Sportomics, Metabolic Health, and Utilization of Functional Medicine Testing

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Jeffrey B. Kreher, MD, FAAP, IFMCP

GENOVA DIAGNOSTICS®

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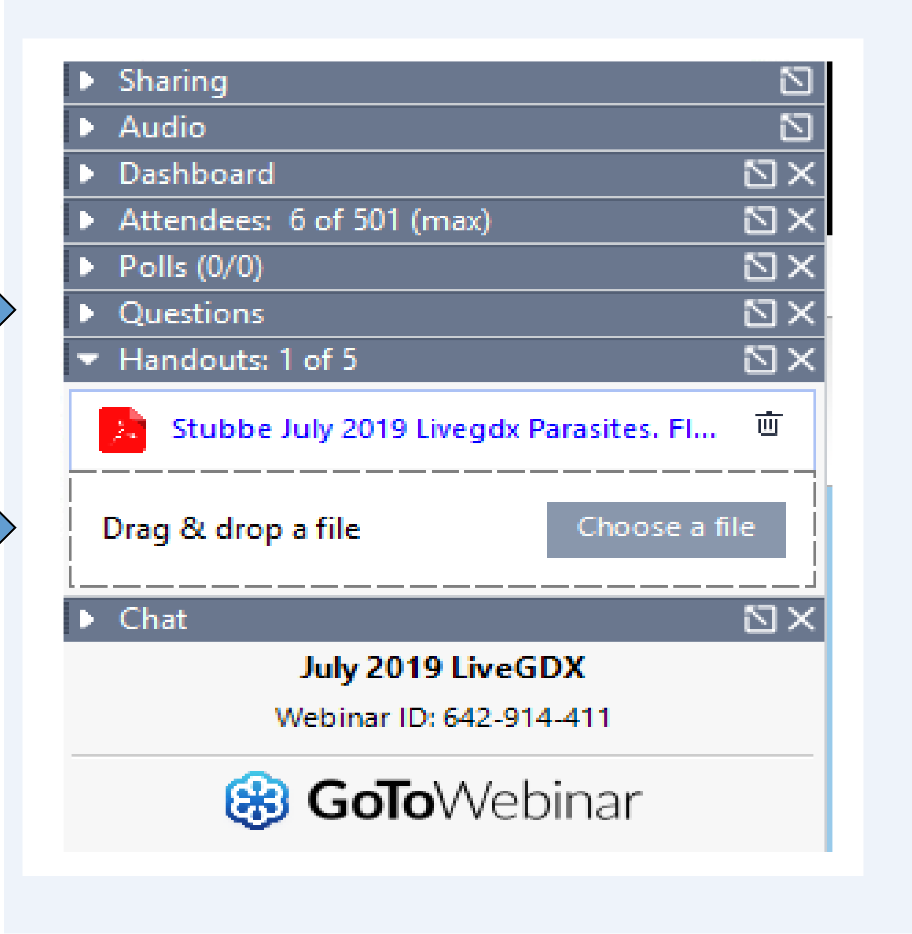
Integrative Functional and Lifestyle Medicine, IFM Certified
Sports Medicine, Physical Activity and Exercise Specialist
Board Certified Internal Medicine and Pediatrics
Certificate of Added Qualification in Primary Care Sports Medicine

Technical Issues & Clinical Questions

Please type any technical issue or clinical question into either the “Chat” or “Questions” boxes, making sure to send them to “Organizer” at any time during the webinar.

We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.



DISCLAIMER: *Please note that any and all emails provided may be used for follow up correspondence and/or for further communication.*

Need More Resources?

Explore

WWW.GDX.NET

for more information and educational resources, including…

LEARN **GDX –** Brief video modules

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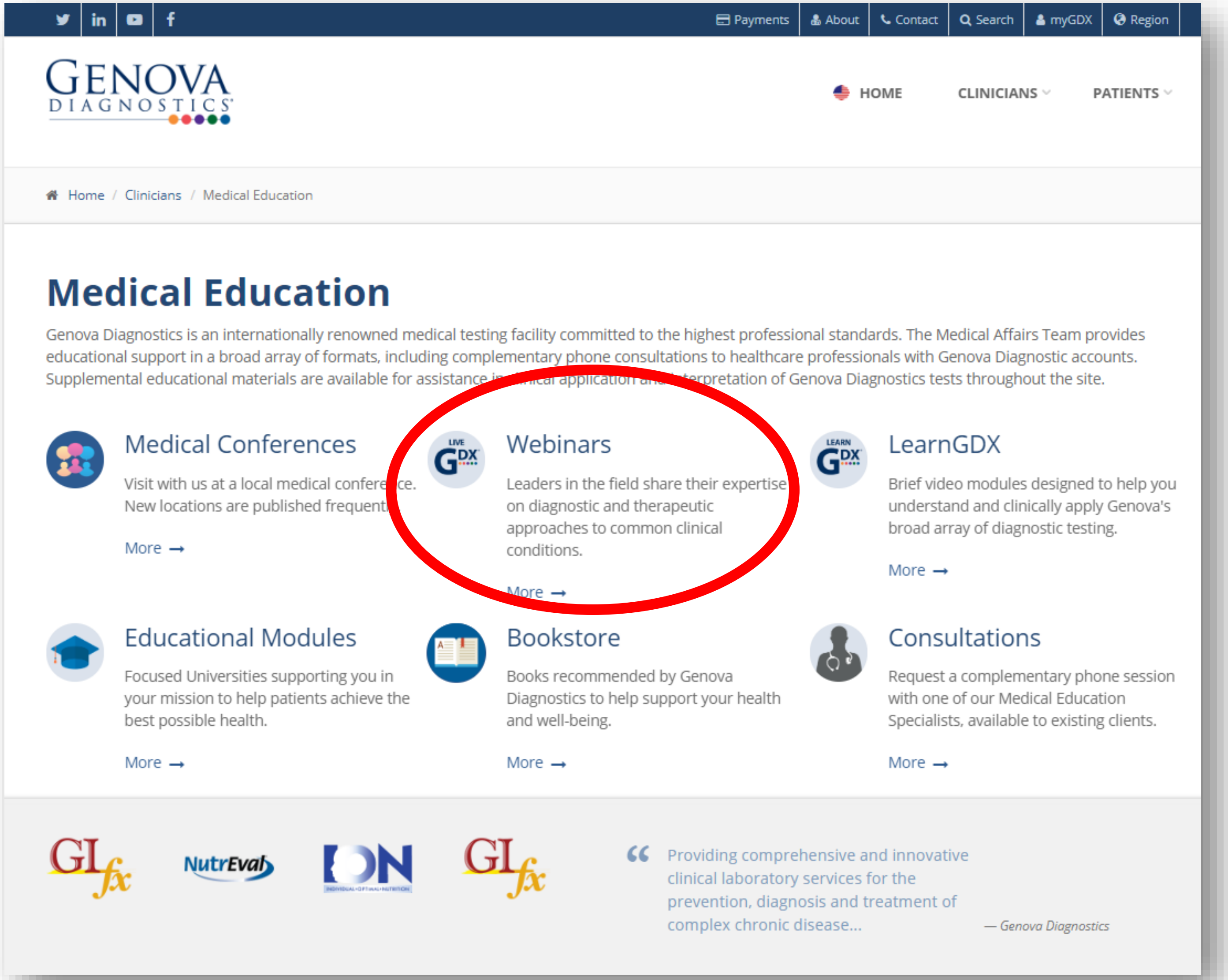
GI University – Focused learning modules

MY **GDX –** Order materials and get results



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Patient Dropship/Online Registration

https://youtu.be/YHd0lD9GVG4

Genova Diagnostics' Patient Dropship/Online Registration

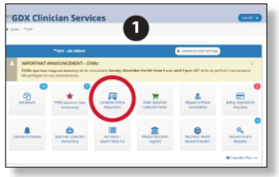
Practitioner Version

Our online test requisition offers practitioners a number of features to assist with the requisition process including:

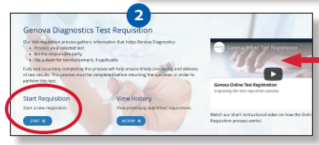
- Improved accuracy/less errors
- Auto-complete information (Practitioner & Patient)

Please follow these steps to try out our new online requisition process. If you have questions, please contact us via the information on the back page.

If the patient won't be logging into PRC to complete the online process, please make sure to have them sign the paper copy of the requisition and include it with their sample submission.

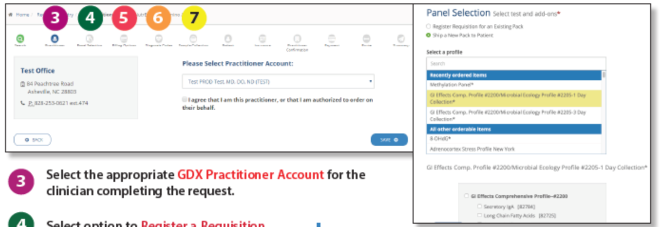


1. Select the Complete Online Requisition button on the myGDX landing page.



Instructional video for guidance.

2. Click Start button to begin GEAR, or click History to view past orders.
   URL to access page after logging into myGDX portal: gdx.net/ereq
   or click on GEAR button from portal landing page



3. Select the appropriate GDX Practitioner Account for the clinician completing the request.

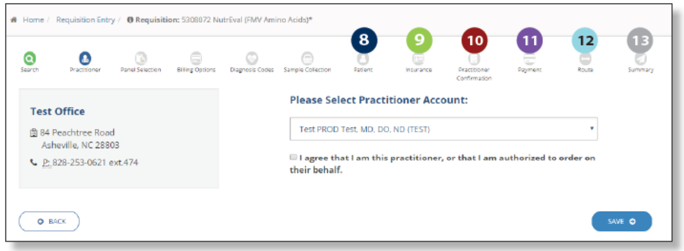
4. Select option to Register a Requisition *(client has kit in office- enter Req #)* or Ship pack to new patient *(type Panel Name - list will filter based on text - or select from drop down menu. After choosing panel, the test selection for the requisition displays below that menu for client to select testing options).*

5. Pick the Billing Option that is applicable for the test.

6. Select or add the appropriate ICD 10 diagnosis code(s).
   If using Medicare please make sure to review the Definition of Medical Necessity

7. A practitioner may now enter Patient Instructions to be included on requisition for Patient dropship orders.
   If registering/ordering multiple kits, additional requisitions will be added on this step by clicking 'Add Another Test'.

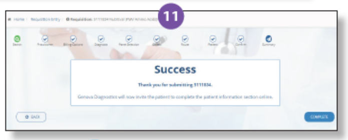
Genova Diagnostics Online Test Requisition



8. **Supply patient information needed for the test to be processed.**
   Patient, Insurance/Payment steps may be skipped if this is not a dropship order. See the skip button at the top of each page. Skipping pages results in GEAR emailing the patient reminding them to complete information.

9. **Patient Insurance Information**
   Provide your patient's insurance information. If insurance information was found for your patient, you may autofill it by selecting their insurance from the provided list.
   You may also upload a copy of the patient's insurance card (front & back) and their driver's license (front & back).

10. **Practitioner Confirmation**
    Please confirm that the data entered is accurate and ready to be submitted.
    You may return and enter any missing information or invite the patient to complete the registration at Step 12.



11. **Payment Page**
    *If the billing option you chose in **Step 4** requires an upfront payment either you or the patient may pay securely.*

12. **Patient Completion (Optional)**
    If there's any missing information you'd like to have the patient complete, provide their name, DOB, and email to send them an invitation to complete the missing information using Genova Diagnostic's Patient Resource Center.

13. **Submission Finalization**
    The final confirmation that the requisition has been completed and is being processed.
    If patient is not logging into PRC to complete information, make sure to have them sign the paper requisition and submit it with their collection pack to Genova.

Please send all questions, comments (positive or negative), and concerns to info@gdx.net. Thank you.

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Objectives for This Presentation

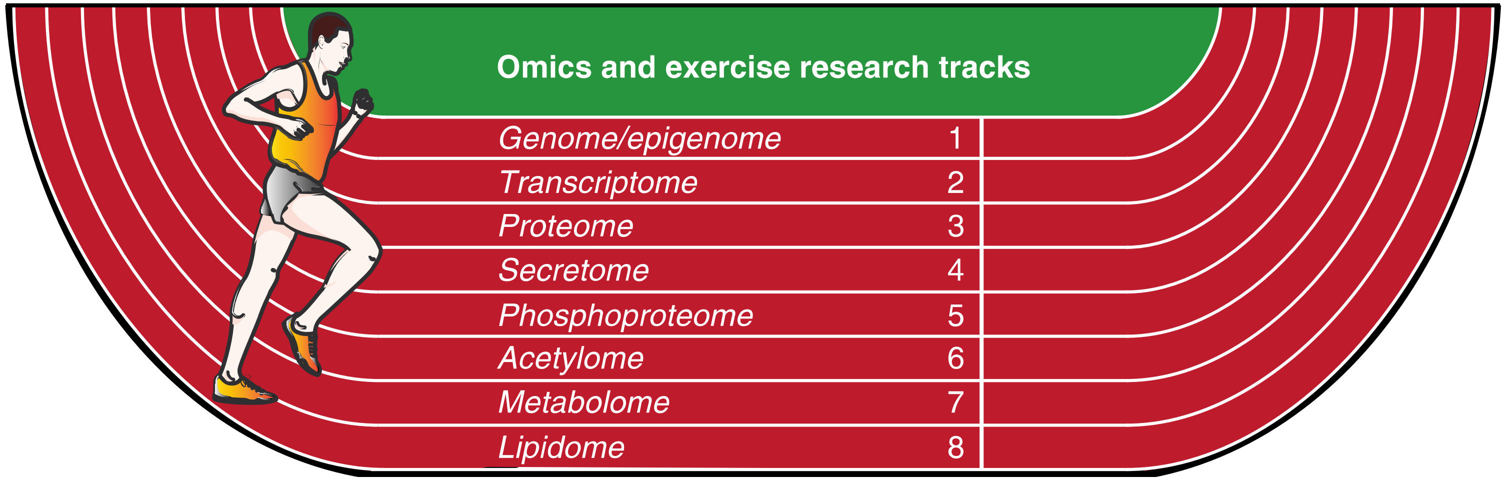
- At the conclusion of this program, participants will be able to:
  - Define Sportomics and its application to Exercise Performance and Metabolic Health
  - Identify and understand changes in metabolome and microbiome associated with exercise
  - Apply metabolomic and microbiome Functional Medicine testing to inform recommendations for improved exercise performance and metabolic health

OUTLINE

- Introduction to “SPORTOMICS”
- Exercise and Metabolome
- Exercise and Microbiome
- Sportomics and Exercise Performance
  - Role of functional medicine testing
- Sportomics and Metabolic Health
  - Role of functional medicine testing

SPORTOMICS . . .

- Applies metabolomics to investigate the metabolic effects of physical exercise on individuals
- Works to advance knowledge in integrative physiology and the systems biology of movement with a goal to translate markers associated with metabolic challenges of training, or competition, to similar stresses of disease settings



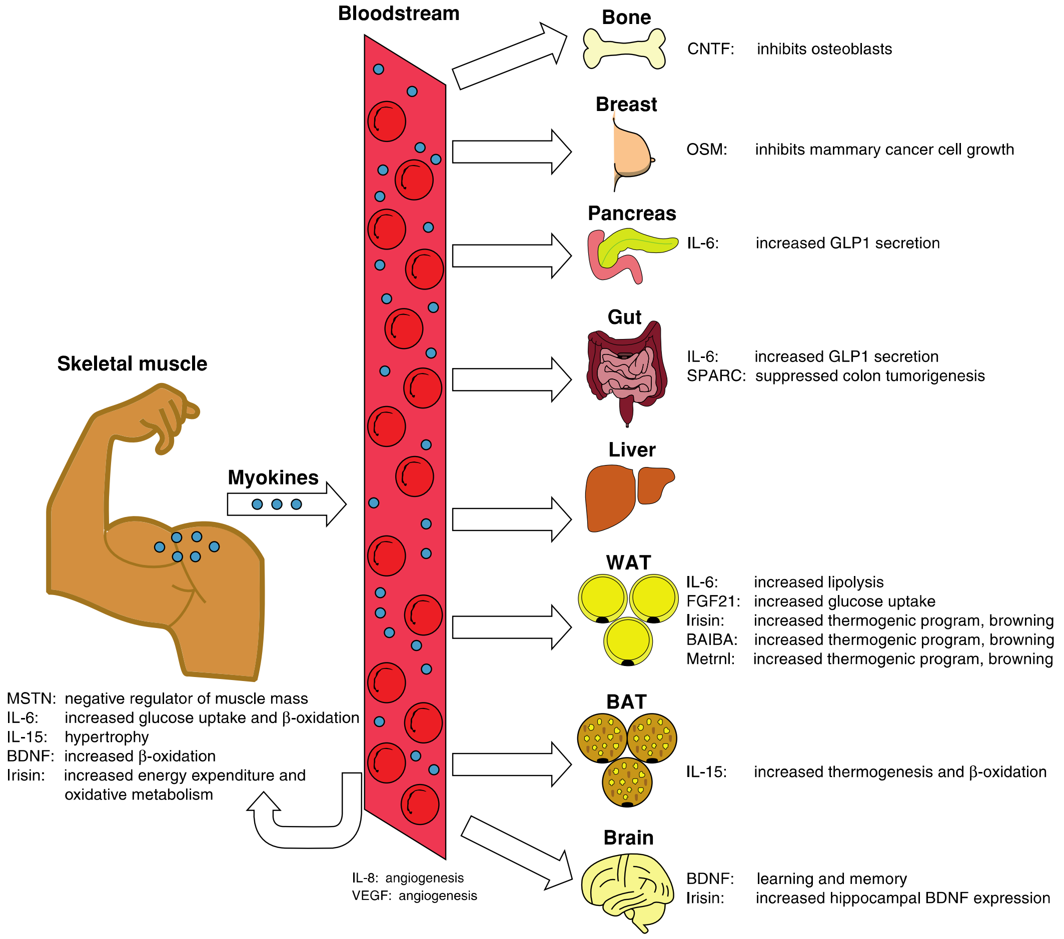
GENOVA DIAGNOSTICS

Bongiovanni T, et al. *Eur Rev Med Pharmacol Sci*. 2019;23(24):11011-11019.
Hoffman NJ. *Cold Spring Harb Perspect Med.* 2017;7(10):a029884.

SPORTOMICS: CLINCIAL RELEVANCE

- EXERCISE = Medicine
  - With a great “benefit to risk” profile
  - Three major clinically relevant questions:
    - What is ”TIPPING POINT”?
      - Where/When/How does exercise become less health promoting?
    - Who are the ”RESPONDERS” vs. “NON-RESPONDERS”?
    - How do you make a “NON-RESPONDER” a “RESPONDER”?

- EXERCISE = INVESTIGATIVE TOOL as a STRESSOR
  to systems biology and integrative physiology



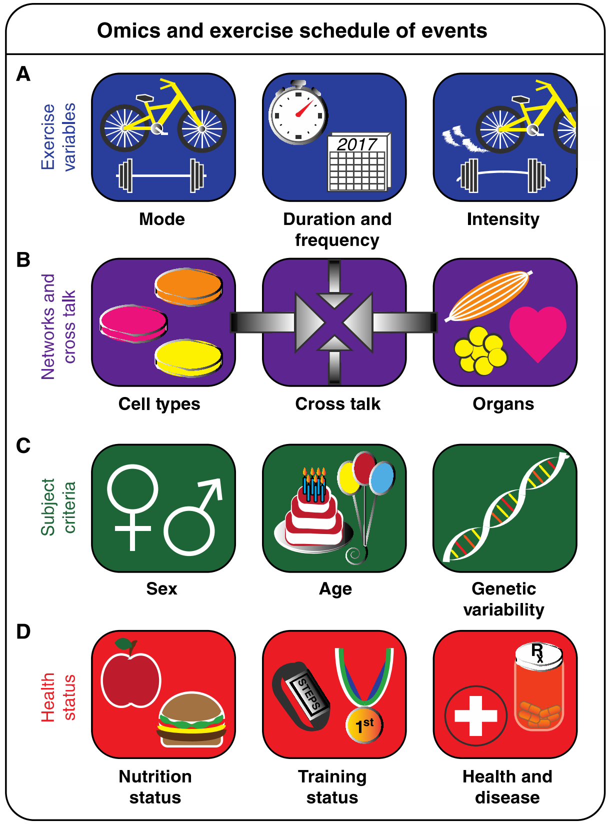
GENOVA DIAGNOSTICS

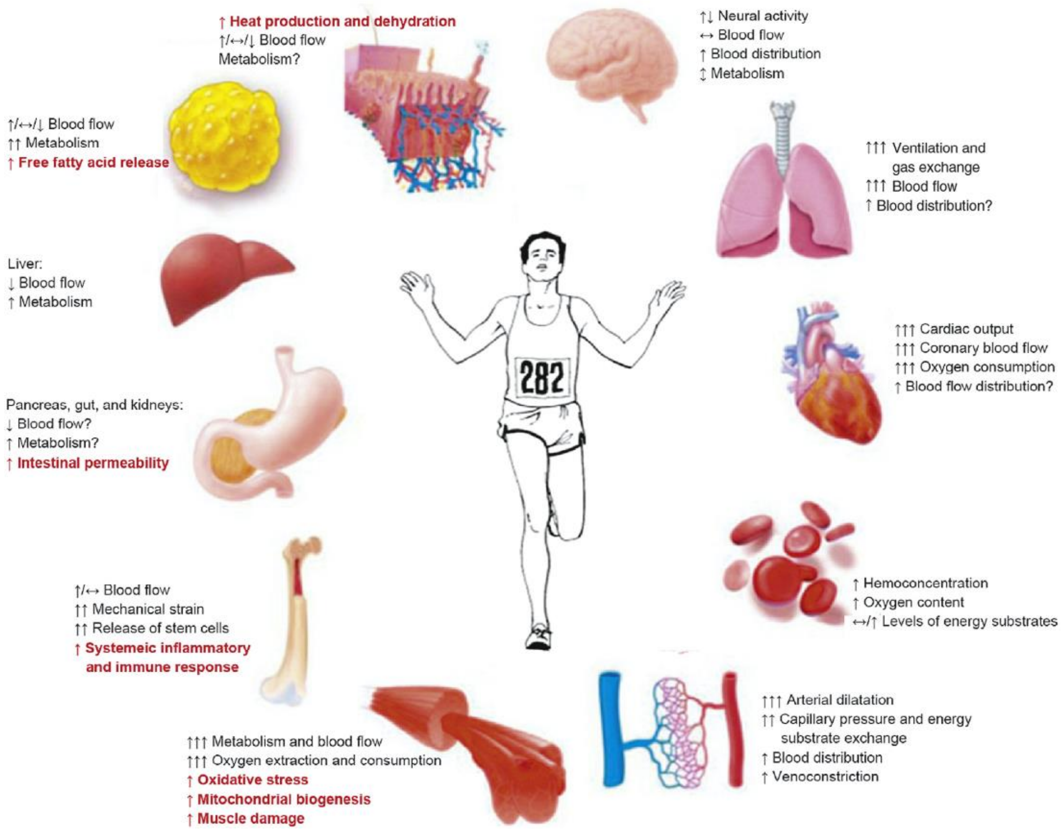
Schnyder S et al. *Bone.* 2015;80:115-125.

SPORTOMICS

MULTI-VARIATE

SYSTEMS BIOLOGY



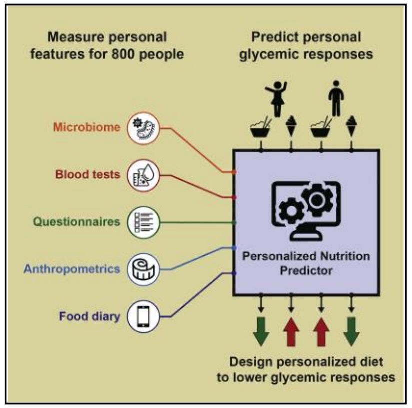


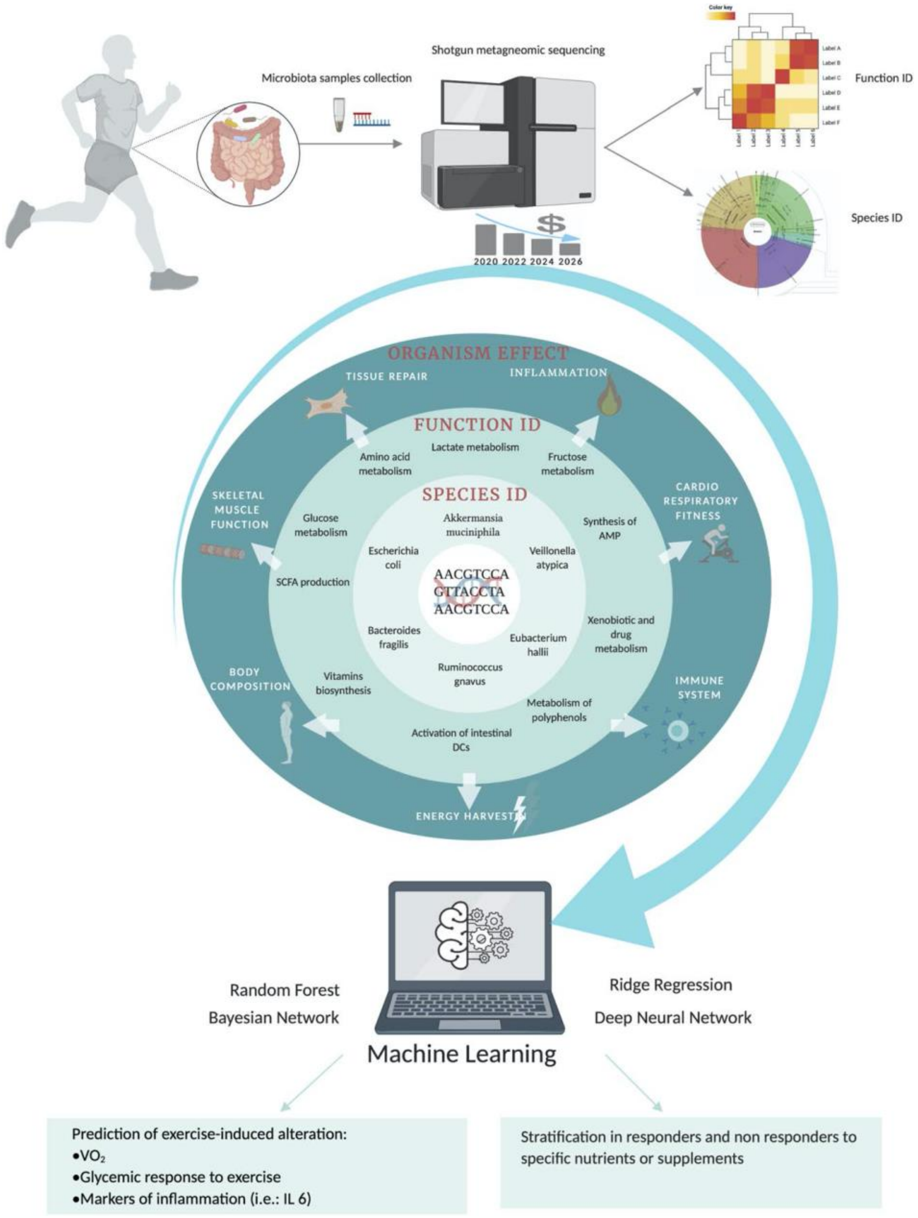
GENOVA DIAGNOSTICS

Mach N, et al. *J Sport Health Sci. 2017;6(2):179-197.*
Hoffman NJ. *Cold Spring Harb Perspect Med.* 2017;7(10):a029884.

SPORTOMICS

- Must go beyond correlation/association studies
- Meta-omics and computational tools
- Potential for machine learning to predict exercise-induce alteration and performance measures to distinguish responders and non responders
  - by Zeevi et al



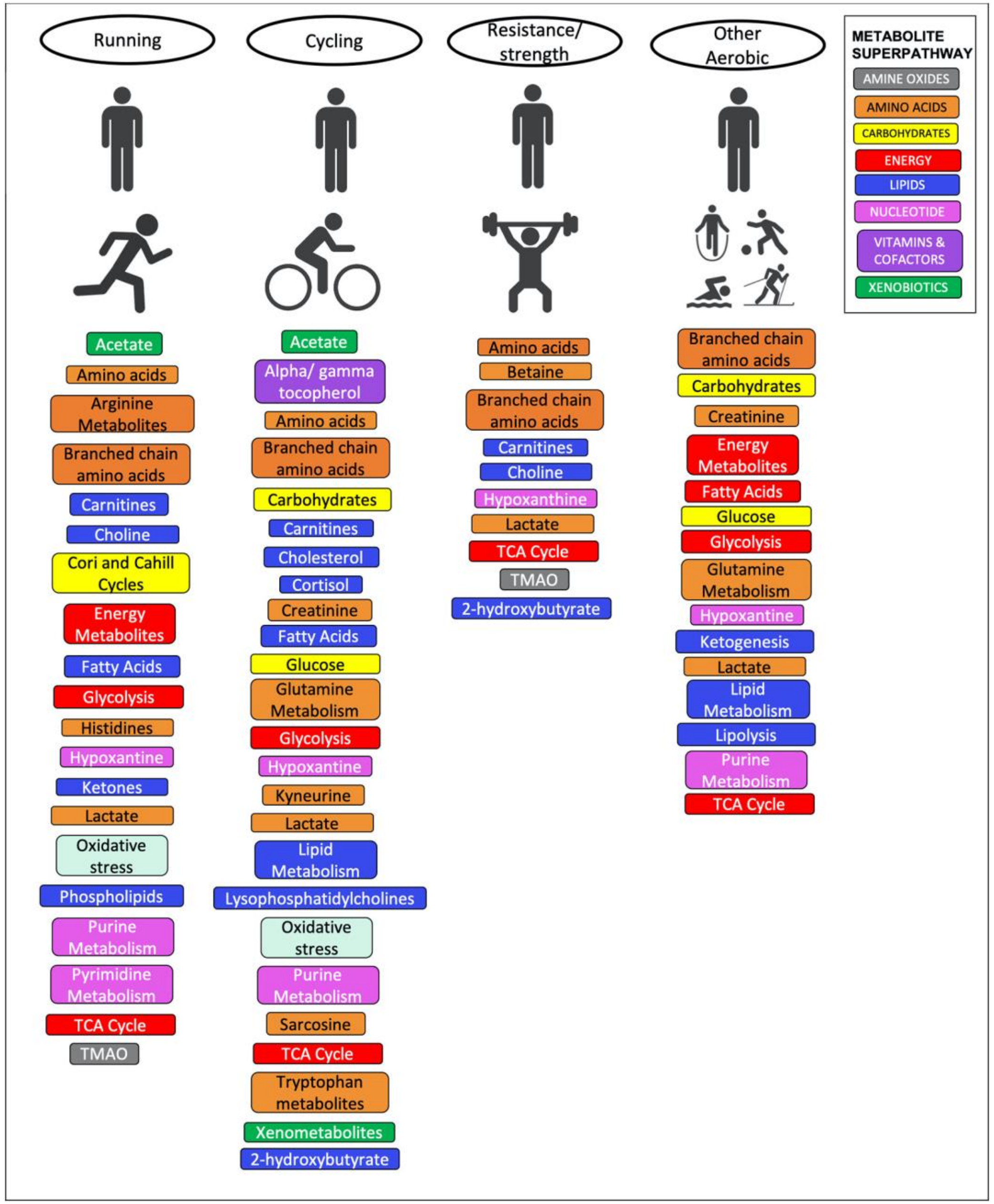


GENOVA DIAGNOSTICS

Mancin L, et al. *Exerc Sport Sci Rev*. 2021;49(1):42-49.
Zeevi D, et al. *Cell*. 2015;163(5):1079-1094.

SPORTOMICS: METABOLOME

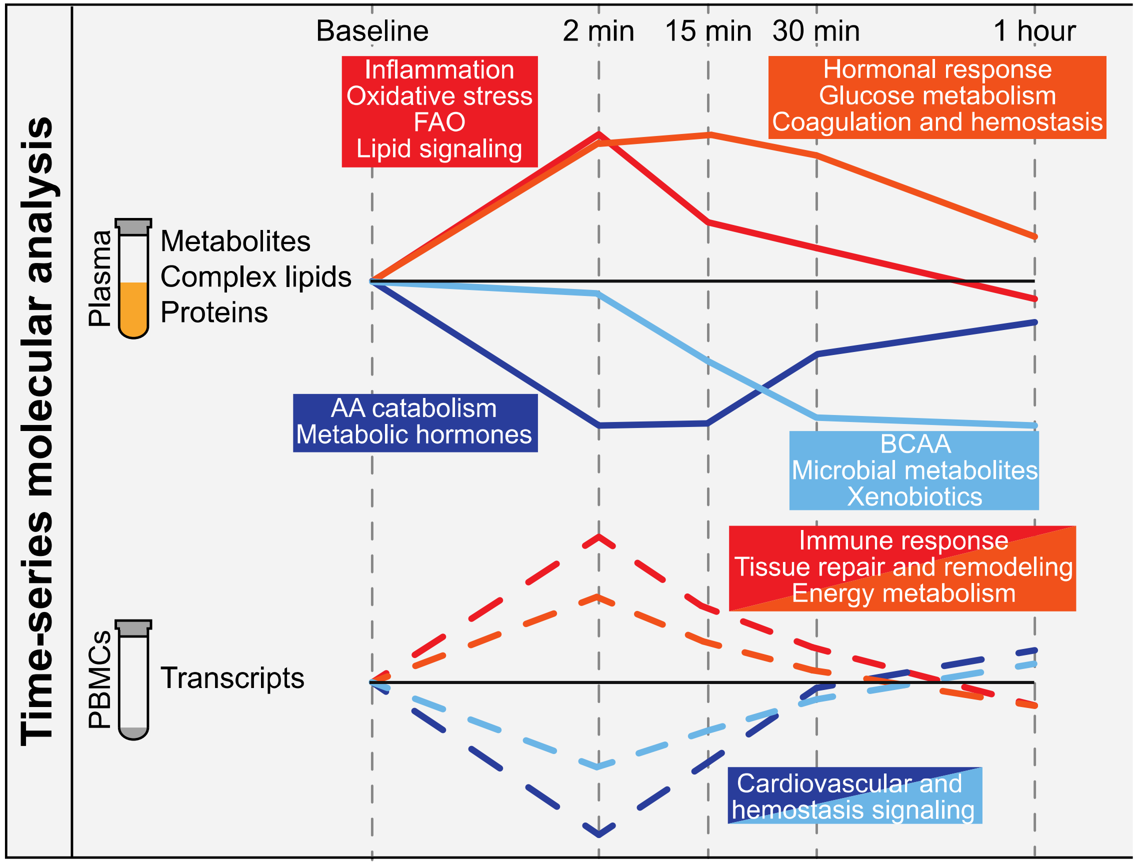
- SUMMARY:
  - Substantial heterogeneity of studies
  - Volume was biggest driver of changes
  - Generally short-lived response to acute exercise
  - However, changes are apparent in consistent movers
  - Multifactorial dose response relationship



Kelly RS, et al. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(12):165936.

SPORTOMICS: METABOLOME

- <u>ACUTE EXERCISE</u>:
  - Responses resolved minutes to hours later
  - Greater changes in less trained in response to marathon [1]
  - INCREASE:
    - Lactate, pyruvate, TCA intermediates, fatty acids, acyl-carnitines, ketone bodies [2]
  - DECREASE:
    - Bile acids [2]

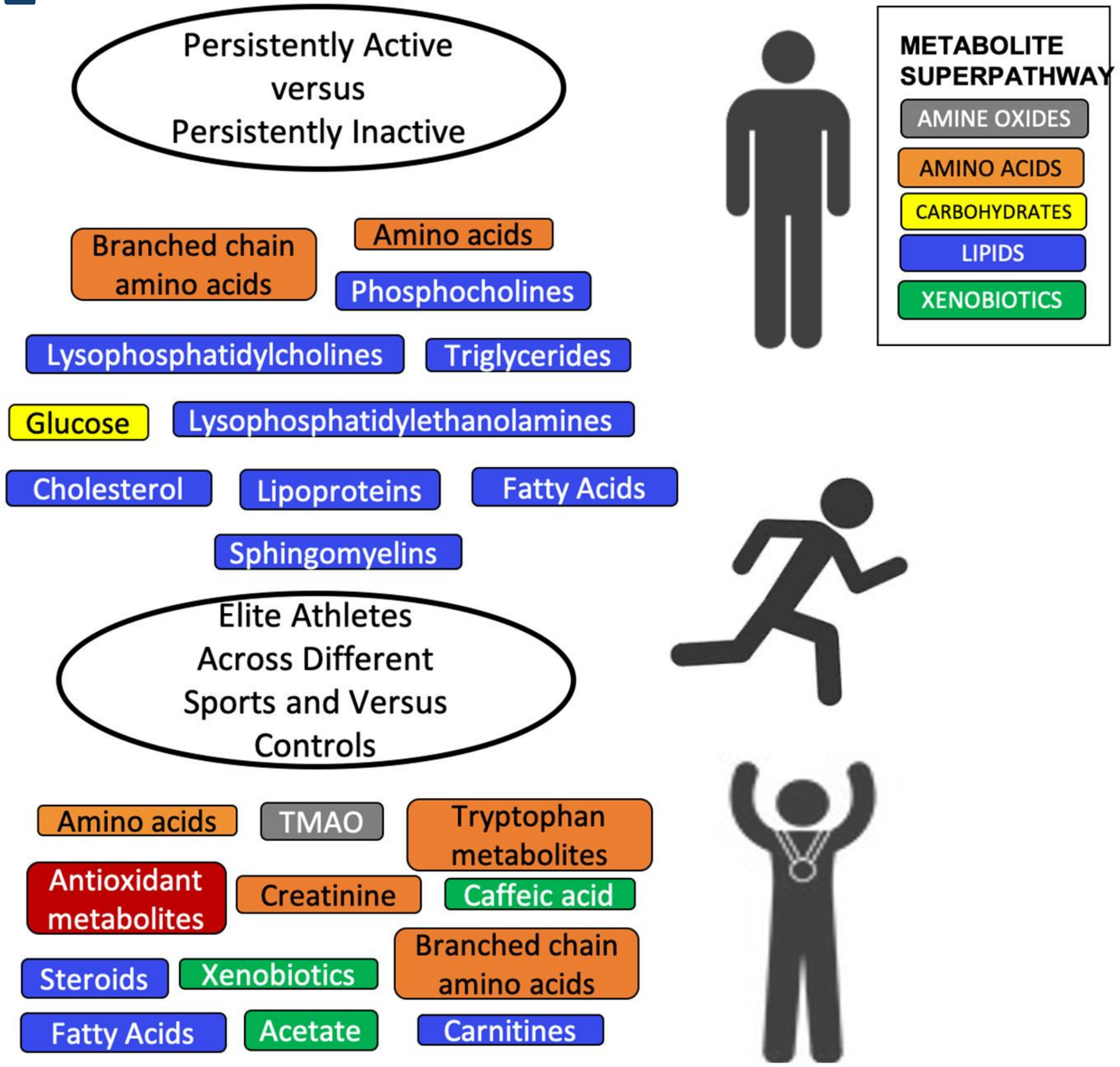


GENOVA DIAGNOSTICS

1. Kelly RS, et al. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(12):1-17.
2. Schranner D, et al. *Sports Med Open*. 2020;6(1):11.
Contrepois K, et al. *Cell*. 2020;181(5):1112-1130.

SPORTOMICS:
METABOLOME & PERFORMANCE

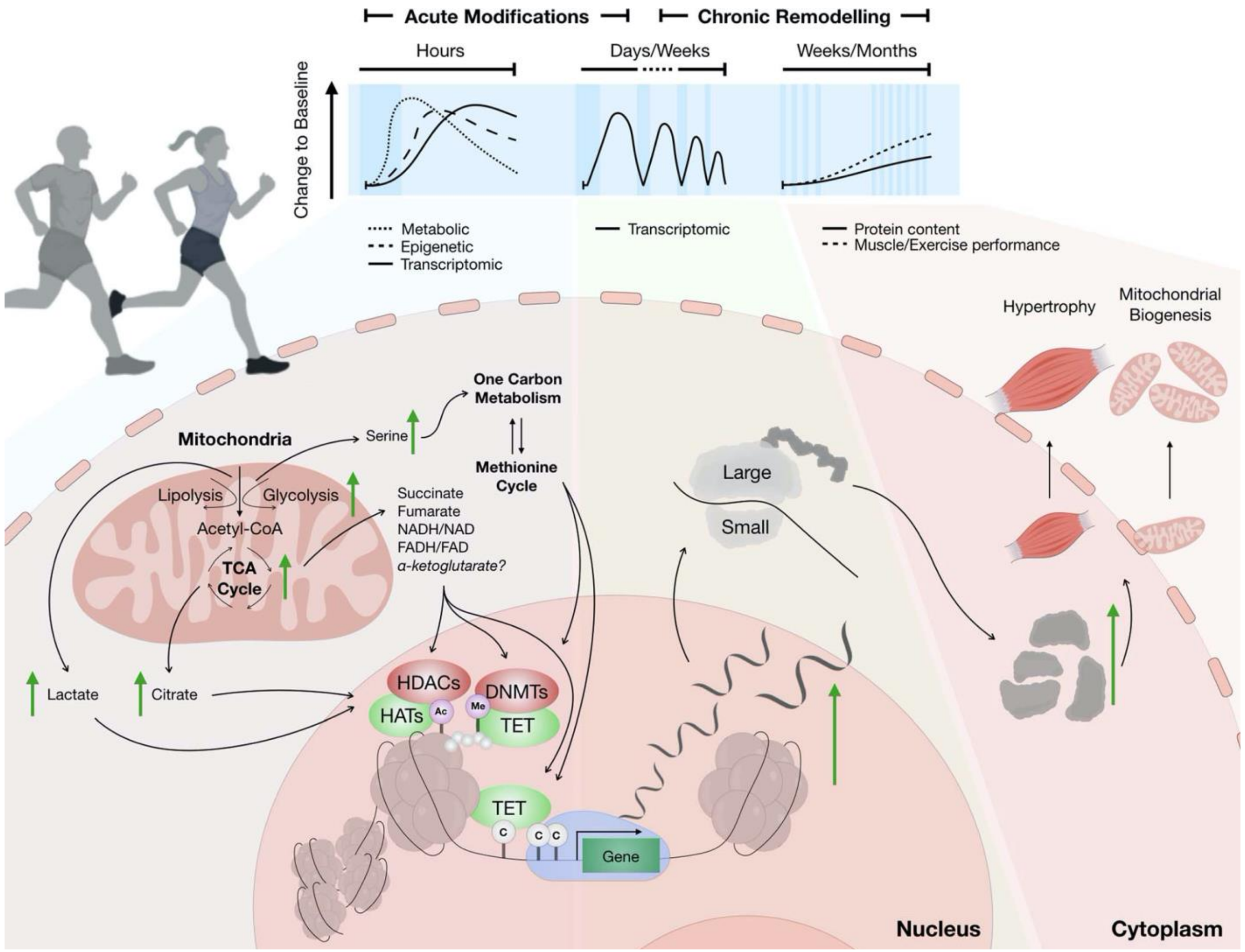
- CHRONIC EXERCISE:
  - “Coherently healthier metabolic profile”
    - Lower amino acids (especially isoleucine)
    - Changes in several lipid metabolites
      - Saturated → polyunsaturated profile
      - Lower VLDL & TG and Higher HDL
  - Difference in intermediary metabolism, fuel substrate utilization, glucose transport, fatty acid oxidation, oxidative stress, steroid biosynthesis, insulin signaling
  - Epigenomic, Transcriptomic, & Proteomic studies are fewer but confirm gene changes



GENOVA DIAGNOSTICS

Kelly RS, et al. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(12):165936.

SPORTOMICS: METABOLOME



Seaborne RA, et al. *Exerc Sport Sci Rev.* 2020;48(4):188-200.

SPORTOMICS: METABOLOME & PERFORMANCE & FUNCTIONAL TESTING

- 38yo year-round athlete
- In winter with significant XC and downhill skiing routine

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	8	3-43
Histidine	212	124-894
Isoleucine	7	3-28
Leucine	15	4-46
Lysine	30	11-175
Methionine	4	2-18
Phenylalanine	21	8-71
Taurine	590	21-424
Threonine	51	17-135
Tryptophan	23	5-53
Valine	19	7-49

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	77	63-356
Asparagine	38	25-166
Aspartic Acid	<dl	<= 14
Cysteine	21	8-74
Cystine	21	10-104
γ-Aminobutyric Acid	1	<= 5
Glutamic Acid	10	4-27
Glutamine	153	110-632
Proline	2	1-13
Tyrosine	27	11-135

Creatinine Concentration

		Reference Range
Creatinine ◆	12.6	3.1-19.5 mmol/L

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic Acid	12	2-47
α-Amino-N-butyric Acid	10	2-25
β-Aminoisobutyric Acid	217	11-160
Cystathionine	18	2-68
3-Methylhistidine	95	44-281

Urea Cycle Markers		Reference Range
Citrulline	2.3	0.6-3.9
Ornithine	5	2-21
Urea ◆	236	168-465 mmol/g creatinine

Glycine/Serine Metabolites		Reference Range
Glycine	139	95-683
Serine	140	40-163
Ethanolamine	182	50-235
Phosphoethanolamine	6	1-13
Phosphoserine	<dl	3-13
Sarcosine	0.5	<= 1.1

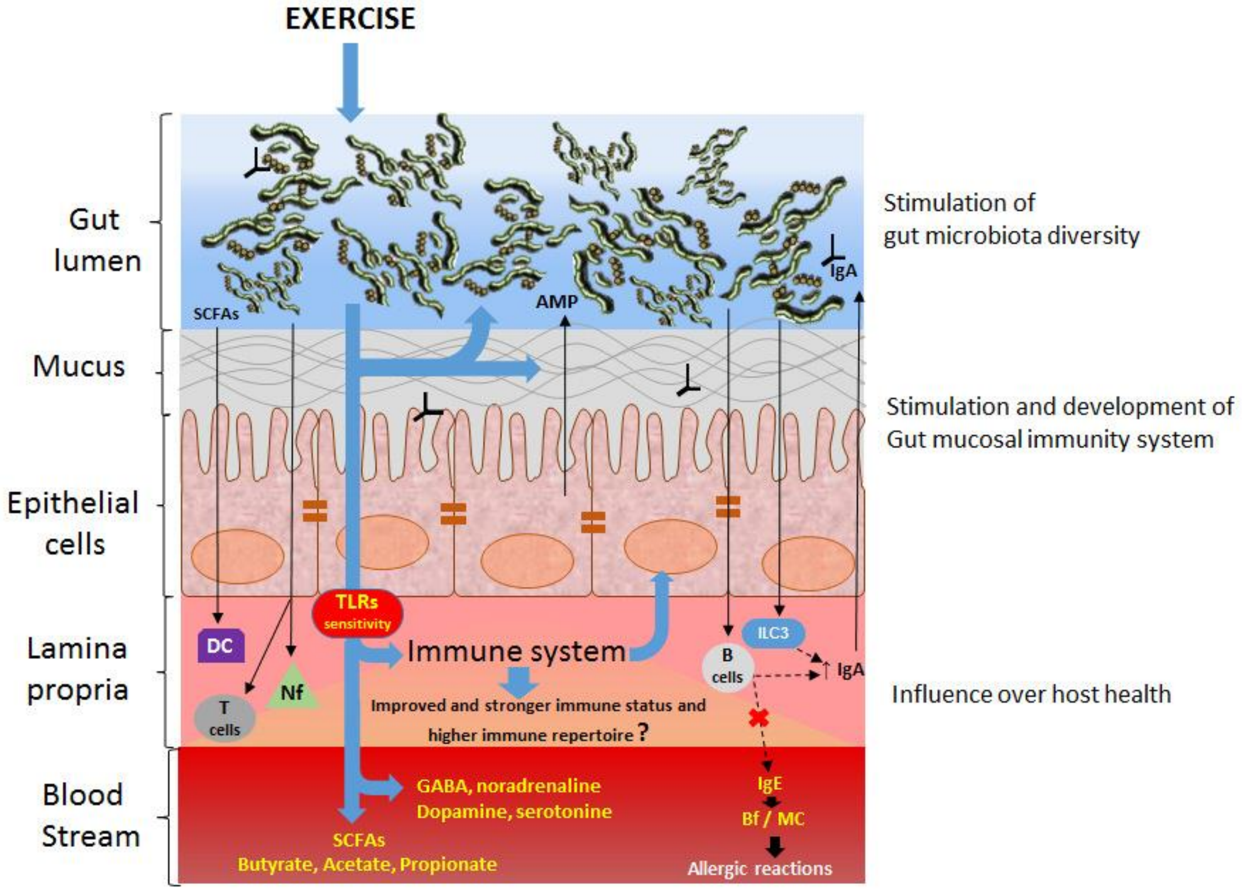
Dietary Peptide Related Markers

		Reference Range
Anserine (dipeptide)	15.5	0.4-105.1
Carnosine (dipeptide)	8	1-28
1-Methylhistidine	1,377	38-988
β-Alanine	13	<= 22

GENOVA DIAGNOSTICS

SPORTOMICS: MICROBIOME

- 2014: 1st report of exercise increasing gut microbial diversity in humans
- Low BMI control and athletes with high BMI significantly higher proportions of *Akkermansia muciniphila*
- Greater microbiome diversity
  - HOWEVER, suggestion that exercise and protein intake were drivers of diversity

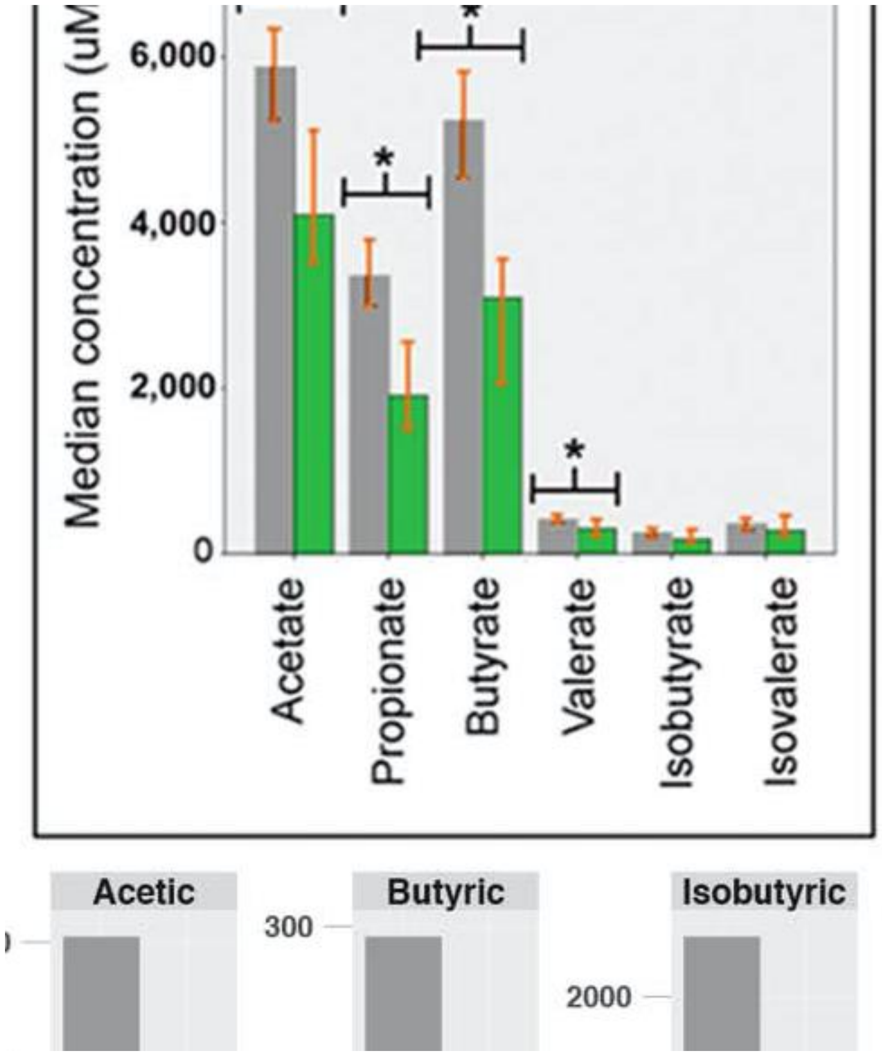


GENOVA DIAGNOSTICS

Bermon S, et al. *Exerc Immunol Rev*. 2015;21:70-79.
Clarke SF, et al. *Gut*. 2014;63:1913-20.

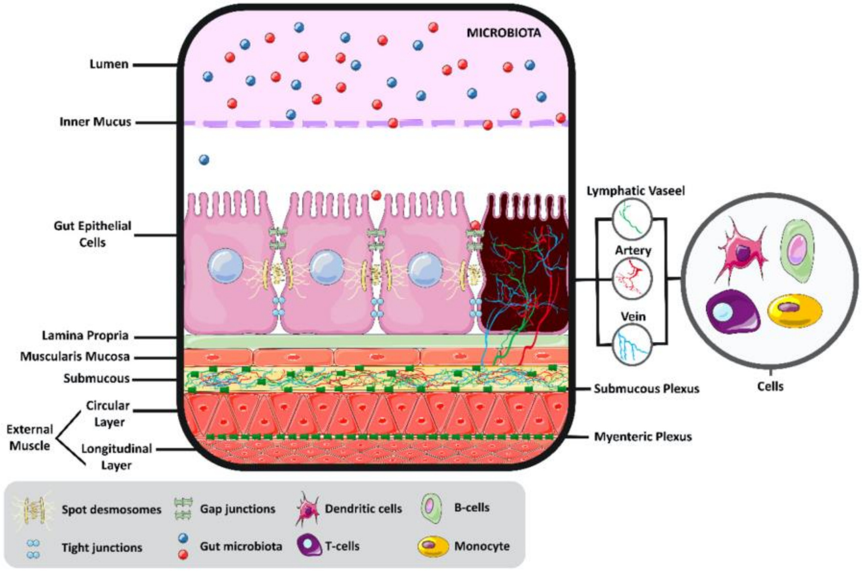
SPORTOMICS: MICROBIOME

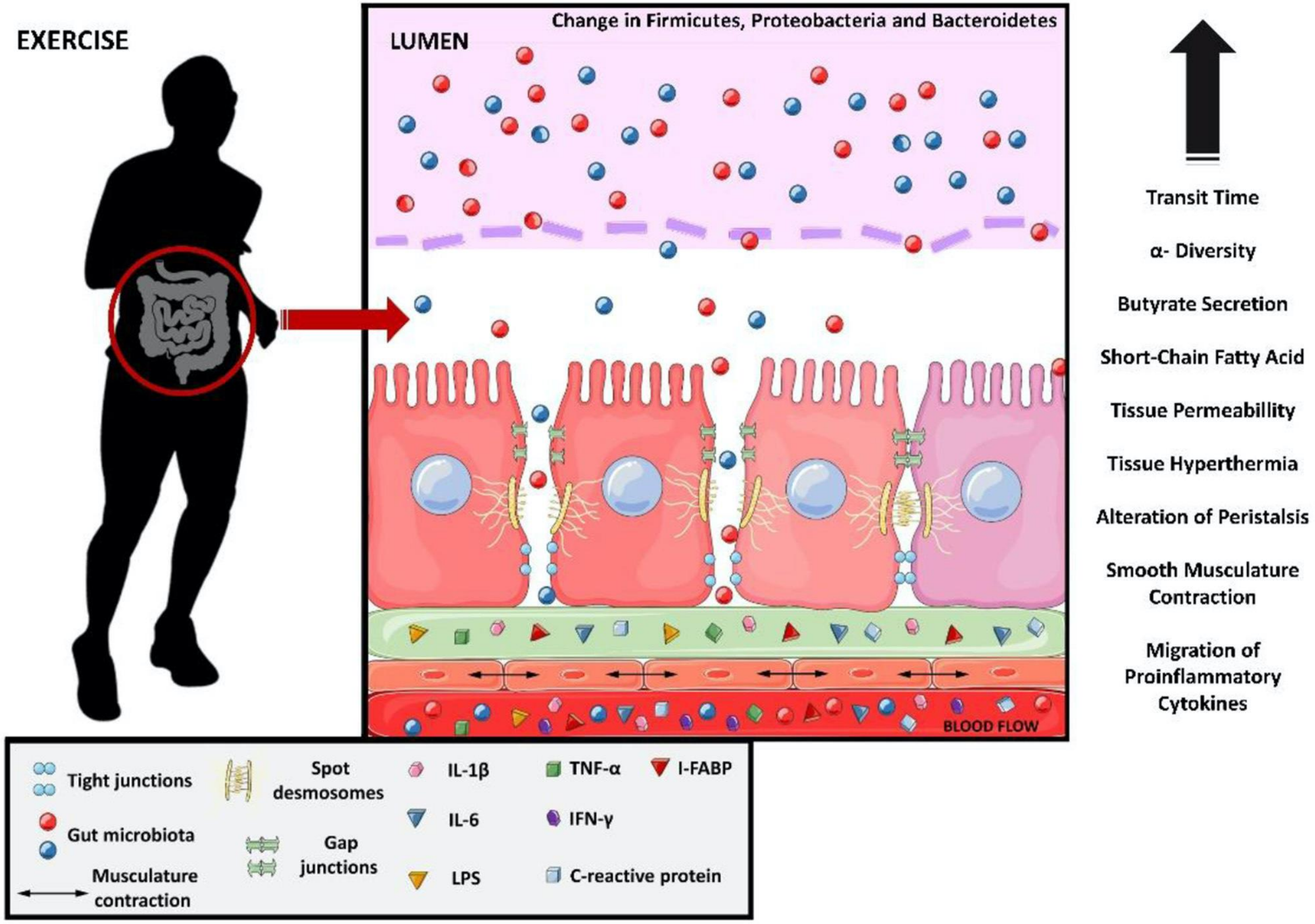
- Greater diversity compared to nonathletes [1,2]
- Greater growth of certain species such as *Akkermansia muciniphila* [1,3,4]
- Relative increase in SCFA [2,5]
- Direct association between VO2max and F/B ratio [6]



1. Clarke SF, et al. *Gut*. 2014;63:1913-20.
2. Barton W, et al. *Gut*. 2018;67(4):625-633.
3. Munukka E, et al. *Front Microbiol*. 2018;9:2323.
4. Bressa C, et al. *PLoS One*. 2017;12(2):e0171352.
5. Estaki M, et al. *Microbiome*. 2016;4(1):42.
6. Durk RP, et al. *Int J Sport Nutr Exerc Metab*. 2019;29(3):249-53.

SPORTOMICS: MICROBIOME

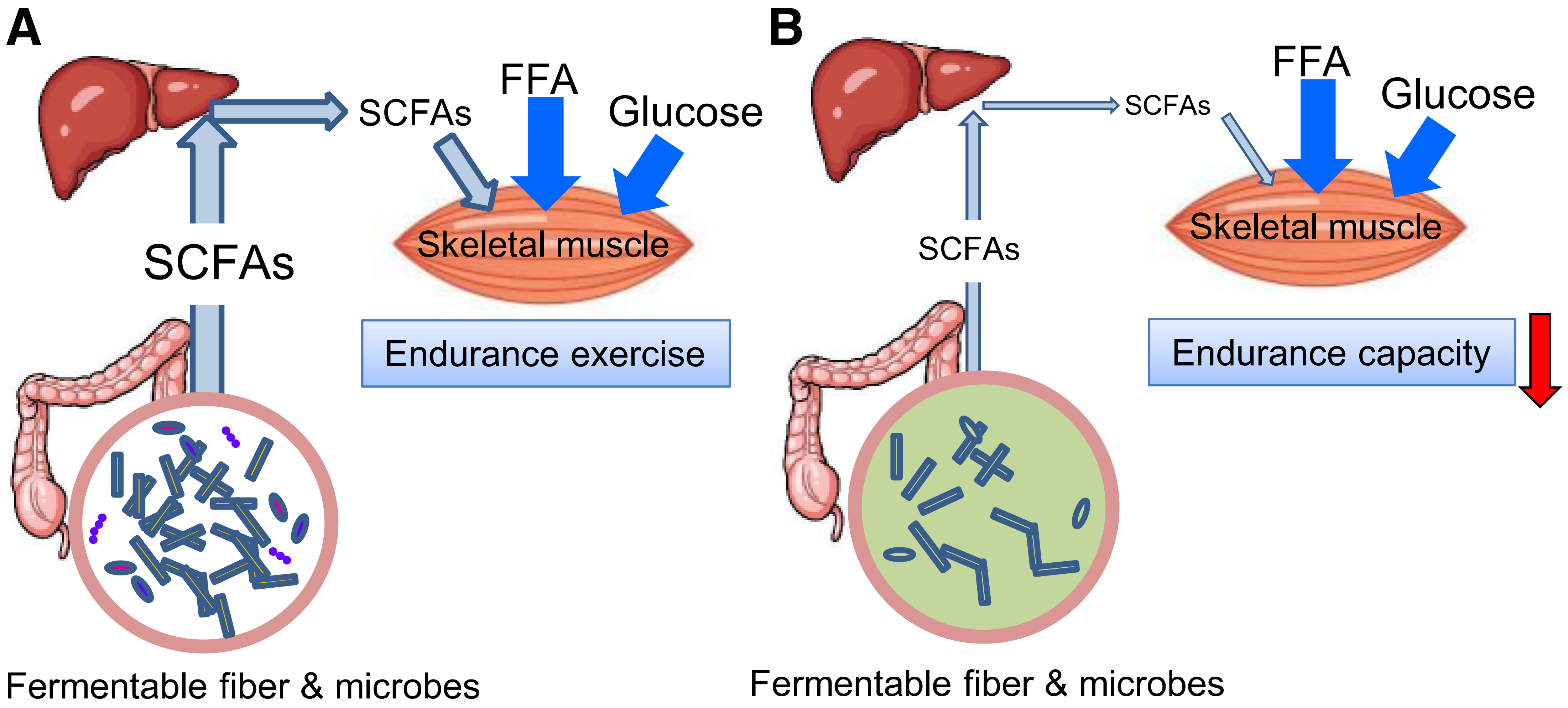




GENOVA DIAGNOSTICS

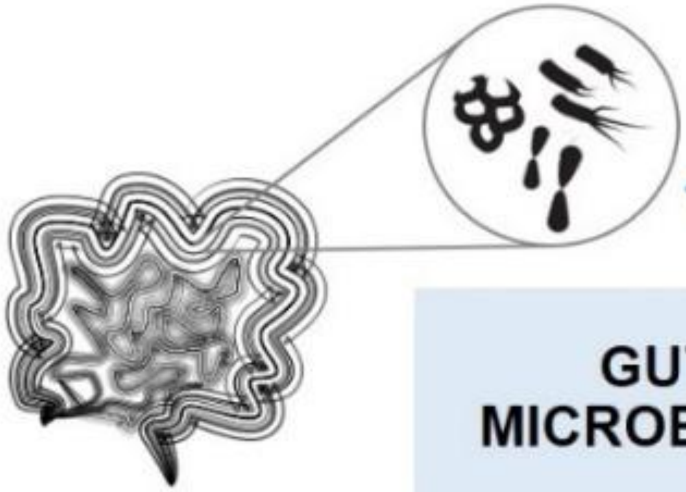
Ribeiro FM, et al. Front Nutr. 2021;8:627289.

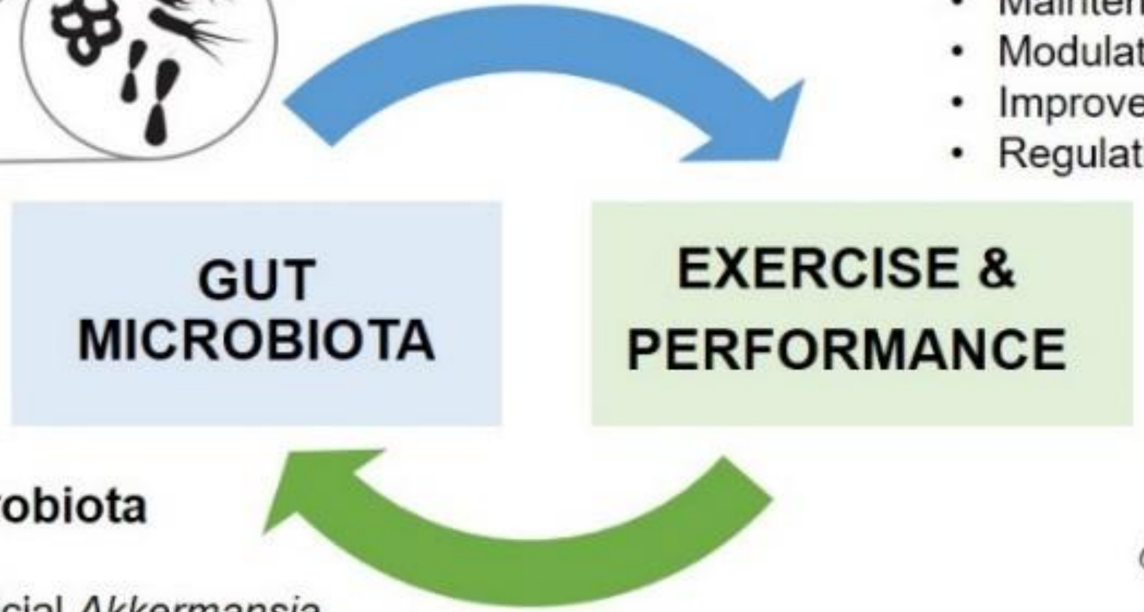
SPORTOMICS:
MICROBIOME & PERFORMANCE



Okamoto T, et al. *Am J Physiol Endocrinol Metab.* 2019; 316(5):E956-E966.

SPORTOMICS:
MICROBIOME & PERFORMANCE





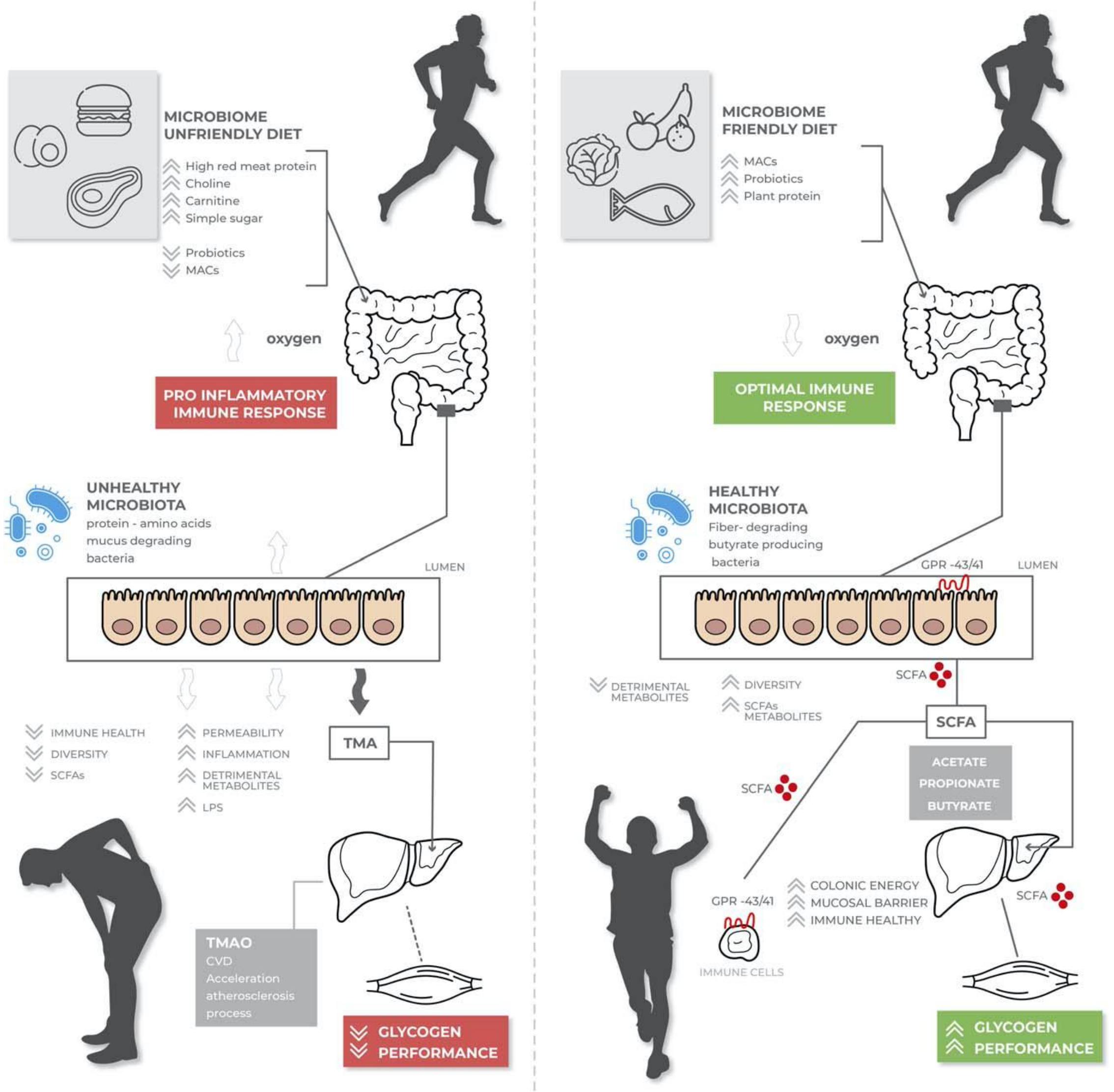
Benefits for the athlete
- Production of bioactive metabolites (i.e.short chain fatty acids, neurotransmitters)
- Maintenance of intestinal barrier function
- Modulation of immune system
- Improved energy harvest and utilization
- Regulation of muscle metabolism

Benefits on the gut microbiota
- Higher microbial richness
- Higher abundancy of beneficial *Akkermansia, Veillonella, Prevotella*
- Selection advantage for lactate-utilizing bacteria

GENOVA DIAGNOSTICS

Marttinen M, et al. *Nutrients.* 2020;12(10):2936.

SPORTOMICS:
MICROBIOME & PERFORMANCE



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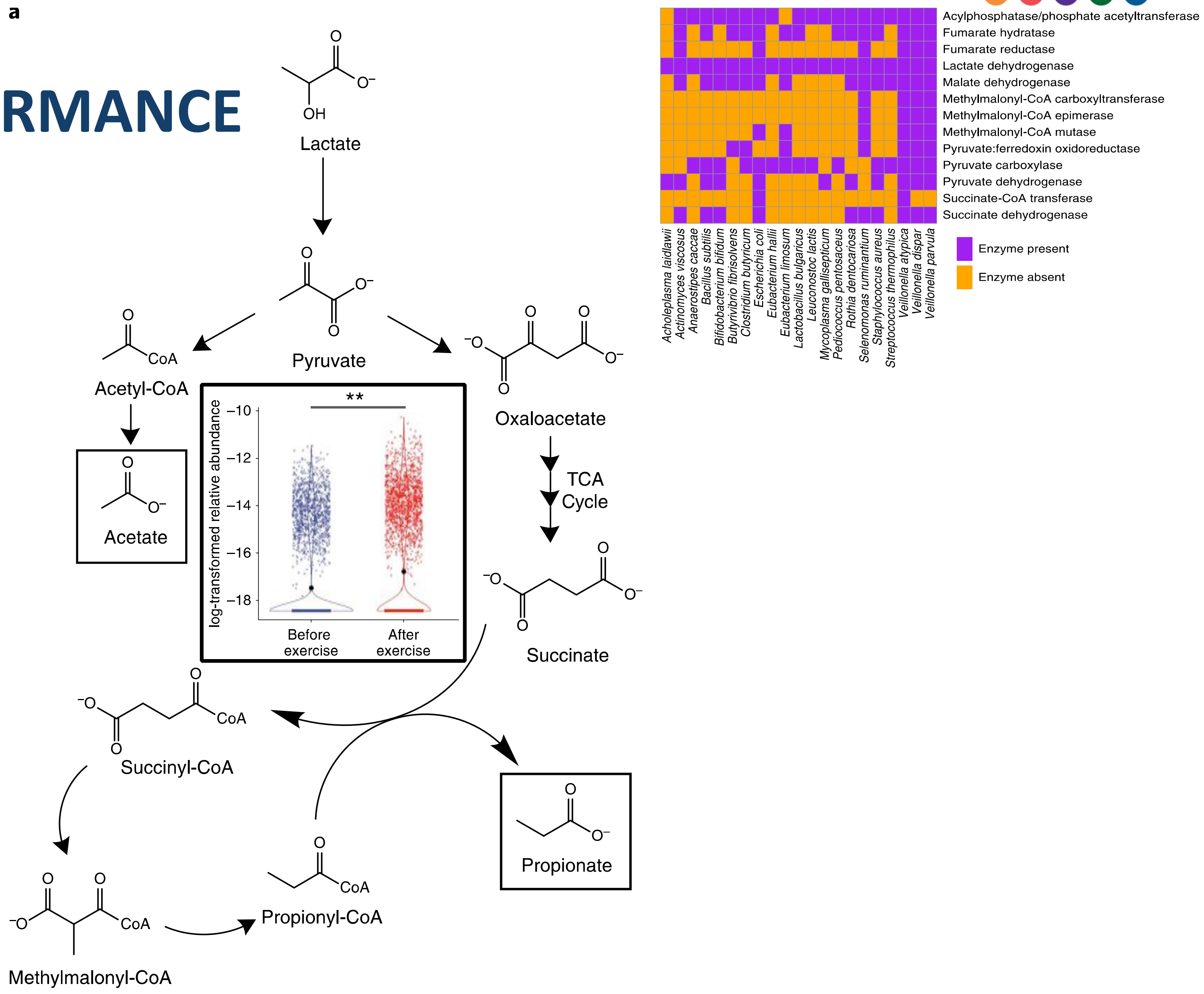
Mancin L, et al. *Exerc Sport Sci Rev*. 2021;49(1):42-49.

SPORTOMICS: MICROBIOME & PERFORMANCE

- INCREASED *Veillonella* spp (esp. *Veillonella atypica*) post marathon
- *Veillonella atypica* gavage → increased exercise performance in mice



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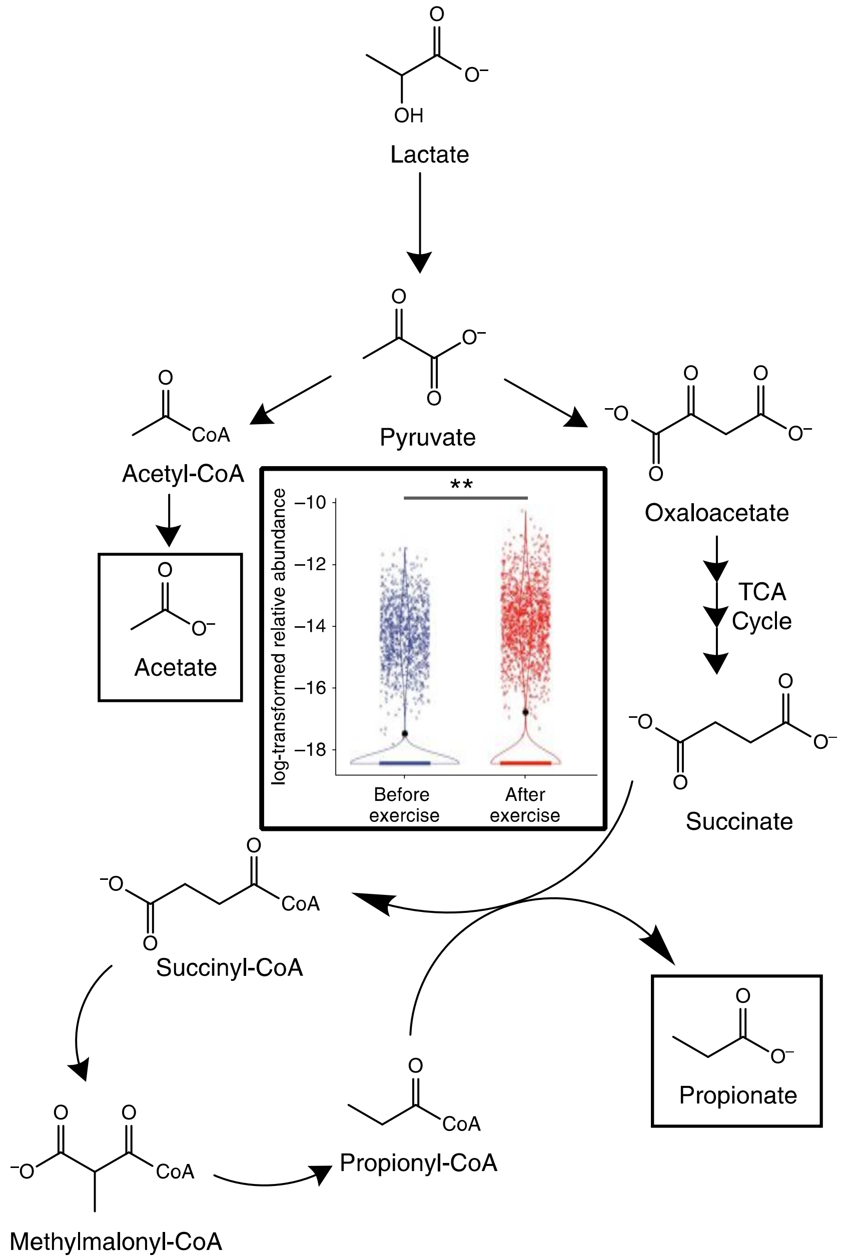
Scheiman J, et al. *Nat Med*. 2019;25(7):1104-9.

SPORTOMICS: MICROBIOME & PERFORMANCE

- IMPROVED EXERCISE PERFORMANCE in mice with *Veillonella atypica* gavage
  - PROPOSED MECHANISM OF ACTION:
    - LACTATE production and conversion into propionate

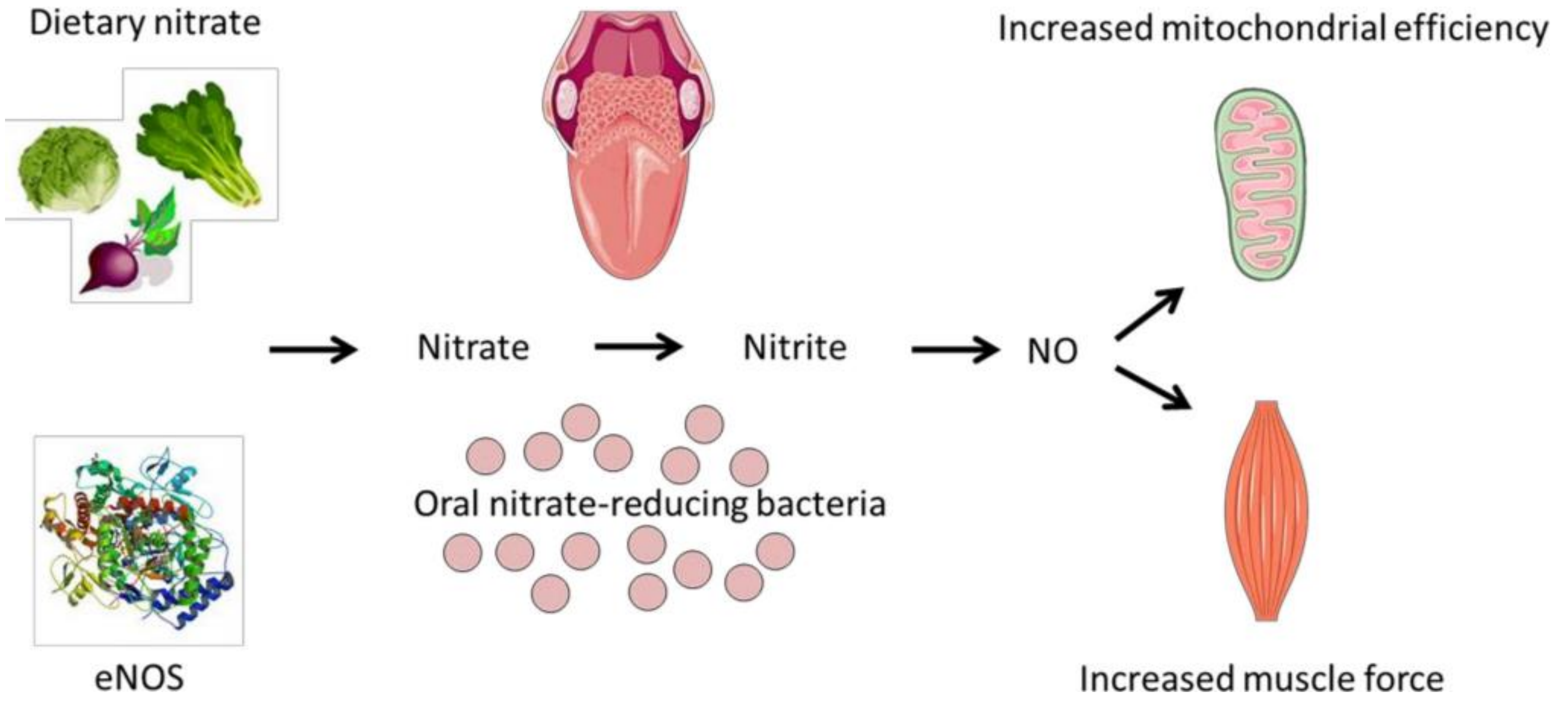
a



Scheiman J, et al. *Nat Med*. 2019;25(7):1104-9.

SPORTOMICS:
MICROBIOME & PERFORMANCE

- *Veillonella* spp. = oral nitrate-reducing bacteria
  - ADDITIONAL PROPOSED MECHANISM OF ACTION: Nitric oxide (NO) production by the oral microbiome



Lundberg JO, *et al*. *Br J Sports Med*. 2021;55(5):243–248.

SPORTOMICS:
MICROBIOME & PERFORMANCE & FUNCTIONAL TESTING

Methodology: DNA by PCR

Gastrointestinal Microbiome (PCR)

Commensal Bacteria (PCR)	Result CFU/g stool		Reference Range CFU/g stool
Bacteroidetes Phylum			
Bacteroides-Prevotella group	2.4E8		3.4E6-1.5E9
Bacteroides vulgatus	1.2E9		<=2.2E9
Barnesiella spp.	3.6E7		<=1.6E8
Odoribacter spp.	7.1E7		<=8.0E7
Prevotella spp.	1.4E8	H	1.4E5-1.6E7
Firmicutes Phylum			
Anaerotruncus colihominis	3.4E7	H	<=3.2E7
Butyrivibrio crossotus	5.0E7	H	5.5E3-5.9E5
Clostridium spp.	2.1E8		1.7E8-1.5E10
Coprococcus eutactus	1.0E8		<=1.2E8
Faecalibacterium prausnitzii	7.5E8		5.8E7-4.7E9
Lactobacillus spp.	1.6E8		8.3E6-5.2E9
Pseudoflavonifractor spp.	3.0E8	H	4.2E5-1.3E8
Roseburia spp.	7.6E7	L	1.3E8-1.2E10
Ruminococcus spp.	1.9E9	H	9.5E7-1.6E9
Veillonella spp.	1.5E8	H	1.2E5-5.5E7
Actinobacteria Phylum			
Bifidobacterium spp.	1.5E8		<=6.4E9
Bifidobacterium longum	1.4E8		<=7.2E8
Collinsella aerofaciens	5.1E8		1.4E7-1.9E9
Proteobacteria Phylum			
Desulfovibrio piger	8.7E7	H	<=1.8E7
Escherichia coli	1.3E8	H	9.0E4-4.6E7
Oxalobacter formigenes	5.0E7	H	<=1.5E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	1.4E8	H	<=8.6E7
Fusobacteria Phylum			
Fusobacterium spp.	2.3E7	H	<=2.4E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	3.1E7		>=1.2E6
Firmicutes/Bacteroidetes Ratio			
Firmicutes/Bacteroidetes (F/B Ratio)	11	L	12-620

Lactate PRODUCER

Lactate DEGRADER

QUINTILE DISTRIBUTION: 1st, 2nd, 3rd, 4th, 5th

SPORTOMICS: MICROBIOME & PERFORMANCE & FUNCTIONAL TESTING

- 40yo with chronic fatigue syndrome, pain amplification syndrome and exercise intolerance – previously failed graded exercise program

Gut Microbiome Metabolites

Metabolic	Result		Reference Range
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	3.1	L	>=23.3 micromol/g
n-Butyrate Concentration	1.2	L	>=3.6 micromol/g
n-Butyrate %	38.7	H	11.8-33.3 %
Acetate %	<DL	L	48.1-69.2 %
Propionate %	60.8	H	<=29.3 %
Beta-glucuronidase	1,063		368-6,266 U/g

Gastrointestinal Microbiome (PCR)**

Commensal Bacteria (PCR)	Result CFU/g stool		Reference Range CFU/g stool
Bacteroidetes Phylum			
Bacteroides-Prevotella group	1.3E8		3.4E6-1.5E9
Bacteroides vulgatus	2.4E7		<=2.2E9
Barnesiella spp.	1.2E7		<=1.6E8
Odoribacter spp.	7.2E6		<=8.0E7
Prevotella spp.	4.8E6		1.4E5-1.6E7
Firmicutes Phylum			
Anaerotruncus colihominis	9.4E5		<=3.2E7
Butyrivibrio crossotus	<DL	L	5.5E3-5.9E5
Clostridium spp.	6.8E8		1.7E8-1.5E10
Coprococcus eutactus	3.8E5		<=1.2E8
Faecalibacterium prausnitzii	6.0E7		5.8E7-4.7E9
Lactobacillus spp.	1.6E8		8.3E6-5.2E9
Pseudoflavonifractor spp.	2.3E7		4.2E5-1.3E8
Roseburia spp.	3.3E7	L	1.3E8-1.2E10
Ruminococcus spp.	5.2E7	L	9.5E7-1.6E9
Veillonella spp.	<DL	L	1.2E5-5.5E7
Actinobacteria Phylum			
Bifidobacterium spp.	2.1E7		<=6.4E9
Bifidobacterium longum	<DL		<=7.2E8
Collinsella aerofaciens	1.7E8		1.4E7-1.9E9
Proteobacteria Phylum			
Desulfovibrio piger	8.6E5		<=1.8E7
Escherichia coli	<DL	L	9.0E4-4.6E7
Oxalobacter formigenes	1.9E6		<=1.5E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	6.4E6		<=8.6E7
Fusobacteria Phylum			
Fusobacterium spp.	1.1E4		<=2.4E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	1.4E7		>=1.2E6
Firmicutes/Bacteroidetes Ratio			
Firmicutes/Bacteroidetes (F/B Ratio)	7	L	12-620

GENOVA DIAGNOSTICS

SPORTOMICS: METABOLIC HEALTH

- LOW cardiorespiratory fitness independent predictor of cardiometabolic disease and mortality [1]

- Exercise capacity more powerful predictor of mortality from cardiometabolic disease than other established risk factors [2]

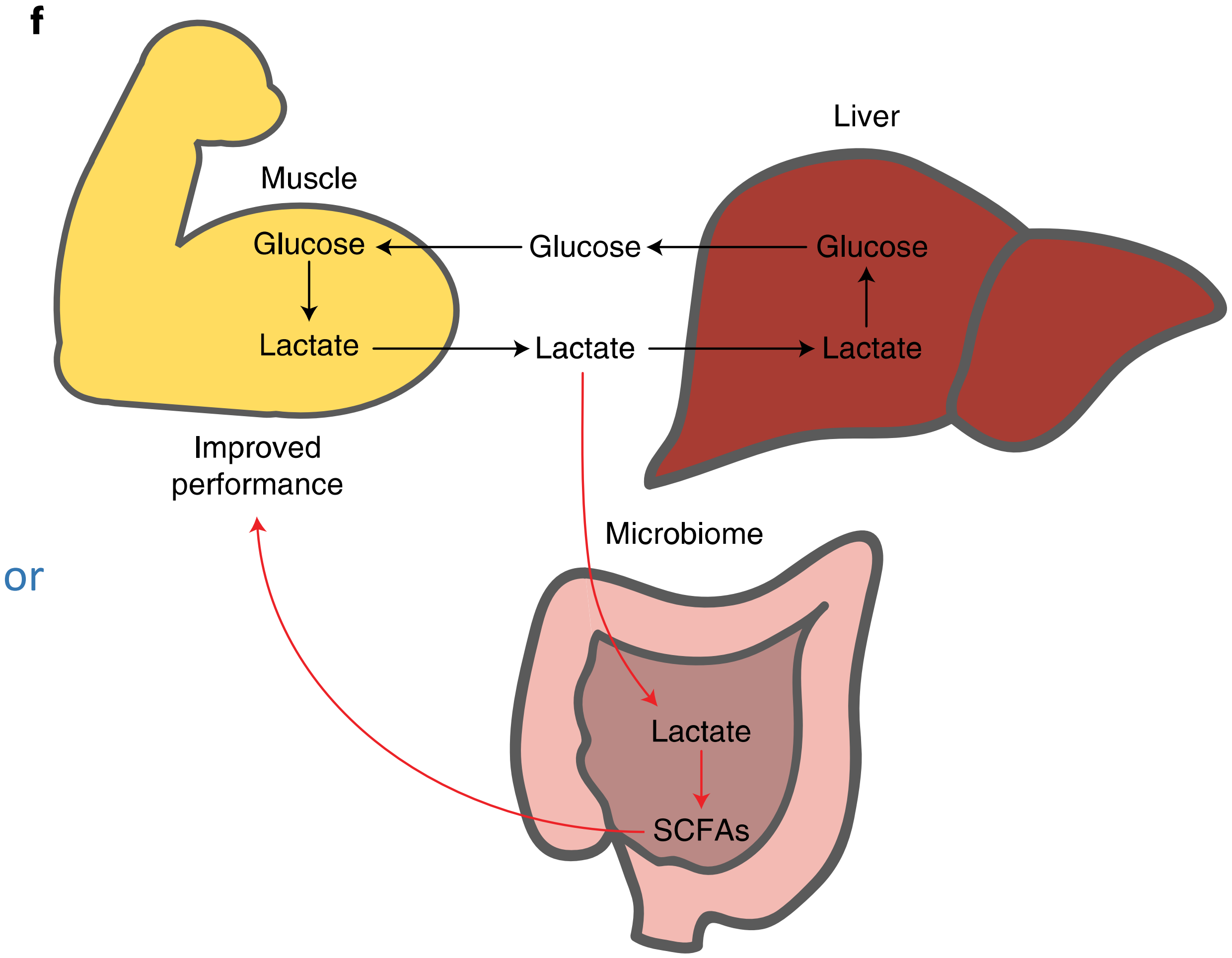
- VO2max is highly correlated with skeletal muscle mitochondrial capacity [3]

GENOVA DIAGNOSTICS

1. Wei M et al. *JAMA*. 1999;282(16):1547-53.
2. Myers J, et al. *N Engl J Med*. 2002:346(11):793-801.
3. van der Zwaard S, et al. *J Appl Physiol*. 2016;121(3):636-45.

SPORTOMICS: METABOLIC HEALTH

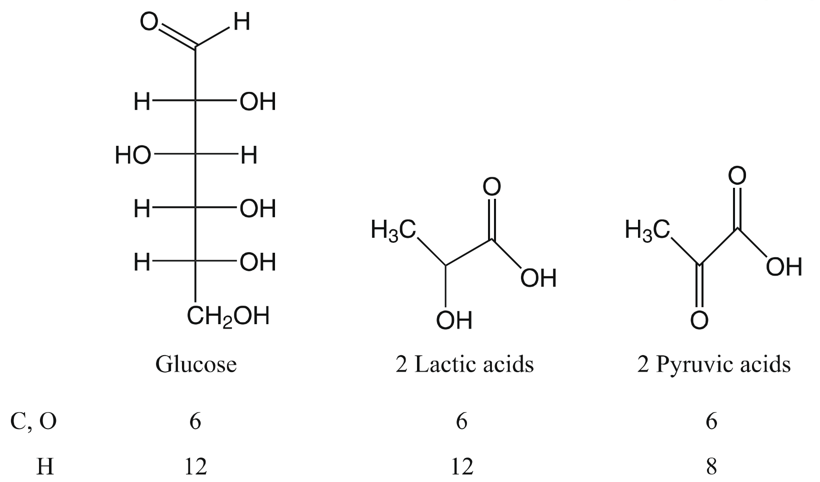
- METABOLIC FLEXIBILITY
  – Ability to appropriately adjust substrate oxidation relative to substrate availability
- LACTATE SHUTTLE:
  – Lactate = gluconeogenic precursor
    - Increased with increased energy expenditure or reduction in energy from aerobic oxidation

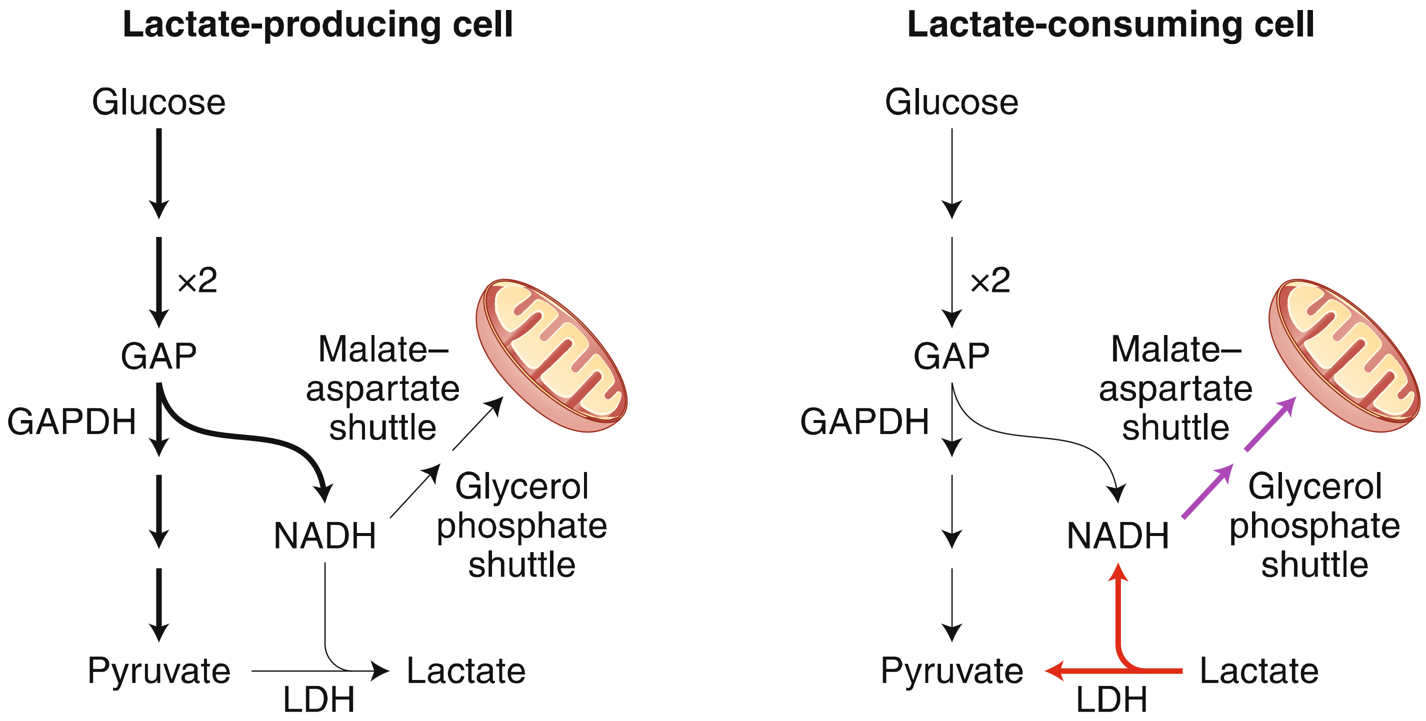


Scheiman J, et al. *Nat Med.* 2019;25:1104-1109.

SPORTOMICS: METABOLIC HEALTH

- **LACTATE**
  - **Glucose as specific fuel and lactate as universal fuel** [1]
    - Lactate as a substrate for generating fuel
    - Radiolabeled lactate → labeling of TCA intermediates greater than radiolabeled glucose [2]



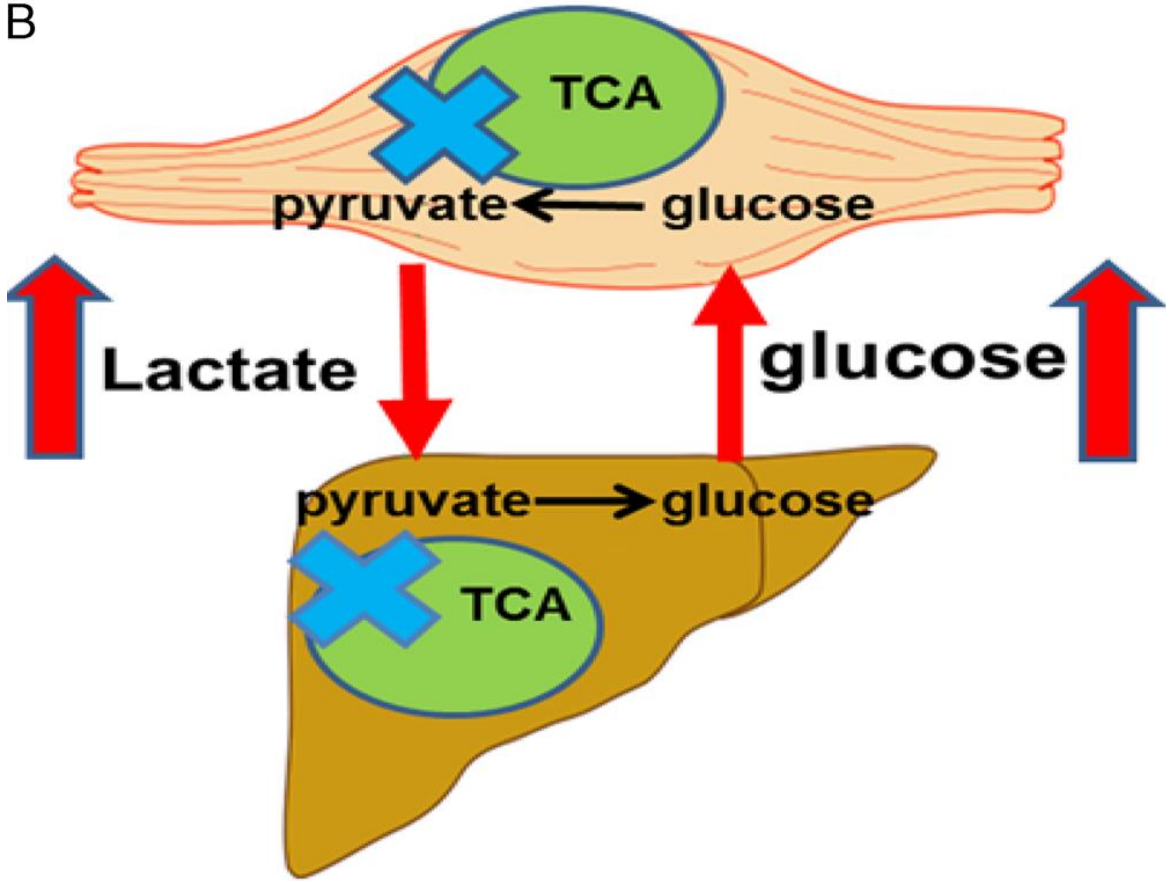


1. Rabinowitz JD, et al. *Nat Metab*. 2020;2:566-571.
2. Hui S, et al. *Nature*. 2017;551(7678):115-118.

SPORTOMICS: METABOLIC HEALTH

- Metabolic Disease
- Obesity
- Insulin Resistance
  - With OBESITY/INCREASED VAT:
    - Skeletal muscle tissue minimally increases glucose oxidation with insulin and preferentially partitions it with net lactate release [1]
  - "VISCIOUS CORI CYCLE" [2]
    - Due to impaired pyruvate oxidation

B



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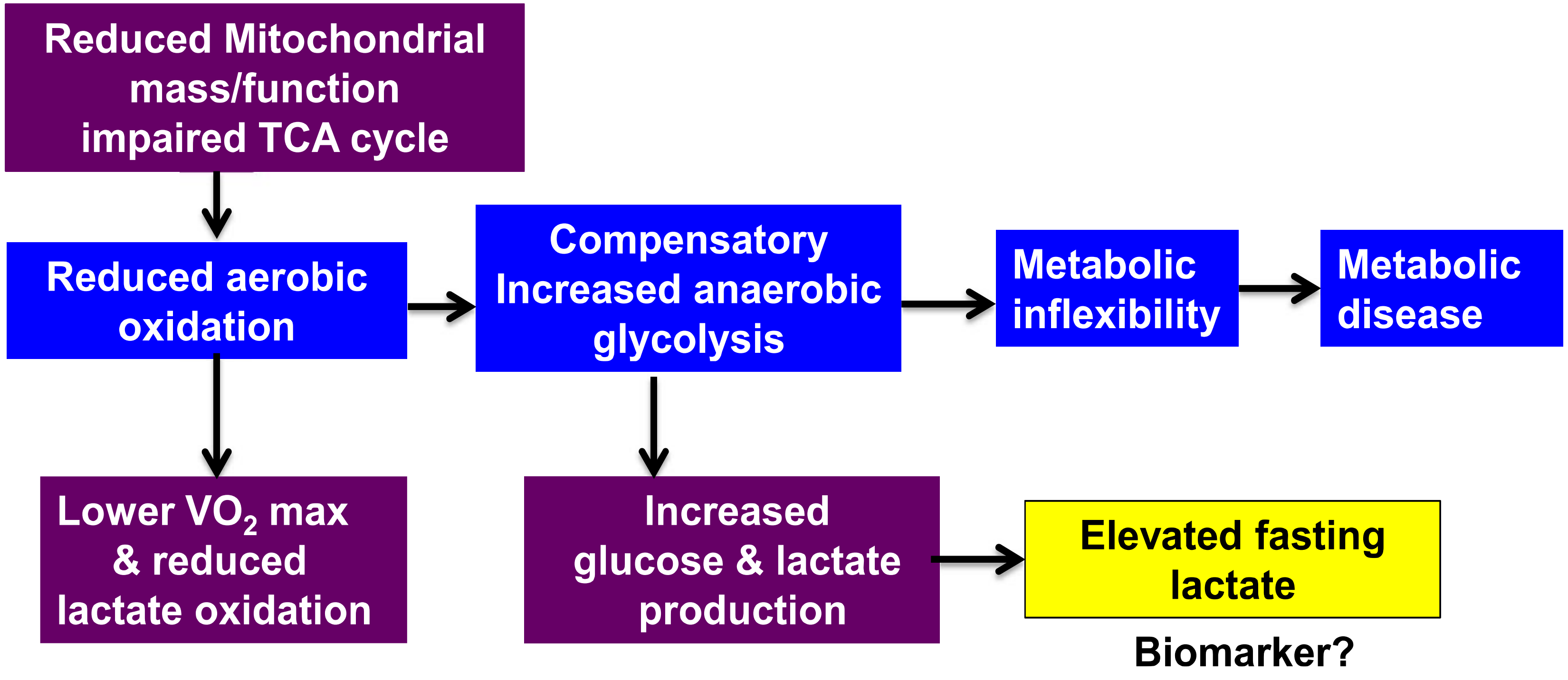
1. Friedman JE, et al. *Metabolism*. 1994;43(8):1047-1054.
2. Broskey NT, et al. *Exerc Sport Sci Rev*. 2020;48(3):119–124.

SPORTOMICS: METABOLIC HEALTH

- Metabolic Disease
- Obesity
- Insulin Resistance



GENOVA DIAGNOSTICS

Broskey NT, et al. *Exerc Sport Sci Rev*. 2020;48(3):119–124.

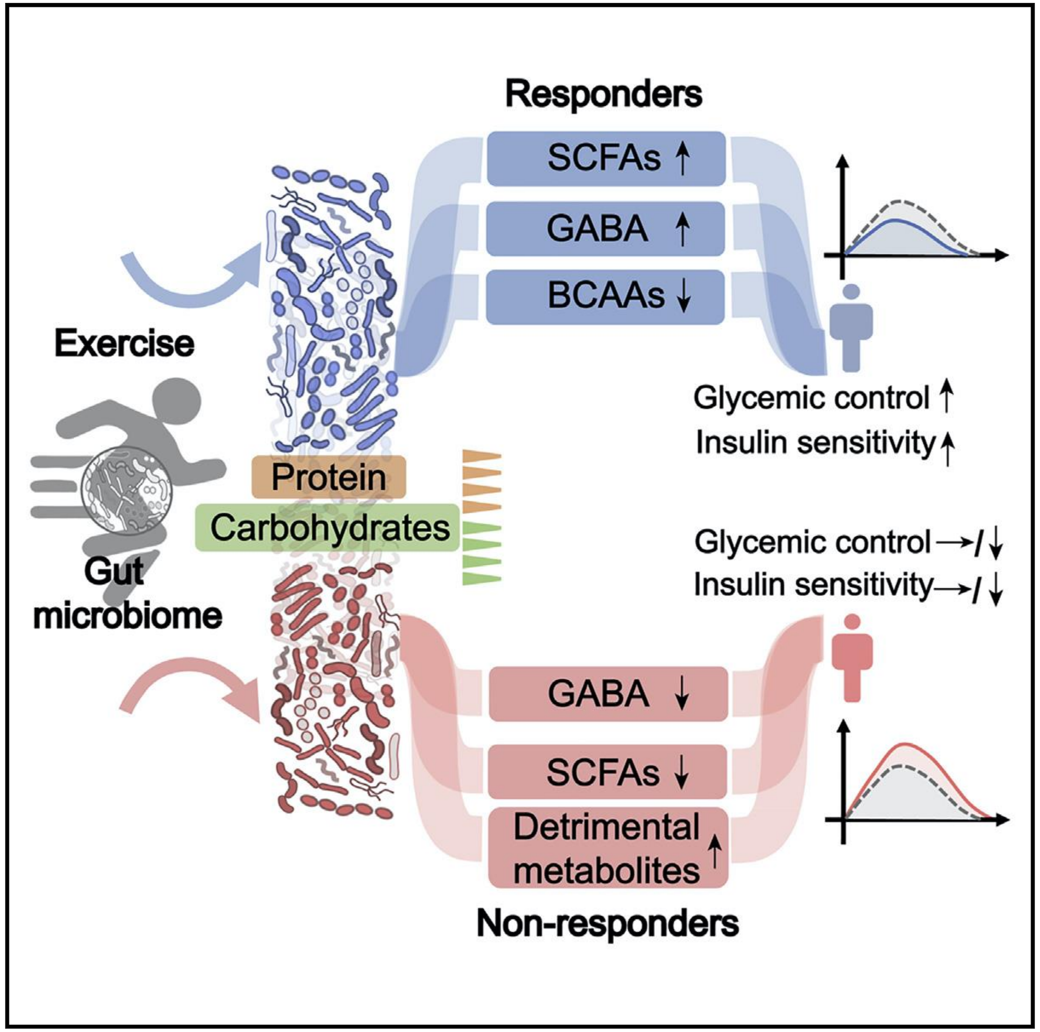
SPORTOMICS:
METABOLIC HEALTH & FUNCTIONAL TESTING

- EVIDENCE of “Vicious Cori Cycle” and impaired metabolic health
  - ELEVATED Lactic Acid
    (especially relative to Pyruvic Acid)
  - LOW Citric acid
    - Often seen in severe obesity
  - LOWER TCA intermediates [1]
    - Labeled by some as “hypometabolic state” or ”mitochondria retraction”
  - +/- HIGHER Malic Acid/Succinic Acid

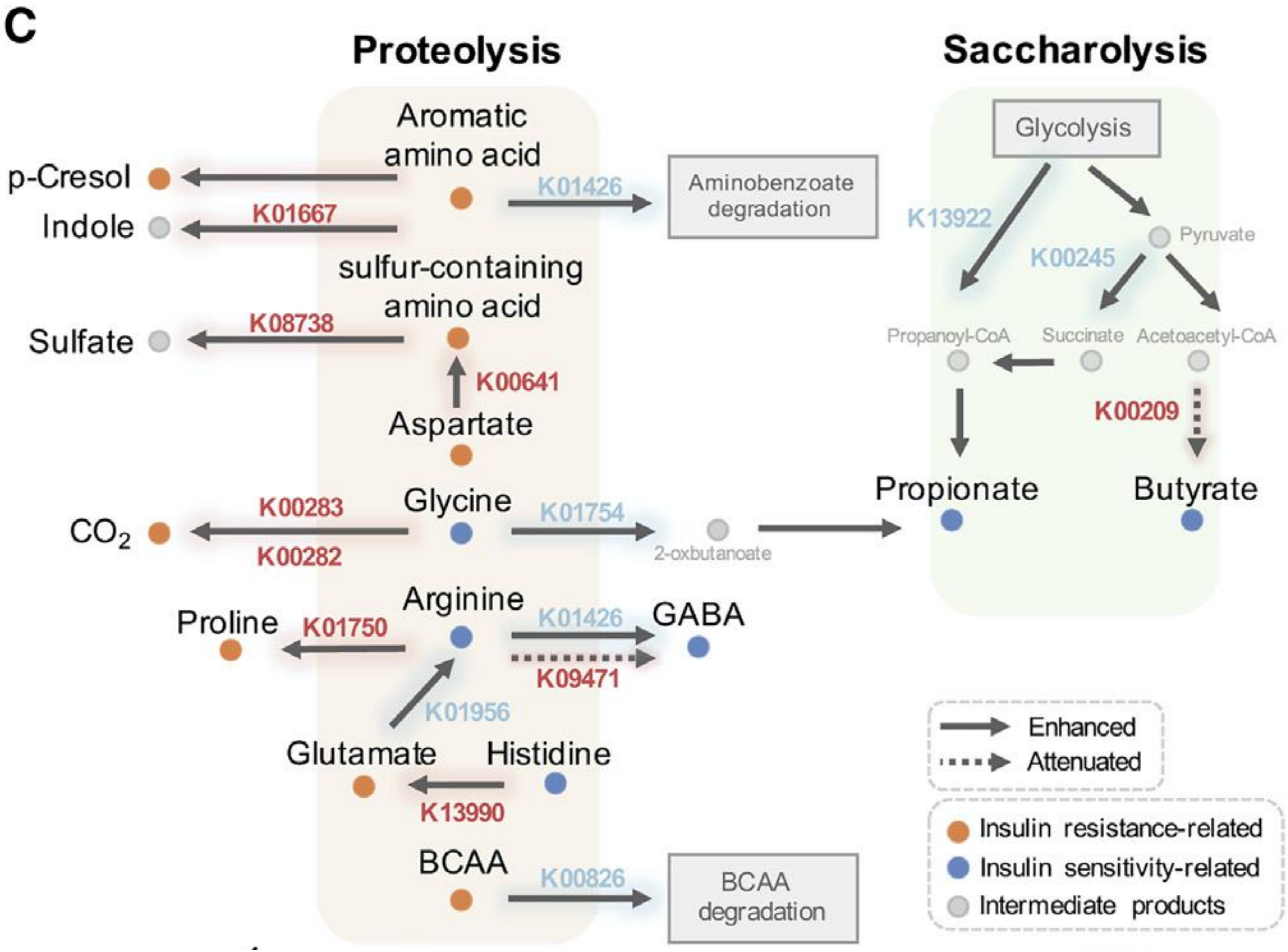
1. Zou K, et al. *Int J Obes*. 2018;43(4):895-905.

SPORTOMICS: METABOLIC HEALTH

- EXERCISE & DIABETES PREVENTION
  - Overweight, prediabetic treatment-naïve males
    - Identified responders to exercise intervention (improved glucose metabolism & insulin resistance)
      - Increased capacity for increased SCFA synthesis
      - Increased capacity for BCAA catabolism
    - FMT of responders improved mice response to exercise
    - Through machine learning then predicted glycemic response to exercise in additional 30 subjects



Liu Y, et al. *Cell Metabolism*. 2020:31(1):77-91.



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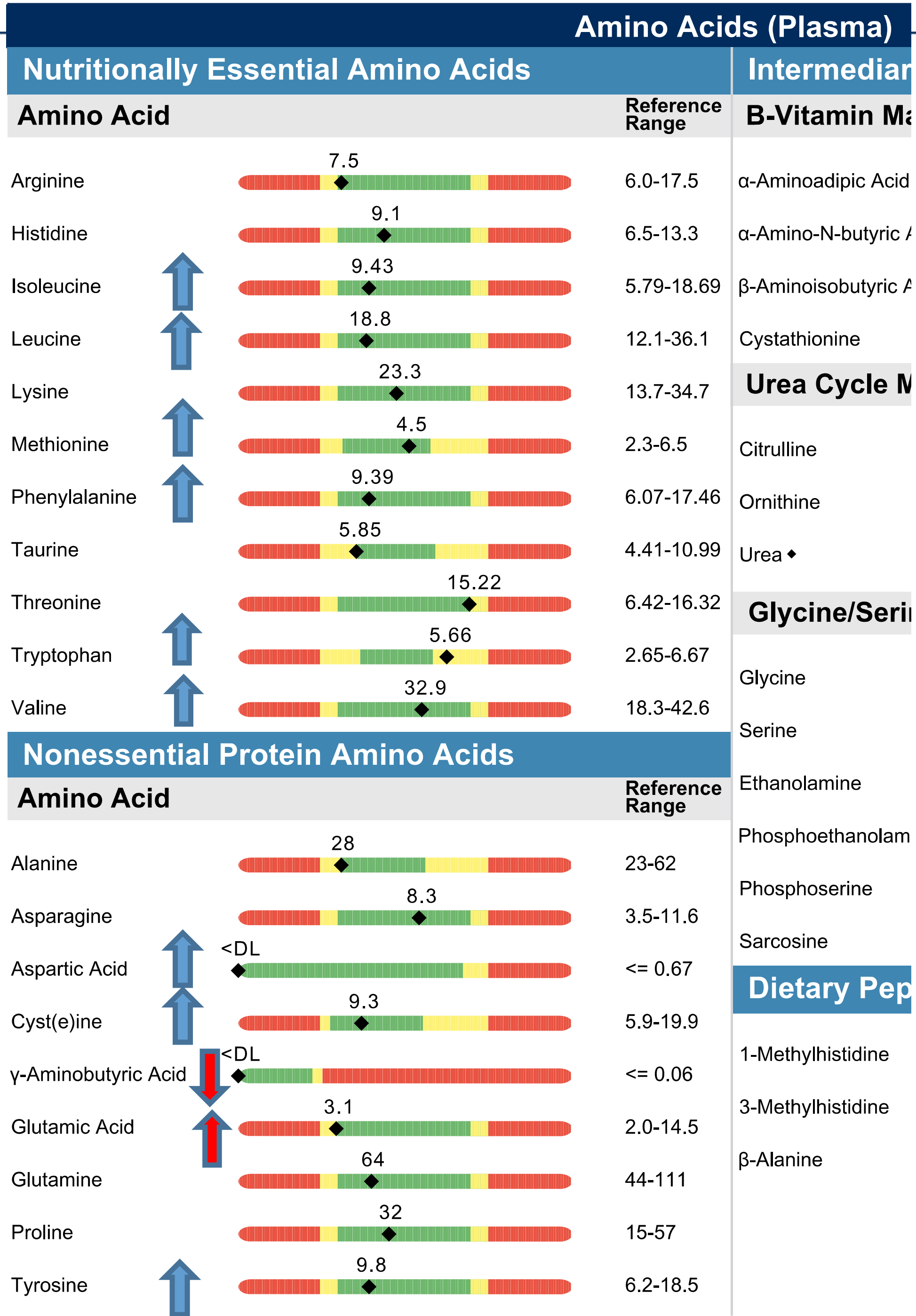
SPORTOMICS: METABOLIC HEALTH & FUNCTIONAL TESTING

- ASSOCIATED w/INSULIN RESISTANCE
  - LOW butyrate (GI Effects)
  - ELEVATED aromatic amino acids (tryptophan, tyrosine, phenylalanine)
  - ELEVATED sulfur-containing amino acids (cysteine, methionine) & aspartate
  - ELEVATED branched chain amino acids (isoleucine, leucine, valine)
  - ELEVATED glutamate with LOWER GABA



Amino Acids (Plasma)

Nutritionally Essential Amino Acids

Amino Acid	Result	Reference Range
Arginine	7.5	6.0-17.5
Histidine	9.1	6.5-13.3
Isoleucine	9.43	5.79-18.69
Leucine	18.8	12.1-36.1
Lysine	23.3	13.7-34.7
Methionine	4.5	2.3-6.5
Phenylalanine	9.39	6.07-17.46
Taurine	5.85	4.41-10.99
Threonine	15.22	6.42-16.32
Tryptophan	5.66	2.65-6.67
Valine	32.9	18.3-42.6

Nonessential Protein Amino Acids

Amino Acid	Result	Reference Range
Alanine	28	23-62
Asparagine	8.3	3.5-11.6
Aspartic Acid	<DL	<= 0.67
Cyst(e)ine	9.3	5.9-19.9
γ-Aminobutyric Acid	<DL	<= 0.06
Glutamic Acid	3.1	2.0-14.5
Glutamine	64	44-111
Proline	32	15-57
Tyrosine	9.8	6.2-18.5

Intermediar

B-Vitamin Ma

α-Aminoadipic Acid

α-Amino-N-butyric A

β-Aminoisobutyric A

Cystathionine

Urea Cycle M

Citrulline

Ornithine

Urea ◆

Glycine/Seri

Glycine

Serine

Ethanolamine

Phosphoethanolam

Phosphoserine

Sarcosine

Dietary Pep

1-Methylhistidine

3-Methylhistidine

β-Alanine

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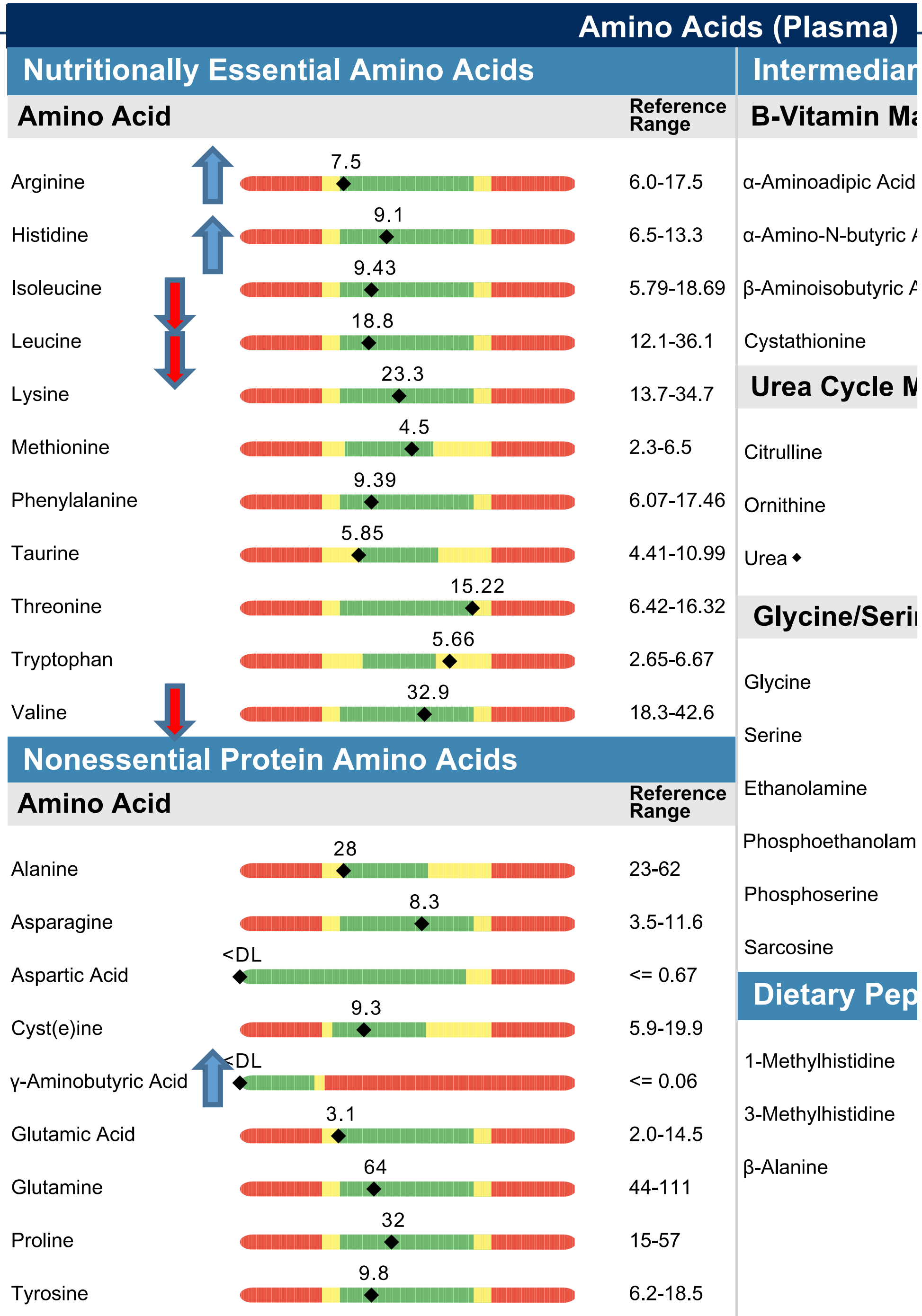
SPORTOMICS: METABOLIC HEALTH & FUNCTIONAL TESTING

- ASSOCIATED w/INSULIN SENSITIVITY
  - ELEVATED SCFAs (GI Effects)
  - ELEVATED histidine, arginine, GABA
  - LOWER branched chain amino acids (isoleucine, leucine, valine)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Tyrosine	9.8	6.2-18.5

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SPORTOMICS:
METABOLIC HEALTH & FUNCTIONAL TESTING

- FUNCTIONAL MEDICINE TESTING INFORMED RECOMMENDATIONS for metabolic health & insulin resistance
  - IF EXERCISING & METABOLIC DISEASE
    - POTENTIAL NON-RESPONDER WITH …
      - Elevated BCAAs and AAAs; Elevated glutamate and Decreased GABA; Elevated cysteine & methionine
    - PROBABLE RESPONDER WITH …
      - Increased Firmicutes & SCFAs; Increased lactate utilizers // (absence of non-responder characteristics)
  - IF NOT EXERCISING & AT RISK FOR METABOLIC DISEASE
    - POTENTIAL RESPONDER WITH …
      - Elevated Bacteroides // Elevated GABA
  - IF NON-RESPONDER OR POTENTIAL NON-RESPONDER
    - Work to elevate SCFAs (fiber, resistant starches, fermented foods/probiotics, butyrate)
    - Decrease exercise volume/intensity

Liu Y, et al. *Cell Metabolism*. 2020:31(1):77-91.

THANK YOU FOR YOUR TIME AND ATTENTION

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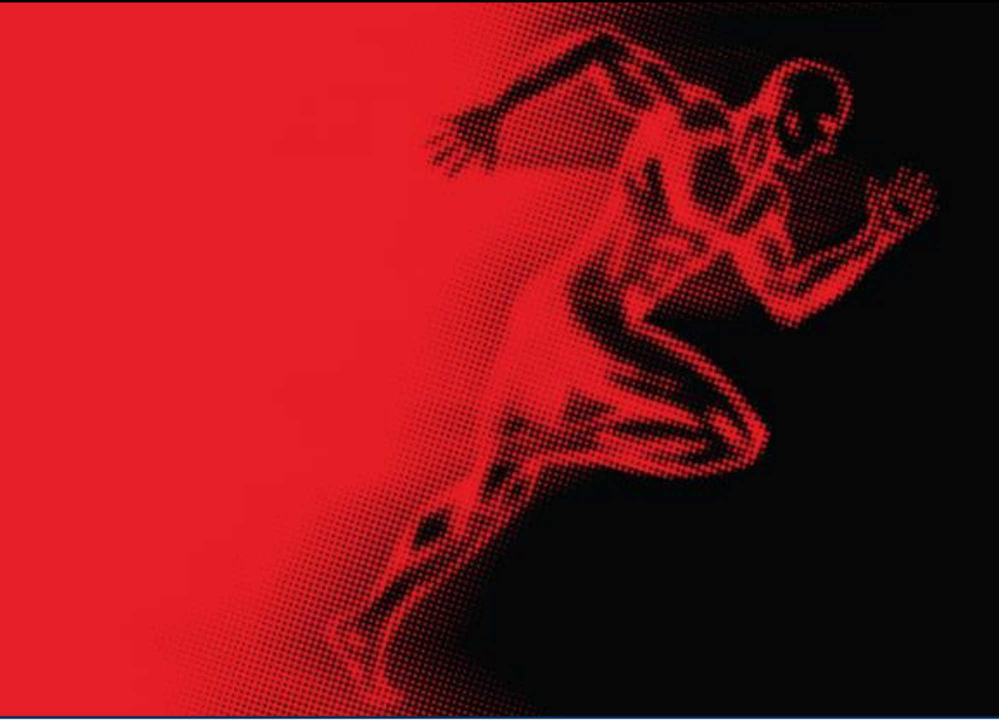

Sportomics, Metabolic Health, and Utilization of Functional Medicine Testing

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