles in older adults
Muscle biopsies compared before and after 4-weeks Mitopure or Placebo

Mitopure induced mitochondrial gene expression similar to aerobic exercise regimens

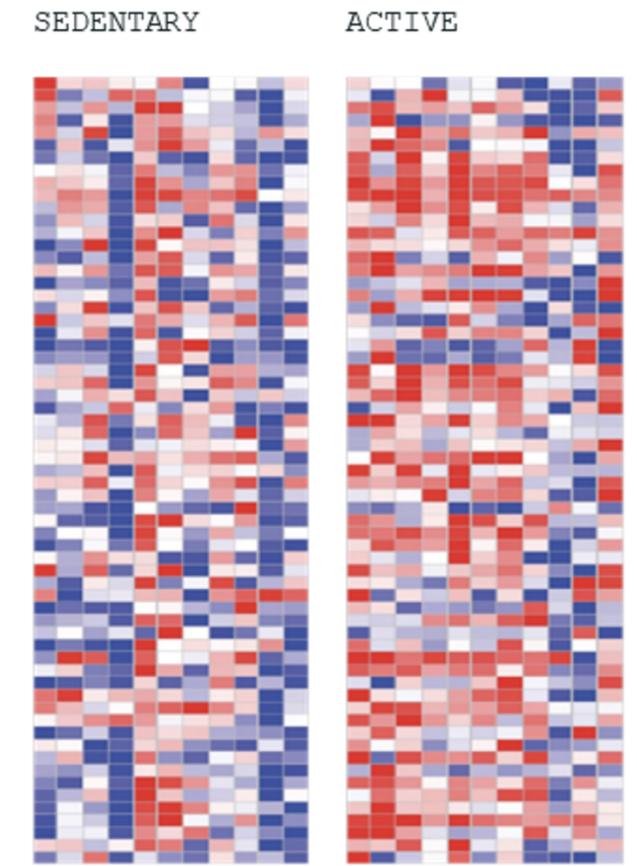
AMAZENTIS PHASE 1
28 DAYS OF TREATMENT WITH MITOPURE™



MIN

MAX

AMAZENTIS
NON-INTERVENTIONAL STUDY



Heatmap represents the genes that are the most significantly changed by the treatment within the GO_MITOCHONDRION genset

nature metabolism 2019

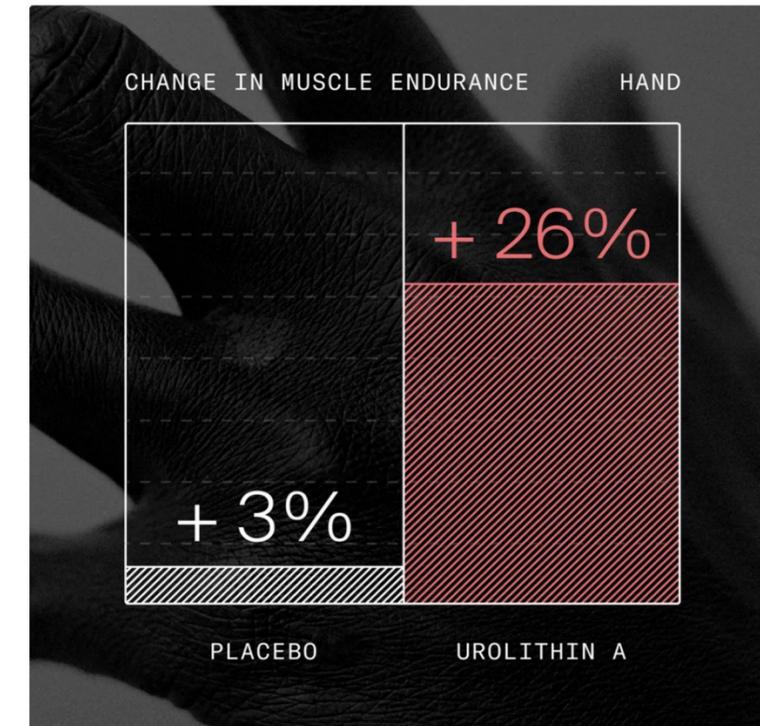
RCT Trial 2: Mitopure statistically improved muscle endurance in older adults

Change from baseline to 2 months
Published in *JAMA Network Open*

Mitopure can increase muscle endurance by upto 17% (leg) and 26% (hand) after 8 weeks*

Isometric testing evaluated time to fatigue (muscle endurance) in hand and leg muscles

Compared to placebo group: 1000mg Mitopure dose improved muscle endurance in a statistically significant manner at 2-months

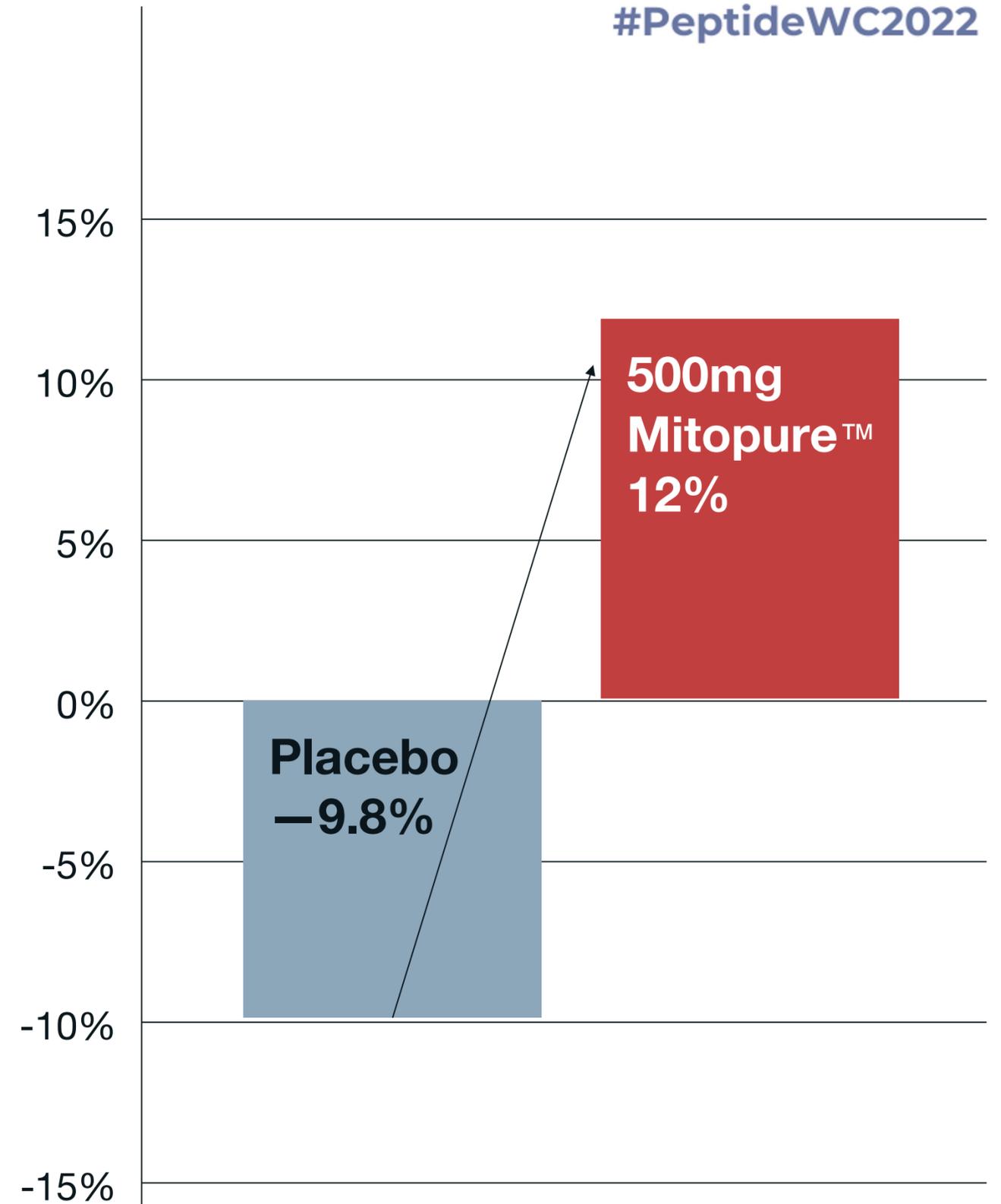


RCT Trial 3: Mitopure statistically improved isokinetic muscle strength in hamstrings in middle-aged adults
Isokinetic muscle strength (peak torque): Change from baseline to 4 months

Mitopure can increase muscle strength by upto 21% after 16 weeks*

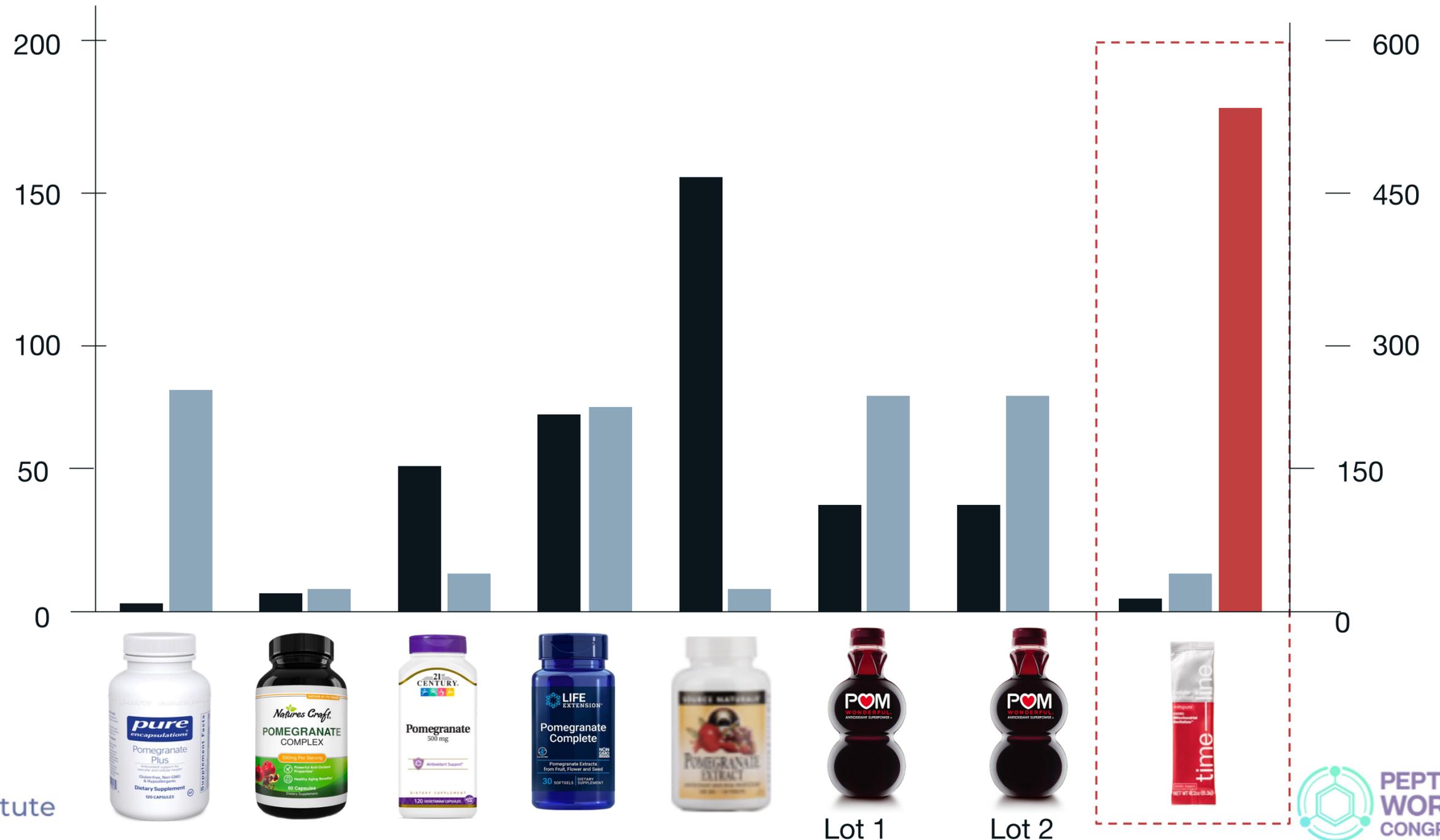
Isokinetic strength testing evaluates lower body muscle core strength

Compared to placebo group: both 500mg and 1g UA doses improved hamstring muscle isokinetic strength in a statistically significant manner



Only product with Mitopure produced detectable levels of Urolithin A

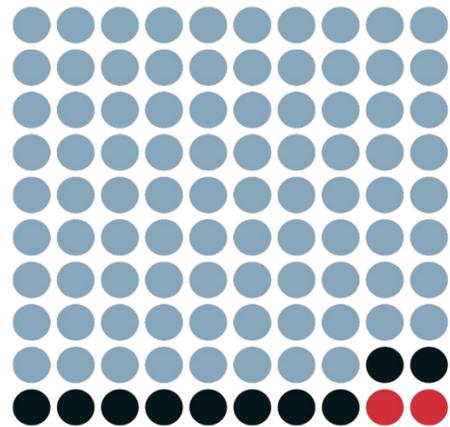
- Ellagic Acid (mg)
- Punicalagins (mg)
- Urolithin A (mg)



Mitopure delivers 6x more Urolithin A than 8 oz pomegranate juice

Baseline Free-living levels

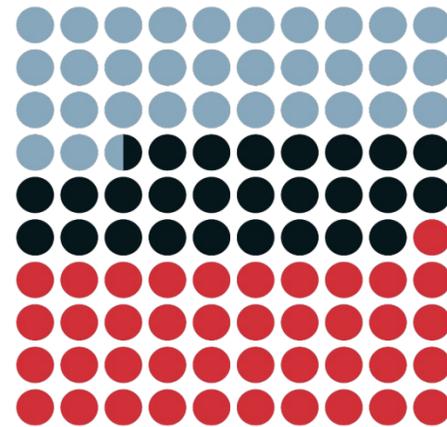
T0 Baseline Total = 100



- 87.8% | No UA producer (<5ng/ml)
- 10.2% | Low UA producer (5-99ng/ml)
- 2% | High UA producer (≥100ng/ml)

24h after Pom. Juice intake

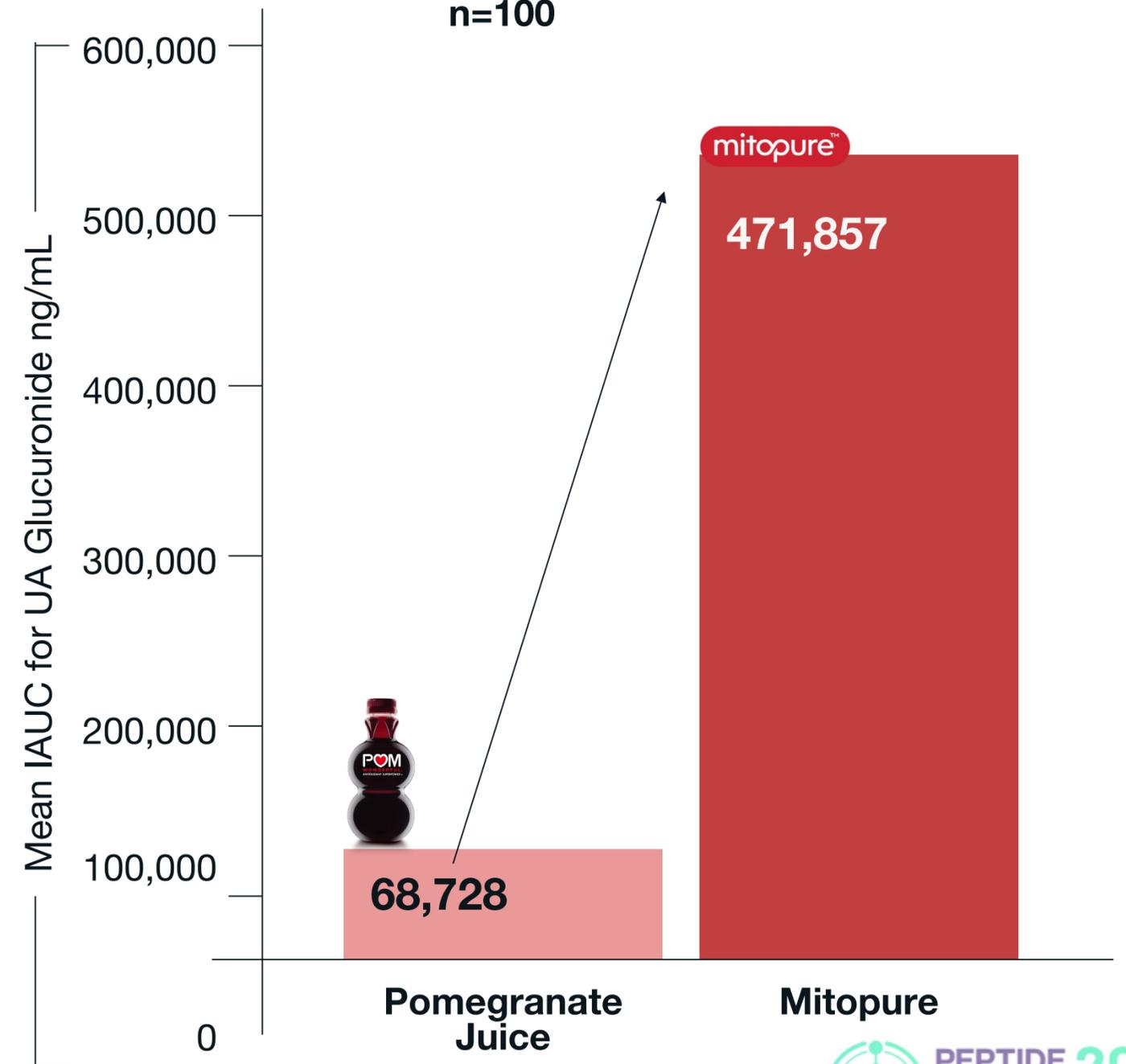
T24h post intake Total = 100



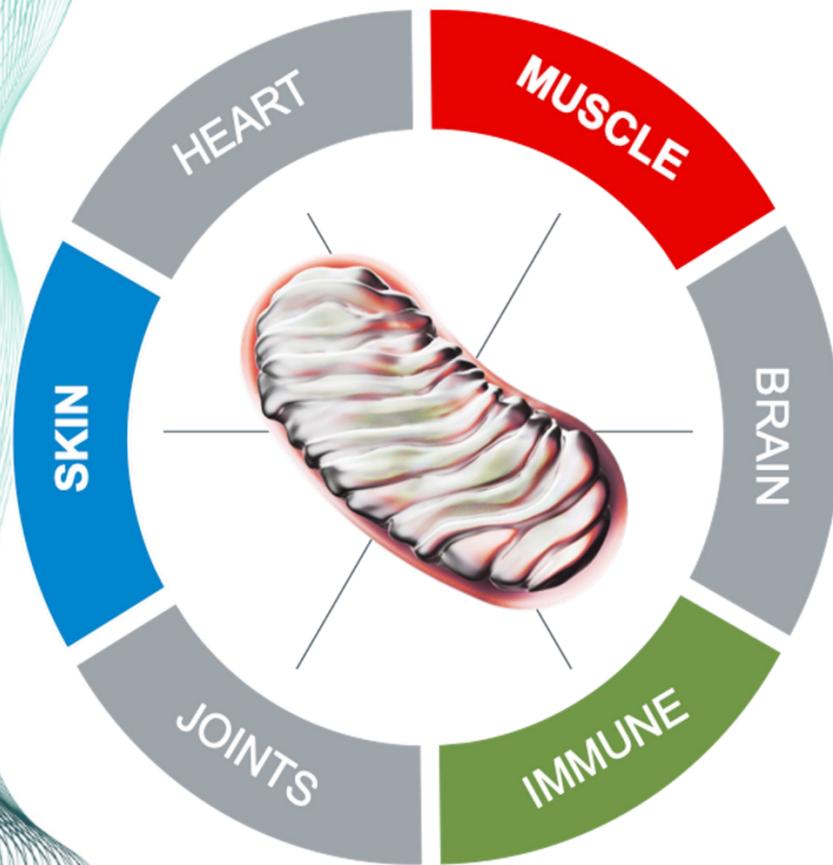
- 32.7% | No UA producer (<5ng/ml)
- 26.5% | Low UA producer (5-99ng/ml)
- 40.8% | High UA producer (≥100ng/ml)

~40% of US population has the appropriate gut microbiome to naturally produce Urolithin A.* This variability can be corrected via Mitopure supplementation that delivers >6x fold more than dietary exposure

Data shown are Mean + SEM, n=100



Today- our clinical program goes beyond muscle. We are targeting immune and skin health benefits with Mitopure



MUSCLE



IMMUNE



SKIN

Sports Nutrition: RCT in Elite athletes on performance and muscle recovery

Immobilization : Unilateral knee immobilization to mimic hospitalization- impact on muscle and mitochondrial health

Impact of Urolithin A on Immune metabolism and immune function in healthy adults

Impact of Urolithin A on metabolic health of immune system post-cancer

UVB-mediated inflammation

Skin Aging- Topical application to improve skin aging

Additional clinical programs are planned with top investigators from top Universities such as Harvard, NorthWestern, UCLA and McGill Universities

Timeline Product Range with Mitopure

Mitopure Powder (Berry)
500mg Mitopure



Mitopure Powder (Ginger)
500mg Mitopure



Mitopure + Protein
20g Whey protein
500mg Mitopure



Mitopure Softgels
500mg Mitopure



Mitopure Challenge
Test kit + Mitopure





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THANK YOU!

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