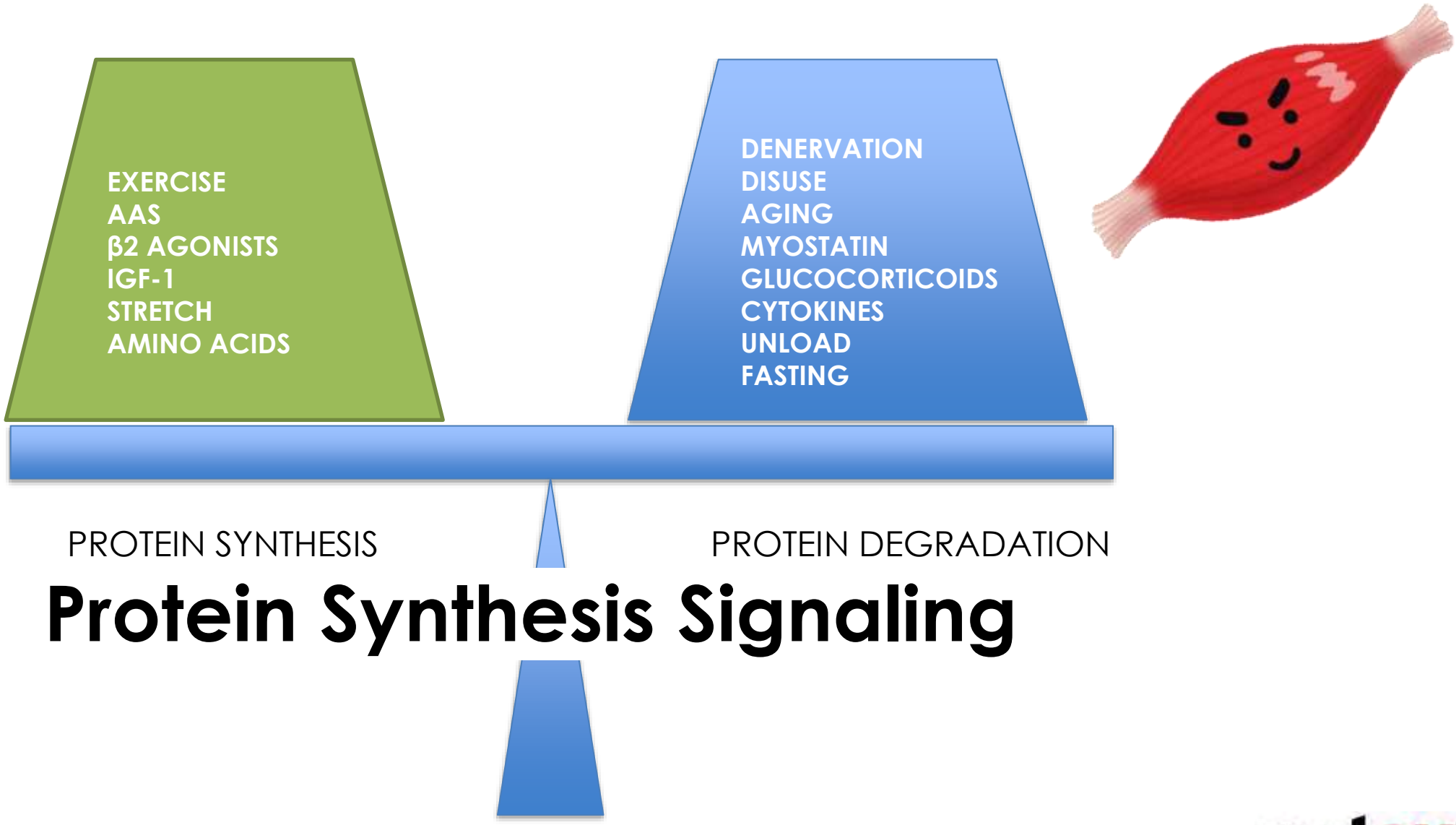
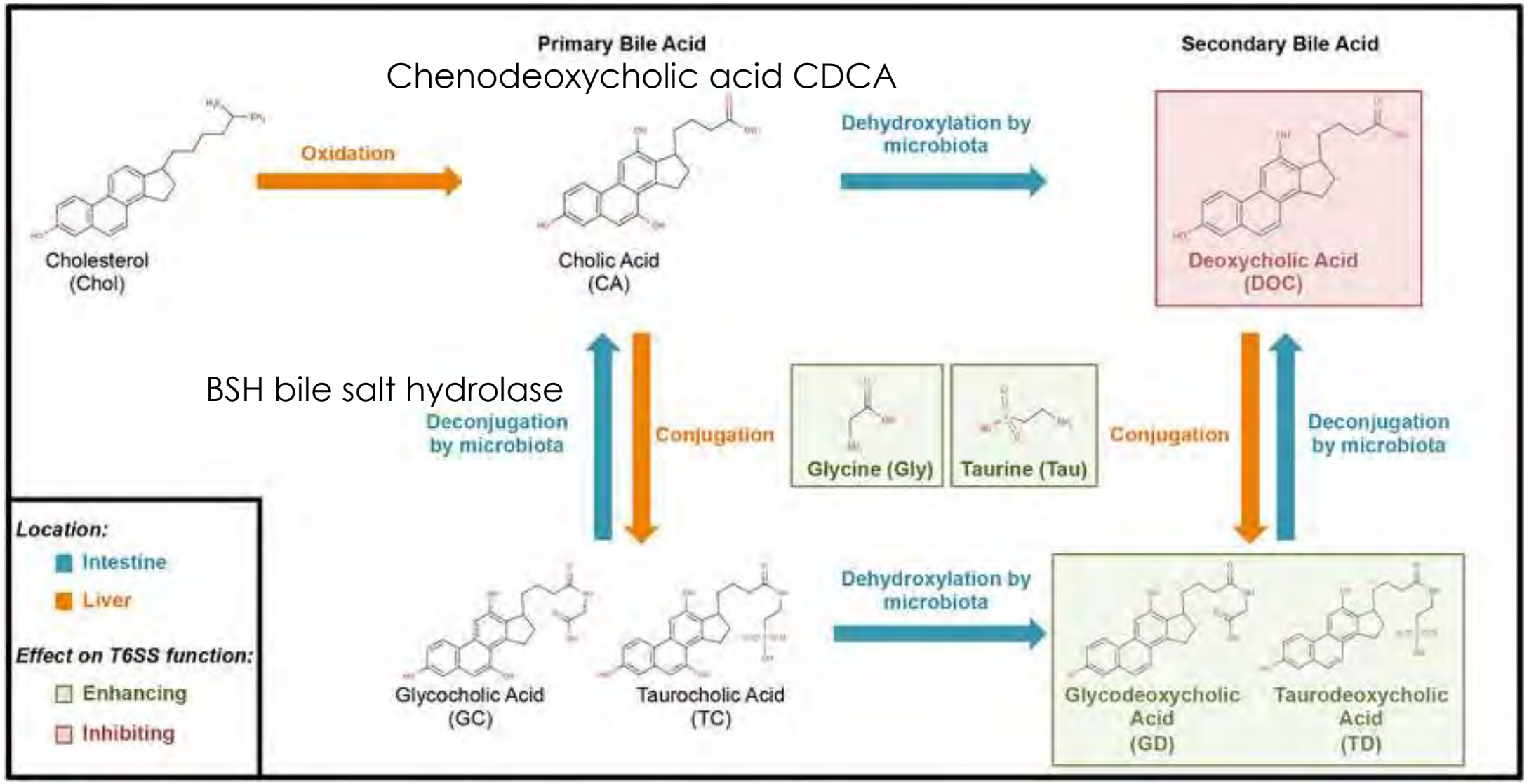
Microbiota e muscolo…



Paoli et al. J Hum Kinet. 2019 Aug 21;68:233-247

Microbiota e muscolo…



Microbiota e muscolo…

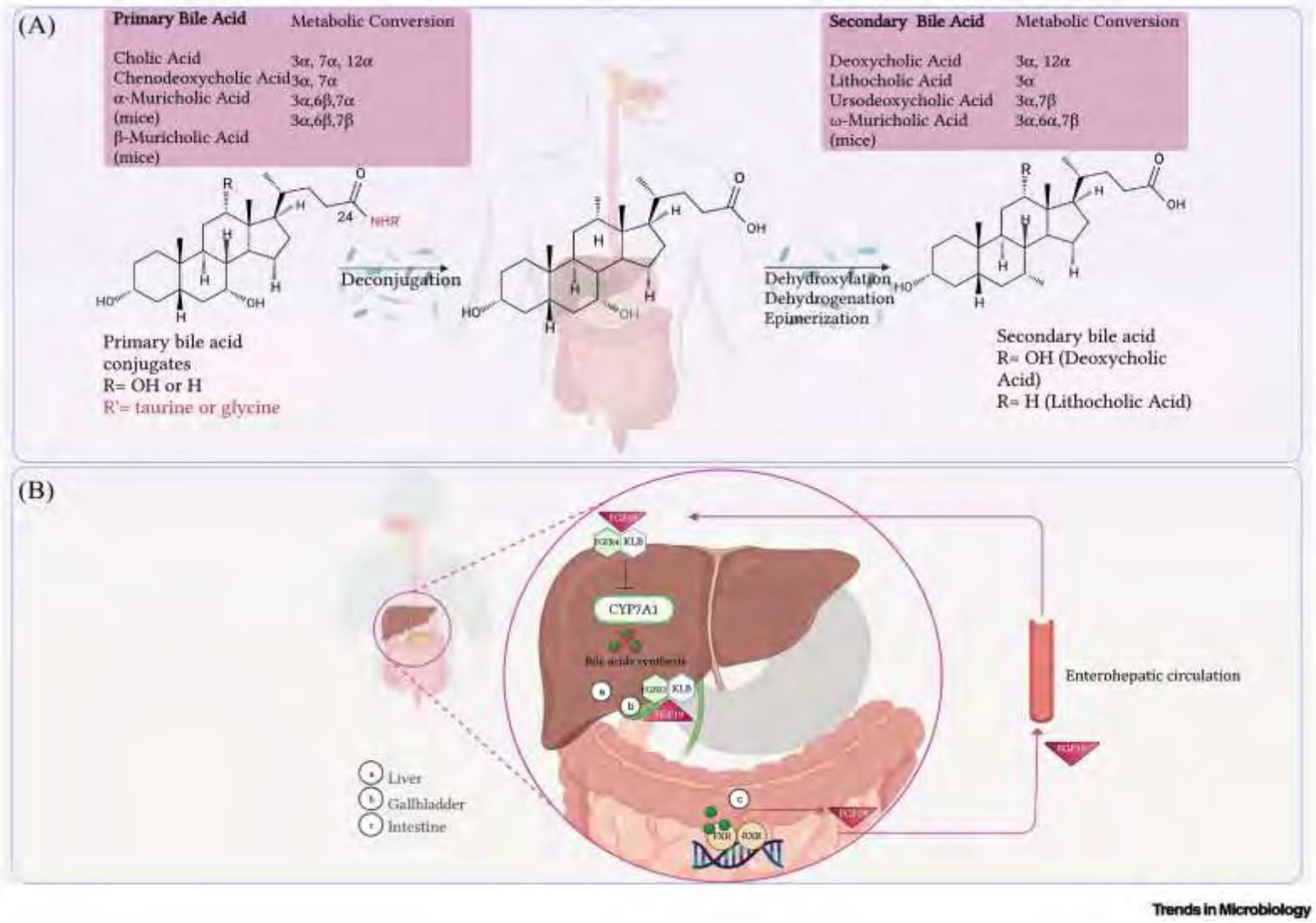
BAs hydrophobic scale: CA < UDCA = CDCA = DCA < LCA.

CA is the most hydrophilic and LCA as the most hydrophobic

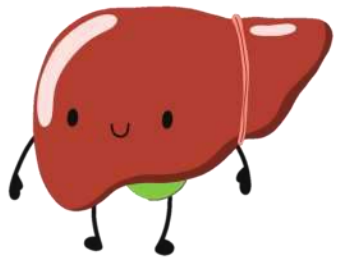
	R1	R2	R3	R4
CA	OH	OH (α)	OH	OH
CDCA	OH	OH (α)	H	OH
UDCA	OH	OH (β)	H	OH
DCA	OH	H (α)	OH	OH
LCA	OH	H (α)	H	OH
G-CA	OH	OH (α)	OH	Glycine
T-CA	OH	OH (α)	OH	Taurine

cholic acid (CA) PRIMARY
chenodeoxycholic (CDCA) PRIMARY
ursodeoxycholic acid (UDCA) SECONDARY
deoxycholic acid (DCA) SECONDARY
lithocholic acid (LCA) SECONDARY

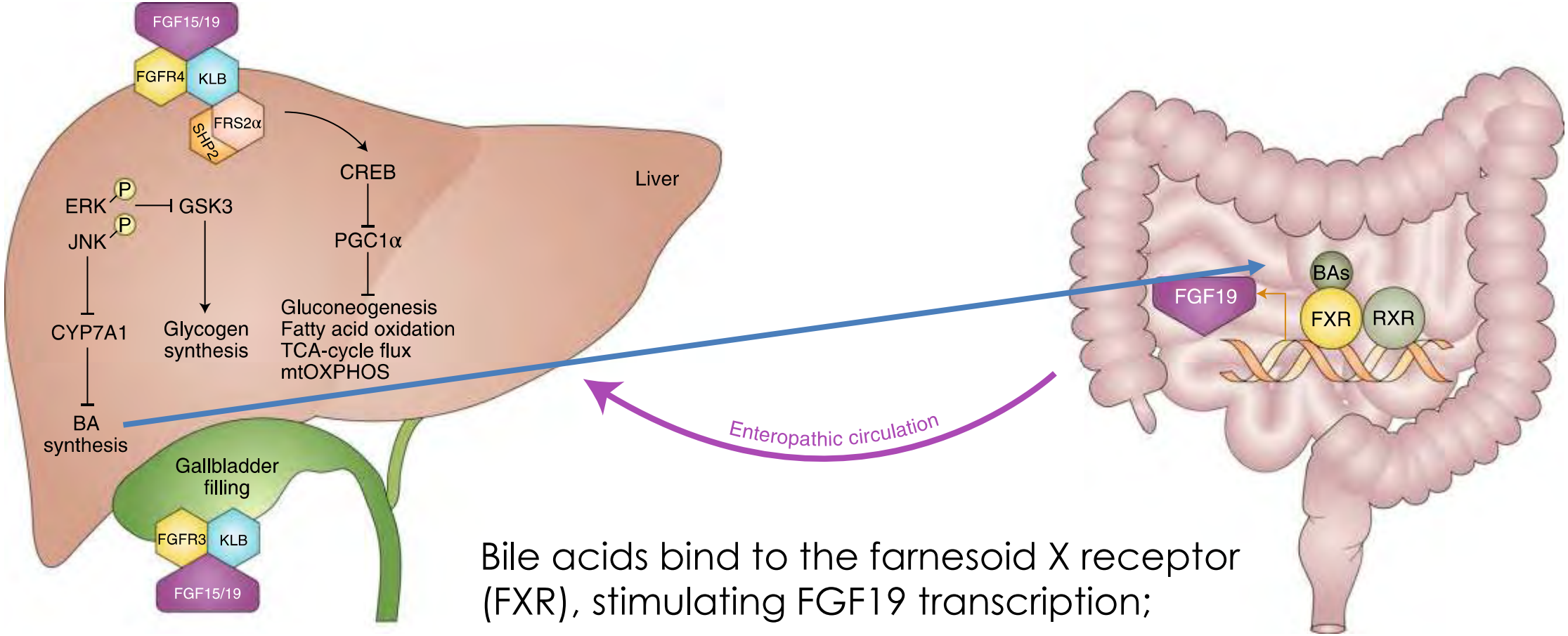
Microbiota e muscolo…



- Bile acids are synthesized from cholesterol in the liver and further metabolized by the gut microbiota into secondary bile acids.
- Bile acid synthesis is under negative feedback control through activation of FXR in the ileum and liver.



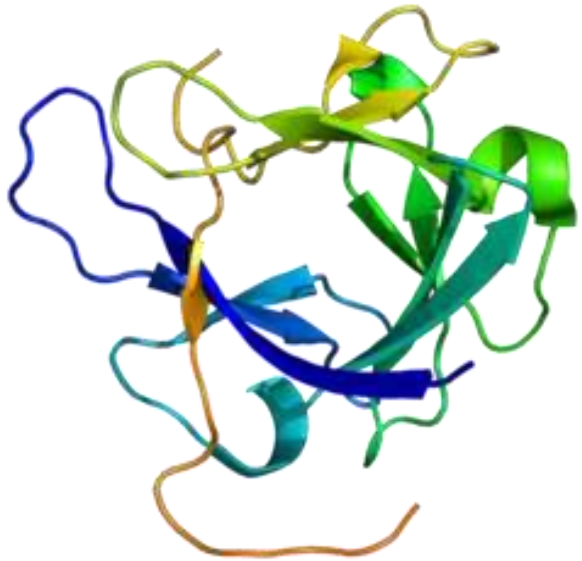
Microbiota e muscolo…



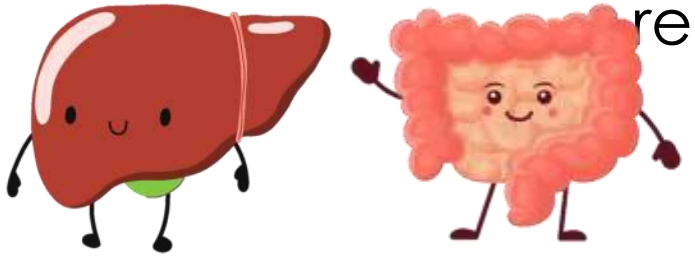
Bile acids bind to the farnesoid X receptor (FXR), stimulating FGF19 transcription;

Gadaleta & Moschetta. Nat Metab. 2019 Jun;1(6):588-594

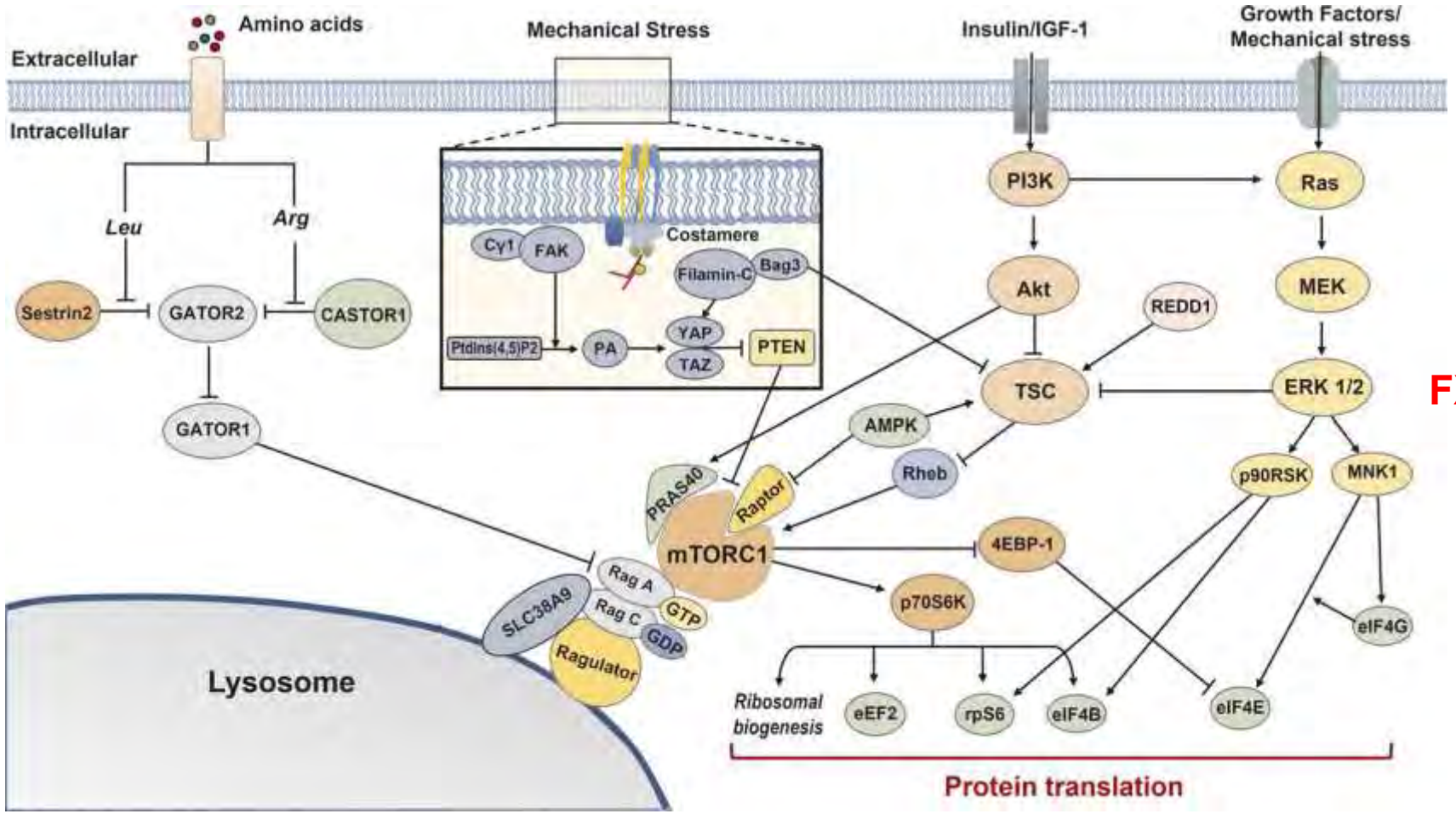
Microbiota e muscolo…



- The fibroblast growth factor (FGF) family is composed of 22 proteins that are involved in a many biological functions, including development, differentiation and metabolism;
- FGF19 (15 in mouse) is produced in the ileum in response to bile acid absorption
- FGF19 then suppressbile acid biosynthesis through down-regulation of CYP7A1 expression, following positive regulation of the JNK and ERK1/2 cascades.



Microbiota ed esercizio…



FXR-FGF15/19

Lim et al. Med Sci Sports Exerc, 2022, 54(9): 1546-1559

Microbiota e muscolo…

FGF15/19 has a protective effect on skeletal muscle.

FGF15/19 stimulates ERK and S6 phosphorylation to induce hypertrophy i.e. an increase of myofiber size

FGF15/19 can also ameliorate sarcopenia and skeletal muscle atrophy induced by glucocorticoid treatment or obesity.

FGF15/19 alleviates obesity-induced muscle atrophy and mitochondrial dysfunction

Microbiota e muscolo…

The conversion of primary bile acids into secondary bile acids relies on the presence of a microbial community.

Germ-free (GF) animals develop bile acid dysmetabolism.

In GF mice or antibiotic- treated mice, the absence of gut microbiota leads to a bile acid pool consisting of mainly primary conjugated bile acids, such as TβMCA

Microbiota e muscolo…

Tauro-β-muricholic acid (TβMCA) is a taurine-conjugated form of the murine-specific primary bile acid β-muricholic acid

It is a competitive and reversible antagonist of the FXR.

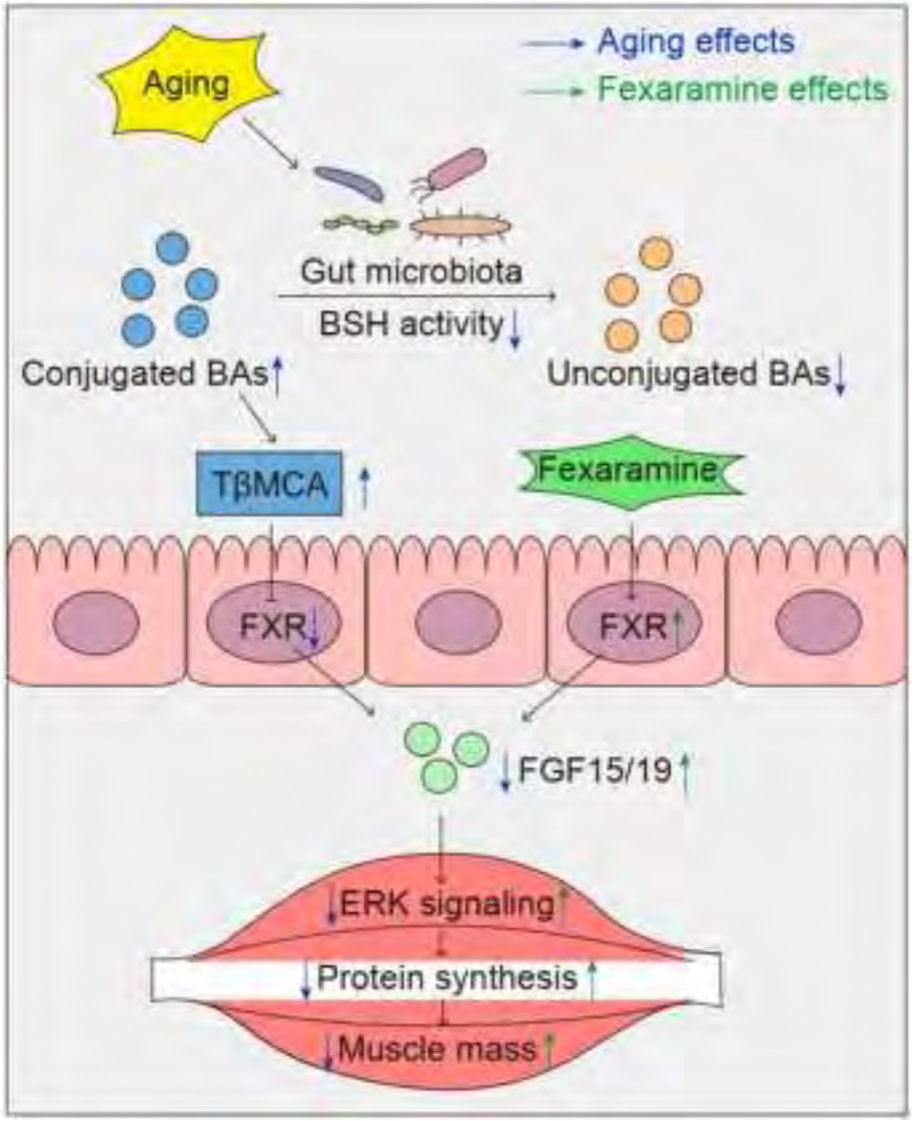
TβMCA accumulates in germ-free mice under normal conditions but is reduced after colonization with feces from a human donor.

Microbiota e muscolo…

The modification of the gut microbiota composition in mice (↓ genus Lactobacillus: the main source of BSH activity), led to the accumulation of FXR antagonists, such as TβMCA, and inhibited the intestinal FXR signaling.

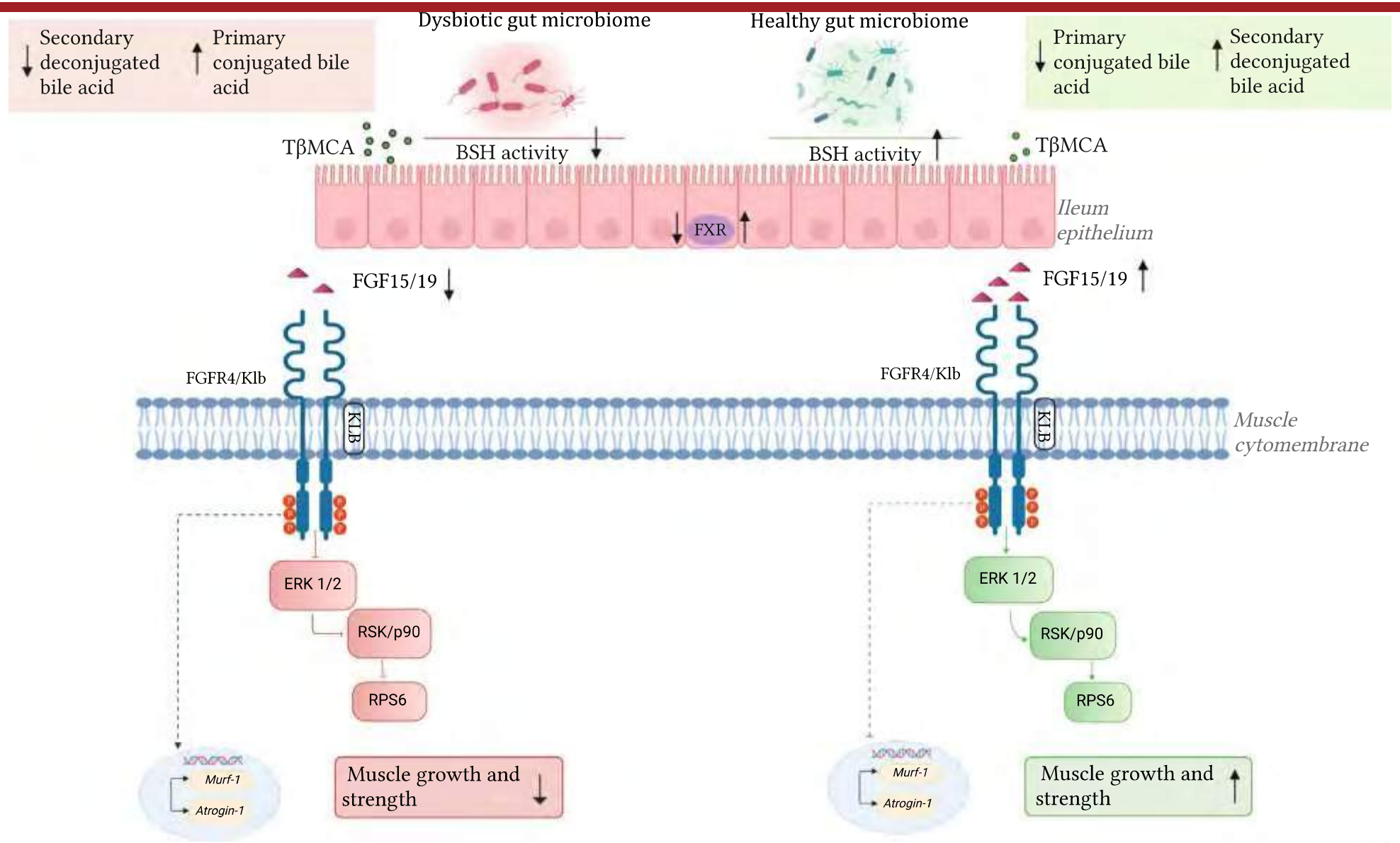
Absence of gut microbiota or antibiotic-induced dysbiosis =
↑ FoxO3, Atrogin-1, Murf-1, and MyoD
↓ ERK 1/2, S6K, AMPK
↓ IGF-1

Microbiota e muscolo…



Qiu et al. Mech Ageing Dev. 2022 Mar;202:111630

Microbiota e muscolo...

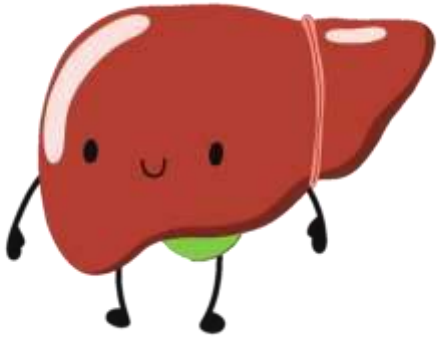


Mancin et al. Trends Microbiol. 2023 Mar;31(3):254-269.

Microbiota e muscolo…

Negative changes of microbiota (dysbiosis) were associated with a decreased conversion of primary bile acids into secondary fecal bile acids (reduction of the secondary:primary bile acid ratio, thus a possible increase in FXR antagonists).

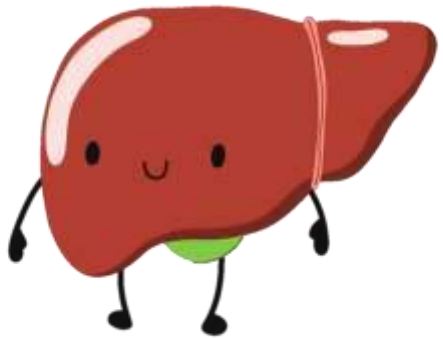
Gut microbiota in cirrhotic patients showed dysbiosis, with a lower prevalence of 7a-dehydroxylating bacteria (*Lachnospiraceae*, *Ruminococcaceae*, and *Blautia*) and a higher abundance of potentially pathogenic bacteria (*Enterobacteriaceae*), compared to controls.



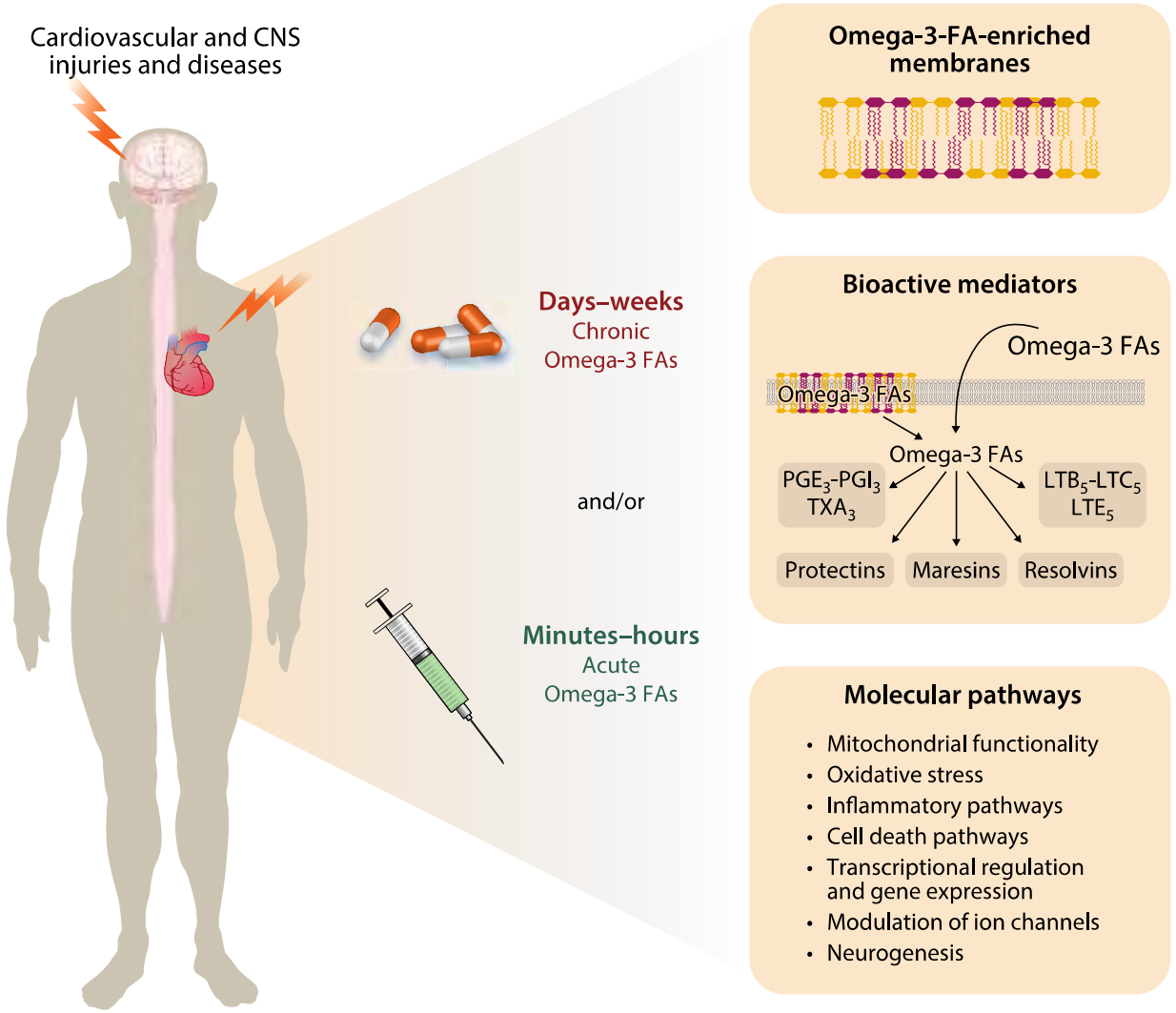
Microbiota e muscolo…

7 days of oral vancomycin administration in male subjects with metabolic syndrome, reduced the amount of Gram-positive intestinal bacteria, especially those belonging to the phylum Firmicutes (Clostridium cluster IV, Lactobacillus plantarum, and various butyrate-producing bacteria, including F. prauszniitzii Faecalibacterium prausnitzii and Eubacterium hallii), which are mainly involved in human bile acid dehydroxylation.

Kakiyama et al. J Hepatol. 2013 May;58(5):949-55
Mancin et al. Trends Microbiol. 2023 Mar;31(3):254-269.



Omega 3, intestino e immunità



An imbalanced consumption of n-3/n-6 PUFAs may lead to gut microbial dysbiosis, in particular, a significant increase in the ratio of Firmicutes to Bacteroidetes, which eventually results in being overweight and obesity.

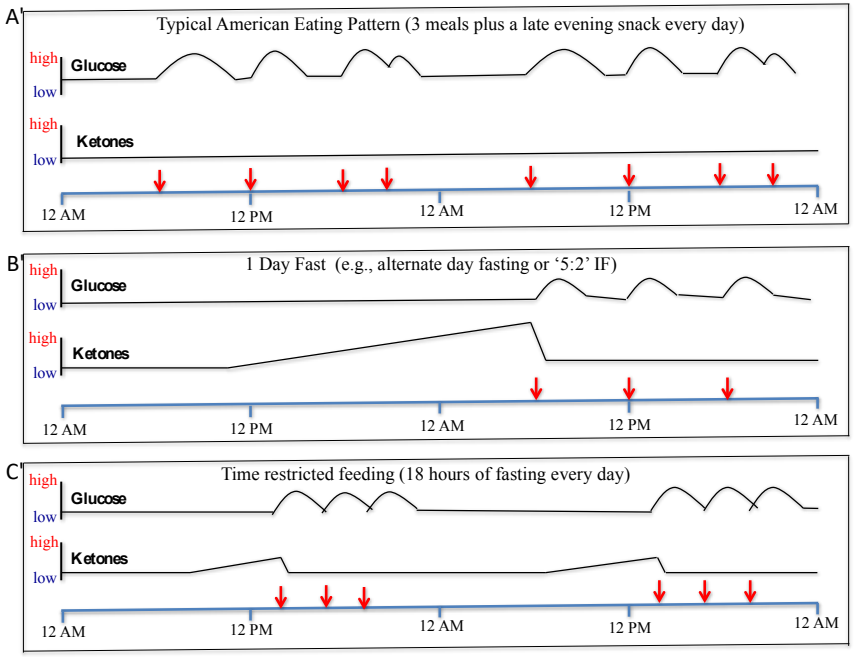
N-3 PUFA deficiency disrupts the microbiota community in metabolic disorders. In addition, accumulating evidence indicates that the interplay between n-3 PUFAs, gut microbiota, and immune reactions helps to maintain the integrity of the intestinal wall and interacts with host immune cells.

Supplementation with n-3 PUFAs may be an effective therapeutic measure to restore gut microbiota homeostasis and correct metabolic disturbances associated with modern chronic diseases.

Zirpoli et al. Annu Rev Nutr. 2020 Sep 23;40:161-187

βHB, fasting, gut, and muscle

Recent findings shows (in mice model) that IF reshapes the gut microbiota, reduces the accumulation of serum BAs, and increases total colonic and fecal BAs. Moreover, IF increases the expression of cholesterol 7α-hydroxylase 1 in liver, but decreases the expressions of both FXR and fibroblast growth factor 15 in the ileum.



Lin et al. Mol Nutr Food Res. 2023 Jul;67(14):e2200595

Trends in
Endocrinology & Metabolism

CellPress

Review

Common and divergent molecular mechanisms of fasting and ketogenic diets

Antonio Paoli, [1,*] Grant M. Tinsley, [2] Mark P. Mattson, [3] Immaculata De Vivo, [4,5] Ravi Dhawan, [5] and Tatiana Moro [1]

β-HB induces the expression of FGF21 and β-Klotho… A NEW PATH TO INVESTIGATE?

Paoli A. Mattson et al. Ageing Research Reviews, 31 Oct 2016, 39:46-58

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CONCLUSIONI

- L'esercizio fisico produce effetti positivi sulla salute ma per raggiungere questo risultato bisogna dosarlo accuratamente: NÉ TROPPO POCO , NÉ TROPPO
- L'uomo si è evoluto per muoversi, ed il suo cervello si è evoluto di conseguenza
- C'è una relazione diretta tra esercizio fisico, microbiota e salute
- Il microbiota influenza le risposte dell'organismo all'esercizio fisico attraverso molteplici connessioni
- Per ottimizzare gli effetti positivi dell'esercizio bisogna tenere in conto anche la salute del microbiota

Esercizio moderato, probiotici, dieta varia e periodi di digiuno aiutano a tenere "in forma" il microbiota" che, a sua volta, ***potenzia gli effetti positivi dell'esercizio***.

UNIVERSITÀ DEGLI STUDI DI PADOVA

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GRAZIE PER L'ATTENZIONE!