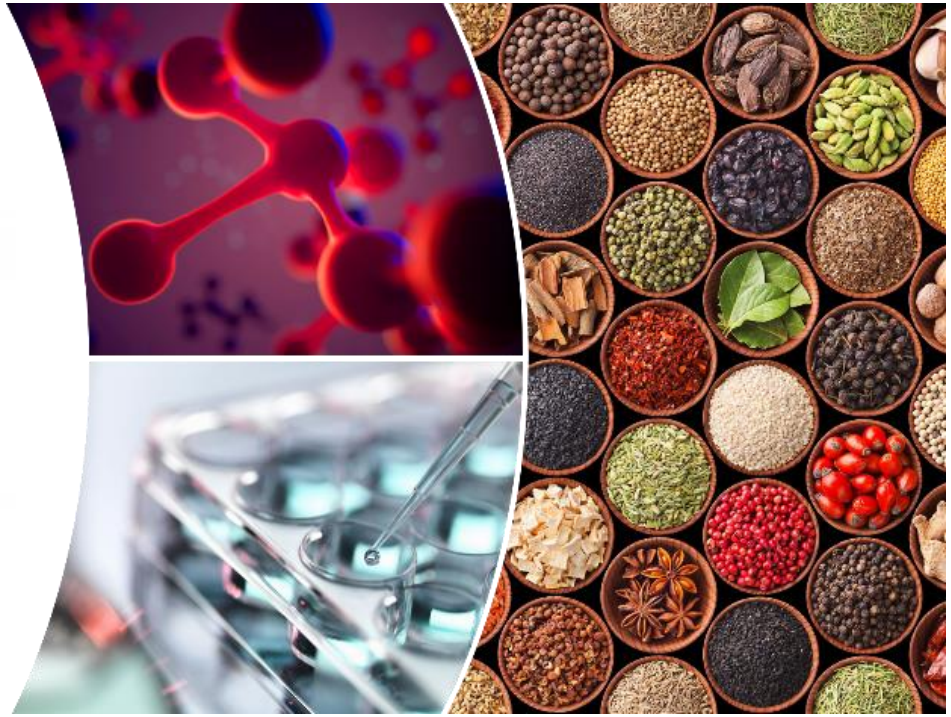


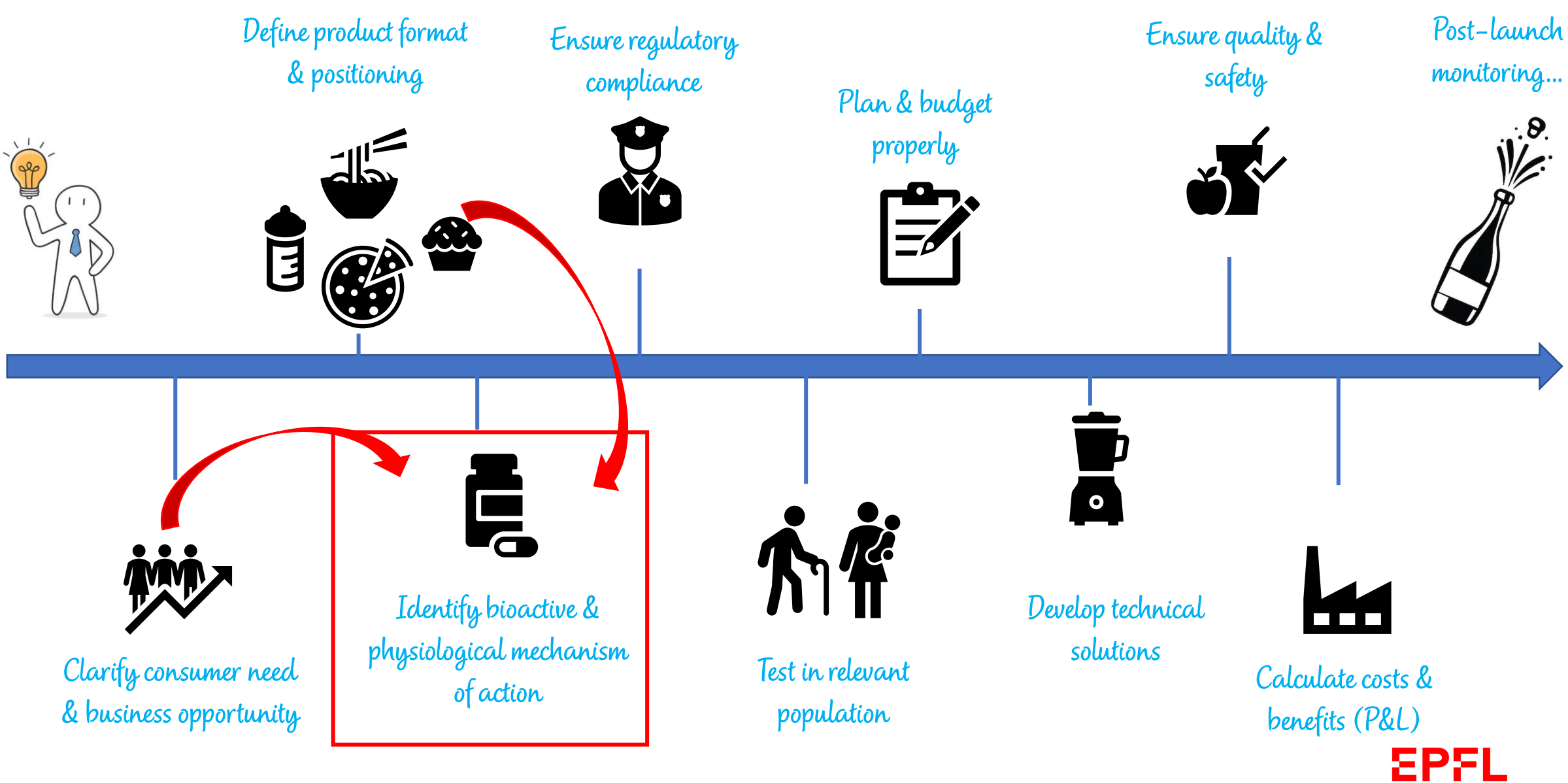
Entrepreneurship in Food & Nutrition Science

Course 2 – Bioactives & pre/probiotics

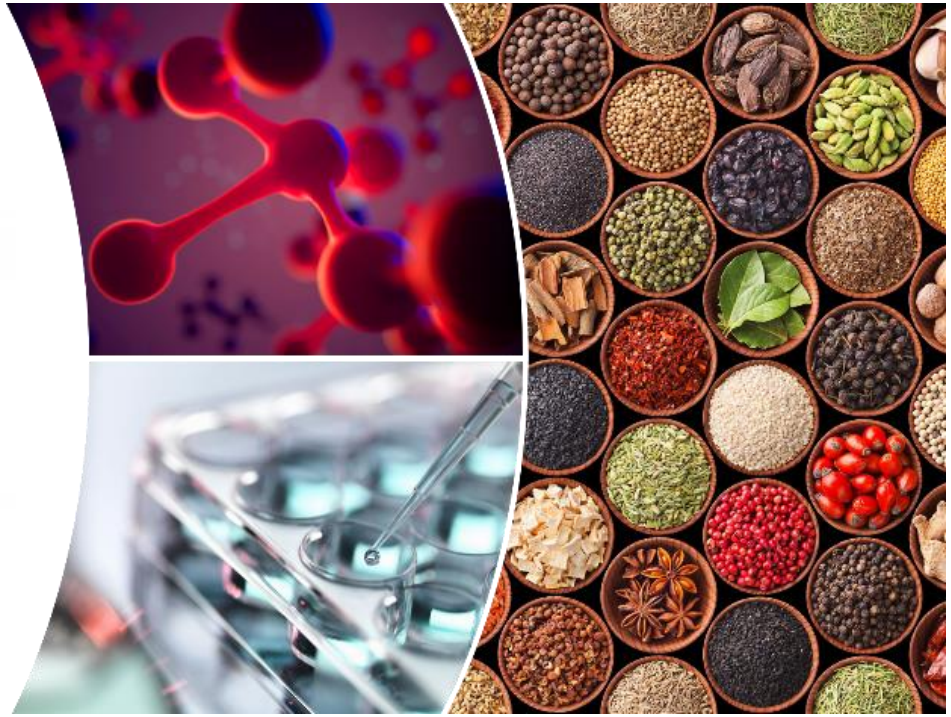
Bioactives & pre/probiotics - Outline

- Natural bioactive food molecules
- Pre/Pro/Post-biotics that modulate the microbiome

Bioactive ingredients for health benefits can drive the product unique value proposition



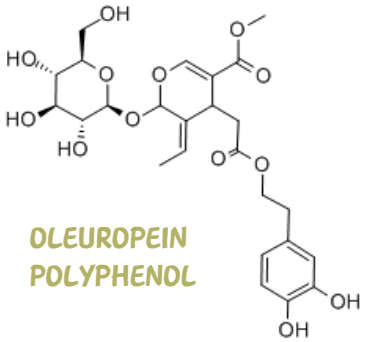
EPFL



Example of olive leave polyphenol for energy and endurance

What it looks like today

A science-rooted **natural ingredient**…



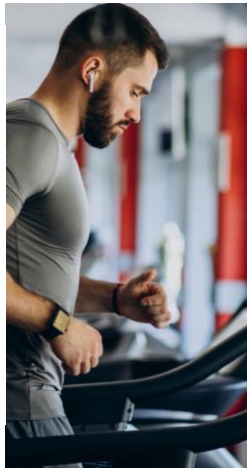
OLEUROPEIN POLYPHENOL

… to stimulate **mitochondria** to boost cellular ATP…

…and increase **muscle energy & sports performance**

Incubated for **open innovation**

ACCELERATOR TEST LAUNCH FOR SPORTS ENERGY

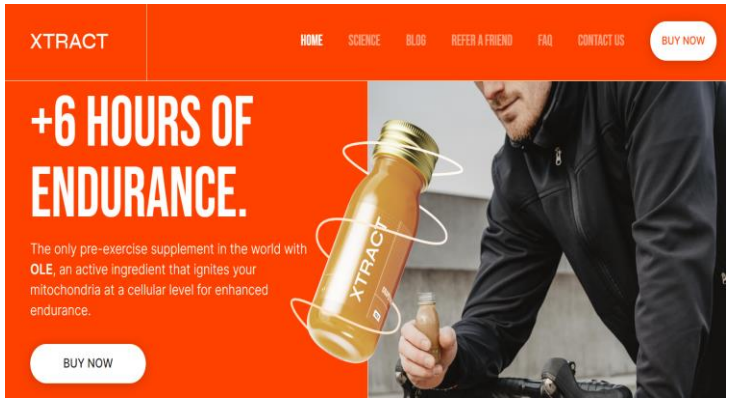


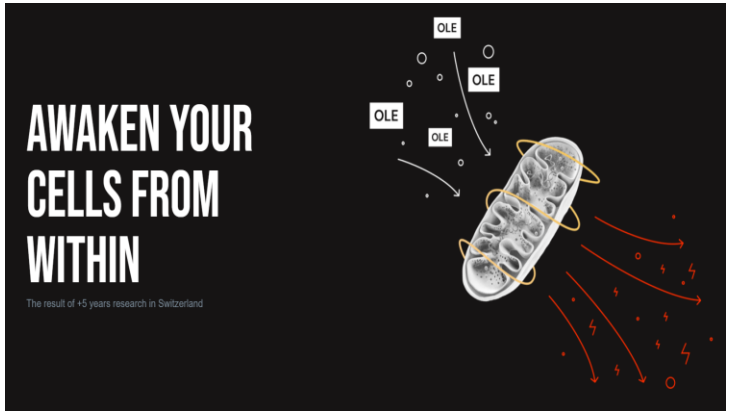
ENERGIZE

The Accelerator
Powered by Nestlé R+D

- MVP «Minimal viable product»
- Consumer communication
- Shop test in Italy

Launched by a **start-up**





https://www.oleus.com

EPFL

From Idea to ~~launch~~ decision… and agility & entrepreneurship !

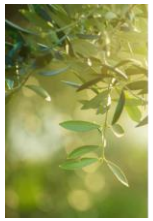
Clarify consumer need & business opportunity

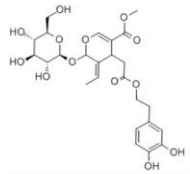
Older people with mobility concerns

Define product format & positioning

High protein healthy aging drink

Identify bioactive & mechanism of action





Ensure regulatory compliance

✓ Food supplement
X Food

Test in relevant population

Develop technical solutions

Calculate costs & benefits (P&L)

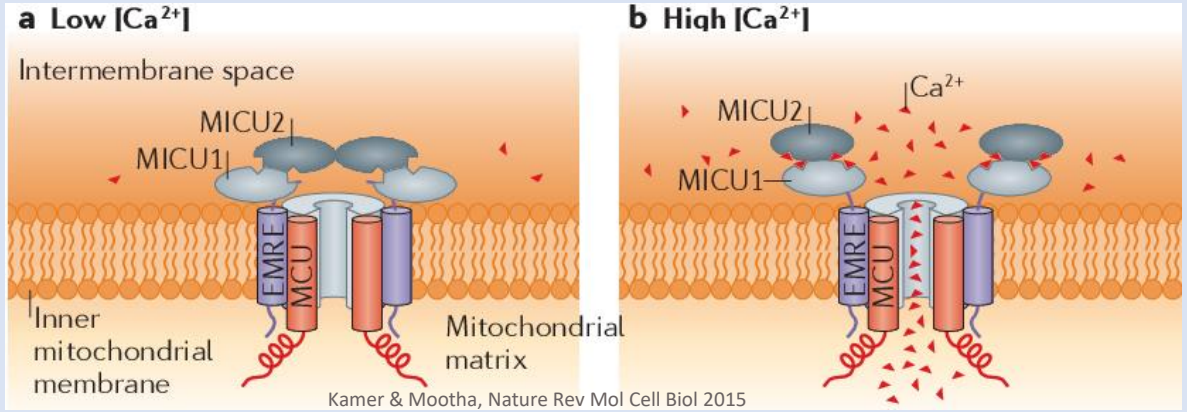
Plan & budget properly

Ensure quality & safety

Post-launch monitoring…

Deep rooted in scientific discovery

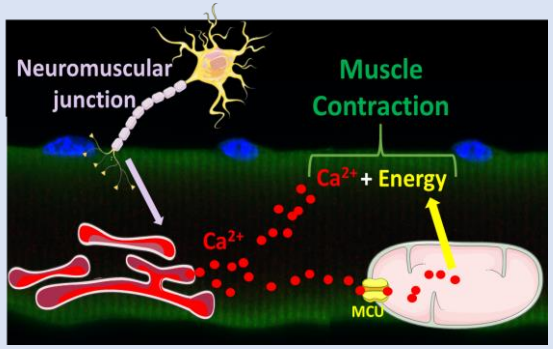
The MCU complex transports Ca2+ in mitochondria



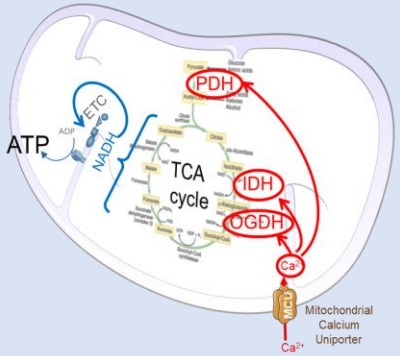
Kamer & Mootha, Nature Rev Mol Cell Biol 2015

De Stefani et al, Nature, 2011 / Baughman et al, Nature, 2011

Mito-Ca controls muscle health via energy production



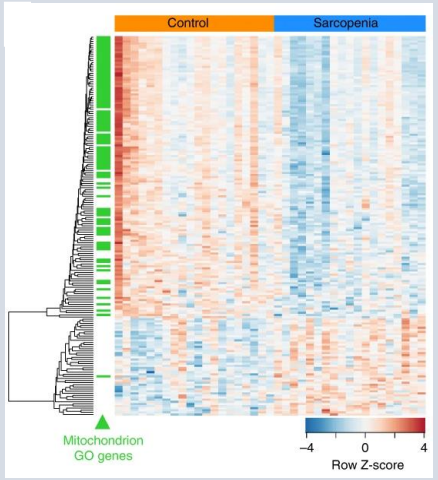
Logan C.V. et al, Nature Genetics, 2014
Lewis-Smith D. et al, Neurology, 2016

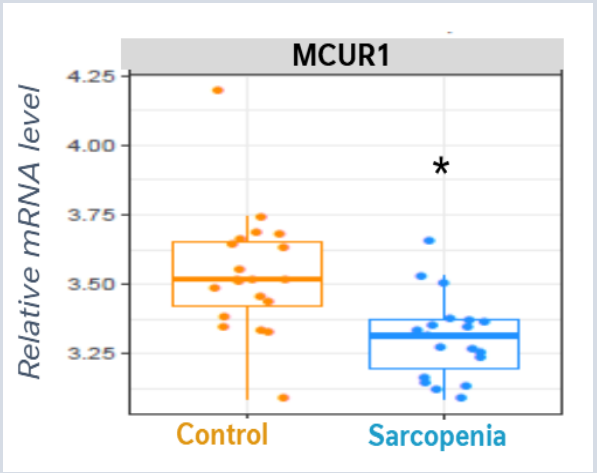


Mammucari et al, Cell Reports 2015
Debattisti et al, Cell Reports 2019

Discovery in a human cohort of muscle aging

- **Mitochondrial dysfunction** is the major transcriptional signature of sarcopenia in human muscle biopsies.
- **Mitochondrial calcium import** is a downregulated pathway in the sarcopenia signature.

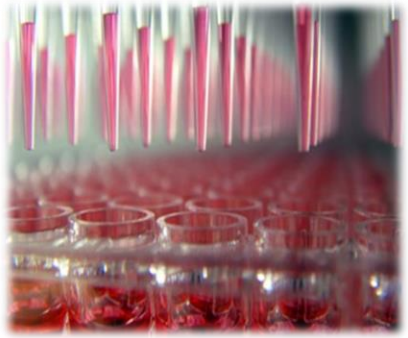


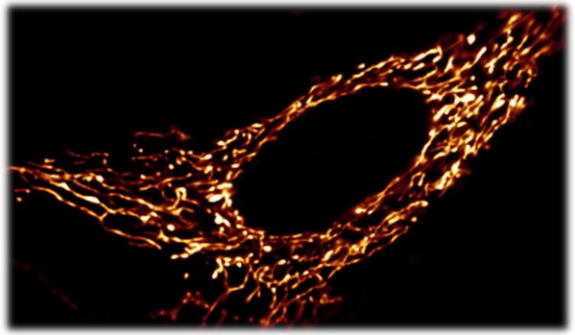


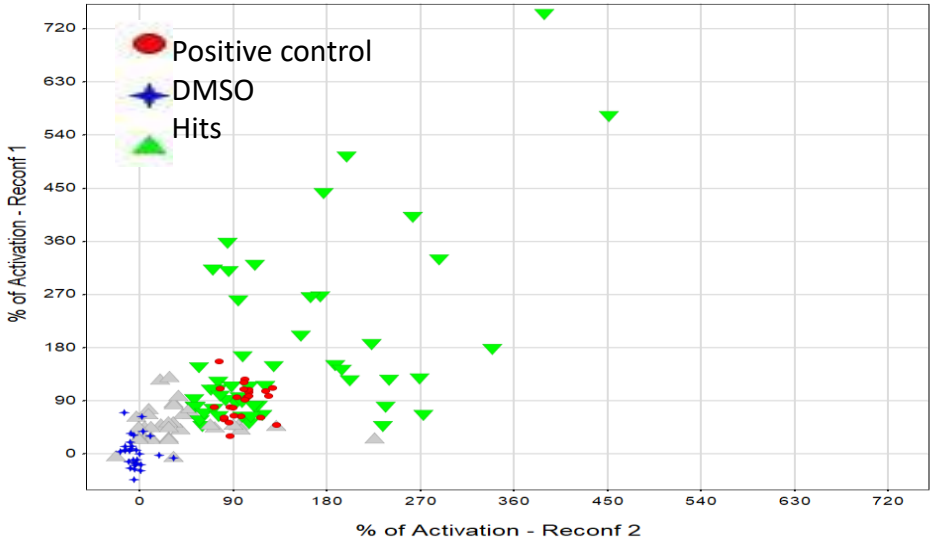
Migliavacca, … & Feige, Nature Comms 2019
Gherardi et al, Cell Metab 2024

Enabled by experimental biology

SCREENING OF 5000 BIOACTIVES WITH MITOCHONDRIAL CALCIUM REPORTER

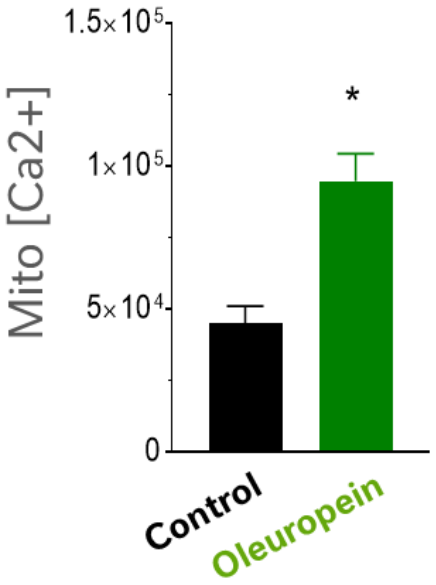




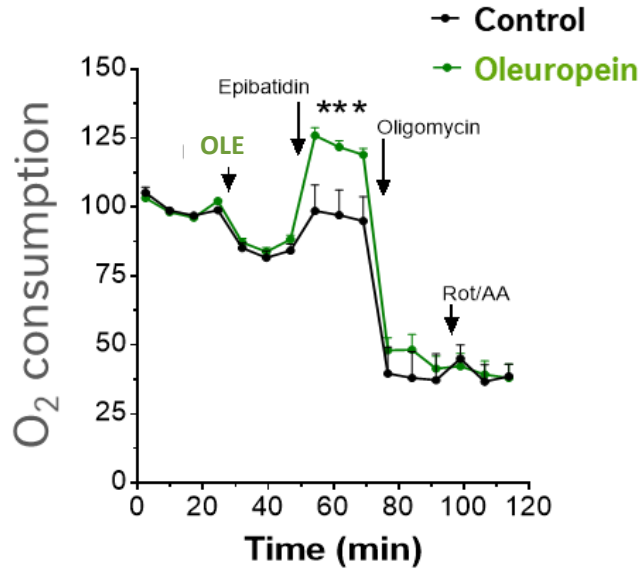


COUNTER-SCREEN & CELLULAR VALIDATION

Mitochondrial Ca^{2+} import



Mitochondrial respiration

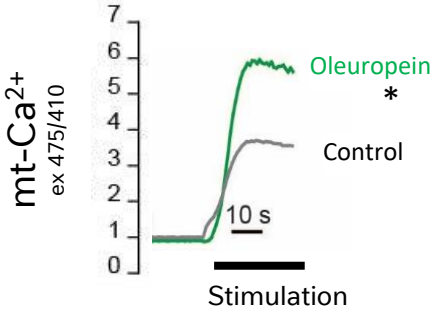


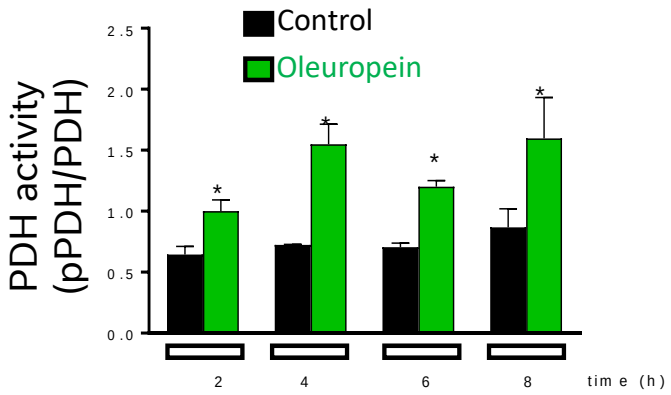
-- Active at 5µM in 5min --

EPFL

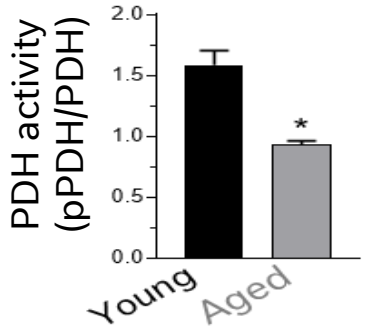
Guided by physiology in model organisms

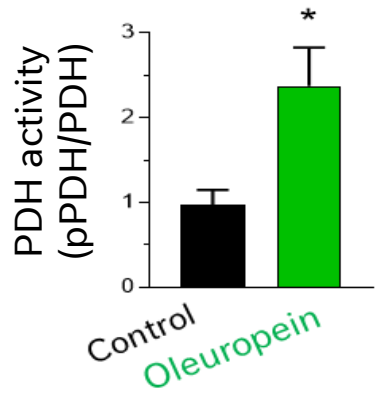
Enhances muscle bioenergetics acutely



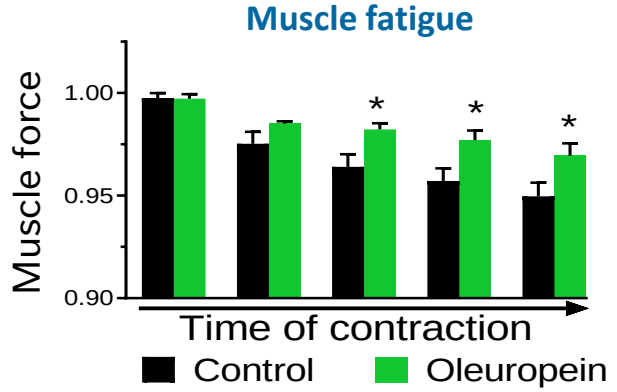


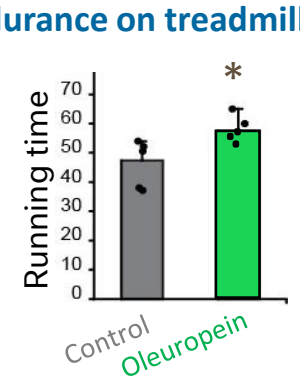
Restores bioenergetic defects during aging





Prevents muscle fatigue





CONSUMER COMMUNICATION

STIMULATES MUSCLE ENERGY ACUTELY

PREVENTS LOW MUSCLE ENERGY DURING AGING

ENDURE FOR LONGER

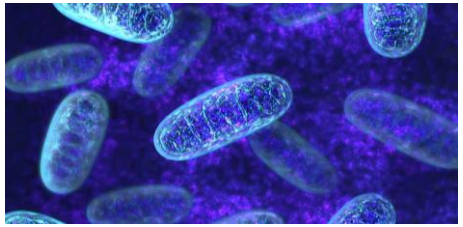
Repurposed via open innovation

The accelerator : translating innovation into a test launch in 6 months

ENERGIZE

The Accelerator
Powered by Nestlé R+D

Scientific discovery	Growth hacking & concept prioritization	Sensory optimization	Communication strategy	Test launch



Optimize taste, color, solubility & stability

A natural plant-based drink to wake up your body to its full energy potential

EPFL

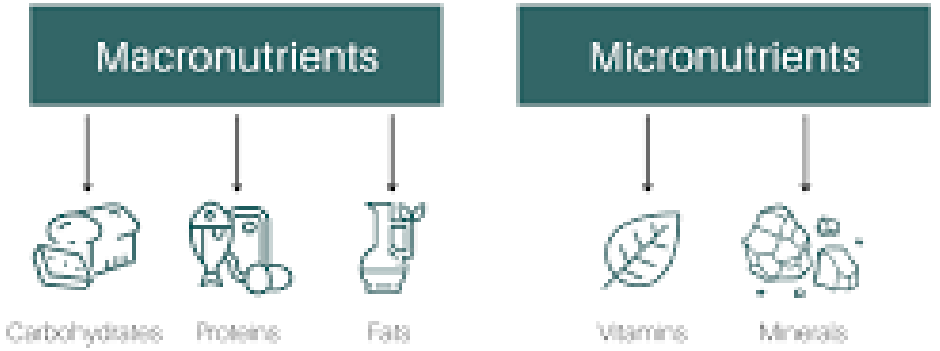
Food metabolites constitute and regulate our cells and organs

"WE ARE WHAT WE EAT"

Ludwig Feuerbach, 1848

June 25, 2007

NUTRIENTS ARE ESSENTIAL FOR LIFE



FOOD BIOACTIVES ARE PHYSIOLOGICALLY ACTIVE (BUT NOT ESSENTIAL)

Examples ?

EPFL

Examples of food bioactives

Bioactive compounds typically occur in small quantities in foods and can be beneficial for health.*

Bioactive compounds are not essential for life but are widely studied for possible health effects.

*EUFIC.org

Compounds	Found in	Function
Polyphenols, flavonoids	All plant foods; studied extensively in cereals, nuts legumes, fruits, vegetables, olive oil, tea, red wine	Anti-oxidant
Phytoestrogens	Soy, flaxseed oil, whole grains	Anti-oxidant, CVD risk
Resveratrol	Red wine, nuts	Anti-oxidant, anti-inflammation
Lycopene	Tomatoes, other fruits	Anti-oxidant
Organosulfur compounds	Garlic, onions	Cardio-protective effects
Epicatechins	Cocoa, tea, apple	Stimulates blood flow

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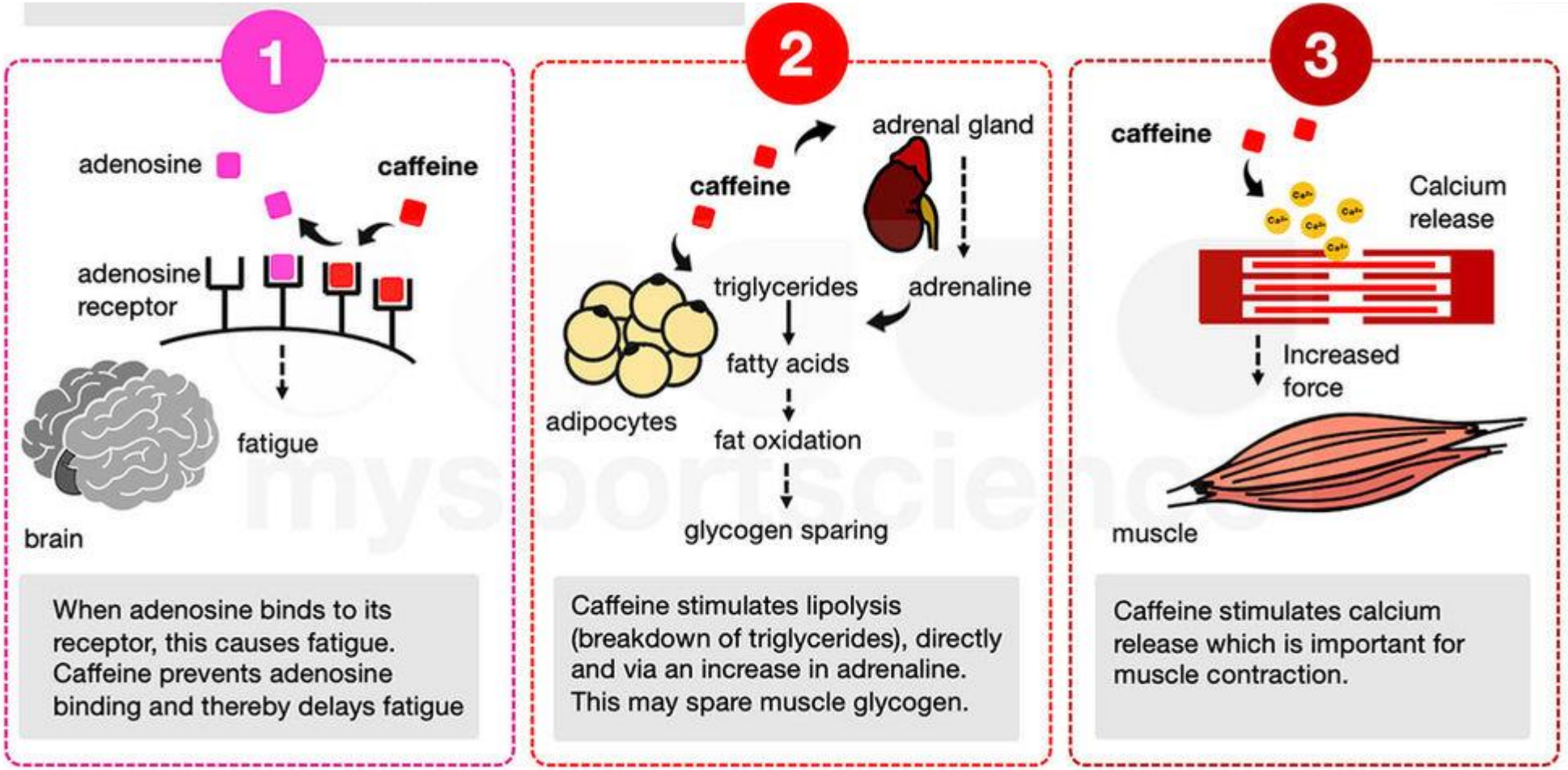
Caffeine is a potent physiological stimulator

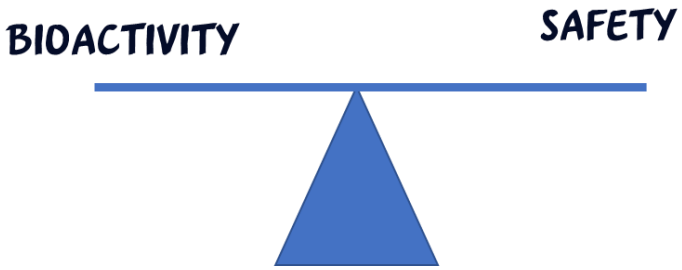
Mechanism of action of caffeine

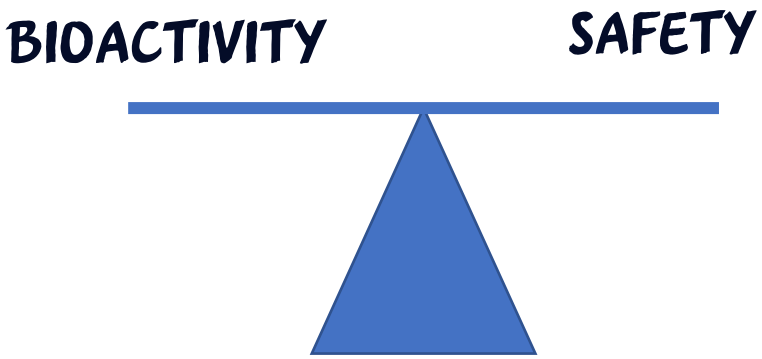


https://www.mysportscience.com/post/how-does-caffeine-work

Bioactivity can have detrimental effects

Up to 5 cups per day





APPROVAL OF NOVEL INGREDIENTS IS HIGHLY REGULATED TO ENSURE CONSUMER PROTECTION

The use of a food substance may be **Generally Recognized as Safe (GRAS)** either through scientific procedures or, for a substance used in food before 1958

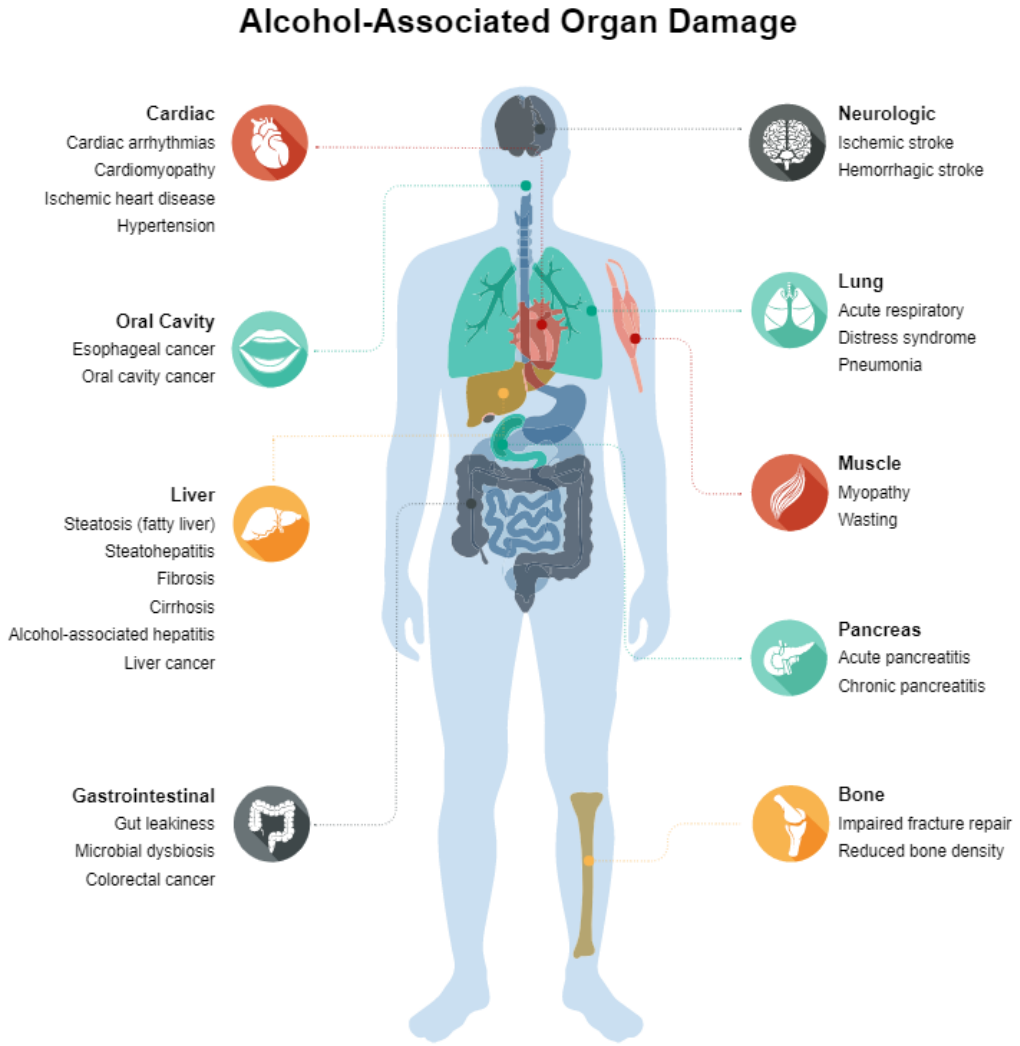
The authorisation and use of novel foods and food ingredients is governed by regulation EC 258/1997

Bioactivity can have detrimental effects

NATURAL ≠ SAFE

APPROVED ≠ HEALTHY

(PUBLIC HEALTH PREVENTION)

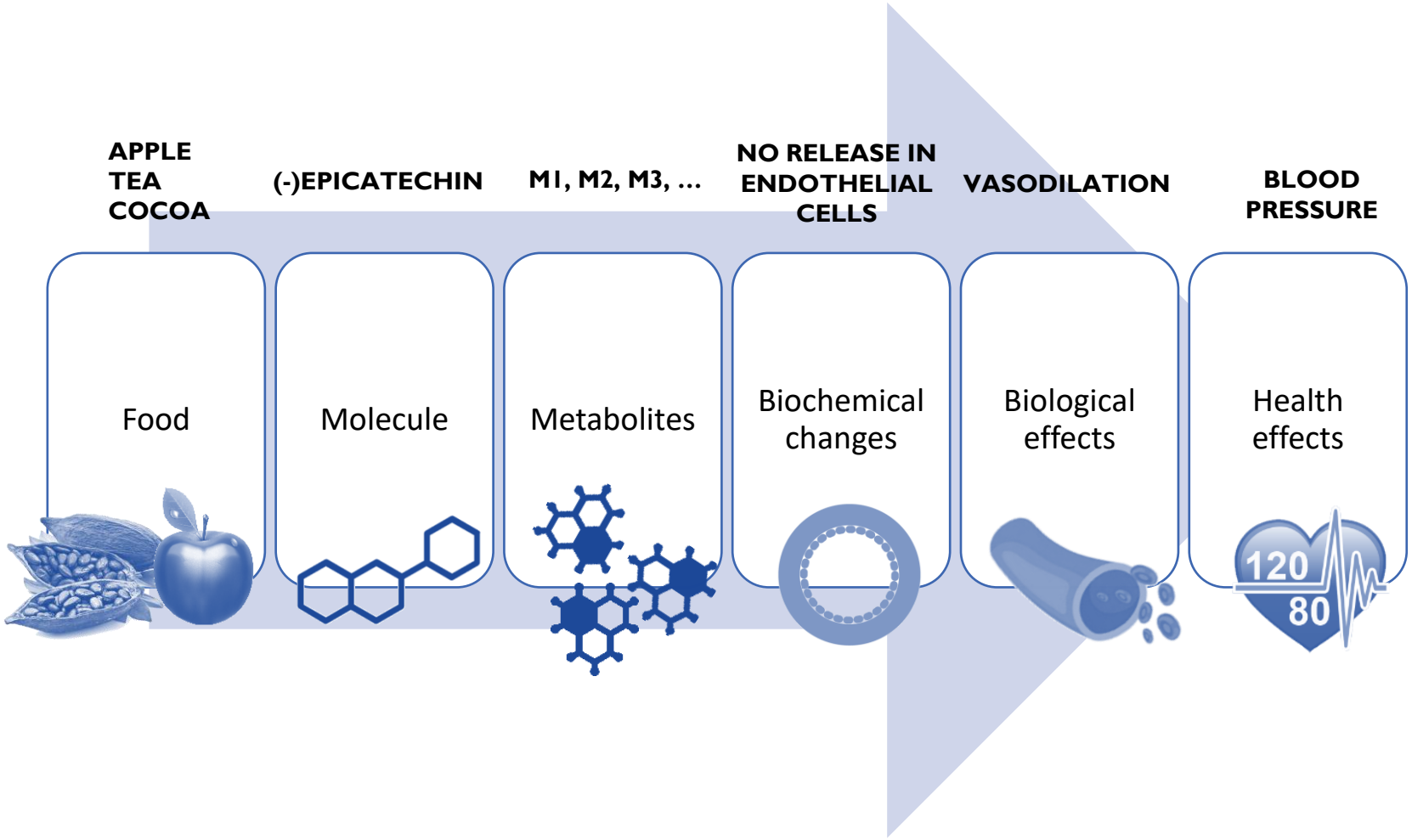


https://www.niaaa.nih.gov/alcohols-effects-health/alcohols-effects-body

EPFL

FROM DIETARY EXPOSURE TO HEALTH BENEFITS

Example of epicatechin from tea & fruits…



EPFL

Health benefits of bioactives discovered via food epidemiology

TEA & COCOA CONSUMPTION IS ASSOCIATED WITH A LOWER RISK OF CARDIOVASCULAR DISEASE (CVD)

- **HIGHER TEA CONSUMPTION ASSOCIATED WITH LOWER CHD RISK**
  Elderly men who drank **≥ 4 cups/day** had a 60% lower risk of fatal CHD when compared to those who drank **< 2 cups/day**.
  Hertog et al. Lancet 1993;342:1007-12

- **HIGHER TEA CONSUMPTION ASSOCIATED WITH LOWER RISK OF STROKE**
  Middle-aged men who drank on average **≥ 5 cups/day** had a 3 times lower stroke incidence (fatal & non-fatal) than those who drank **< 2.5 cups/day**.
  Keli et al. Arch Intern Med 1996;156:637-42

- **HIGHER COCOA CONSUMPTION ASSOCIATED WITH LOWER CVD RISK**
  in elderly men, Intake of approximately **4.2g cocoa/day** (~10g dark chocolate) was associated with a 50% lower CVD mortality compared to **no cocoa intake**.
  Buijsse et al. Arch Intern Med 2006;116:411-7

EPFL

Health benefits of bioactives discovered via nutrient epidemiology

HIGHER INTAKES OF FLAVAN-3-OLS & EPICATECHIN (KEY POLYPHENOLIC COMPOUNDS IN TEA & COCOA) WERE ASSOCIATED WITH A LOWER RISK OF CORONARY HEART DISEASE (CHD)

- **HIGHER FLAVAN-3-OLS INTAKE ASSOCIATED WITH LOWER CHD RISK**
  In elderly men, higher intake of flavan-3-ols (mean intake **124 mg/day** vs. **25 mg/day**) was associated with a 50% lower risk of fatal CHD.
  Arts et al. Am J Clin Nutr 2001;74:227-32

- **HIGHER EPICATECHIN INTAKE WAS ASSOCIATED WITH LOWER CHD RISK**
  In elderly men, higher intake of epicatechin (mean **intake 21.9 mg/day** vs. **7.9 mg/day**) was associated with a 38% lower risk of fatal CHD.
  Dower et al. Am J Clin Nutr 2016;104:58-64

EPFL

The hype of neutraceuticals

NUTRACEUTICAL (NUTRIENT + PHARMACEUTICAL) IS NOT AN APPROVED TERM

A NATURAL BIOACTIVE IS EITHER:

-Food

Regular consumption

-Food supplement

Proactive health management for specific use

-Medical food (FSMP EU)

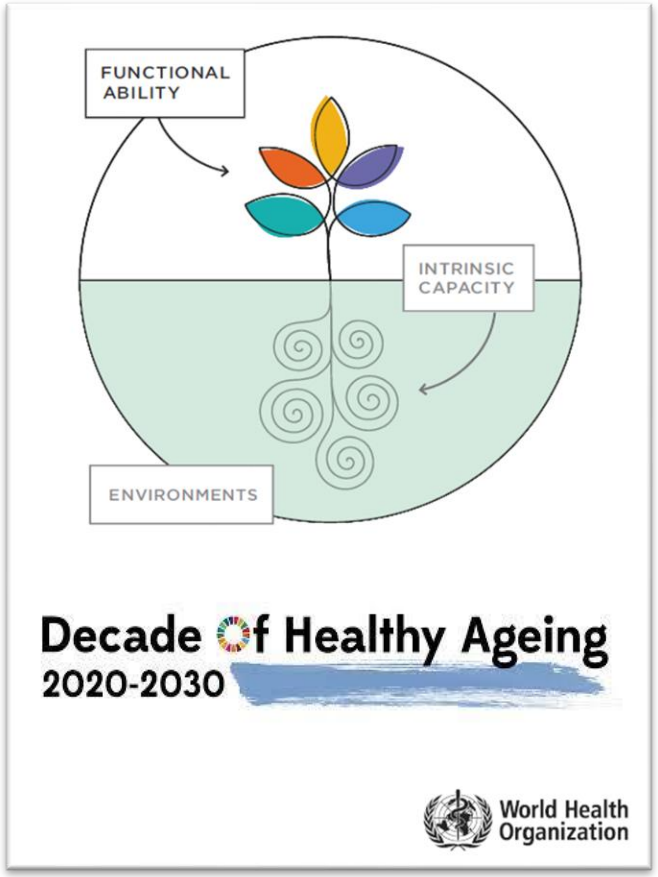
Dietary management of a medical condition

-Drug

Treatment of disease

EPFL

Example of bioactives that slow down aging



Silver economy is **$7 trillion** with equal split US-EU-CN and expected to **double by 2032**

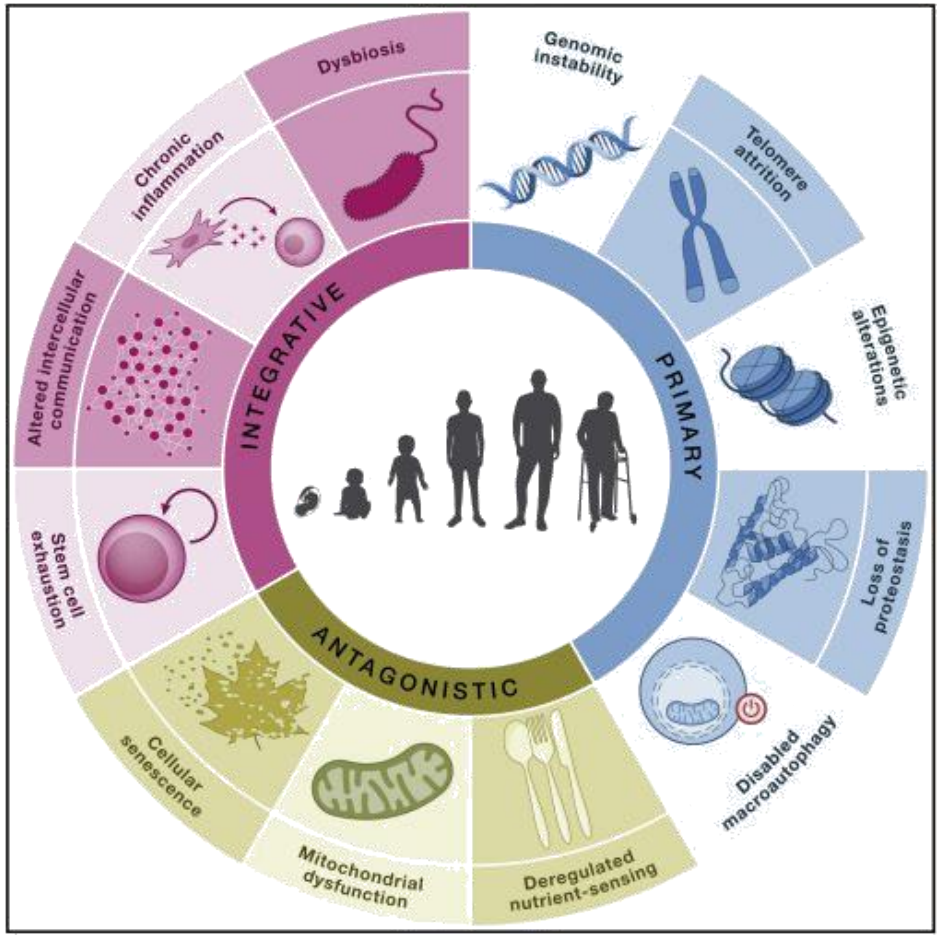
65+ concentrate **50% of health care costs**

Source: Scott AJ, Lancet 2021 / Li et al, Risk Manag Health Polic 2020

EPFL

Discovery of healthy aging bioactives via biological mechanisms

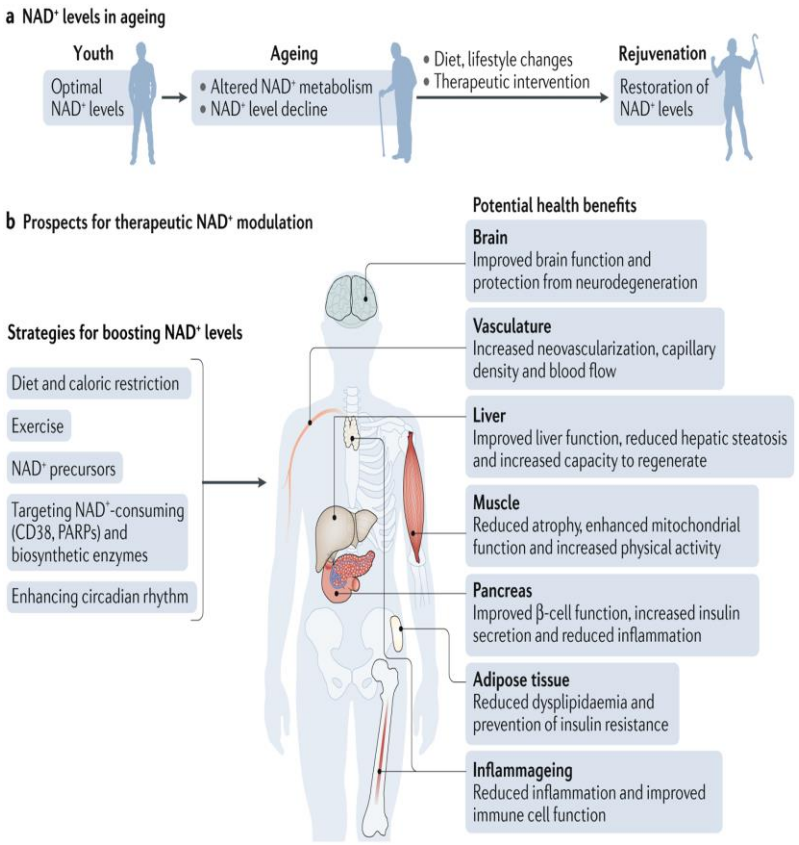
HALLMARKS OF AGING



Lopez-Otin et al, Cell 2013 / Lopez-Otin et al, Cell 2023

EPFL RESEARCH ON HALLMARKS OF AGING WITH BIOACTIVES

(EXAMPLE OF NAD+ PRECURSORS)



Covarrubias et al, Nature Reviews 2021

EPFL | NEWS

A vitamin that stops the aging process of organs

https://actu.epfl.ch/news/a-vitamin-that-stops-the-aging-process-of-organs/

Science

AGING

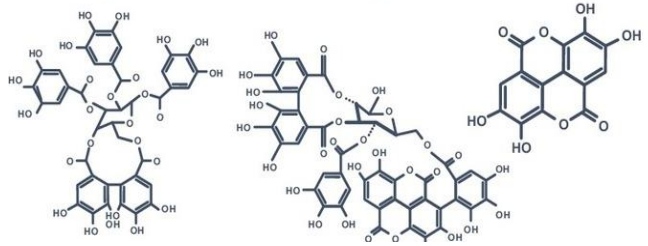
NAD⁺ repletion improves mitochondrial and stem cell function and enhances life span in mice

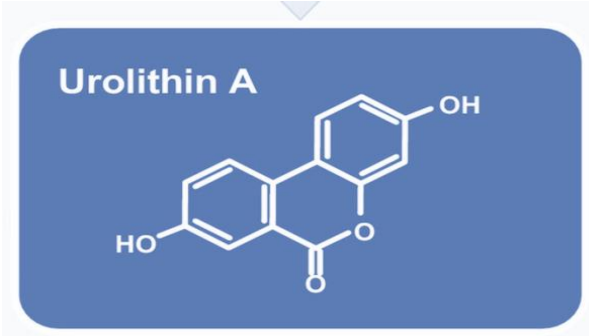
Zhang et al, Science 2016

EPFL

Example of Urolithin A

Ellagitannins and ellagic acid

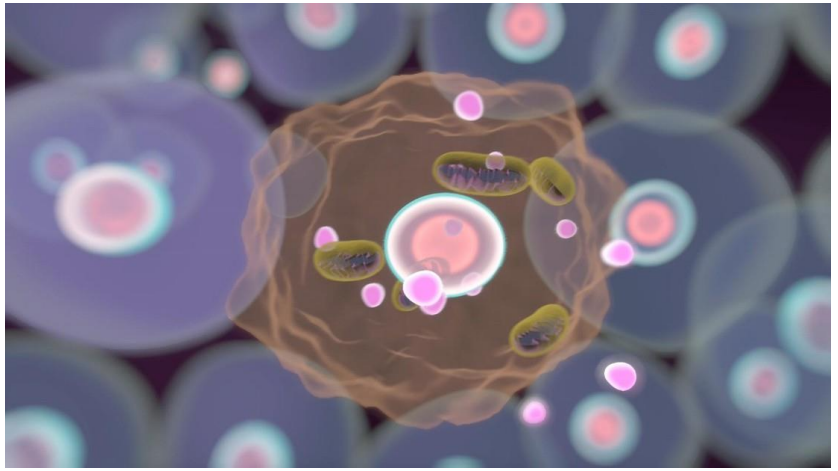




nature medicine

Urolithin A induces mitophagy and prolongs lifespan in *C. elegans* and increases muscle function in rodents

Dongryeol Ryu[1,5], Laurent Mouchiroud[1,5], Pénélope A Andreux[1,2,5], Elena Katsyuba[1], Norman Moullan[1], Amandine A Nicolet-dit-Félix[1], Evan G Williams[1], Pooja Jha[1], Giuseppe Lo Sasso[1], Damien Huzard[3], Patrick Aebischer[4], Carmen Sandi[3], Chris Rinsch[2] & Johan Auwerx[1]



MITOPHAGY IS THE CELLULAR RECYCLING OF DAMAGED MITOCHONDRIA

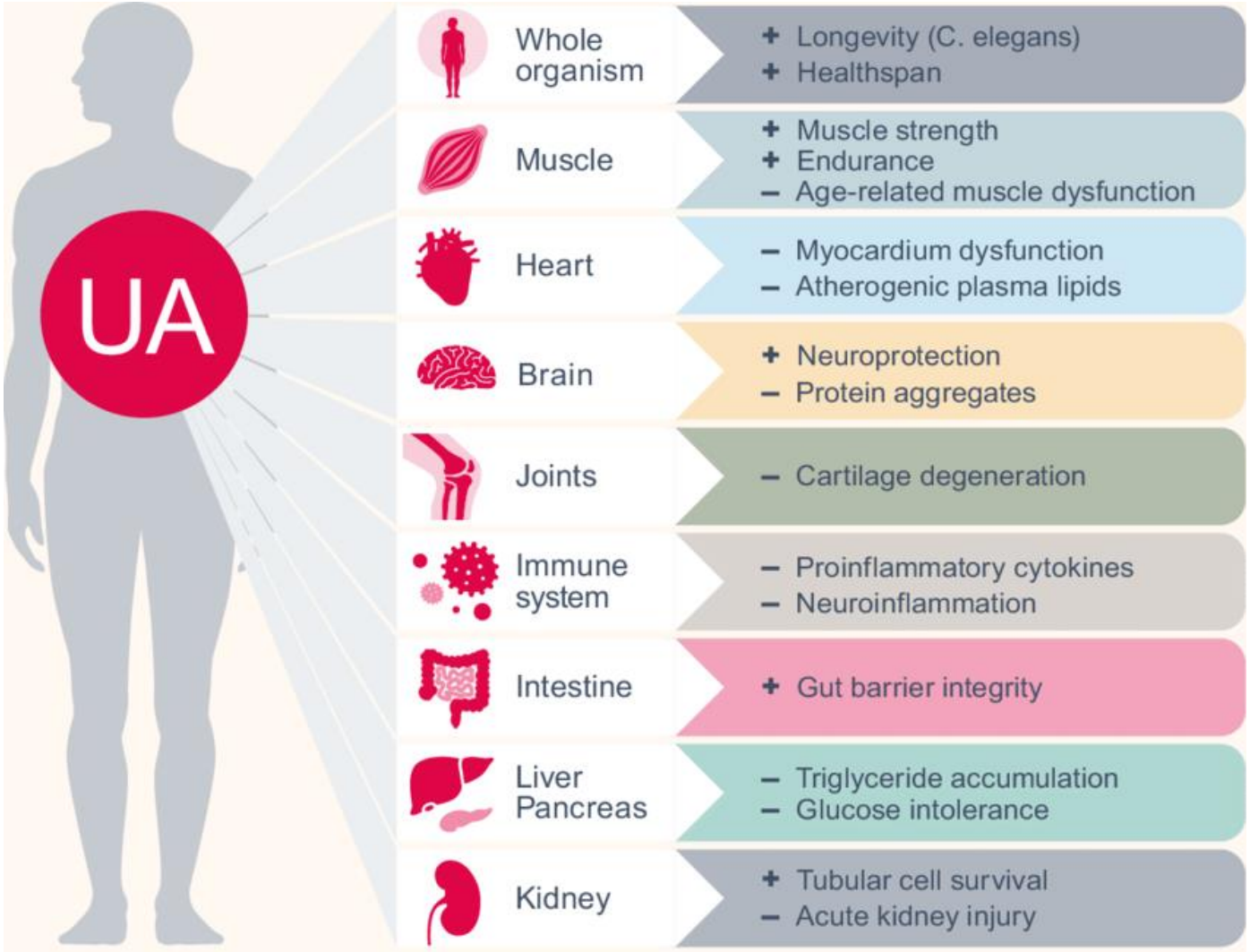
https://actu.epfl.ch/news/pomegranate-finally-reveals-its-powerful-anti-agin/

EPFL

Urolithin A: discovered & explained from EPFL

https://youtu.be/Lf1vCyfaosE

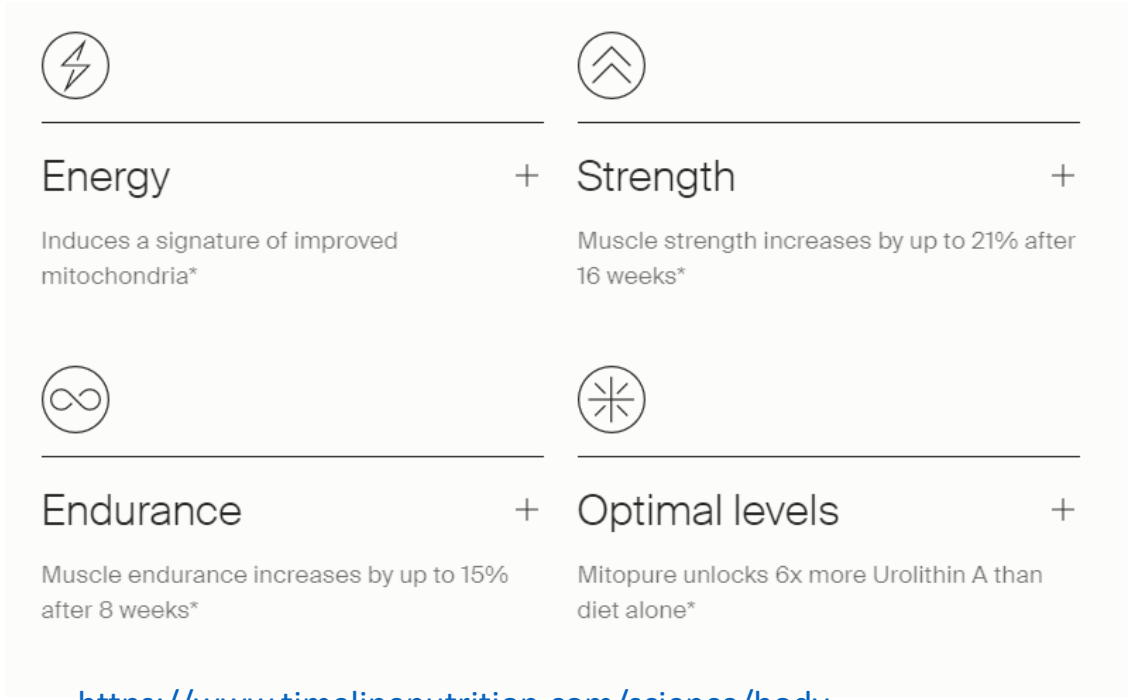
Urolithin A has broad health benefits



D'Amico et al, Trends Molecular Medicine 2021

EPFL

Urolithin A is beneficial for cellular & muscle health during aging in humans



https://www.timelinenutrition.com/science/body


nature metabolism

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nature › nature metabolism › letters › article

Letter | Published: 14 June 2019

The mitophagy activator urolithin A is safe and induces a molecular signature of improved mitochondrial and cellular health in humans

Pénélope A. Andreux, William Blanco-Bose, Dongryeol Ryu, Frédéric Burdet, Mark Ibberson, Patrick Aebischer, Johan Auwerx, Anurag Singh & Chris Rinsch

Nature Metabolism **1**, 595–603 (2019) | Cite this article


JAMA Network Open

Original Investigation | Nutrition, Obesity, and Exercise

Effect of Urolithin A Supplementation on Muscle Endurance and Mitochondrial Health in Older Adults
A Randomized Clinical Trial

Sophia Liu, PhD; Davide D'Amico, PhD; Eric Shankland, PhD; Saakshi Bhayana, BS; Jose M. Garcia, MD, PhD; Patrick Aebischer, MD; Chris Rinsch, PhD; Anurag Singh, MD, PhD; David J. Marcinek, PhD


Cell Reports Medicine Open access

ARTICLE | VOLUME 3, ISSUE 5, 100633, MAY 17, 2022

Urolithin A improves muscle strength, exercise performance, and biomarkers of mitochondrial health in a randomized trial in middle-aged adults

Anurag Singh [5, 6] • Davide D'Amico [5] • Pénélope A. Andreux • ... Patrick Aebischer • Johan Auwerx • Chris Rinsch • Show all authors • Show footnotes

Open Access • DOI: https://doi.org/10.1016/j.xcrm.2022.100633 • Check for updates


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Article | Open Access | Published: 11 June 2021

Nutrition and Health (including climate and ecological aspects)

Direct supplementation with Urolithin A overcomes limitations of dietary exposure and gut microbiome variability in healthy adults to achieve consistent levels across the population

Anurag Singh, Davide D'Amico, Pénélope A. Andreux, Gillian Dunngalvin, Timo Kern, William Blanco-Bose, Johan Auwerx, Patrick Aebischer & Chris Rinsch

https://actu.epfl.ch/news/compound-with-anti-aging-effects-passes-human-tria/

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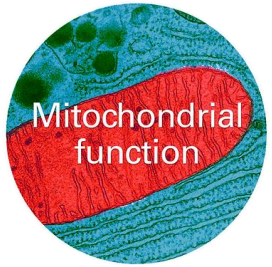
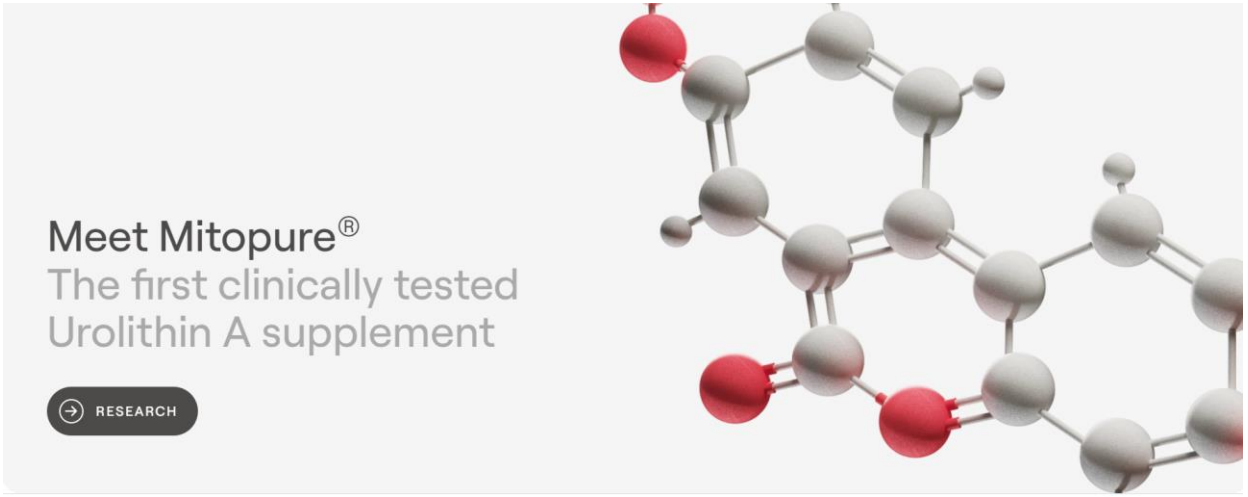
Urolithin A was valorized in a local start-up

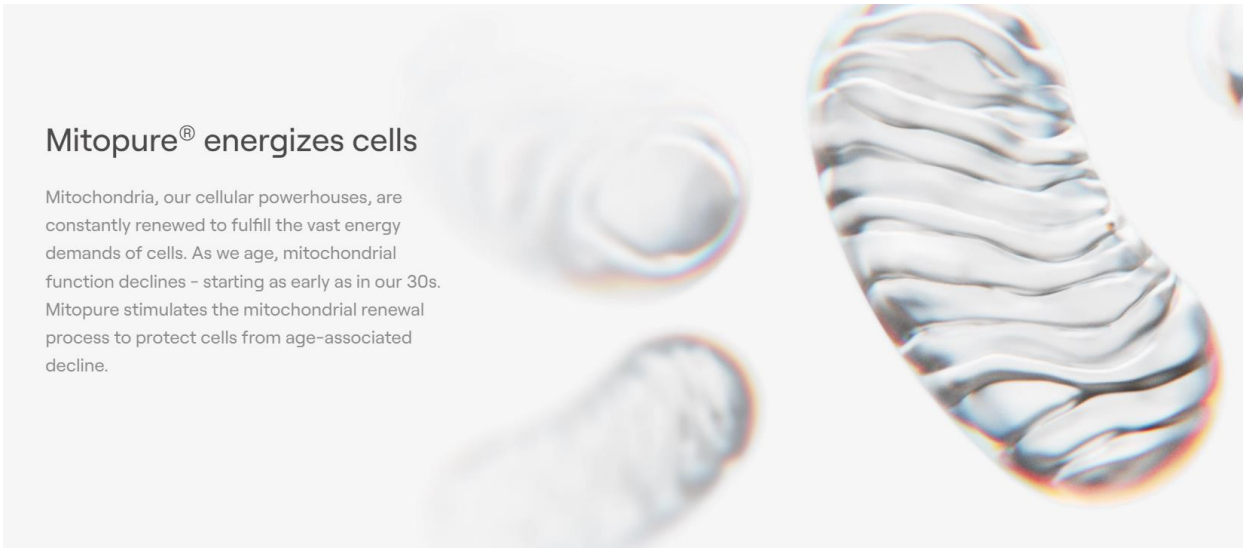
Amazentis

EPFL Innovation Park

Amazentis is an innovative life science company dedicated to employing breakthrough research and clinical science to bring advanced therapeutic nutrition products to life.







https://www.amazentis.com/

https://www.mitopure.com/
https://www.timelinenutrition.com/

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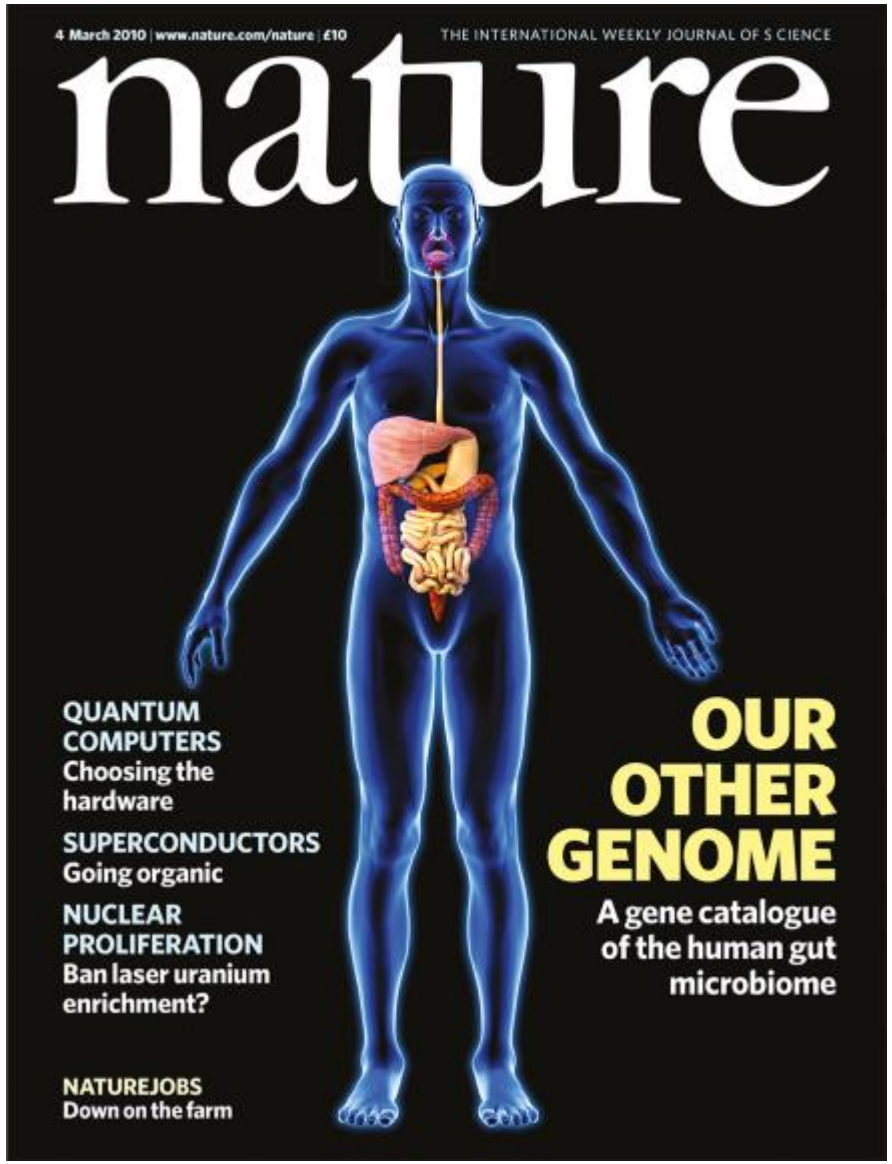
The gut microbiome



Qin et al, Nature 2010

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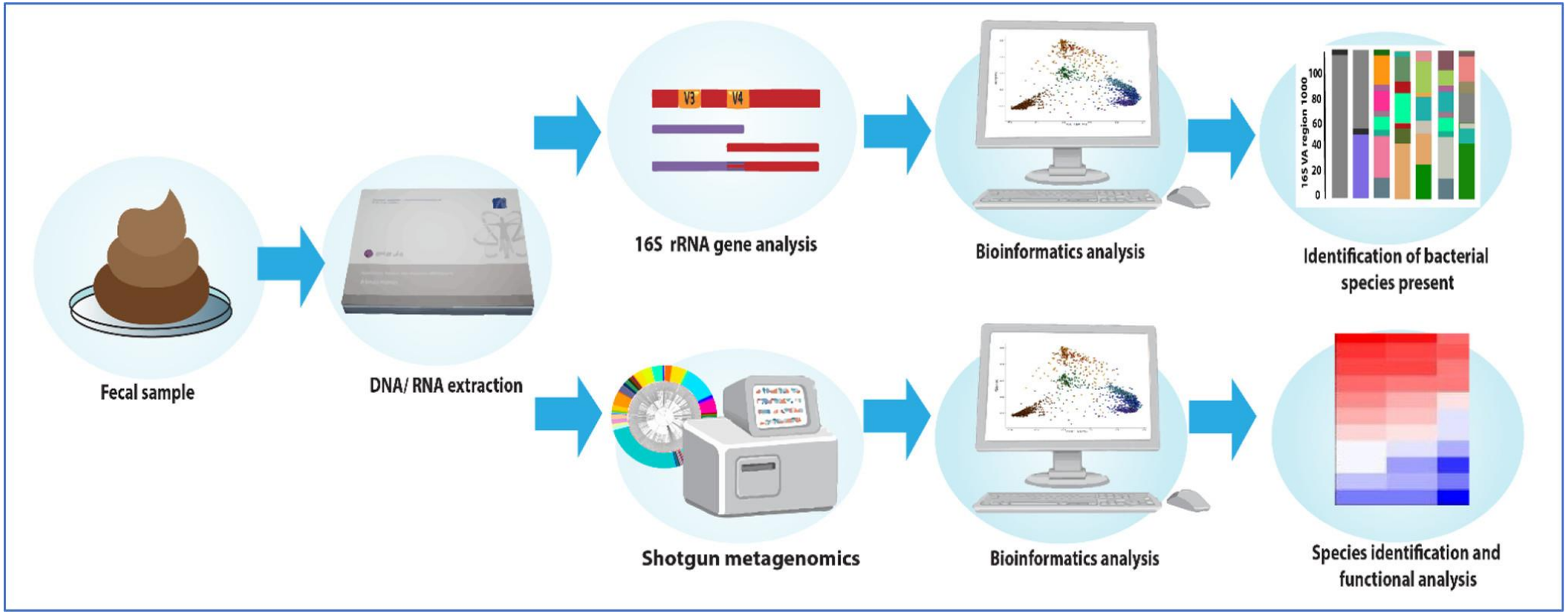
How to analyse the microbiome

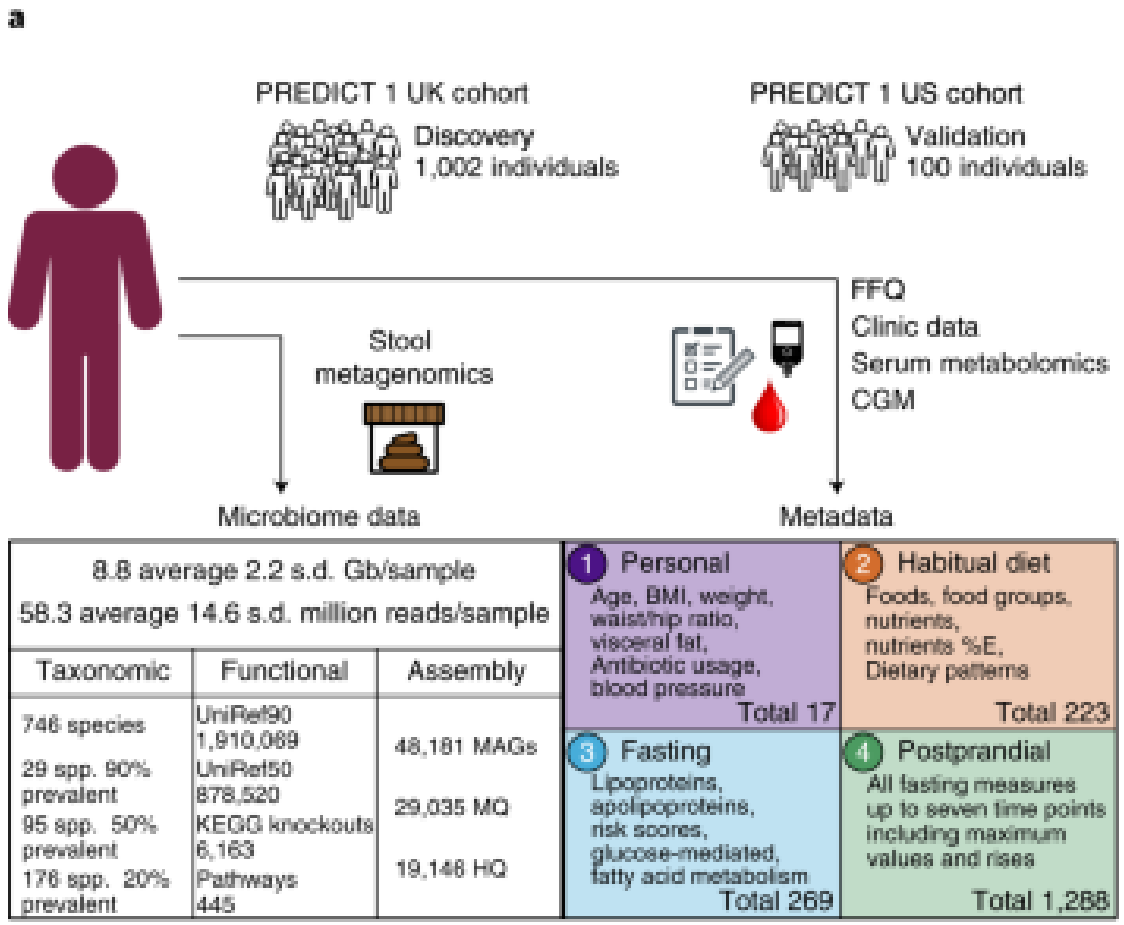


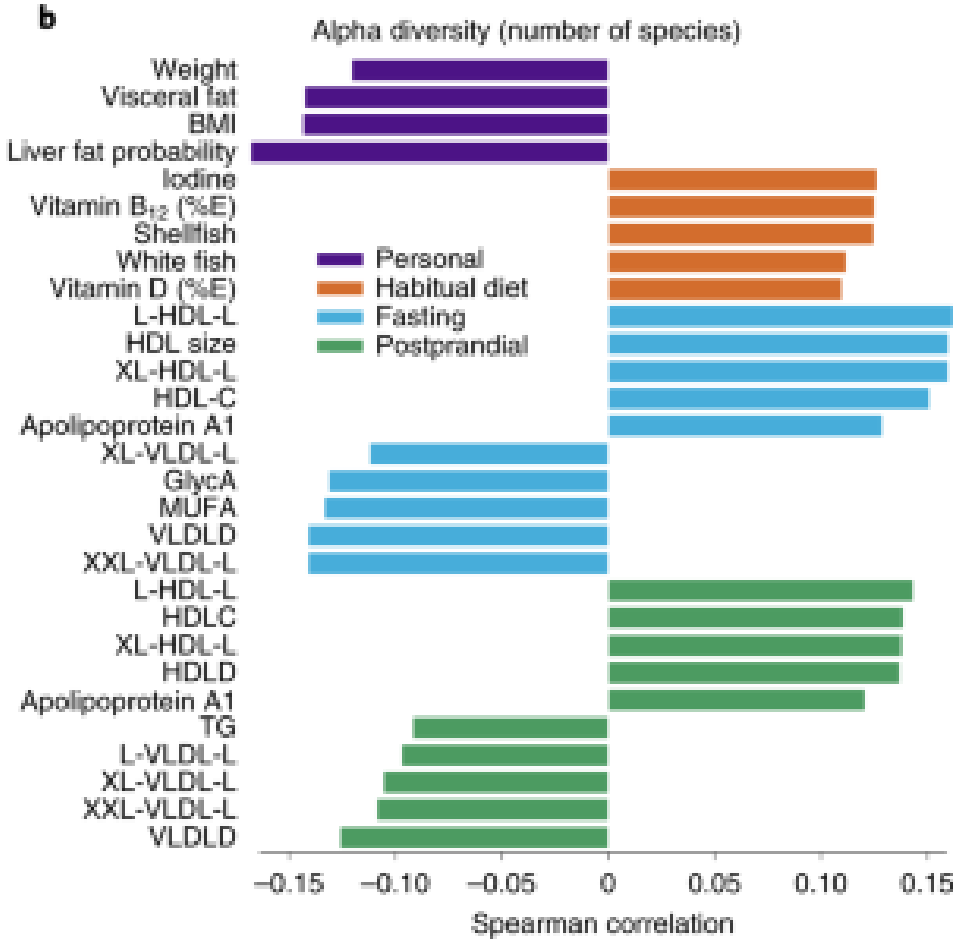
Challenges of gut microbiome analyses

- Bioinformatic deconvolution of a highly complex ecosystem
- Genome annotations are based on known species
- Functional gene annotations suffer from experimental culture basis (anaerobic bacteria more challenging to study)
- Human analyses from stools are delayed spatially and temporally

The diversity of the gut microbiome associates with health

Example of cardiometabolic health in adults





Asnicar et al, Nature Medicine 2021

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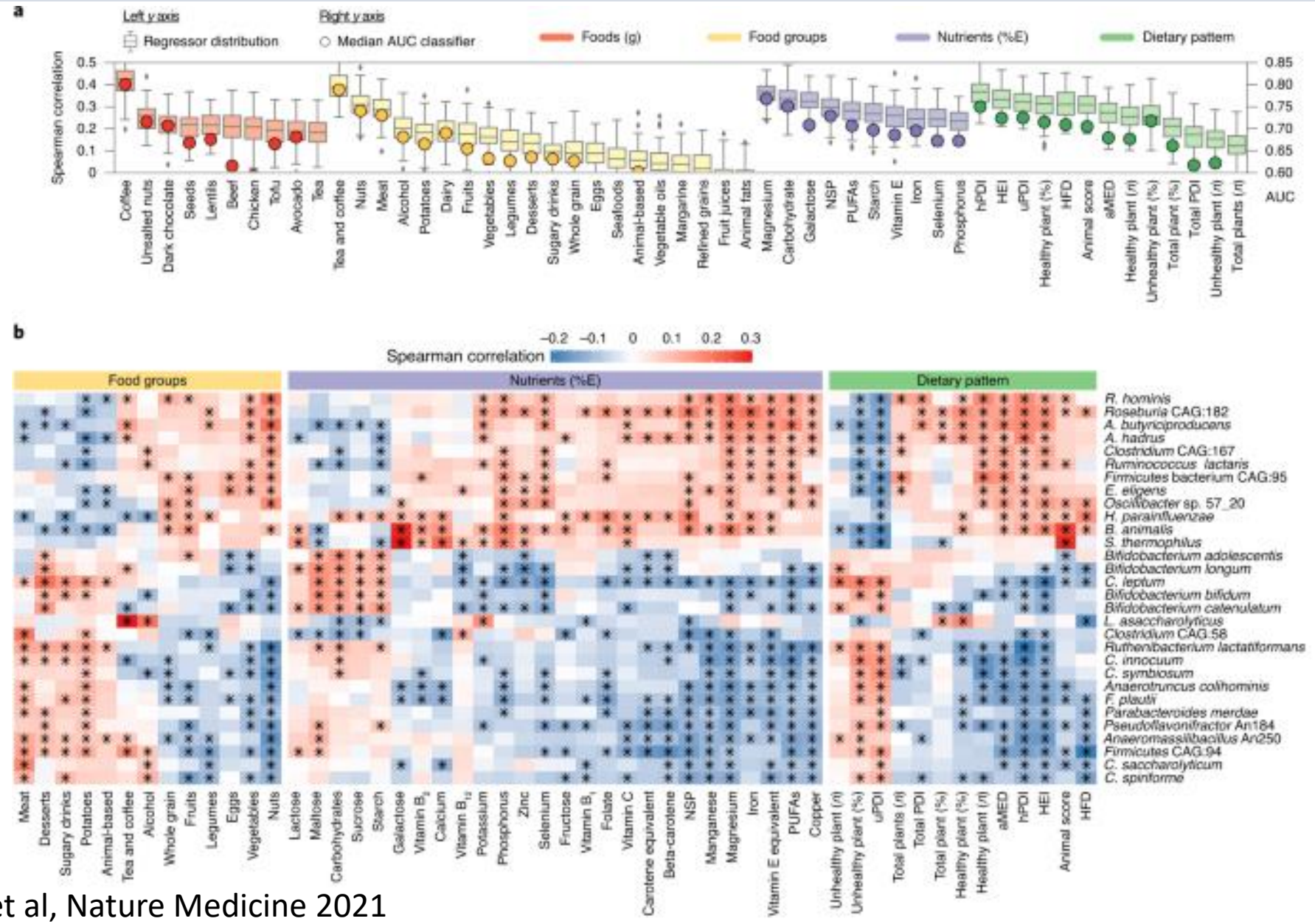
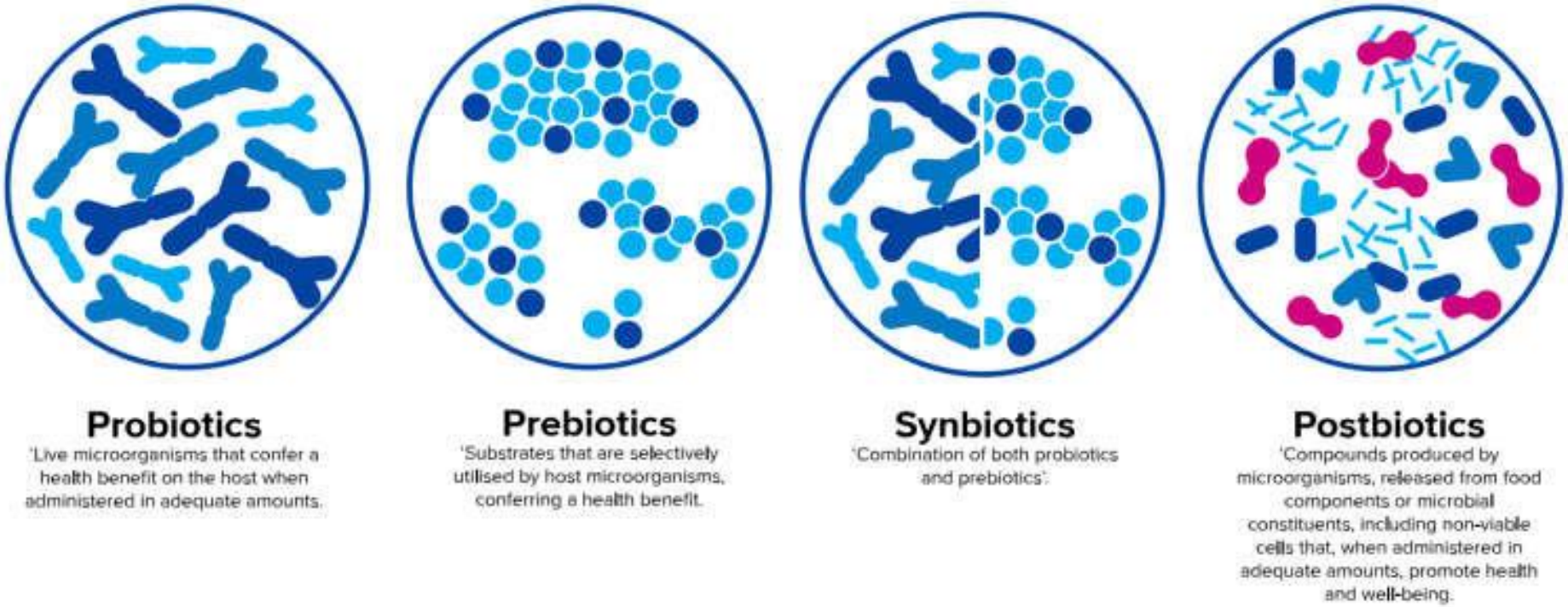
Food feeds and shapes the gut microbiome



Asnicar et al, Nature Medicine 2021

How is the gut microbiome modulated for health benefits ?



Salminen et al, Nutrients 2020

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Prebiotics

Prebiotics

What are prebiotics?

Substrates that are selectively utilized by host microorganisms conferring a health benefit. Simply put, they are food for beneficial microbes that live on or in us.

What do you look for on the label?

The word 'prebiotic' is seldom used on the label. Look for:

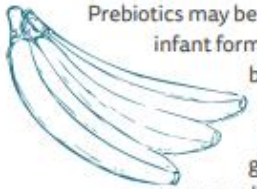
- Galactooligosaccharides (GOS)
- Fructooligosaccharides (FOS)
- Oligofructose (OF)
- Chicory fiber
- Inulin

ISAPP

Connecting science, microbes and health

Prebiotics in food

Some prebiotics (oligofructose and inulin) can be found in onions, garlic, bananas, chicory root, Jerusalem artichokes, but typically are present at low levels. To increase your daily intake, include prebiotic supplements or foods with added prebiotics as part of your diet. Prebiotics may be added to yogurts, infant formula, cereals, breads, biscuits/cookies, desserts or drinks. Try to get at least 5 grams of prebiotics in your diet every day. Eating whole grains, fruits and vegetables, and other fiber-rich foods can help.



Prebiotics in mother's milk

Human milk provides a rich source of prebiotics to the nursing baby. They support infant's health by encouraging beneficial gut microbes.

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What are probiotics?

Live microorganisms which ☑

when administered in **adequate amounts** ☑

confer a **health benefit** on the host. ☑

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How do probiotics work ?

PROBIOTICS INTERACT WITH...

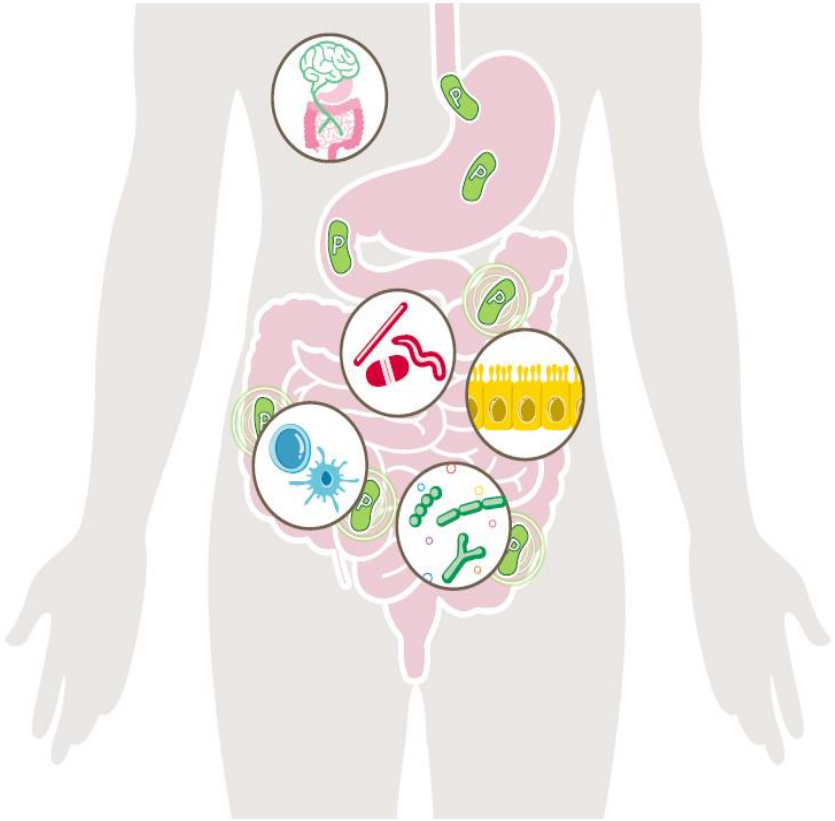
Brain through the vagus nerve

Pathogens

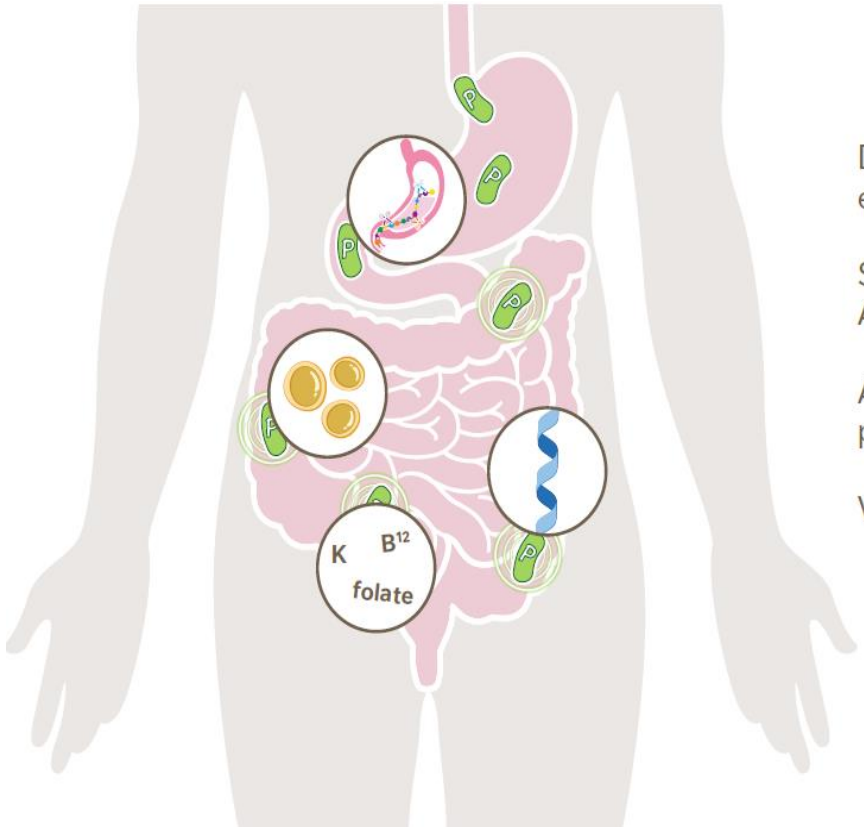
Gut cells

Immune cells

Microbiome



... AND PRODUCE POSTBIOTICS LIKE:



Digestive enzymes

Short Chain Fatty Acids

Anti-microbial peptides

Vitamins

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Examples of health benefits delivered by probiotics

Reduces crying time in colicky babies

Mitigate allergic symptoms

Protects against infections

Supports immune function

Improves gut transit and function

Reduces anxiety

A probiotic links a bacterial strain to a health benefit

EACH PROBIOTIC IS UNIQUELY IDENTIFIED...

Lactobacillus *johnsonii* La1

Genus Species Strain

... AND PROVIDES SPECIFIC BENEFITS

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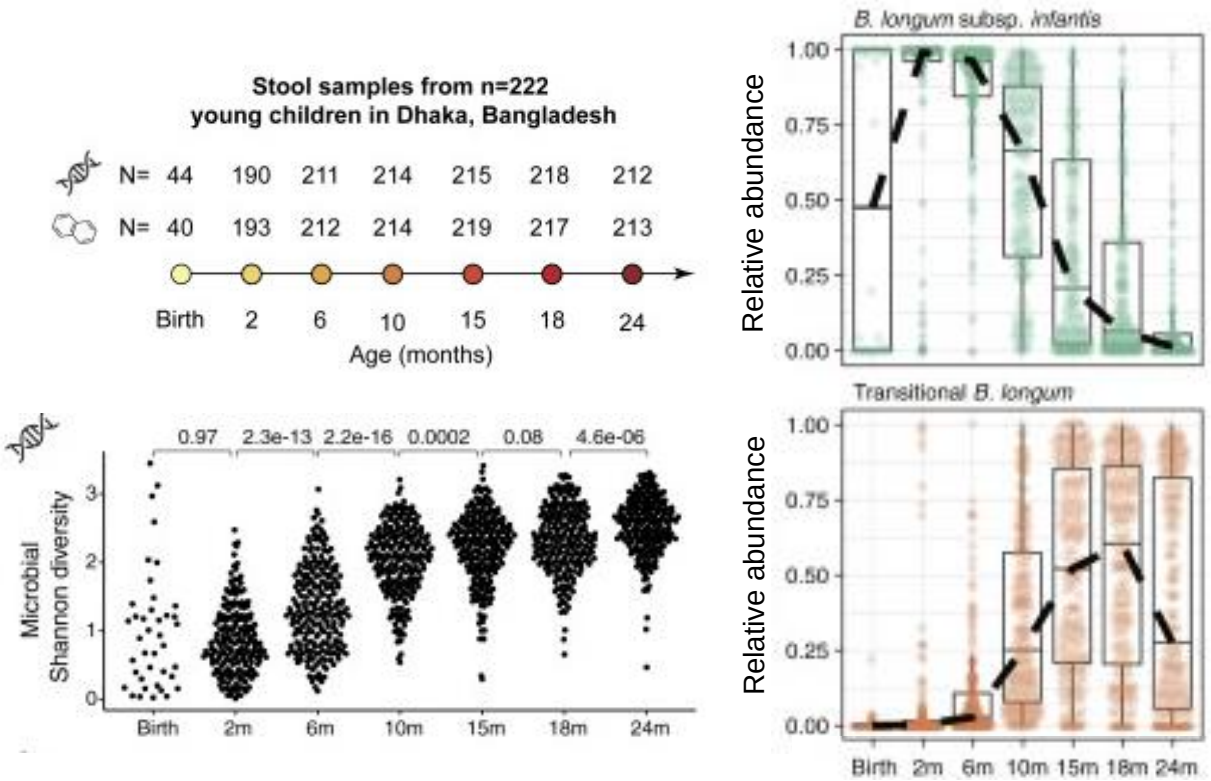
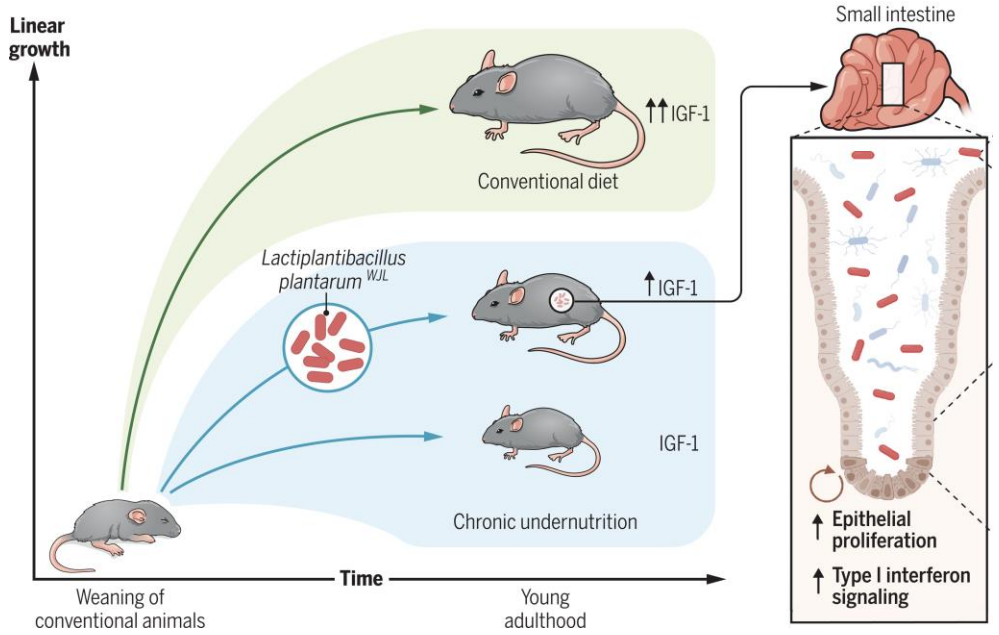
Examples of discovery of novel probiotics

Discovery of a transitional strain that supports the milk to solid food diversification in infants



Vatanen et al, Cell 2022

Discovery of a strain that stimulates faltered growth



Schwarzer et al, Science 2023

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Materials for project work

- Reason to believe
- Preclinical assays

Mechanism of action is the pilar of differentiation and population selection

Clarify consumer need & business opportunity

Define product format & positioning

Identify bioactive & physiological mechanism of action

Ensure regulatory compliance

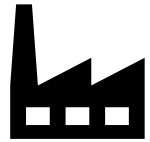
Plan & budget properly

Test in relevant population

Develop technical solutions

Ensure quality & safety

Calculate costs & benefits (P&L)



Post-launch monitoring...

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Is novelty an advantage ?

Is the technology mature?

Are consumers ready (know & trust)?

Is the price acceptable?

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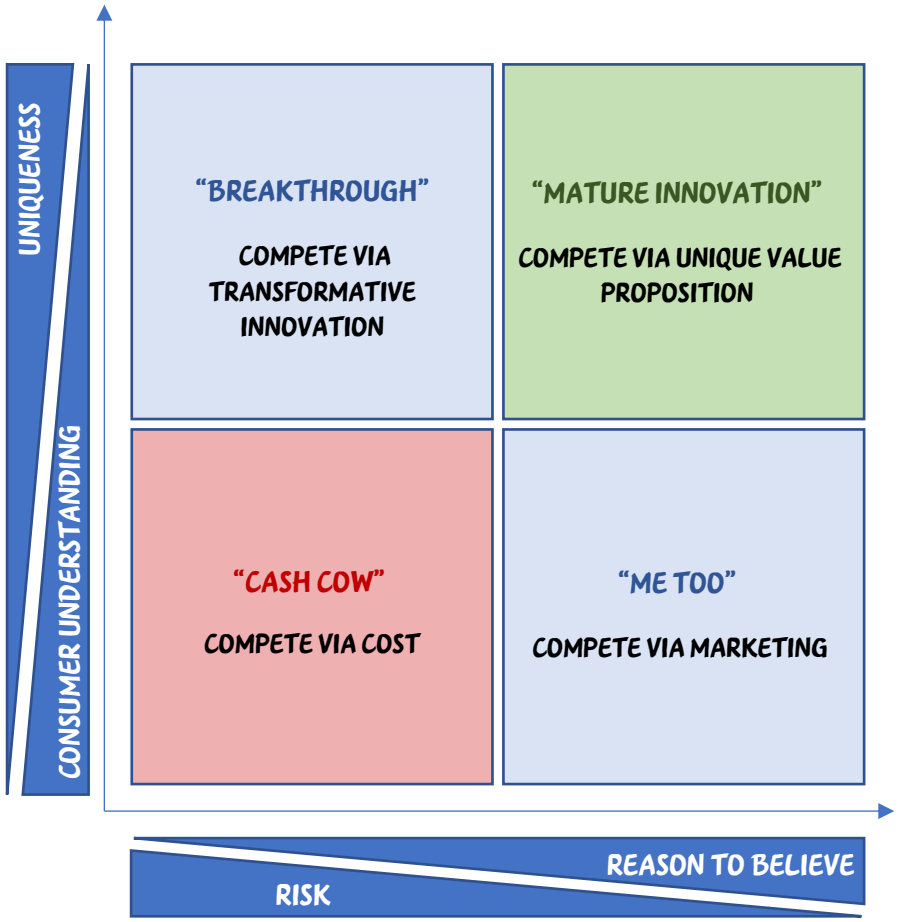
Innovation balance: uniqueness vs risk



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What are strong reasons to believe for nutrition & health

- Exisiting **interventional clinical trials**:
  - With ingredient in same population
  - With ingredient in a different population
  - With different ingredient targeting similar mechanism

- **Observational clinical trial or epidemiology** linking the ingredient to a health benefit

- Exisiting **preclinical science** on ingredient or mechanism of action:
  - Ingredient➲health benefit
  - Ingredient➲mechanism & mechanism➲health benefit

- **Human genetics** (+ mouse genetics if translation of model well validated)

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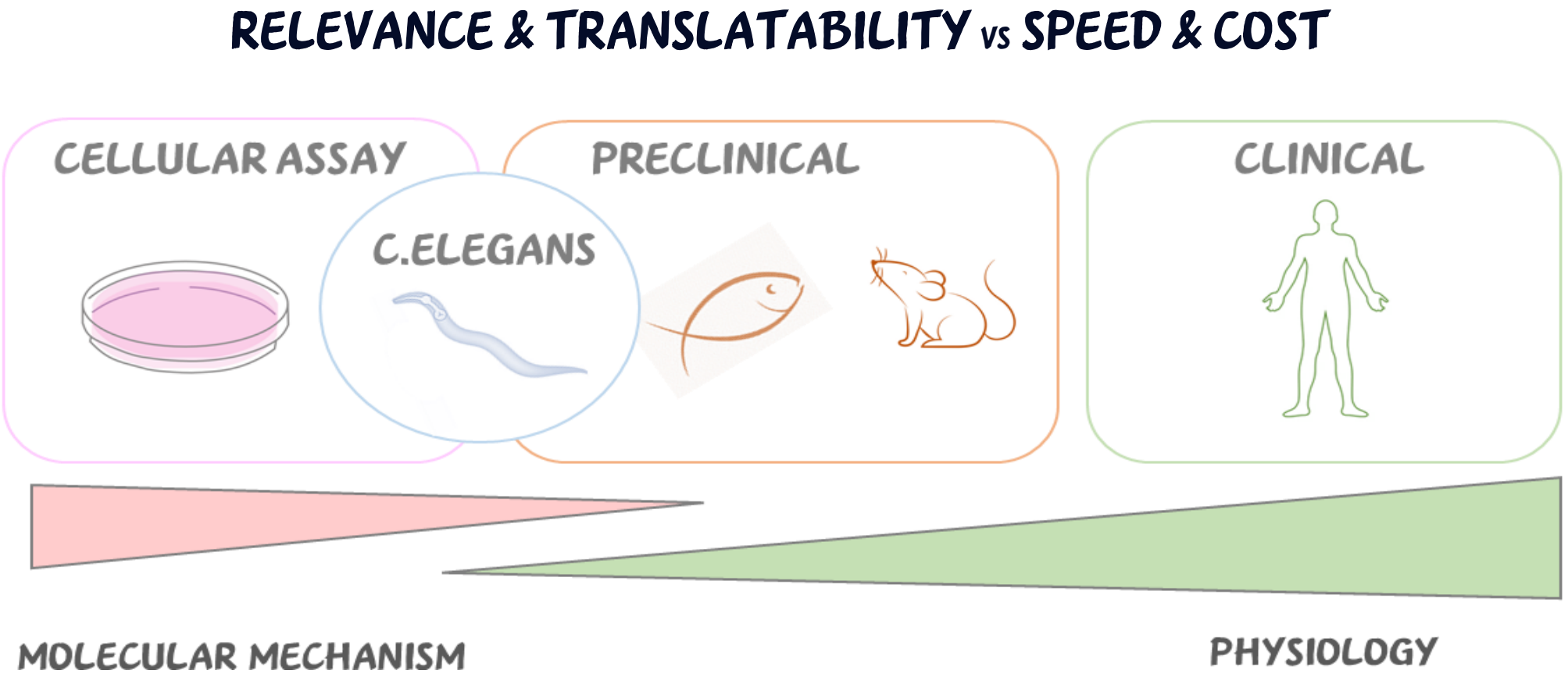
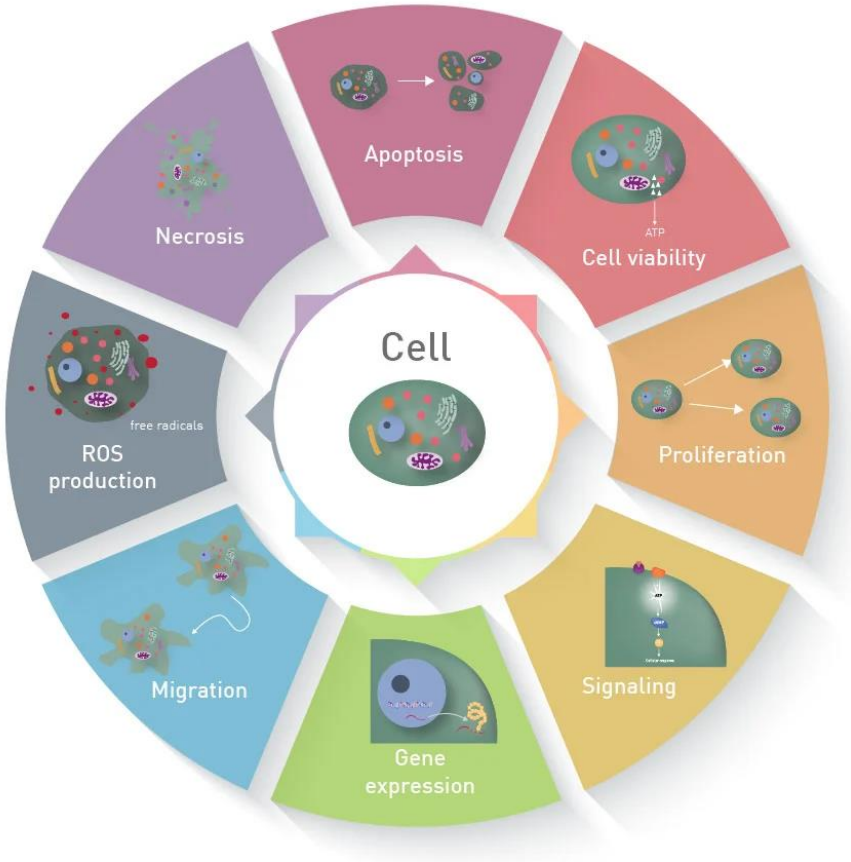
How to chose a preclinical model



There is no perfect model: need to understand if the model predicts well the final physiology

Biochemical & cellular assays

	Biochemical Assays	Cell Based Assays
DEFINITION	Biological assays are target based in-vitro biochemical tools for analyzing biomolecules quantitatively or qualitatively	Cell based assays are physiology-based assays that allow the detection of the response of biological organisms to a particular substance or biomolecule
SIGNIFICANCE	Target-based	Physiology-based
PURPOSE	Detect and quantify the activity of biomolecules/drugs	Allow the detection of the response of biological organisms/ systems to a particular substance

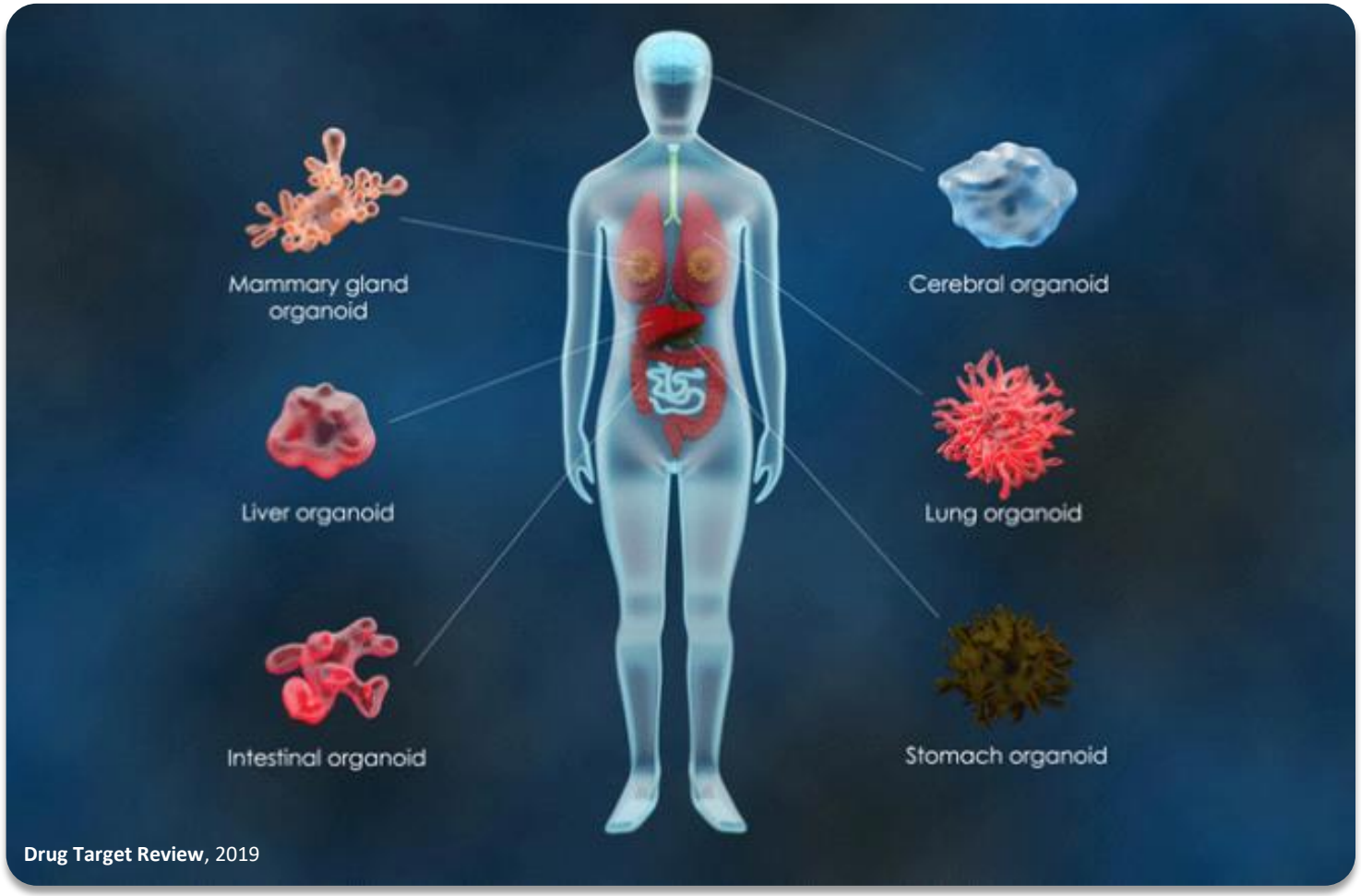


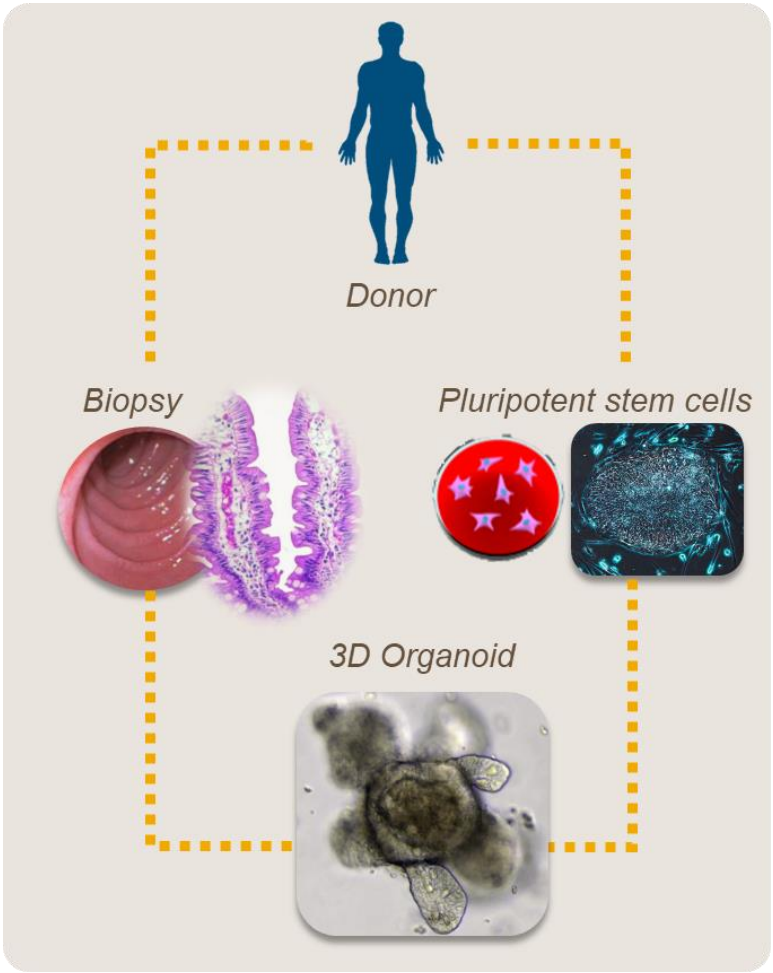
Does the nutrient reach the circulation?

Does the nutrient enter cells?

Organoids

A 3D non-animal *ex-vivo* approach to study human organ function





Advantages: 3D organization / specialization & communication of ≠ cell types / simplified physiological function
Limitations: doesn't model nutrient absorption & organ cross-talk

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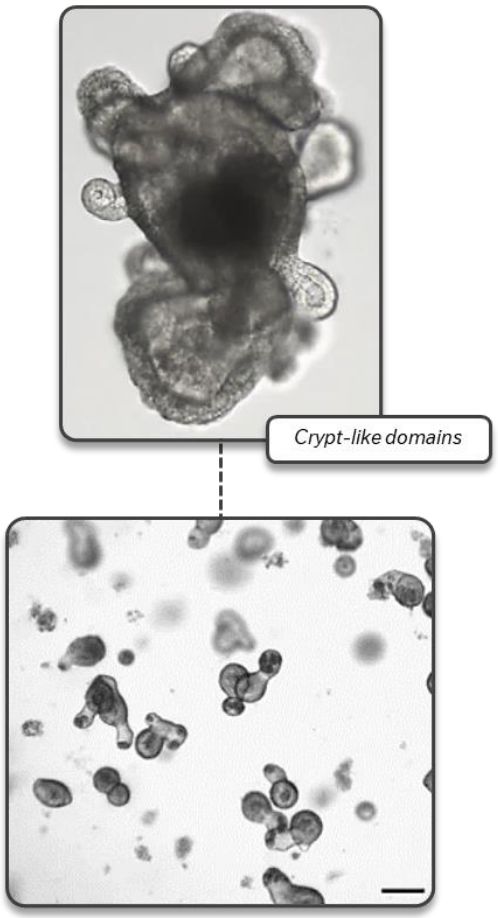
Example of intestinal organoids

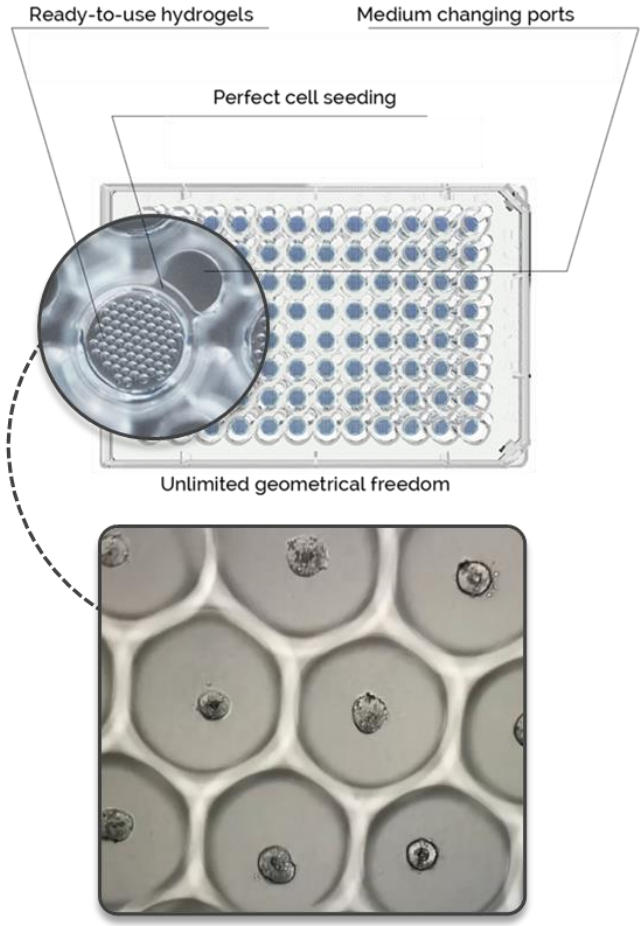
Towards modelling diet–microbiome–host interactions

1st Gen: *Self-organizing biopsy-derived mini-gut organoids*



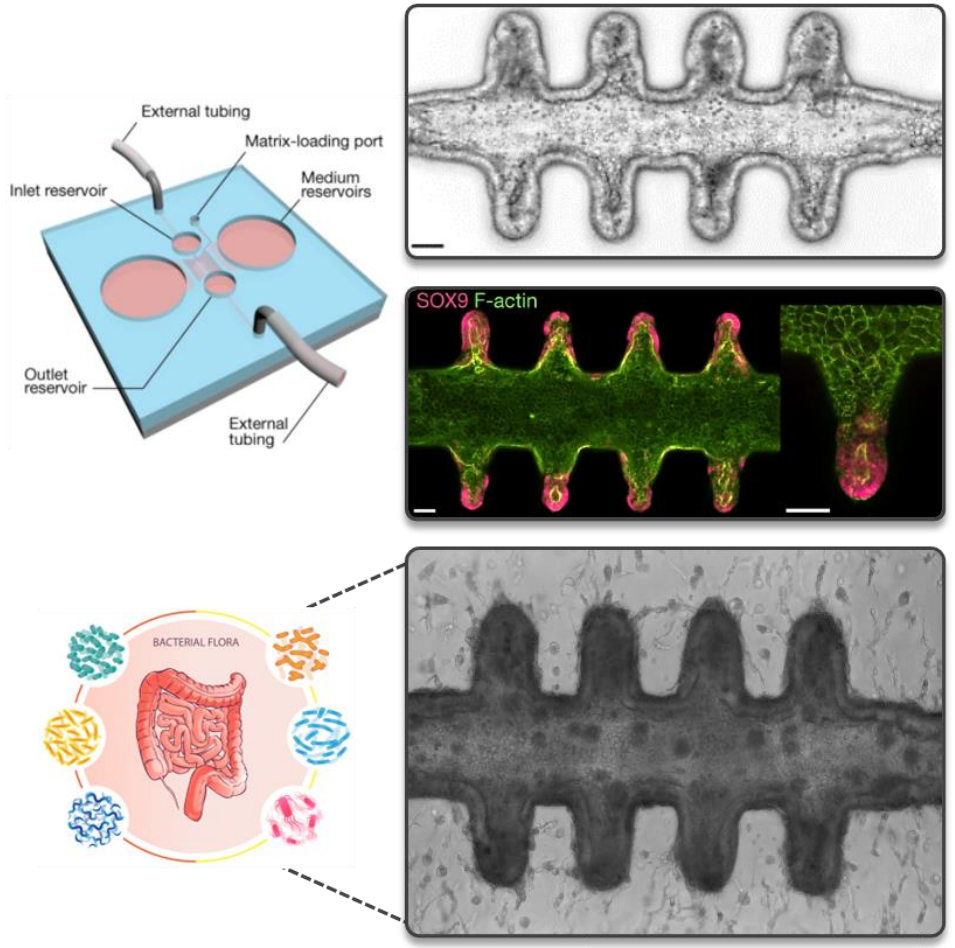
T. Sato et al. **Nature** *(2009)*

2nd Gen: *High-throughput automated organoid culture in microcavity arrays*



N. Brandenberg, S. Hoehnel, F. Kuttler et al. **Nat. Biomed. Eng.** *(2020)*

3rd Gen: *Tube-shaped mini-guts using organoids-on-a-chip platform*



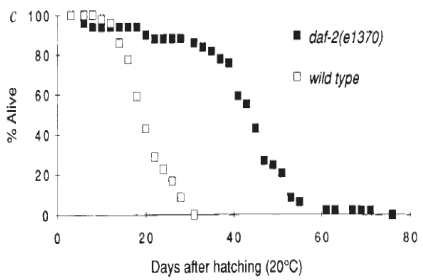
SUNBIOSCIENCE

M. Nikolaev et al . **Nature** *(2020)*

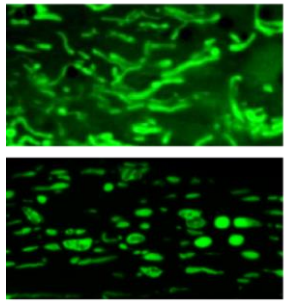
C. elegans: A simple living organism to study complex biology

- ✓ Eukaryotic nematode
- ✓ Multicellular and multi-tissular
- ✓ Short-lived
- ✓ Easy to manipulate genetically
- ✓ No ethics approval

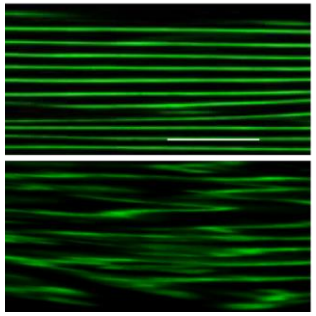
Lifespan studies

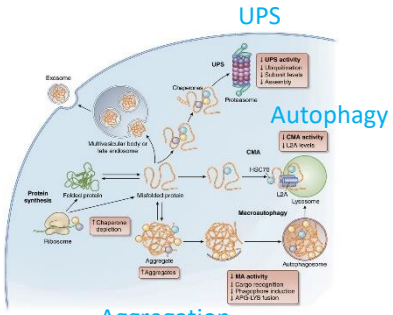


Mitochondrial interventions

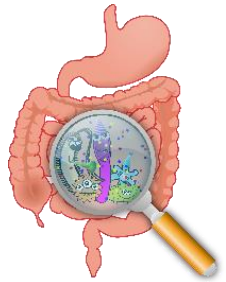


Muscle homeostasis

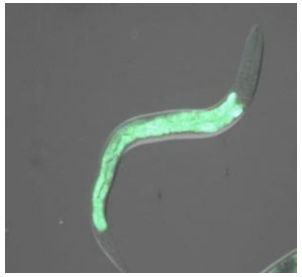




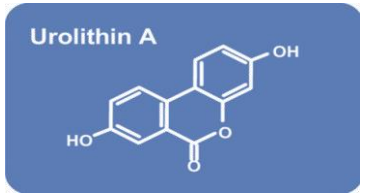
Proteostasis/ aggregation

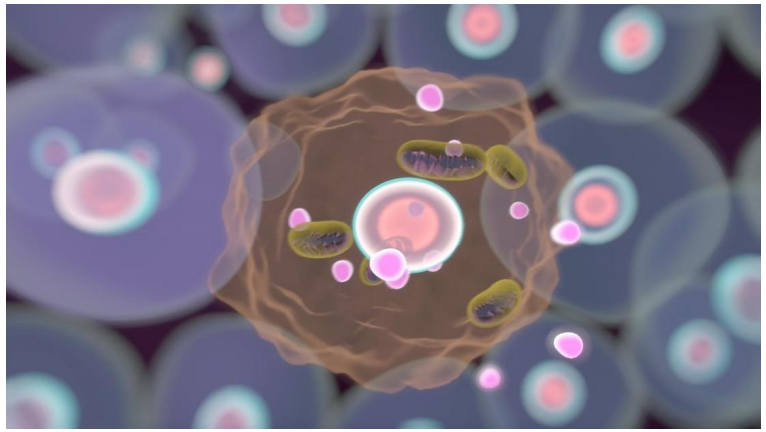


Gut function



Example of c. elegans application for the health benefits of Urolithin A





nature medicine

Urolithin A induces mitophagy and prolongs lifespan in *C. elegans* and increases muscle function in rodents

Dongryeol Ryu[1,5], Laurent Mouchiroud[1,5], Pénélope A Andreux[1,2,5], Elena Katsyuba[1], Norman Moullan[1], Amandine A Nicolet-dit-Félix[1], Evan G Williams[1], Pooja Jha[1], Giuseppe Lo Sasso[1], Damien Huzard[3], Patrick Aebischer[4], Carmen Sandi[3], Chris Rinsch[2] & Johan Auwerx[1]

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Example of c. elegans application for the health benefits of Urolithin A

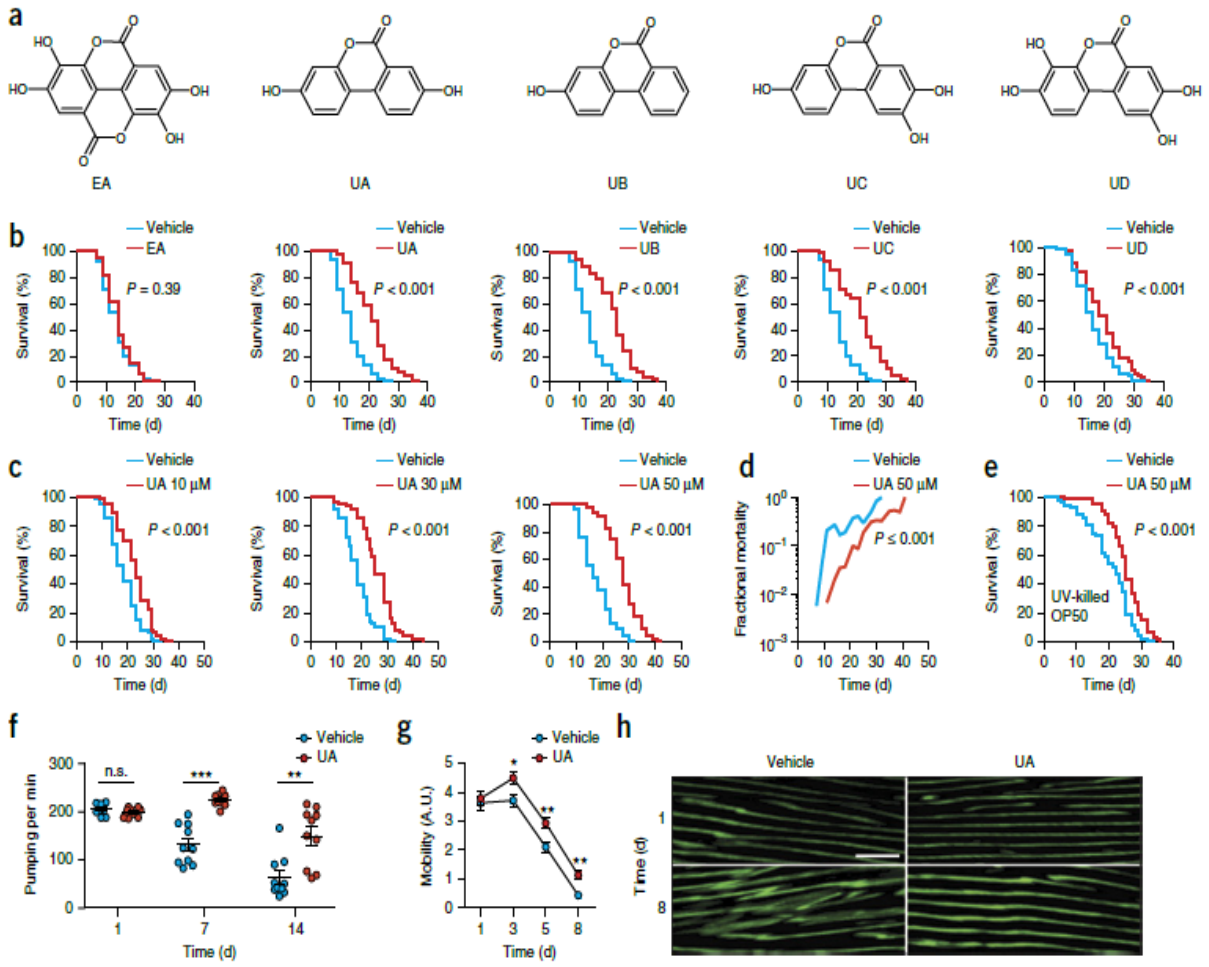


Figure 1 UA improves fitness and extends lifespan. (**a**) Chemical structures of EA and its derived metabolites UA, UB, UC and UD. (**b**) Lifespan of worms treated with 50 µM EA, UA, UB, UC or UD, or with vehicle (1% DMSO). (**c**) Lifespan of worms treated with 10, 30 or 50 µM UA, or the corresponding concentration of vehicle. (**d**) Mortality rate in worms treated with 50 µM UA or vehicle. (**e**) Lifespan of worms maintained on UV-killed OP50 bacteria treated with 50 µM UA or vehicle. For **b**,**c**,**e**, *P* values represent comparison with vehicle calculated using log rank test. (**f**) Pharyngeal pumping at days 1, 7 and 14 of adulthood in worms treated with 50 µM UA or vehicle ($n = 10$). Values are mean ± s.e.m. n.s., not significant; $^{**}P \leq 0.01$, $^{***}P \leq 0.001$ by unpaired *t* test. (**g**) Mobility of worms in arbitrary units (A.U.) at days 1, 3, 5 and 8 of adulthood in worms treated with 50 µM UA or vehicle ($n = 10$). Values are mean ± s.e.m. $^{*}P \leq 0.05$, $^{**}P \leq 0.01$; by two-way analysis of variance (ANOVA) followed by Bonferroni post-tests. (**h**) Representative images ($n = 5$ images per group) of muscle morphology at days 1 and 8 of adulthood of $p_{myo\text{-}3}$MYO-3::GFP worms treated with 50 µM UA or vehicle. Scale bar, 8 µm. Data are representative of at least two independent experiments. See also **Supplementary Figures 1–3** and **Supplementary Tables 1** and **2**.

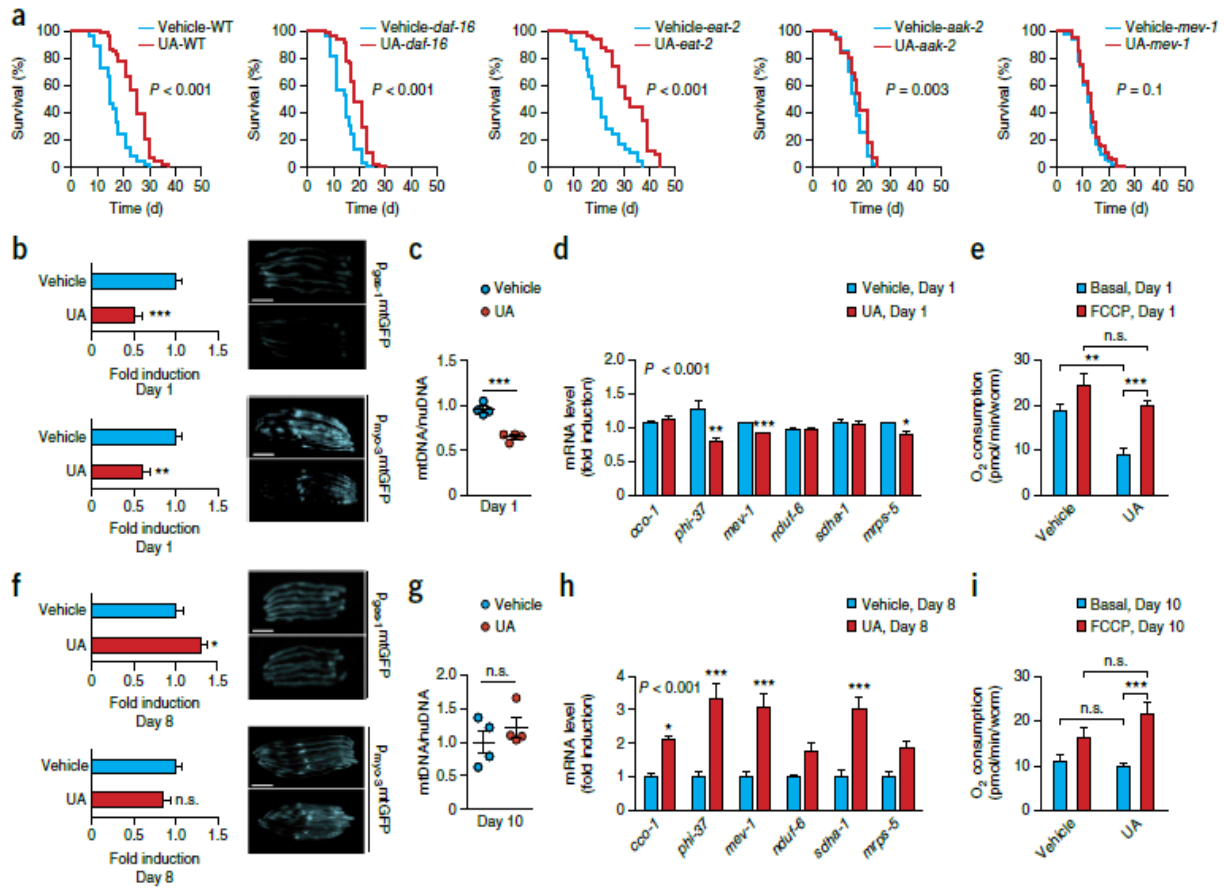


Figure 2 UA alters mitochondrial functions in *C. elegans*. (**a**) Lifespan of wild-type, *daf-16(mu86)*, *eat-2(ad465)*, *aak-2(ok524)* and *mev-1(kn1)* mutants treated with UA or vehicle. *P* values compared with vehicle calculated using log-rank test. (**b**) Representative images (right, $n = 3$) and GFP quantification (left, $n = 8$) of mitochondrial content at day 1 of adulthood in intestinal ($p_{ges\text{-}1}$mtGFP; top) and muscle ($p_{myo\text{-}3}$mtGFP; bottom) mito::GFP reporter strains treated with UA or vehicle. (**c**) mtDNA/nuDNA ratio at day 1 of adulthood in wild-type worms treated with UA or vehicle ($n = 4$). For **b**,**c**, $^{**}P \leq 0.01$, $^{***}P \leq 0.001$; by unpaired *t* test. (**d**) Gene expression at day 1 of adulthood in wild-type worms treated with UA or vehicle ($n = 5$). $^{*}P \leq 0.05$, $^{**}P \leq 0.01$, $^{***}P \leq 0.001$; by one-way ANOVA. (**e**) Respiration at basal level and after short-term incubation with 10 µM FCCP on day 1 of adulthood in wild-type worms treated with UA or vehicle ($n = 5$). $^{**}P \leq 0.01$, $^{***}P \leq 0.001$; n.s., not significant; by two-way ANOVA followed by Bonferroni post-tests. (**f**) Representative images (right, $n = 3$) and GFP quantification (left, $n = 8$) of mitochondrial content at day 8 of adulthood in intestinal ($p_{ges\text{-}1}$mtGFP; top) and muscle ($p_{myo\text{-}3}$mtGFP; bottom) mito::GFP reporter strains treated with UA or vehicle ($n = 8$). (**g**) mtDNA/nuDNA ratio on day 10 of adulthood in wild-type worms treated with UA or vehicle ($n = 4$). For **f**,**g**, $^{*}P \leq 0.05$; n.s., not significant; by unpaired *t*-test. (**h**) Gene expression on day 8 of adulthood in wild-type worms treated with UA or vehicle ($n = 5$). $^{*}P \leq 0.05$, $^{***}P \leq 0.001$; by one-way ANOVA. (**i**) Respiration at basal level and after short-term incubation with 10 µM FCCP on day 10 of adulthood in wild-type worms treated with UA or vehicle ($n = 5$). $^{***}P \leq 0.001$; n.s., not significant; by two-way ANOVA followed by Bonferroni post-tests. For **b**,**f**, scale bars, 250 µm. UA was used at 50 µM. Values are mean ± s.e.m. Data are representative of at least two independent experiments. See also **Supplementary Figure 3** and **Supplementary Table 1**.

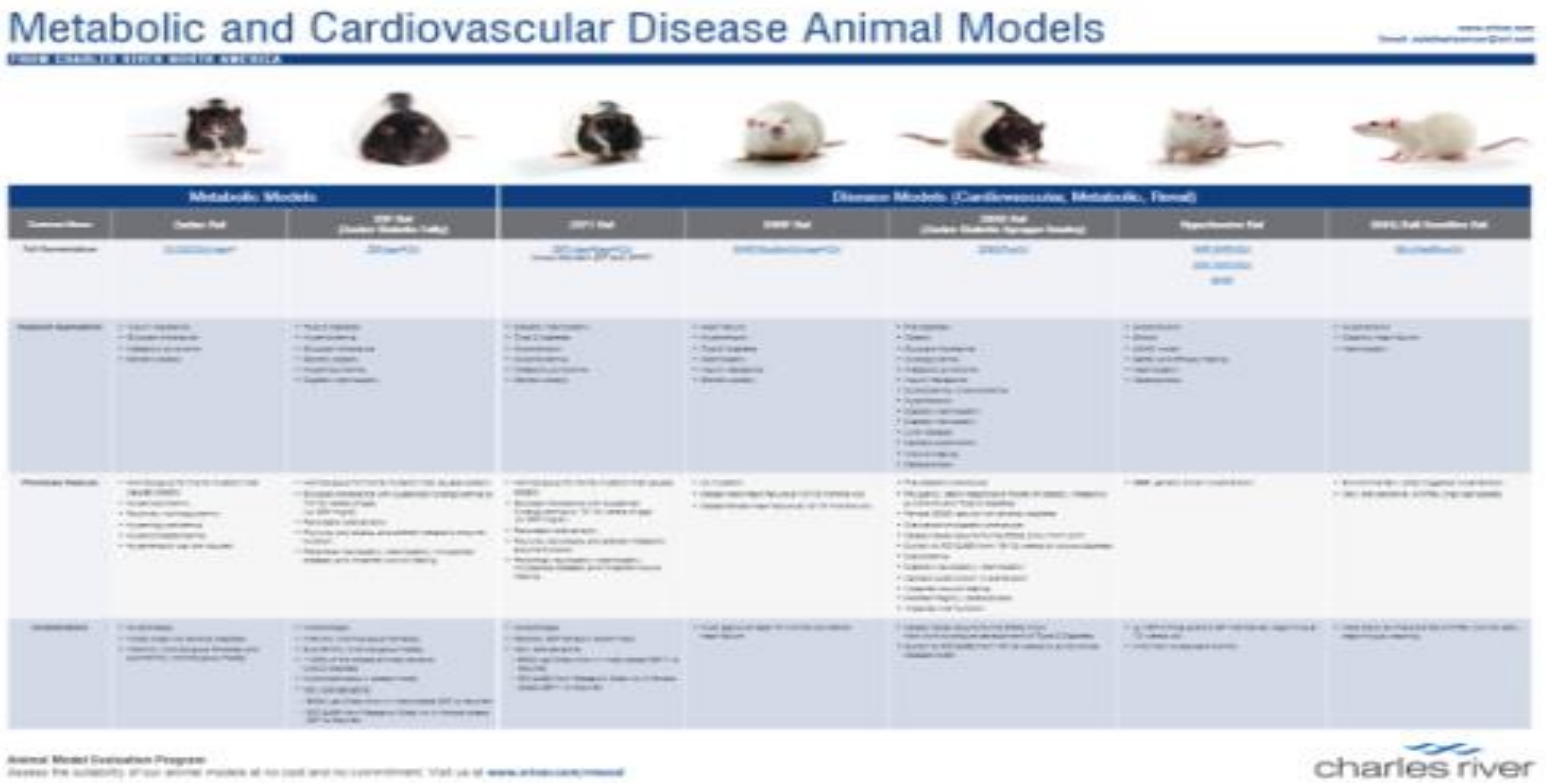
Animal models for nutrition science

RATS **MICE**

Genetically identical

Environmental conditions controlled

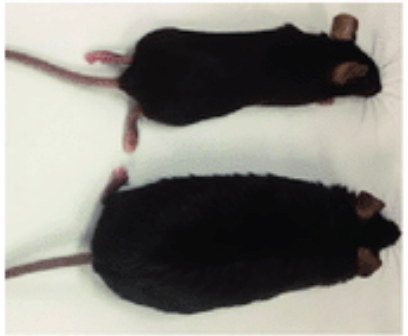
Applications:
Safety
Genetic modifications
Diet-induced phenotypes



https://www.criver.com/user/login?destination=/info-pi-rm-resources-metabolic-cardiovascular-disease-animal-models-na

FARM ANIMALS

(VERY RARE, FOR COMPLEX PHYSIOLOGY)



Normal diet

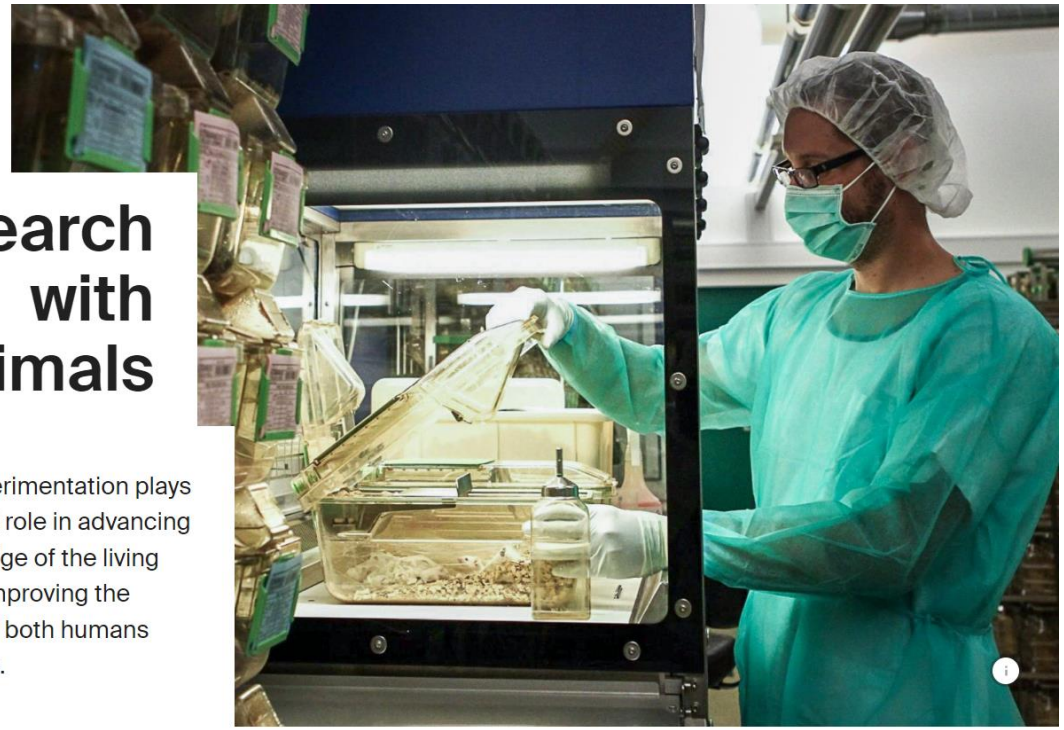
High fat diet (12 weeks)

db/db mice
Leptin receptor mutant

EPFL

Animal research at EPFL

https://www.epfl.ch/research/experimentation-research-with-animals/



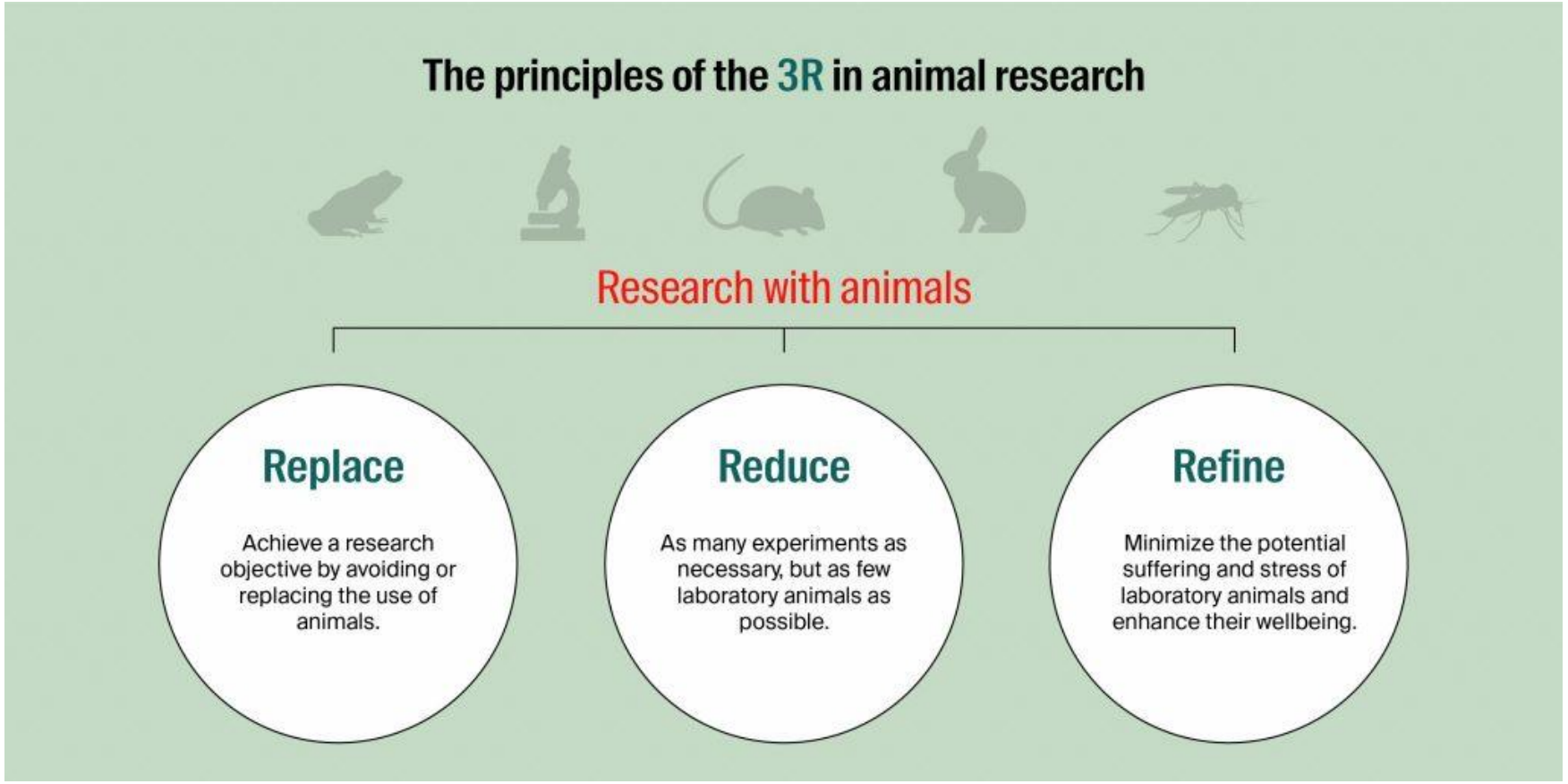
Research with animals

Animal experimentation plays a significant role in advancing our knowledge of the living world and improving the wellbeing of both humans and animals.

Ethics & 3R

Animal research is regulated in Switzerland (project approval & training of researchers)

https://www.blv.admin.ch/blv/en/home/tiere/tierversuche.html



https://swiss3rcc.org/

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