OPTIMIZING PERFORMANCE

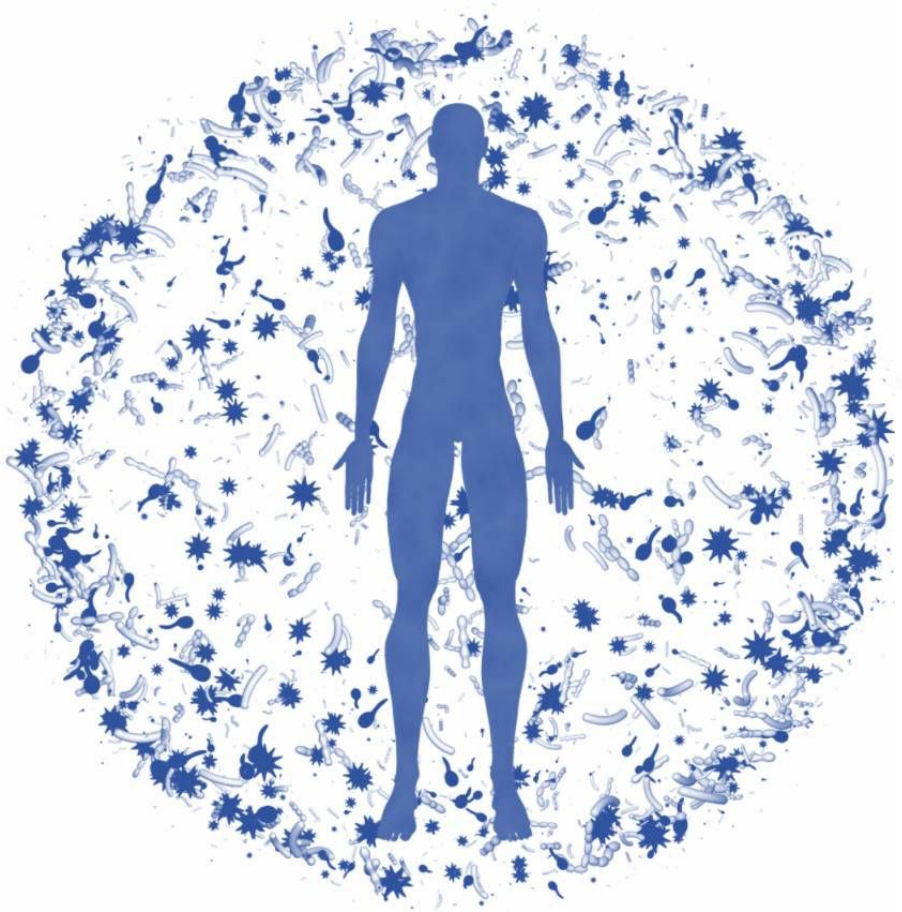
THE MICROBIOME-MITOCHONDRIA CONNECTION

SHAWN MANSKE, ND

Biocidin Botanicals

OBJECTIVES

- Review the role of the microbiome in affecting overall health
- Understand the interactions between the mitochondria and microbial metabolites
- Explore how exercise influences the microbiome and mitochondrial function and, vice versa
- Discuss interventions that target the microbiome and mitochondria, that can optimize exercise and sports performance



OUR MICROBIOME

THE PASSENGERS AS CO-PILOTS

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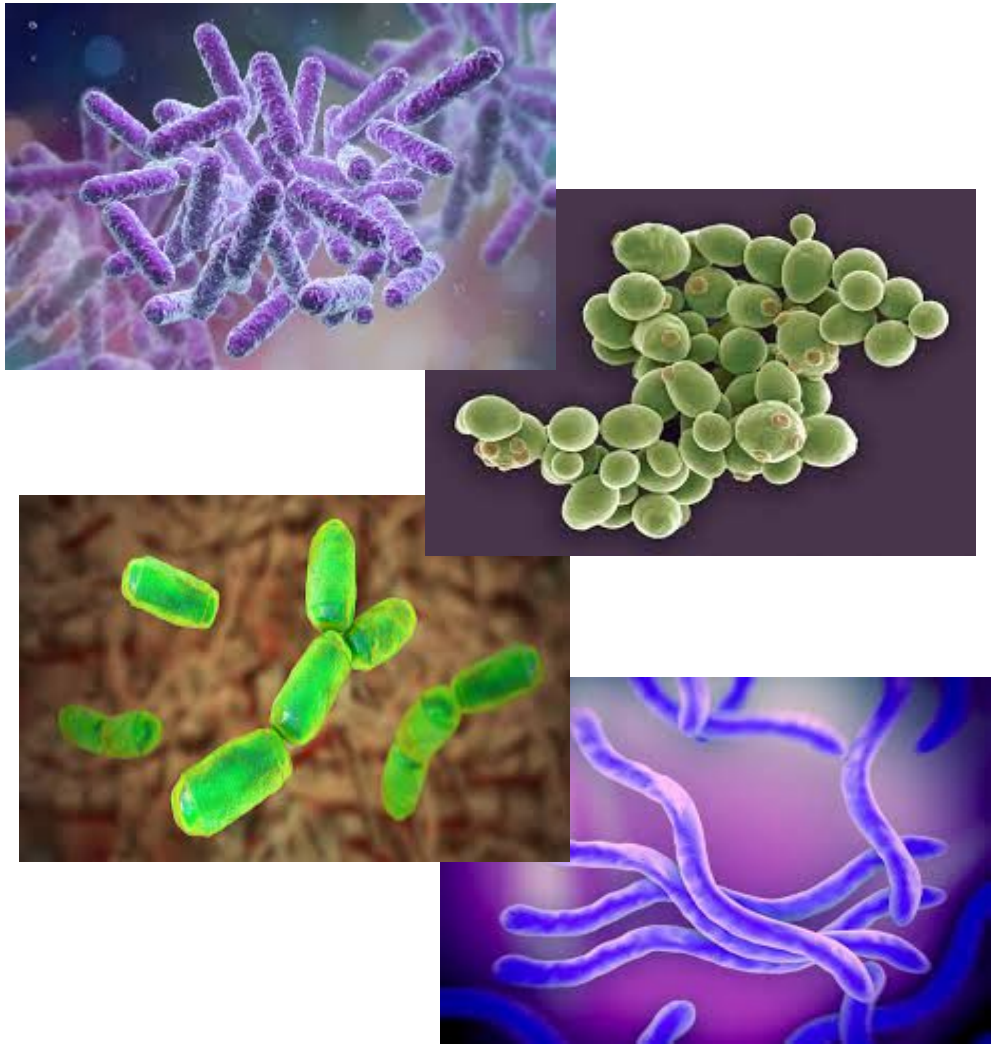
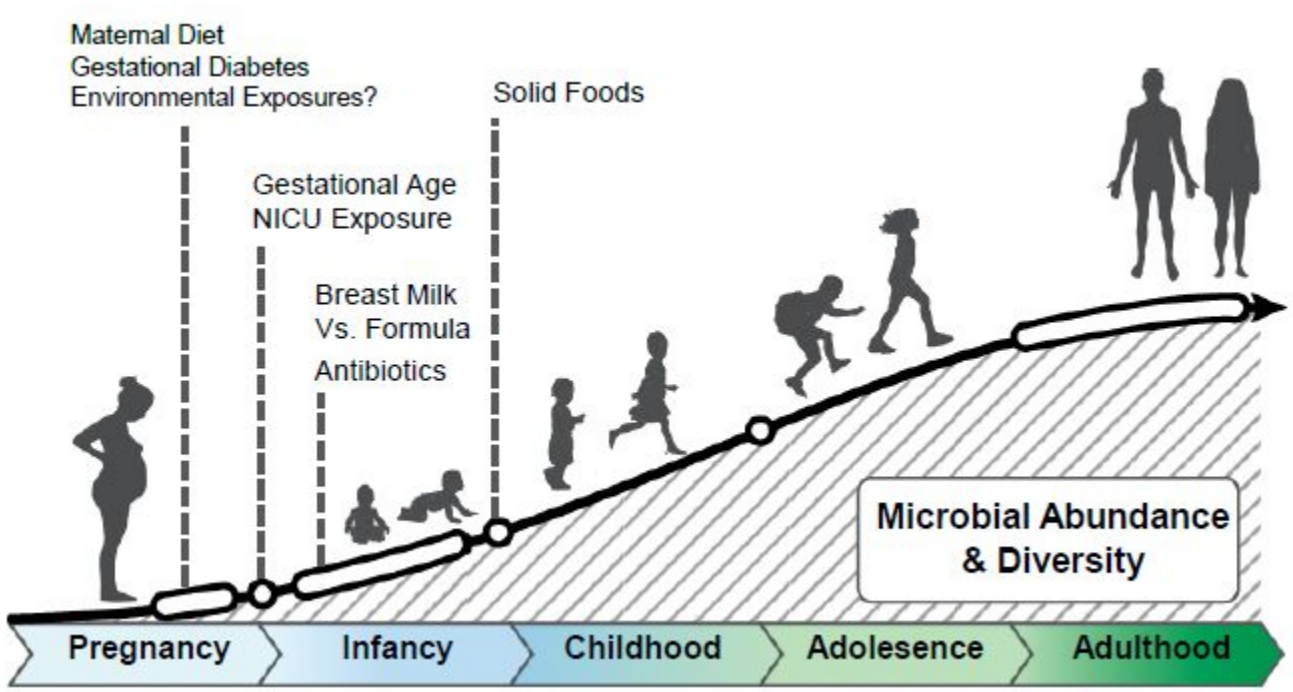
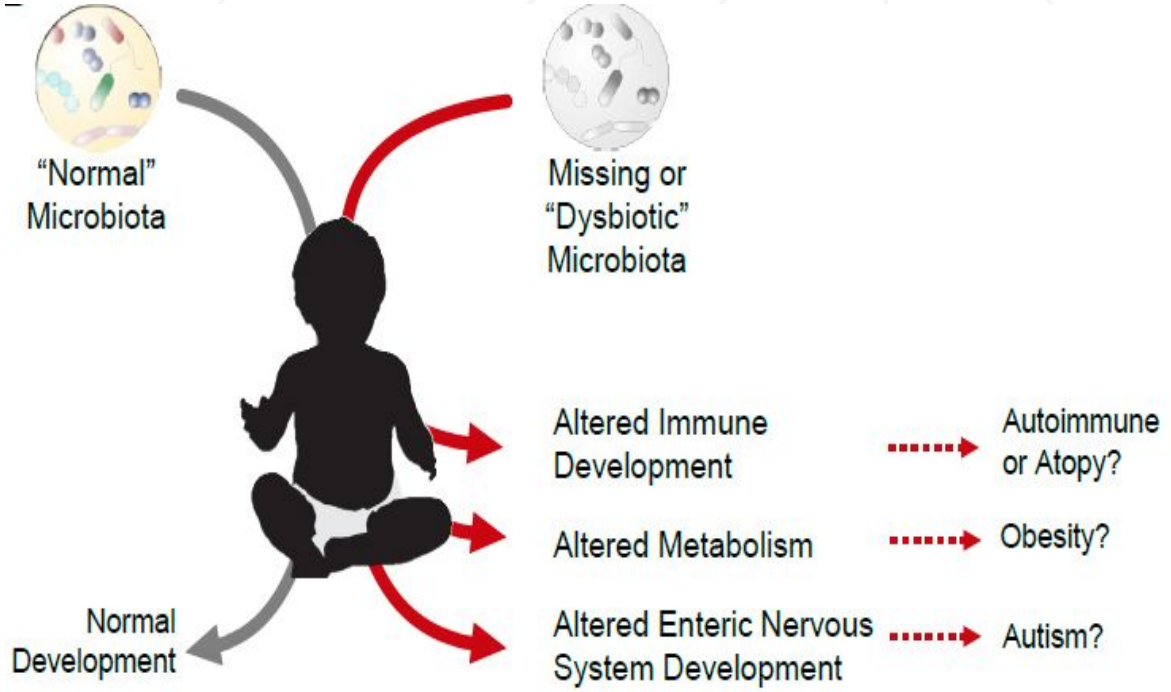
THE MICROBIOME

- The microbiome describes the microorganisms coexisting in or on our bodies – bacteria, fungi and yeasts, viruses, archaea, and parasites.
- Estimated that 80-95% reside in the gastrointestinal tract, while the remaining can be found in the lungs and respiratory tract; bladder and urinary tract; fluid of the eyes; and on the skin.
- Trillions co-exist with us in numbers on par with our own human cells – approximately 37 trillion.
- Microbial genes total 2-3 million; human genes 23,000 (vast microbial gene products).
- Microorganism types include commensals, non-commensals, opportunistic, and pathogenic.



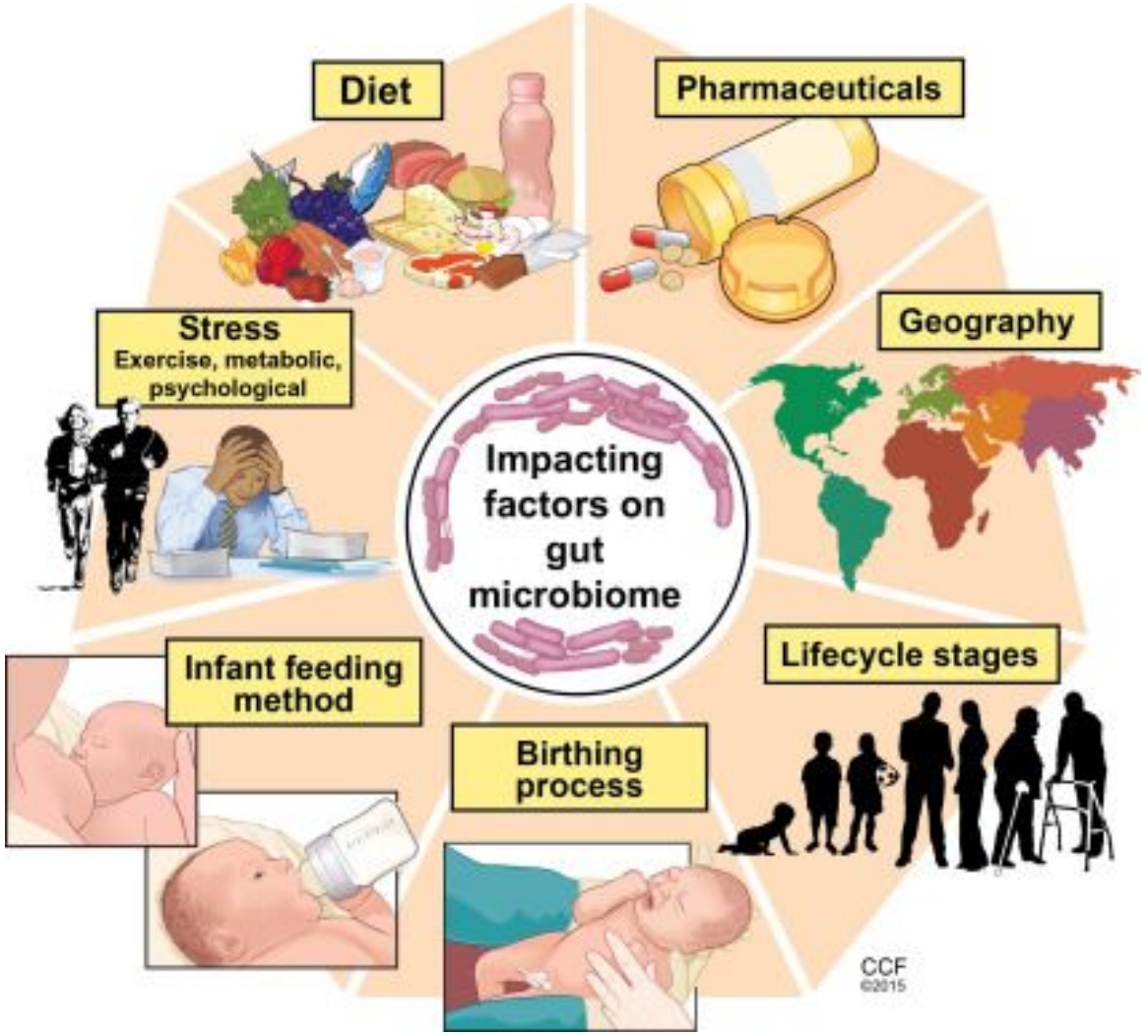
MICROBIOME DEVELOPMENT





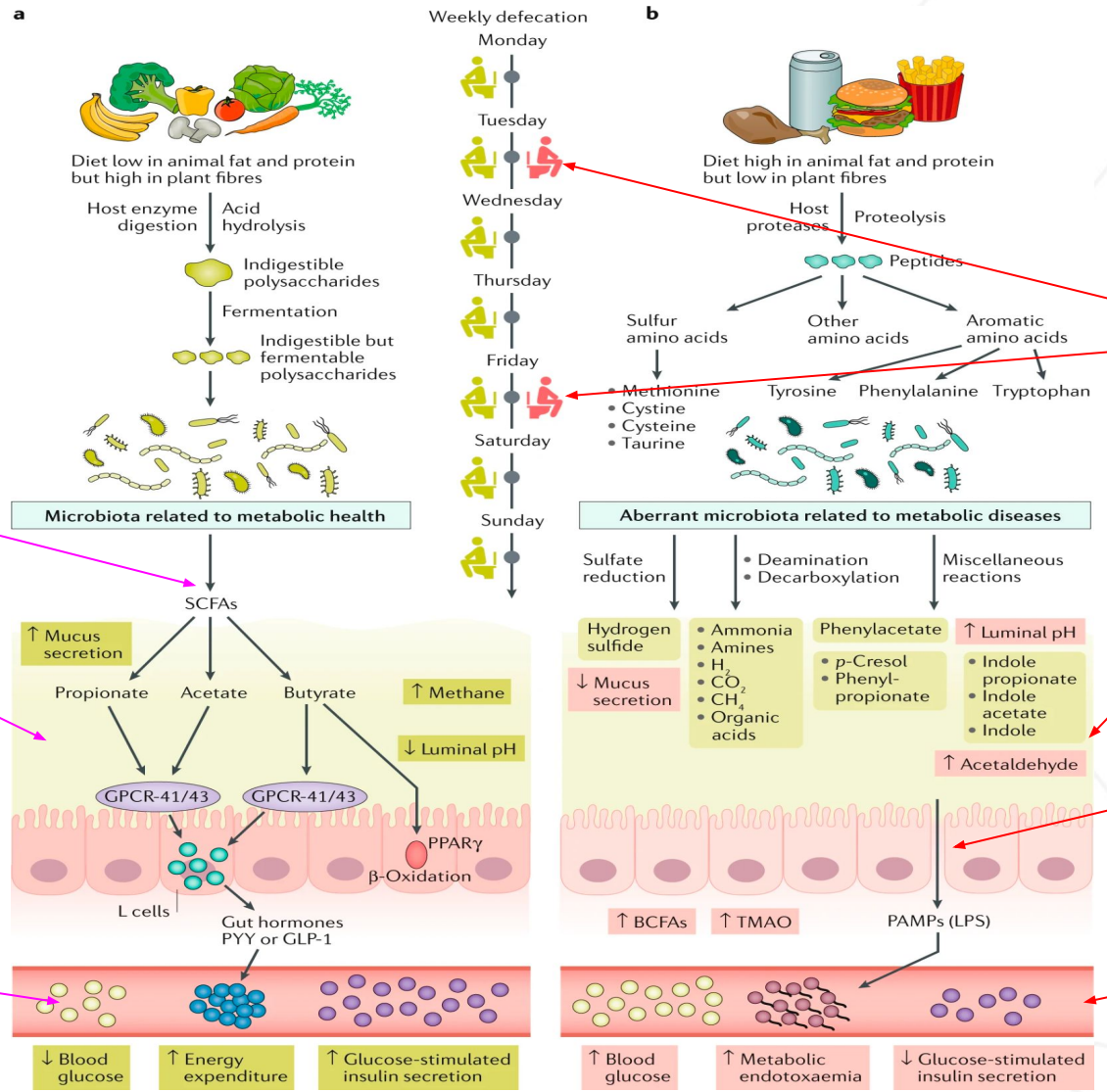
https://www.ncbi.nlm.nih.gov/books/NBK481567/

INFLUENCES ON THE MICROBIOME



https://www.sciencedirect.com/topics/immunology-and-microbiology/gut-microbiome

DIET INFLUENCES THE MICROBIOME TO AFFECT METABOLISM



Short Chain Fatty Acids

Thick Mucus Layer

Blood Sugar

Reduced Defecation

Reduced Mucus Layer

Leaky Gut

Systemic Inflammation

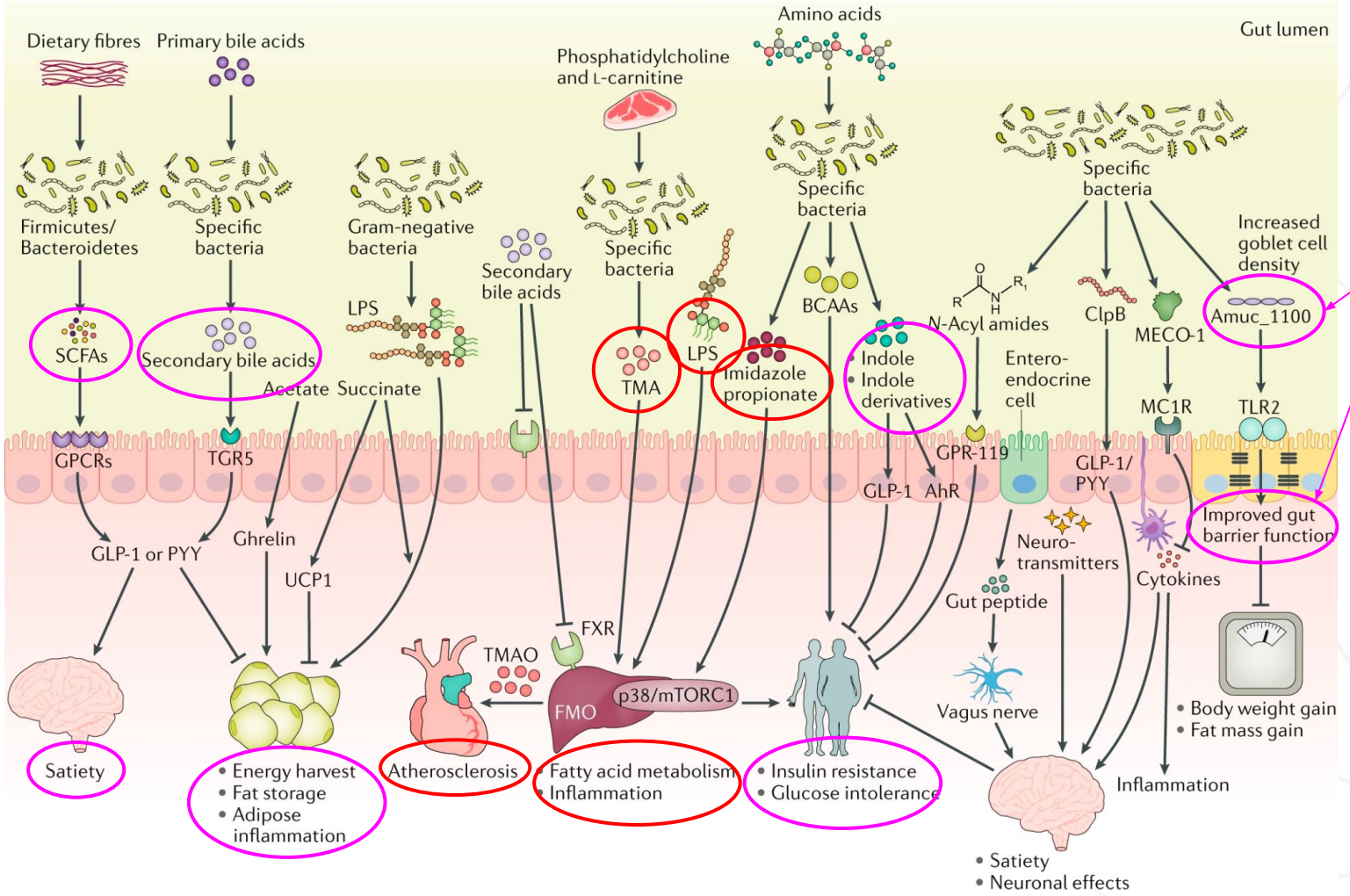
https://www.nature.com/articles/s41579-020-0433-9

MICROBIAL METABOLITES THAT ALTER METABOLISM

- Short Chain Fatty Acids (SCFA)
- 2^0 Bile Acids
- Lipopolysaccharide (LPS)
- Trimethylamine (TMA)
- Branched Chain Amino Acids (BCAA)
- N-acyl amide
- Bacterial synthesized neurotransmitters (Trps), ex:serotonin

https://www.nature.com/articles/s41579-020-0433-9

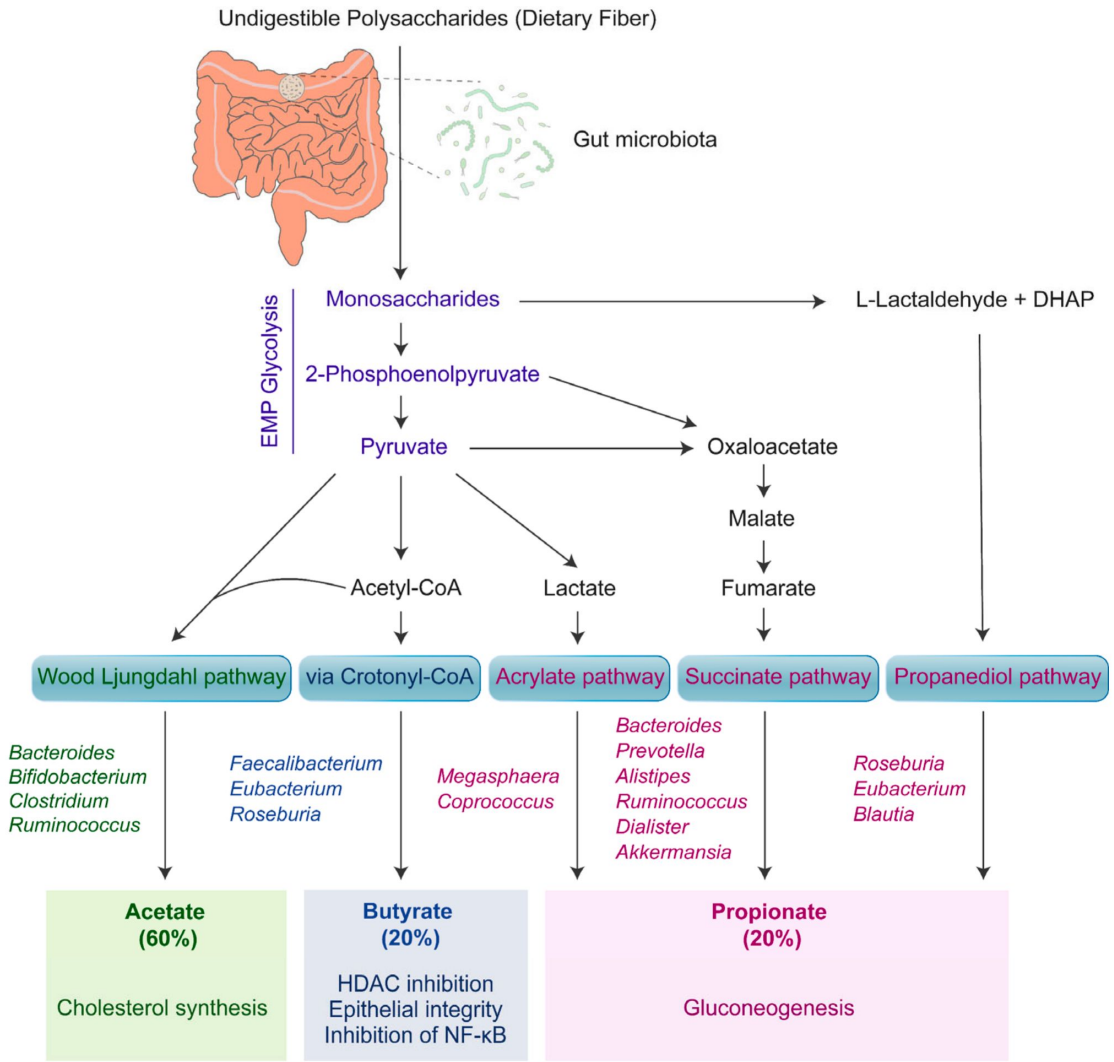
MICROBIAL METABOLITES ALTER METABOLISM



https://www.nature.com/articles/s41579-020-0433-9

BACTERIAL SHORT CHAIN FATTY ACID PRODUCTION

Keystone Species
Akkermansia
Faecalibacterium
Roseburia
Ruminococcus
Bifidobacterium spp.

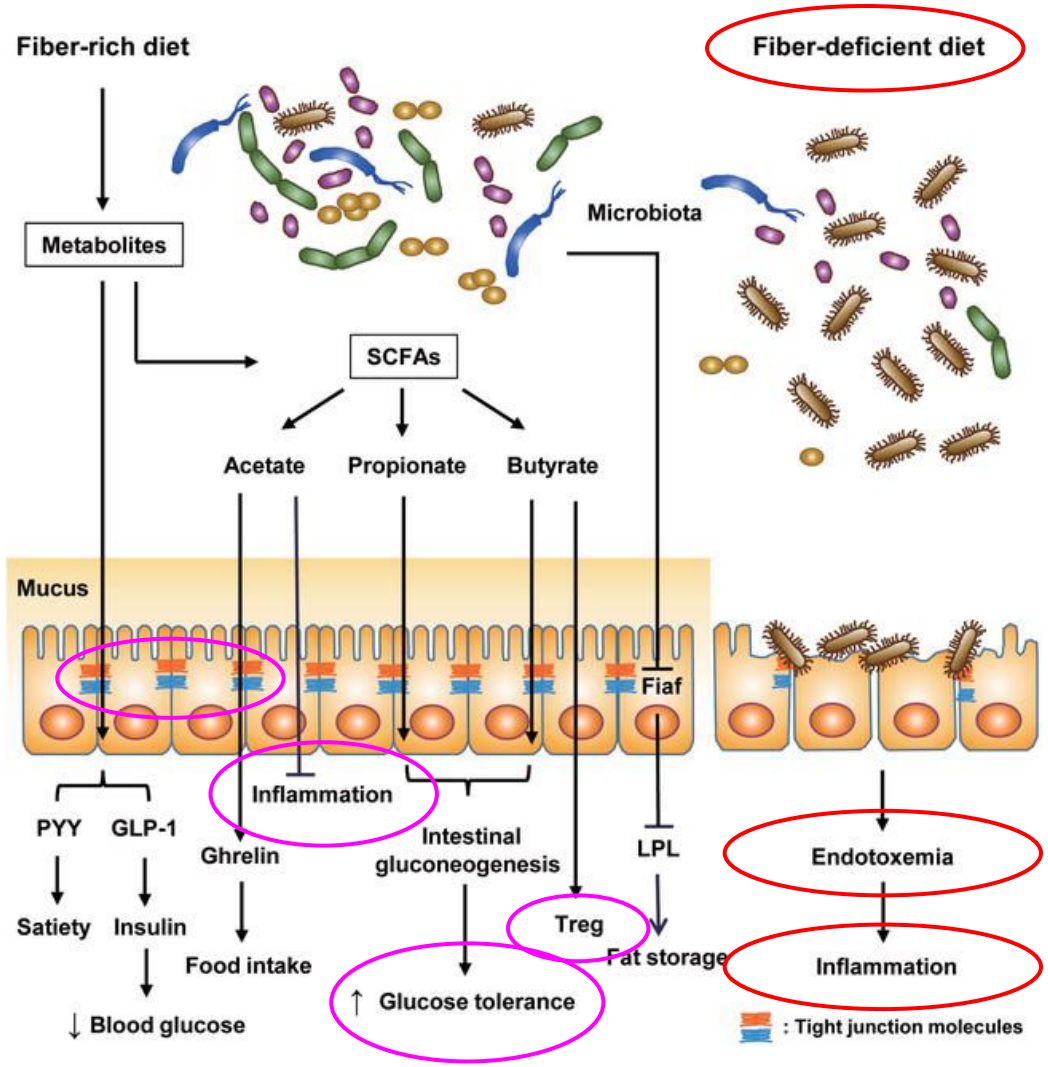


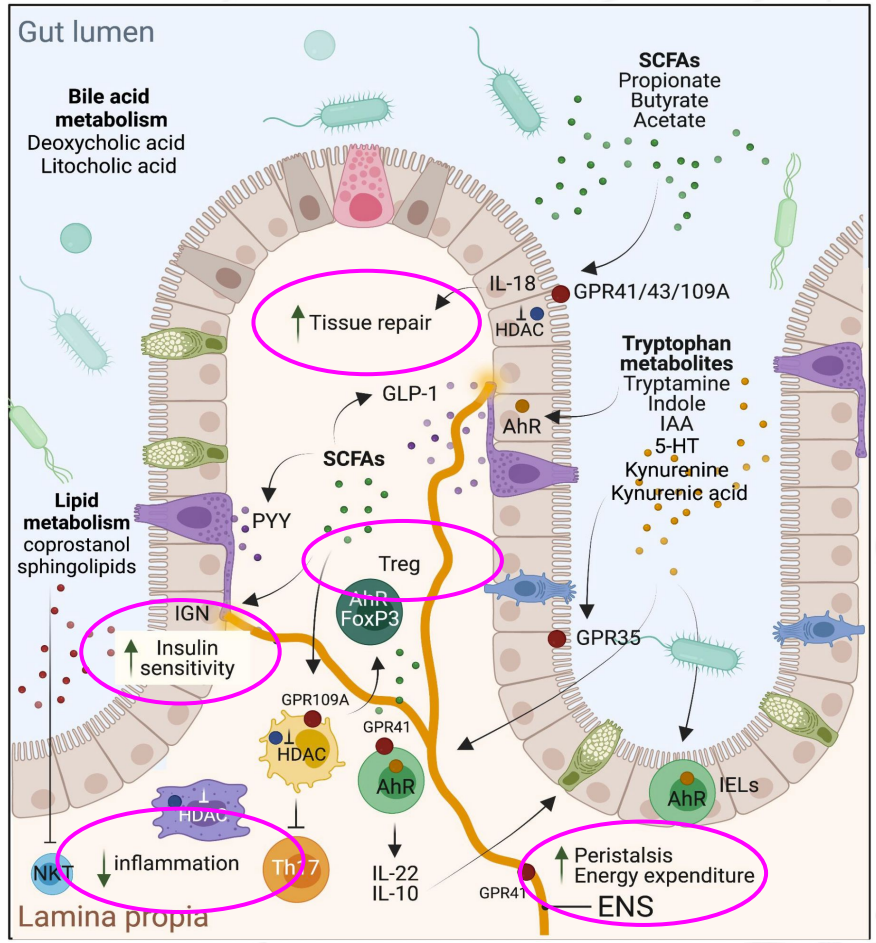
Keystone Species
"microbial keystone taxa are highly connected taxa that individually or in a guild exert a considerable influence on microbiome structure and functioning irrespective of their abundance across space and time. These taxa have a unique and crucial role in microbial communities, and their removal can cause a dramatic shift in microbiome structure and functioning."

https://pubmed.ncbi.nlm.nih.gov/29789680/

https://www.mdpi.com/1422-0067/23/5/2679

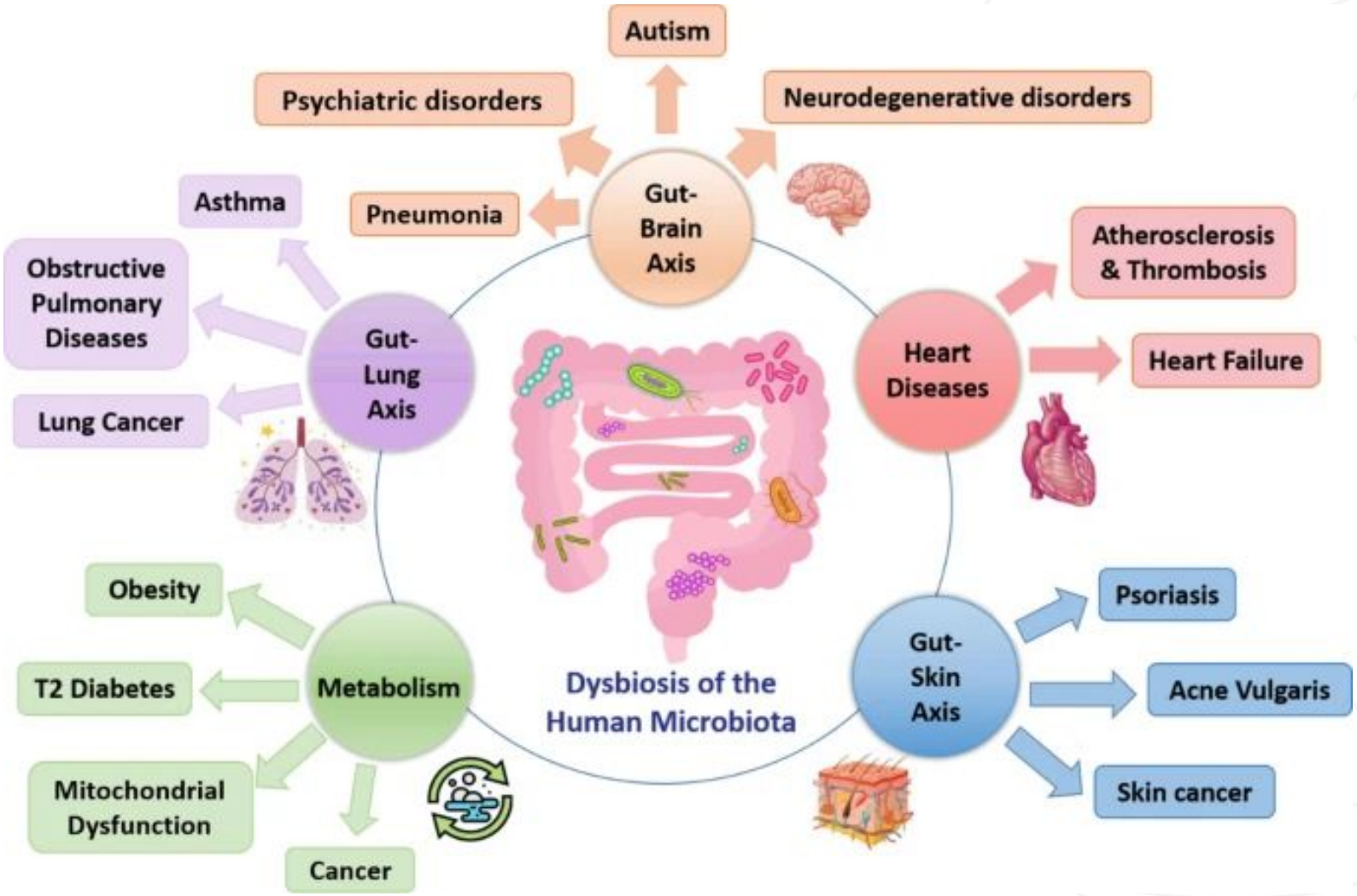
SCFAS AND INTESTINAL BARRIER FUNCTION





https://www.intechopen.com/chapters/73646
https://www.frontiersin.org/articles/10.3389/fcell.2021.719072/full

DYSBIOSIS AND DISEASE



https://pubmed.ncbi.nlm.nih.gov/35255932/

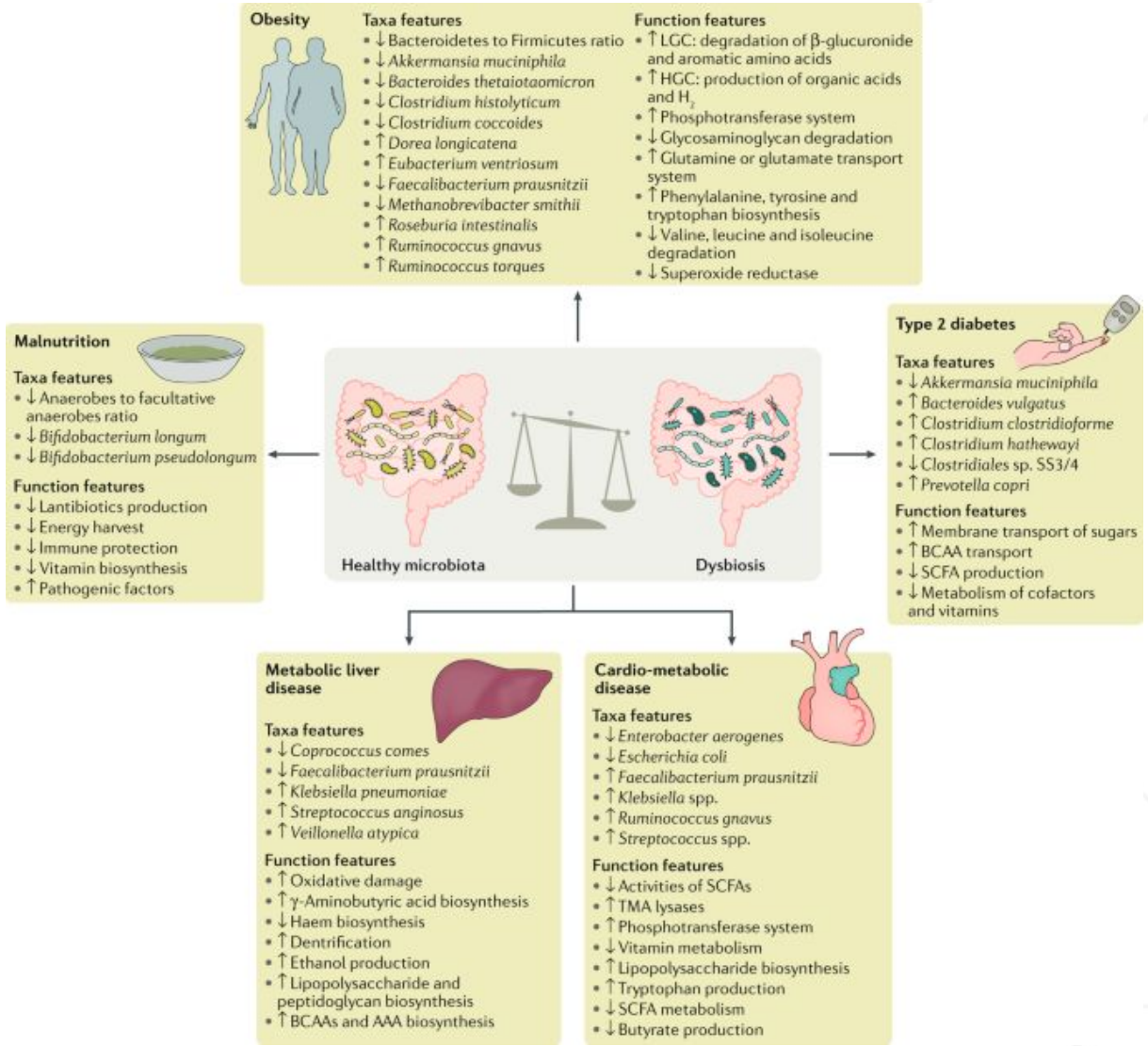
MICROBIOME DISTURBANCES IN DISEASE

Lowered Microbial Diversity

Reduced Commensal Microbes

Increased Pathogenic Microbes

Shift In Functional Activities



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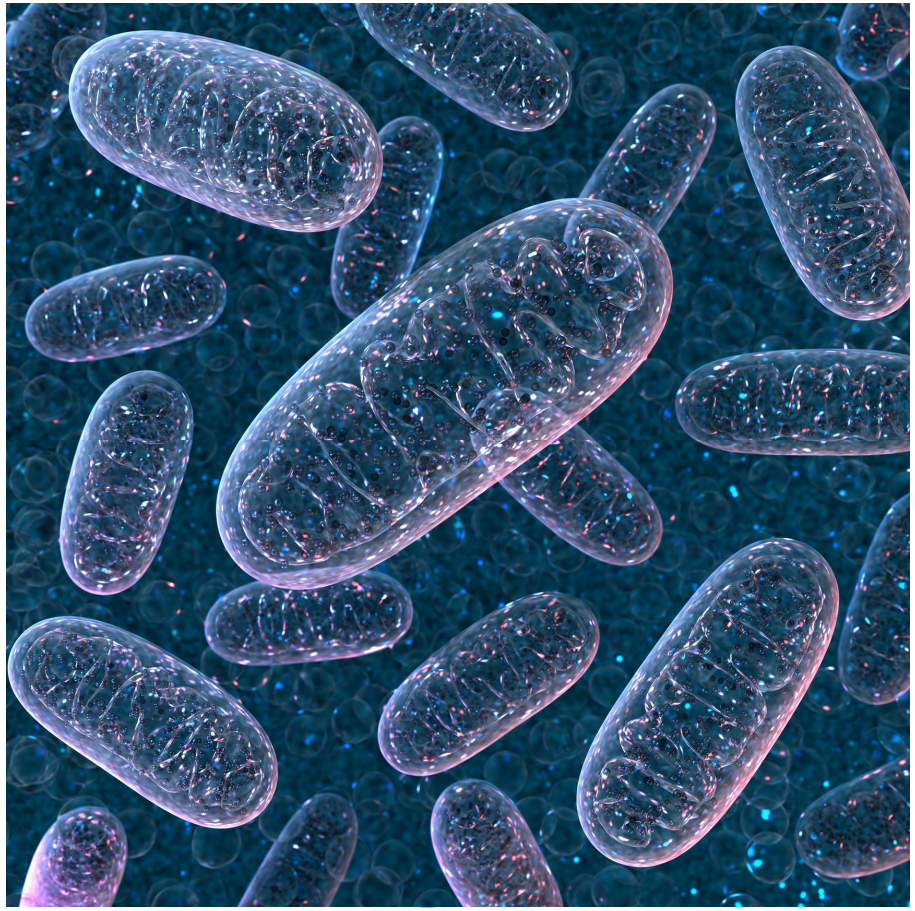
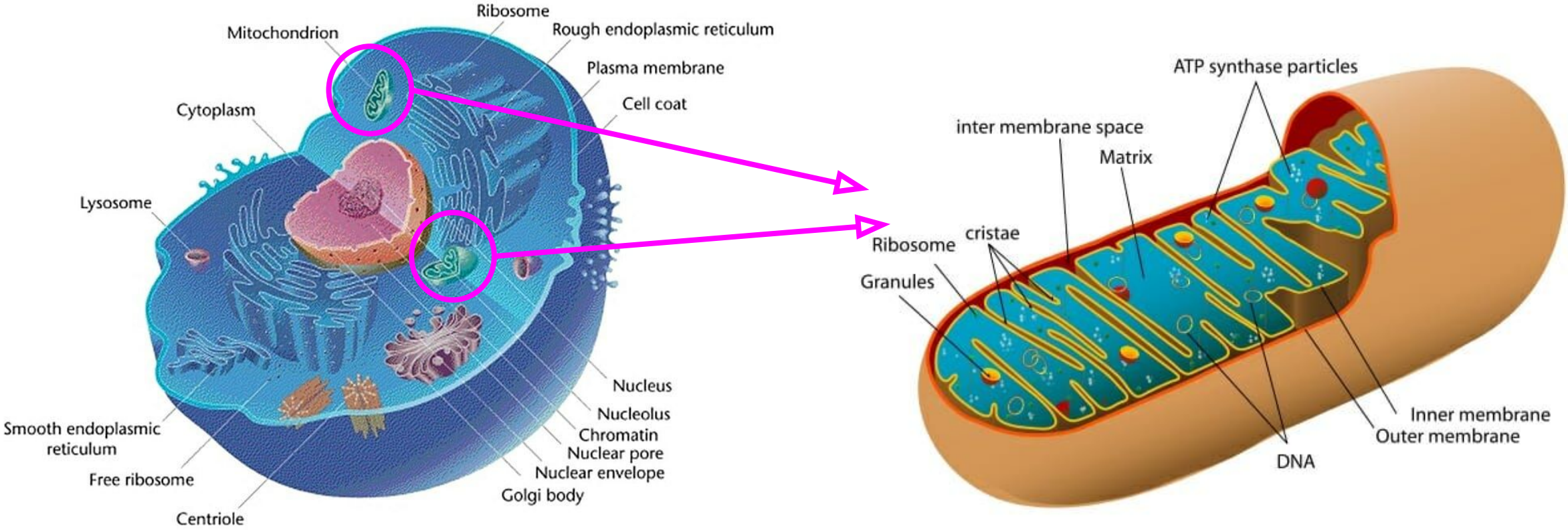


MITOCHONDRIA

CELLULAR ENERGY PRODUCERS

Biocidin Botanicals™

THE CELL AND MITOCHONDRIA



https://commons.wikimedia.org/wiki/File:Animal_mitochondrion_diagram_en_%28edit%29.svg

MITOCHONDRIA: WHAT DO THEY DO?

PRODUCTION OF ATP – CELLULAR ENERGY

Perhaps the most well-known role of mitochondria is the production of ATP, the energy currency of cells.

CALCIUM HOMEOSTASIS

Mitochondrial calcium exchange is the flow of calcium in and out of a cell's mitochondria, a process important in metabolic regulation and cell death.

REGULATION OF INNATE IMMUNITY

Innate immunity is the inborn system that recognizes and responds to infection by pathogens, providing immediate, non-specific defence.

PROGRAMMED CELL DEATH

Apoptosis is the highly controlled process of programmed cell death, necessary during intrauterine development, mopping up damaged cells, and maintaining cell numbers.

STEM CELL REGULATION

Mitochondria are thought to play crucial roles in the maintenance of pluripotency, differentiation, and reprogramming of induced pluripotent stem cells.

MITOCHONDRIAL DYSFUNCTION

DYSFUNCTION WITHIN THE MITOCHONDRIA LINKED TO DISEASE

When mitochondria stop functioning, the cell they are in is starved of energy. Depending on the type of cell, symptoms can vary widely.

As a general rule, cells that need the largest amounts of energy, such as heart muscle cells and nerves, are affected the most by faulty mitochondria.

FREE RADICAL THEORY OF AGING

Theory states that reactive oxygen species (ROS) are produced in mitochondria as a byproduct of energy production. These highly charged particles damage DNA, fats, and proteins.

Due to the damage caused by ROS, the functional parts of mitochondria are damaged. When the mitochondria can no longer function optimally, further ROS are produced, accelerating cellular damage and contributing to the aging process.

ROS-INDUCED MITOCHONDRIAL DYSFUNCTION

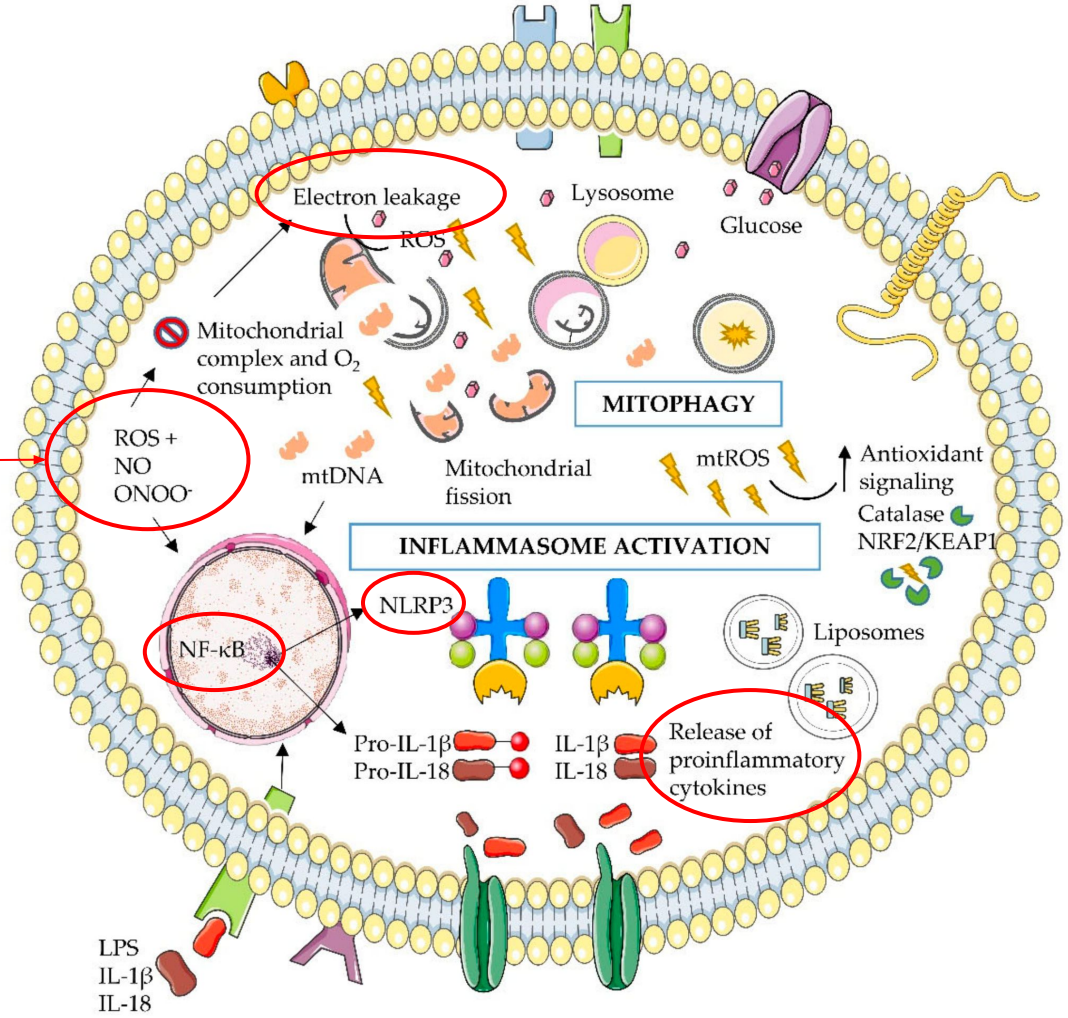
Systemic Inflammation

Excess Glucose

Excess Fatty Acids

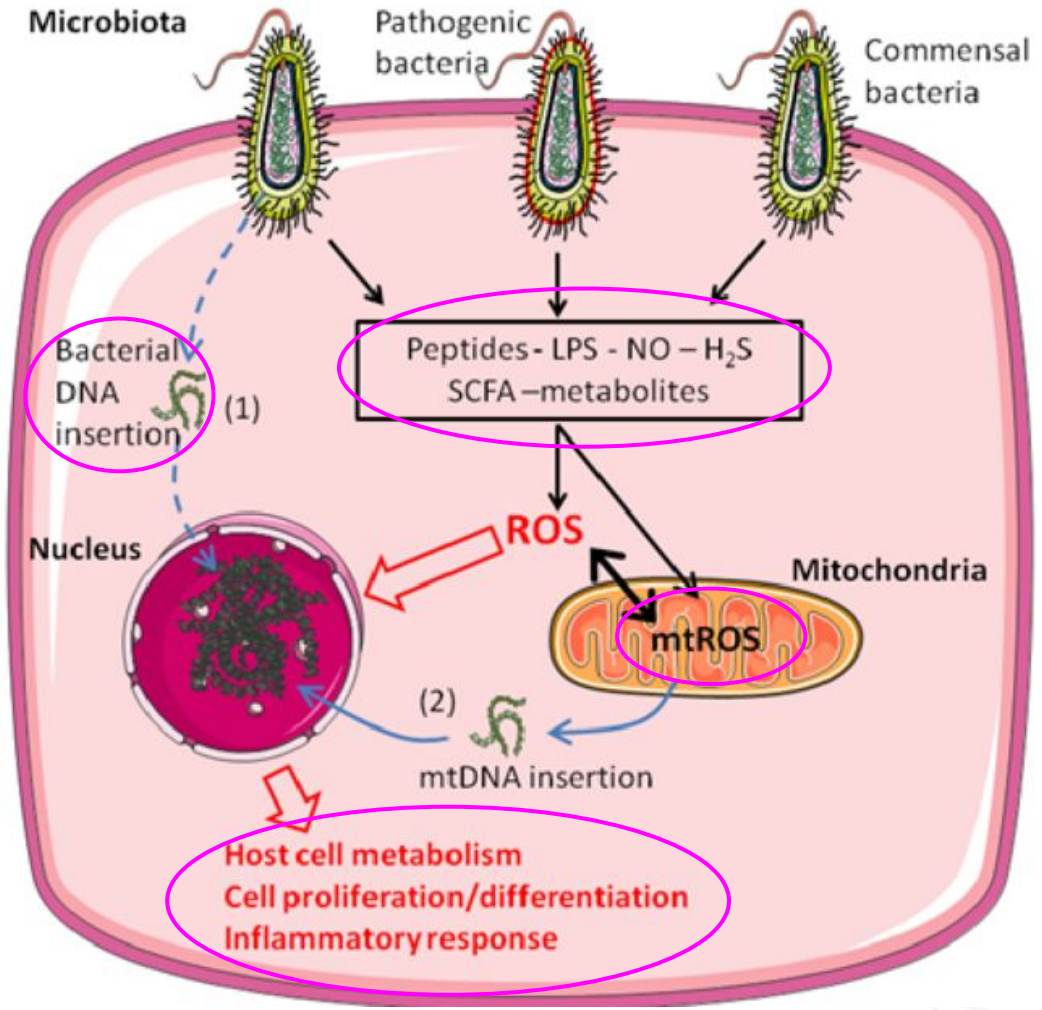
Microbial Metabolites

Environmental Toxins



https://www.mdpi.com/2076-3921/9/9/848#

MICROBIOTA-MITOCHONDRIAL COMMUNICATION

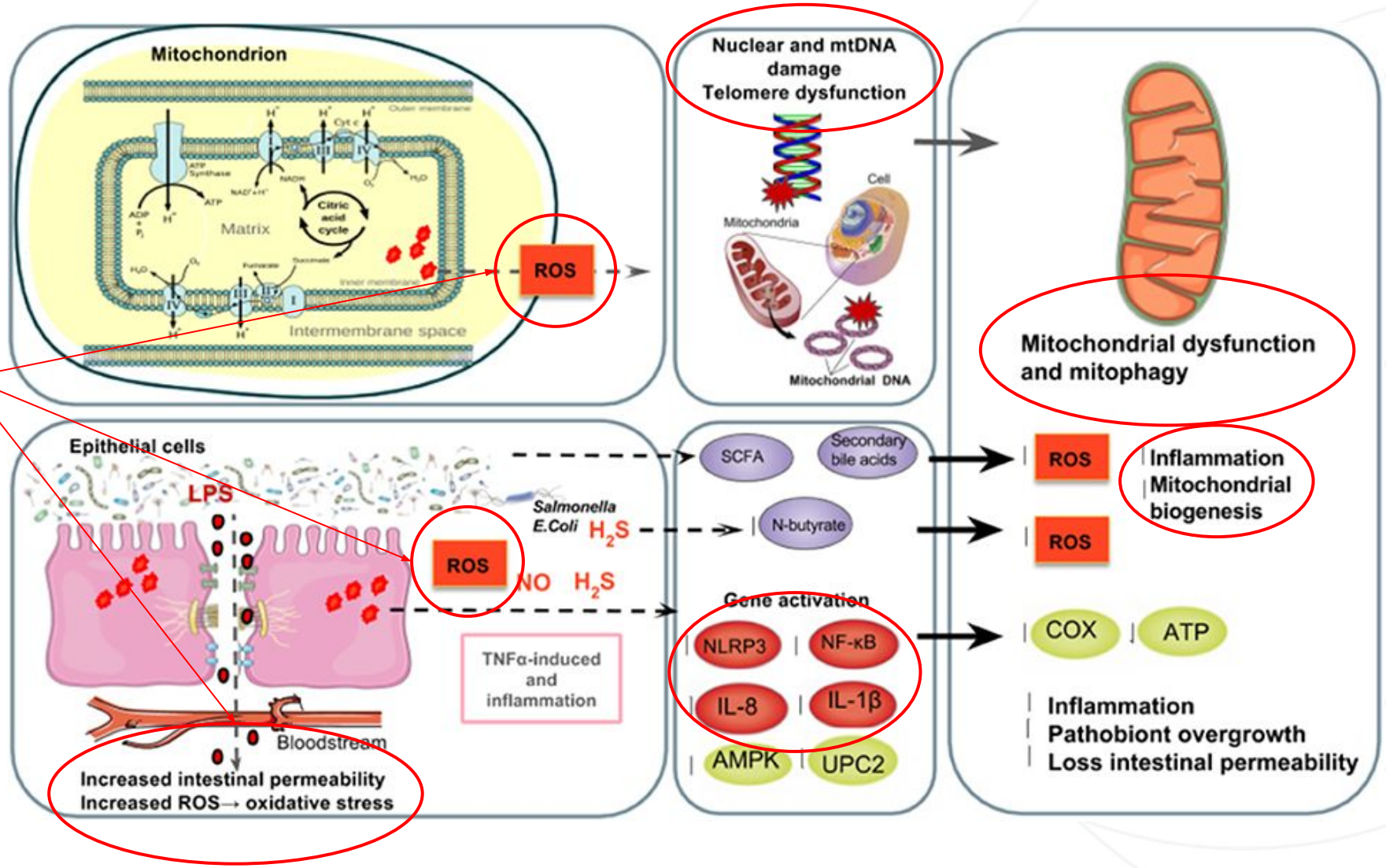


https://pubmed.ncbi.nlm.nih.gov/26429302/

EXERCISE ASSOCIATED MITOCHONDRIAL ROS PRODUCTION

Poorly Trained Individuals

Excessive Training or Competition



https://www.frontiersin.org/articles/10.3389/fphys.2017.00319/full

EXERCISE

- Exercise is widely accepted as a promising therapeutic strategy for human health, as it modulates specific metabolic signaling pathways.

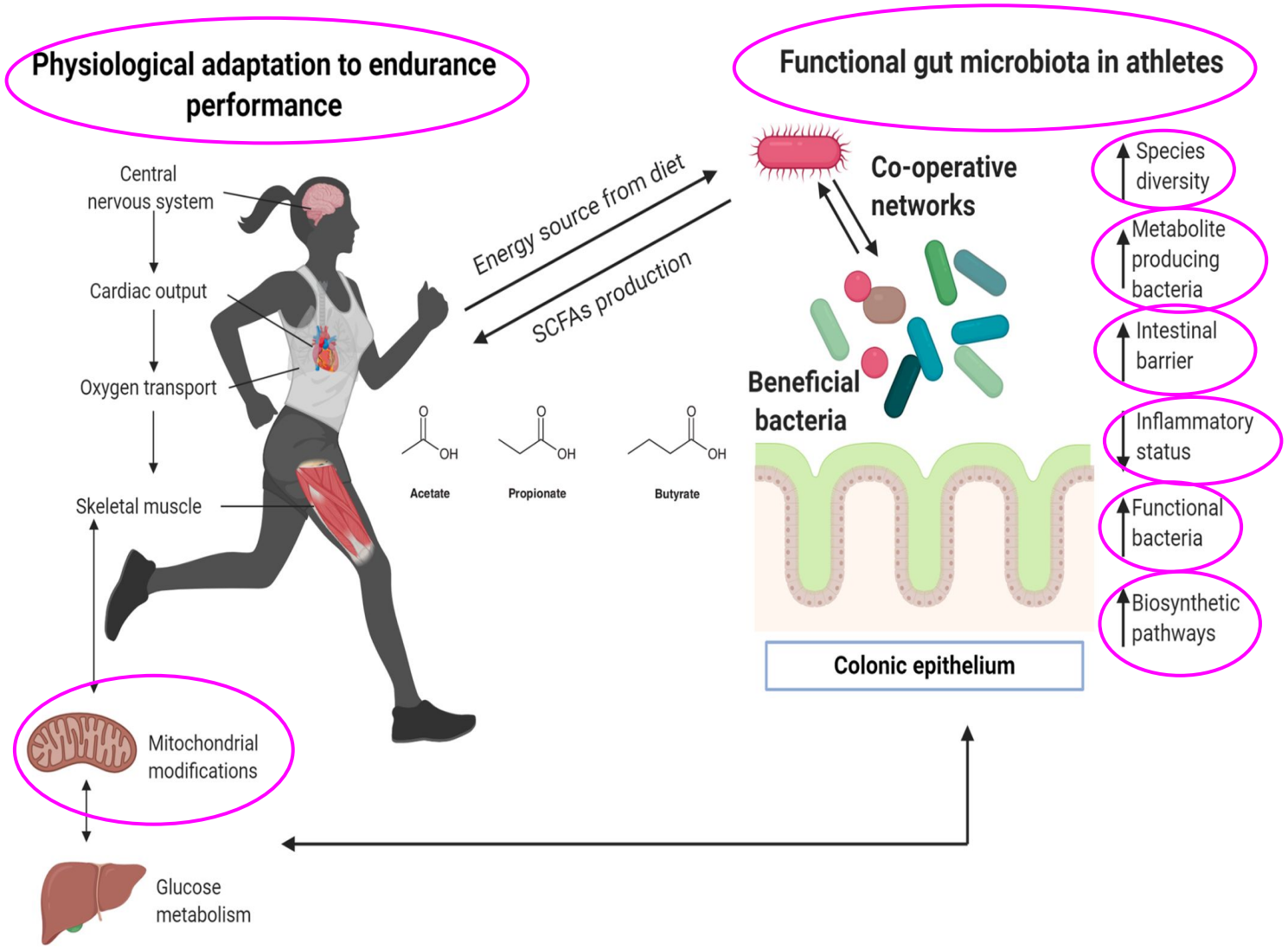
- Physical exercise directly benefits skeletal muscle metabolism and systemic energy homeostasis.

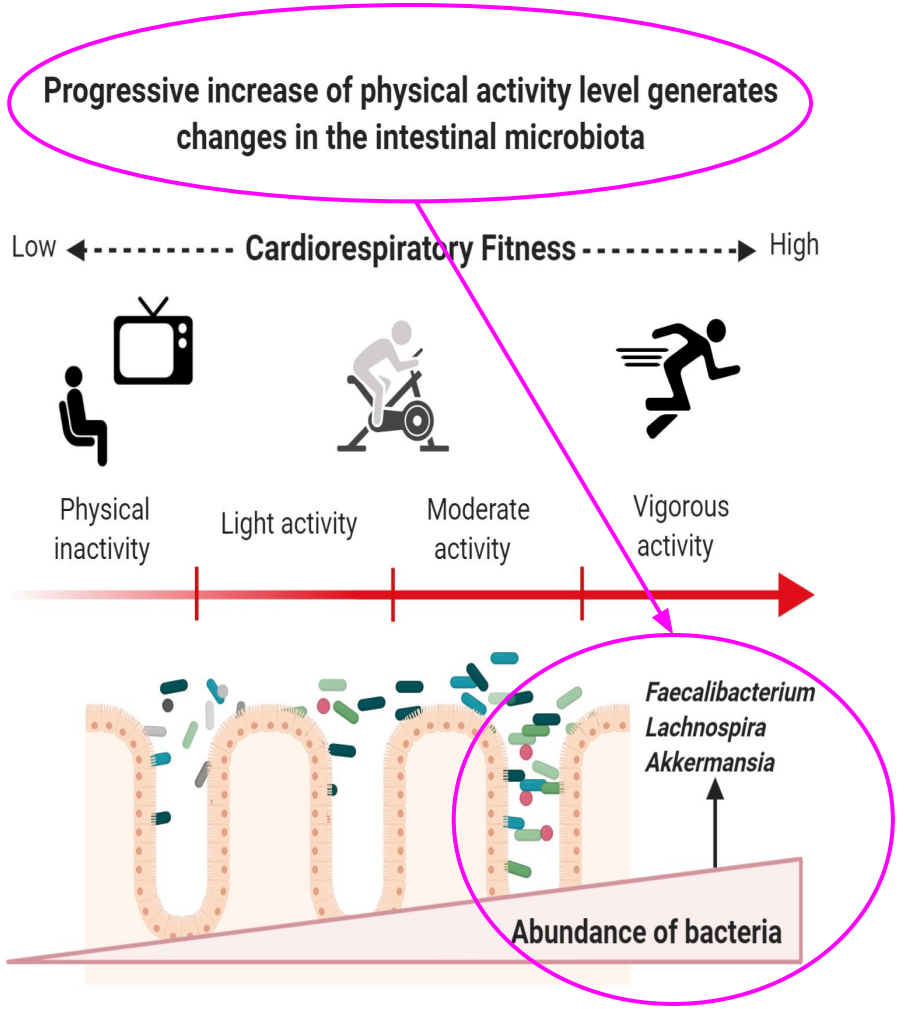
- Mitochondria are vital for exercise and performance because of their role in ATP production and β-oxidation of fatty acids.

- Exercise also affects genes associated with glucose and lipid metabolism which provides fuel for mitochondrial energy production.

- Exercise has direct impacts on the microbiome

EXERCISE AND MICROBIOME ADAPTATIONS





https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0247039

➔ Microbiome composition was different based on

- Type of sport
- Number of sports
- Level of activity

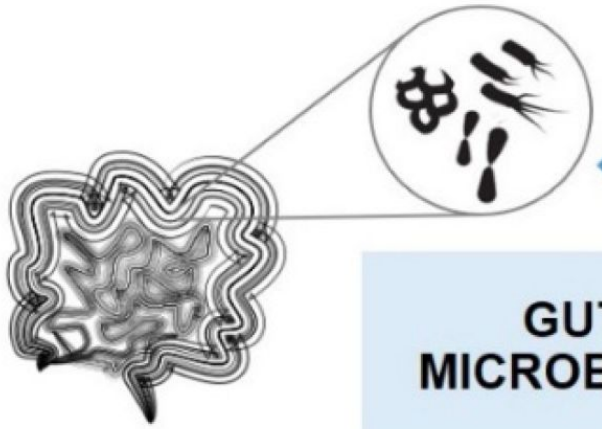
➔ Endurance sports
➔ Compared with sedentary

CHARACTERISTIC CLADES OF THE MICROBIOTA OF ATHLETES ACROSS DIFFERENT DISCIPLINES AND SEDENTARY ADULTS EXPOSED TO TRAINING

Cyclists	Cyclists and rugby players	Cyclists and sedentary adults exposed to exercise
❑*Eubacterium* ❑*Methanobrevibacter* • **Activities of interest**: Branched aminoacid and carbohydrate metabolism	❑*Akkermansia** • **Activities of interest**: Mucin-degrading activity	❑*Ruminococcaceae** ❑*Ruminococcus** • **Activities of interest:** Branched aminoacid and carbohydrate metabolism
Endurance athletes and rowers	**Marathoners**	**Rowers**
❑*Firmicutes* • **Activities of interest**: Galactose metabolism, D-alanine, histidine and primary bile acid biosynthesis, Tricarballylic, 3-metylglutaconic, vanillylmandelic, quinolinic and kynurenic acids and thymine metabolism	❑*Veillonella** • **Activities of interest**: Lactate metabolism	❑*Actinobacteria* ❑*Bacteroidetes* ❑*Clostridiales* ❑*Dorea* ❑*Proteobacteria* ❑*Roseburia* ❑*Subdoligranulum* • **Activities of interest:** Branched aminoacid and carbohydrate metabolism, ATP metabolism, sugar transport systems, butyrate producers (*Roseburia*, *Subdoligranulum*), insulin sensitivity (*Dorea*)
Rugby players	**Multiple sports**	**Multiple sports and sedentary adults**
❑*Erysipelotrichaceae** • **Activities of interest**: Phenylacetylglutamine derived from phenylalanine metabolism, creatinine kinase and bilirubin metabolism	❑*Anaerostipes* ❑*Bacteroides* ❑*Bifidobacterium* ❑*Clostridium* ❑*Faecalibacterium** ❑*Lachnospiraceae** ❑*Lactobacillus* ❑*Streptococcus* • **Activities of interest:** cis-aconitate, succinic acid, lactate and creatinine metabolism, butyrate producers (*Anaerostipes*, *Faecalibacterium*, *Lachnospiraceae*), sugar alcohol fermentation (*Streptococcus*)	❑*Prevotella** • **Activities of interest**: L-lysine, branched chain amino acid and carbohydrate metabolism pathways
Sedentary adults		
❑*Coprococcus** ❑*Parasutterella**		

https://www.oaepublish.com/mrr/article/view/5458

EXERCISE-INDUCED MICROBIAL CHANGES & ATHLETIC BENEFITS



GUT MICROBIOTA

EXERCISE & PERFORMANCE

Benefits for the athlete

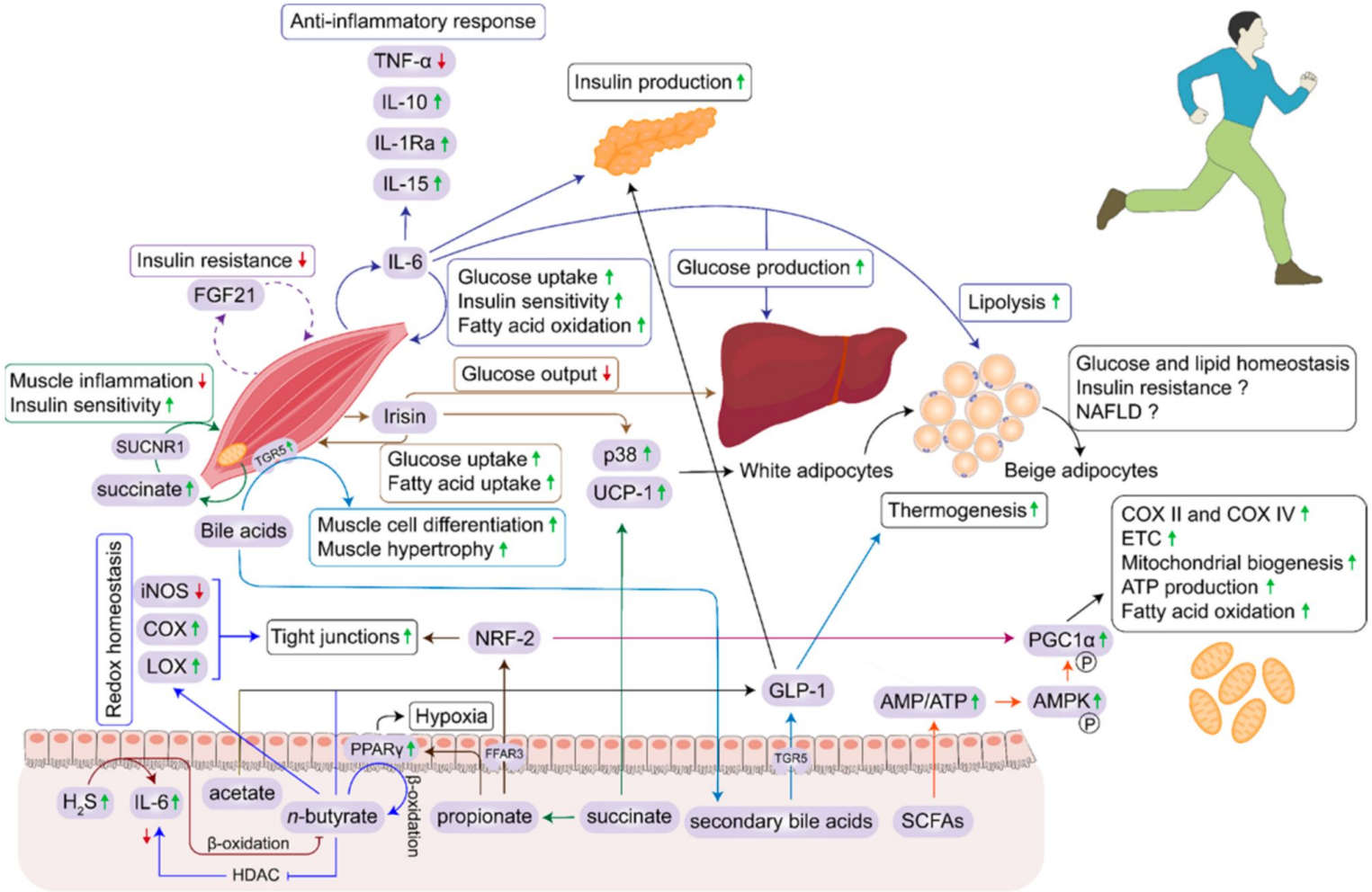
- Production of bioactive metabolites (i.e.short chain fatty acids, neurotransmitters)
- Maintenance of intestinal barrier function
- Modulation of immune system
- Improved energy harvest and utilization
- Regulation of muscle metabolism

Benefits on the gut microbiota

- Higher microbial richness
- Higher abundancy of beneficial *Akkermansia, Veillonella, Prevotella*
- Selection advantage for lactate-utilizing bacteria

https://www.mdpi.com/2072-6643/12/10/2936#

INTERPLAY OF EXERKINES AND MICROBIOTA-DERIVED METABOLITES



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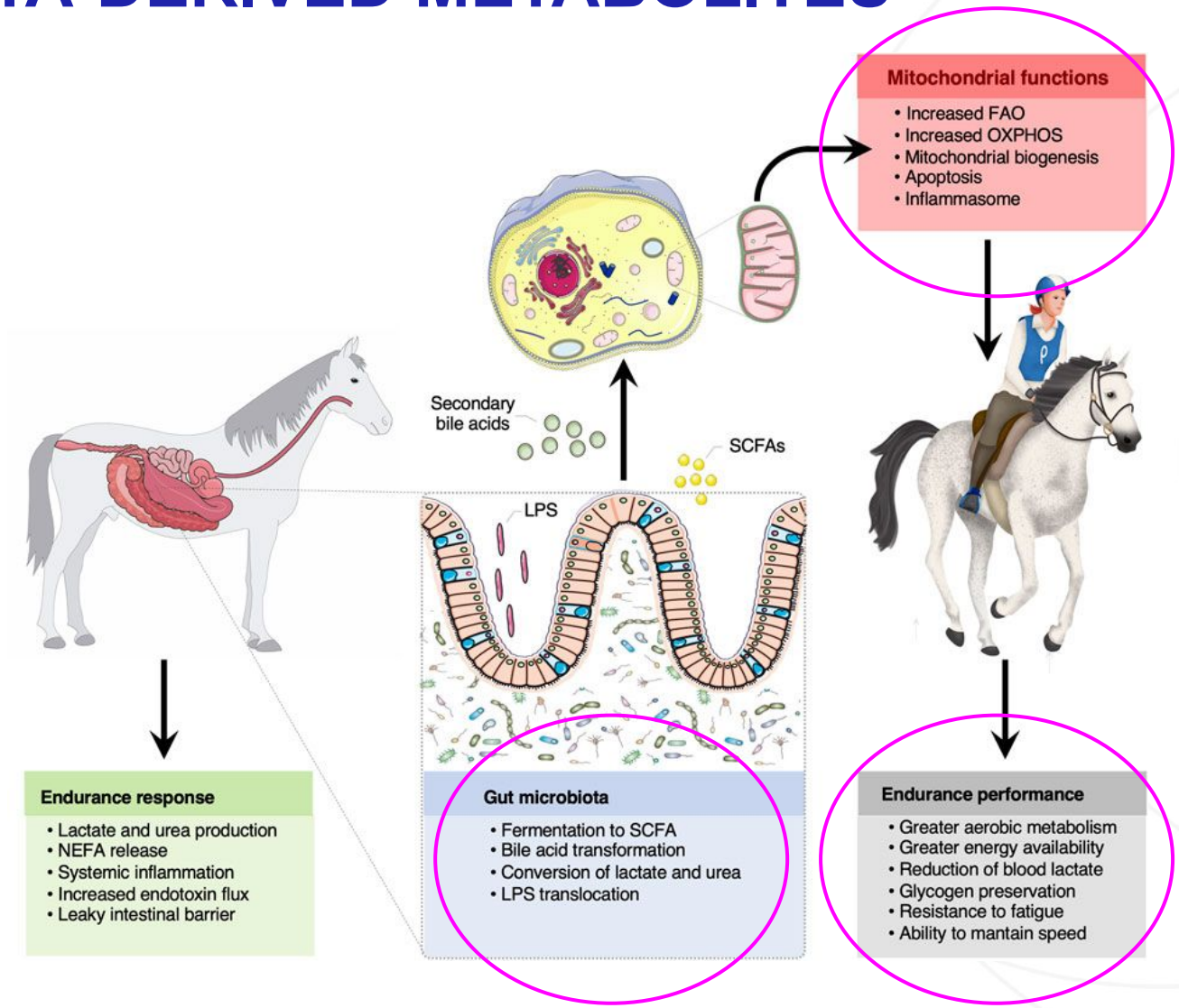

https://www.frontiersin.org/articles/10.3389/fmolb.2021.656204/full

International Journal of
Molecular Sciences

MDPI

Review

Intertwined Relationship of Mitochondrial Metabolism, Gut Microbiome and Exercise Potential

Saba Imdad [1,2]

"The three-way interaction of the gut microbiome, mitochondria, and exercise intervention can coherently induce a greater impact on the remodelling of the human physiological processes for a balanced and healthy outcome. The appropriate contribution of these factors for human health is evident. Each component has its interdependency on the other, through which they each modulate one another in a dynamic and complex manner."

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interplay of exerkines and microbiota-derived metabolites is displayed in Figure 3.

OPTIMIZING THE MICROBIOME AND MITOCHONDRIA FOR EXERCISE PERFORMANCE

- Diet and lifestyle have big impacts on the health and balance of the microbiome, as well as the health and function of mitochondria
  - Antioxidant rich, plant based, anti-inflammatory diet, devoid or low in processed foods, sugars, additives, etc.
    - Rich in a diverse array of vegetables, low sugar fruits
    - Probiotics, fermented foods, prebiotic fibers, and resistant starches
  - Exercise and movement
    - Daily, moderate activity combined with high-intensity interval training
    - Combination of strength and aerobic training
  - Mitochondrial targeted nutritional supplementation and botanicals
  - Hydration – ensure adequate water intake
  - Time spent outdoors in nature, sunlight
  - Stress reducing practices and activities
  - Avoid exposure to toxins

OPTIMIZING EXERCISE AND PERFORMANCE

Optimize Microbiome

- Antioxidant Rich, Plant-based, Organic Diet
- Fermented Foods and Probiotics
- Prebiotic Fibers and Resistant Starches
- Repair Intestinal Permeability
- Microbial Balancing Botanical Extracts
- Exercise

Optimize Mitochondrial Function

- Exercise
- Adequate Sleep
- Avoid Toxins
- Sunlight
- Stress Reduction
- Antioxidant Rich, Plant Based Organic Diet
- Targeted Supplements and Botanical Extracts

Support Recovery & Resilience Pathways

- Adequate Sleep and Rest
- Stress Reduction
- Adrenal
- Inflammation modulation with Supplements and Botanical Extracts

CONCLUSIONS

- The interaction of the gut microbiome, mitochondria, and exercise intervention can induce a significant impact on the remodelling of physiological processes for balanced and healthy outcomes.
- Each component has its interdependency on the other, through which they each modulate one another in a dynamic and complex manner.
- Exercise can positively impact the microbial diversity and mitochondrial performance and reduce the risk of many metabolic and non-transferable diseases.
- Understanding of the mechanism of microbial response to exercise can pave the way for the development of novel therapeutic and nutritional strategies to modulate and customize the microbiota, as well as enhance athletic potential and overall health.
- Targeting both the microbiome and the mitochondria with diet, lifestyle, nutritional supplementation and botanicals can lead to improved performance and exercise outcomes.