MICROBIOME MEDICS

Diabetes, Cancer and the Gut Microbiome

Dr Sheena Fraser

Objectives

- 1. Understand gut microbiome function and link with disease
- 2. Metabolic syndrome and inflammation
- 3. Cancer and metabolic syndrome
- 4. Solutions

MICROBIOME MEDICS

What is the gut microbiome?

highest microbial density (colon);most researched

mostly bacteria

>100 trillion microorganisms > 1000 different species

unique ‘fingerprint’

ACTIVE PARTICIPANTS NOT PASSIVE PASSENGERS

new ‘organ’

What makes a healthy gut microbiome?

- composition
- diversity
- abundance
- richness
- resilience
- healthy GM not defined

MICROBIOME MEDICS

What makes an unhealthy gut microbiome?

- **Composition**:↓ GM diversity ↓ beneficial microbes ↑potential pathogens
- **Function**: ↓beneficial anti-tumour metabolites, ↑harmful pro-tumour metabolites, high pH

MICROBIOME MEDICS

Function of gut microbiome

MICROBIOME MEDICS

PROTECTION FROM PATHOGENS

METABOLITE FACTORIES

IMMUNE DEVELOPMENT & FUNCTION

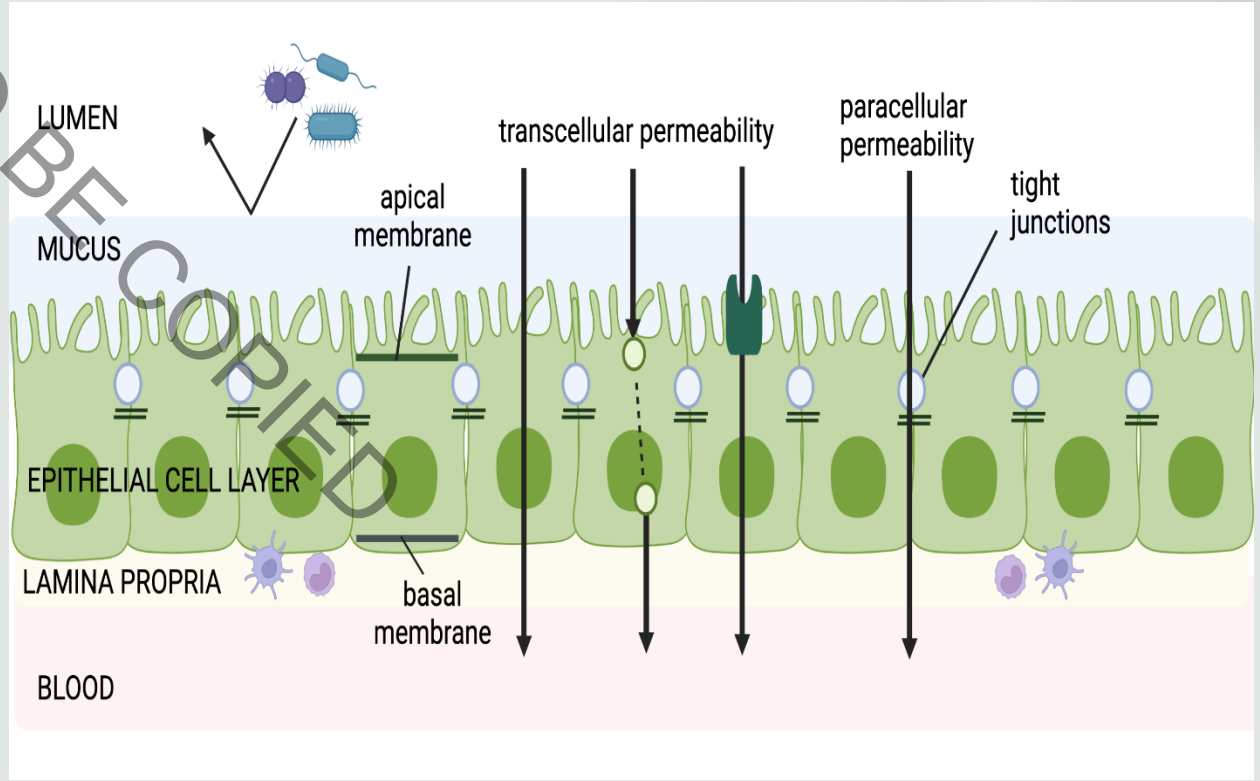
DRUG METABOLISM

MICROBIOME MEDICS

GM protective Mechanisms include:

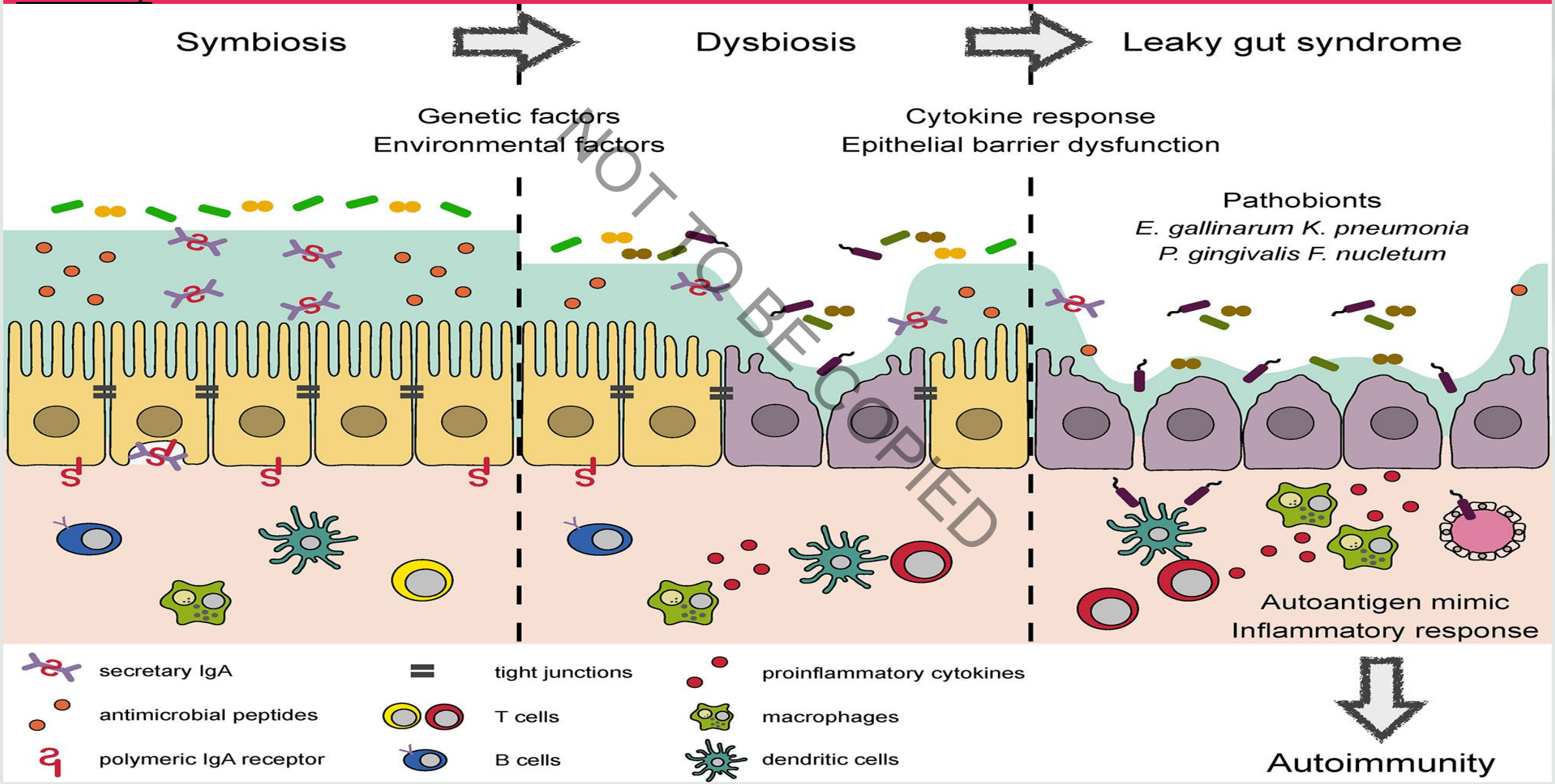
- competition & weapons (AMPs)
- barrier (mucus layer, tight junctions)
- short chain fatty acids (SCFAs) e.g., butyrate
- Butyrate=colonocyte energy source

Increased intestinal permeability AKA "leaky gut"



Camilleri M. Human Intestinal Barrier: Effects of Stressors, Diet, Prebiotics, and Probiotics. Clin Transl Gastroenterol. 2021 Jan;12(1):e00308.

Increased Intestinal Permeability (aka 'Leaky Gut')



Lipopolysaccharide (LPS)

- Derived from pathogenic gram negative bacteria
- Product of bacterial wall
- creates inflammation
- Leaks into blood stream vial “leaky gut” creating inflammation elsewhere in body
- High levels found in patients with obesity, metabolic syndrome and T2DM

MICROBIOME MEDICS

What are Short Chain Fatty Acids ?

Fibre

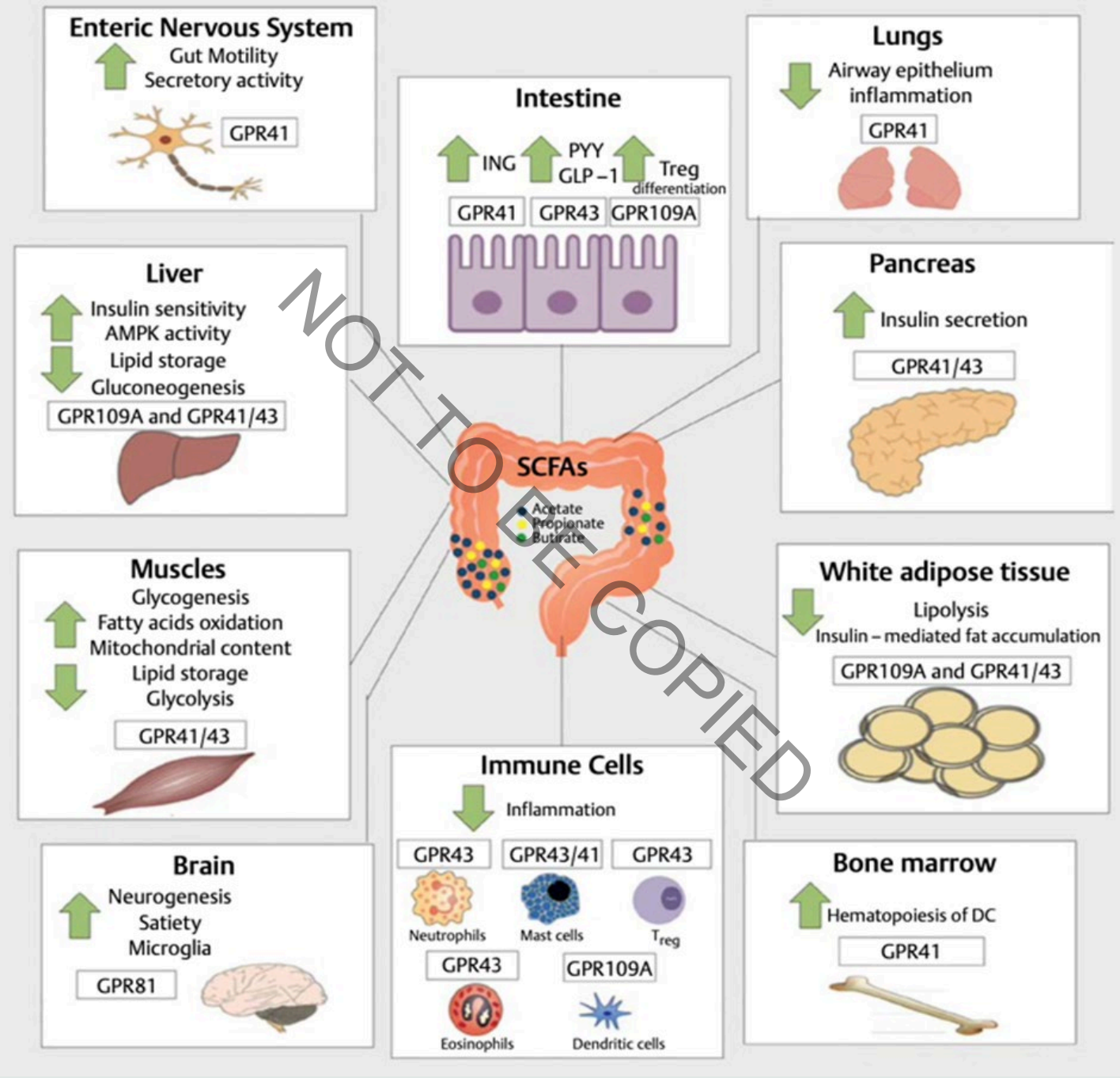
Fermentation

- SCFAs are microbial metabolites (butyrate, acetate, propionate)

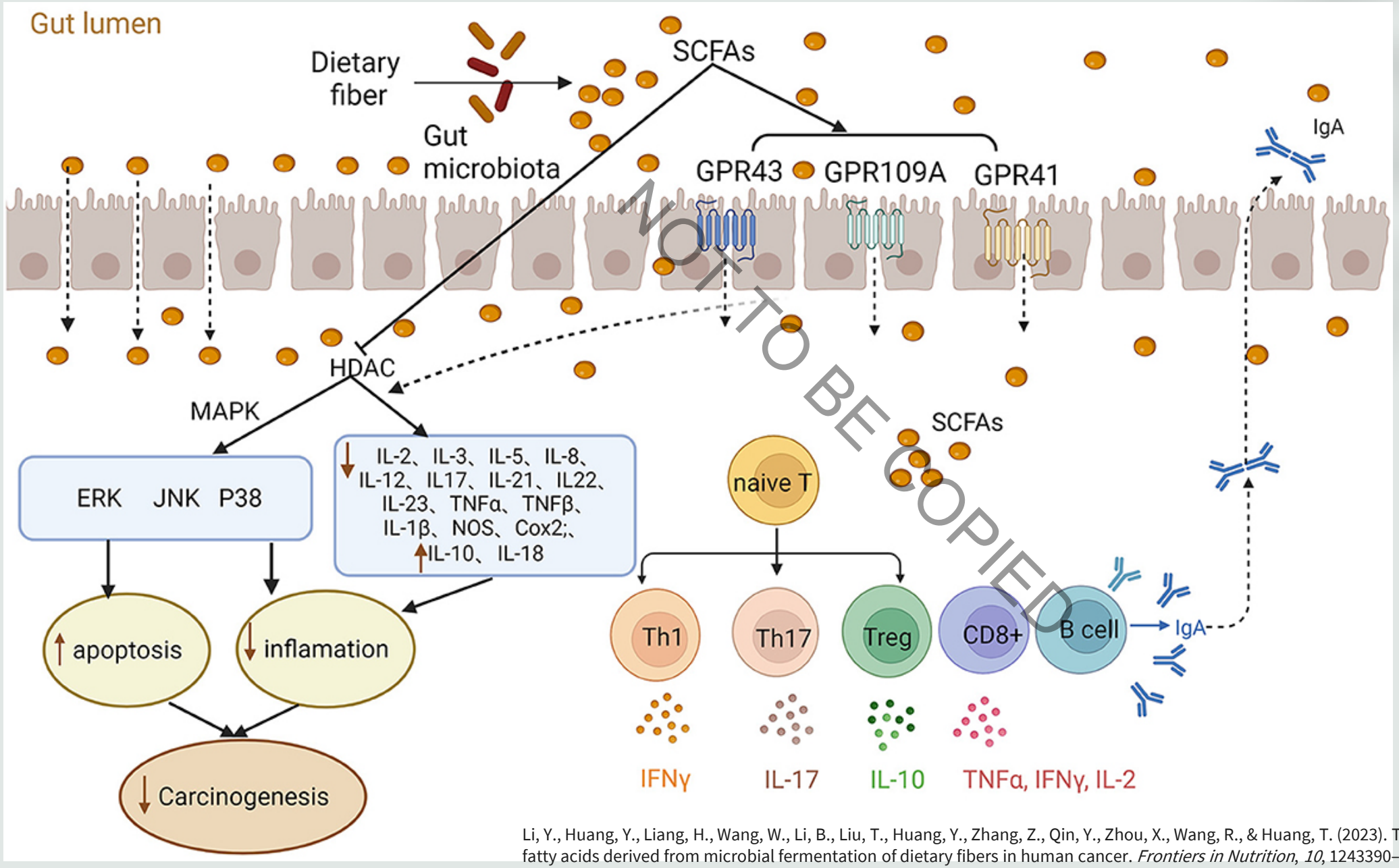
SCFAs bind receptors

- **SCFAs bind to specific SCFA receptors**

MICROBIOME MEDICS

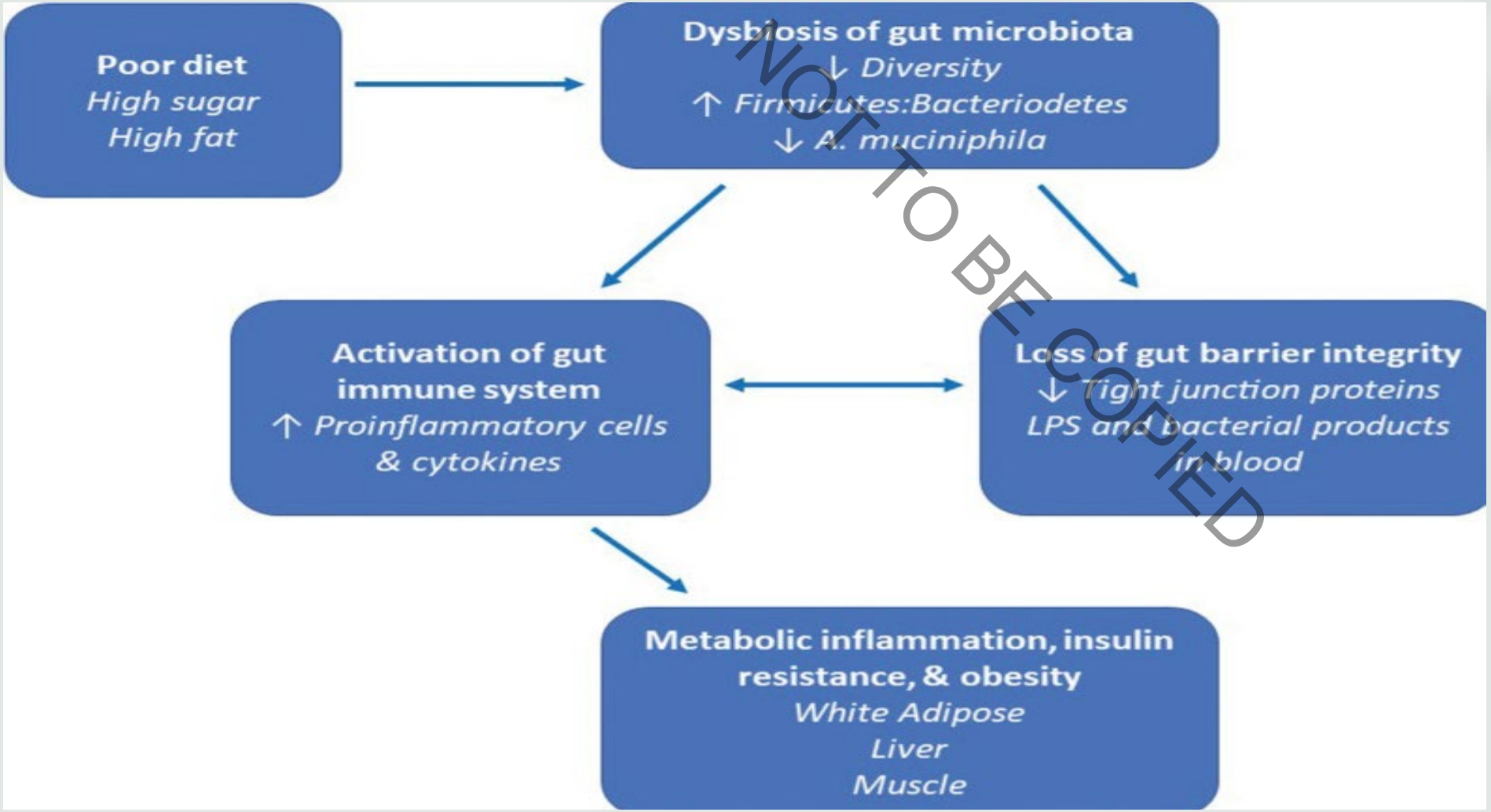


SCFA's

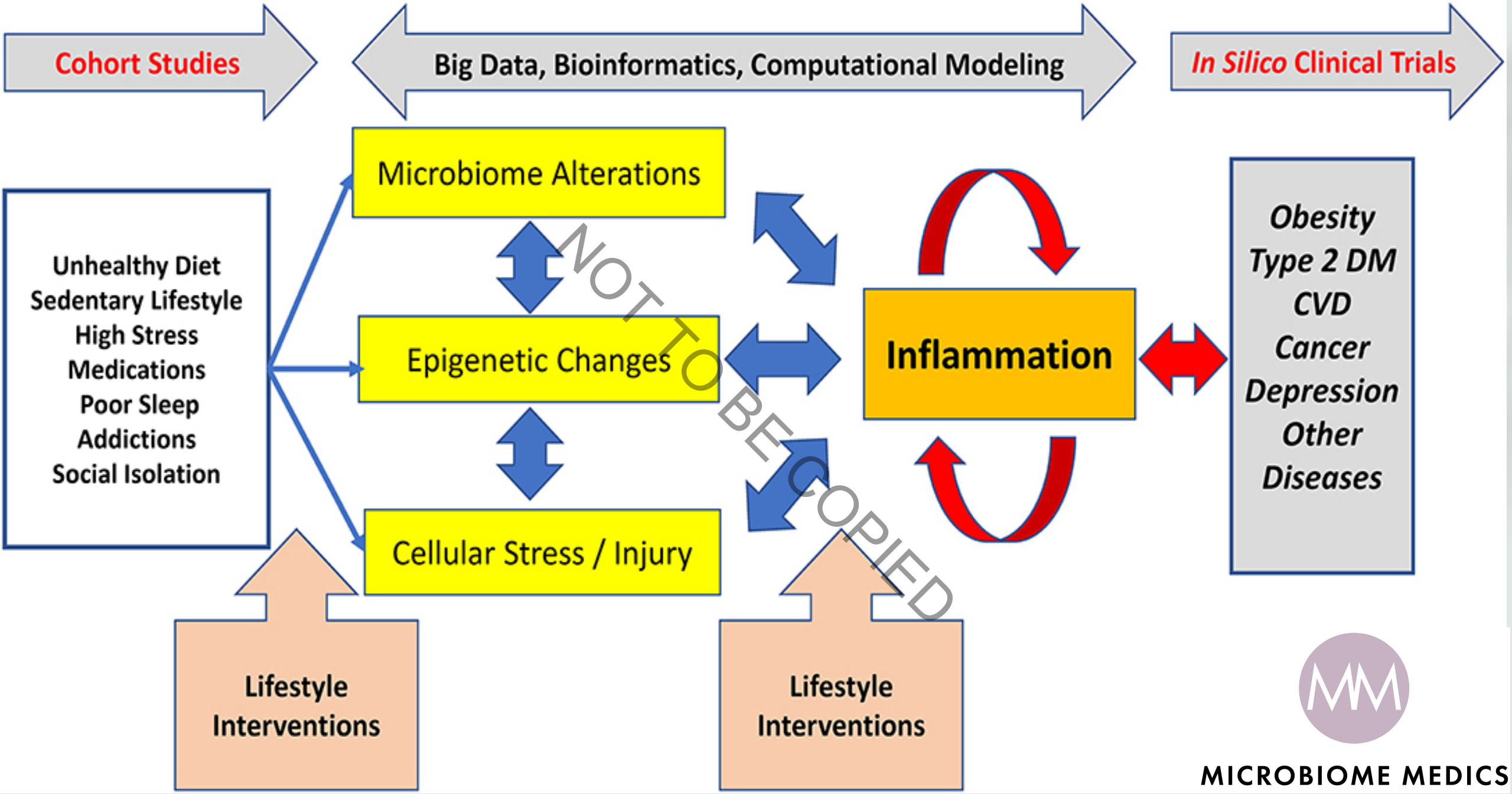


Li, Y., Huang, Y., Liang, H., Wang, W., Li, B., Liu, T., Huang, Y., Zhang, Z., Qin, Y., Zhou, X., Wang, R., & Huang, T. (2023). The roles and applications of short-chain fatty acids derived from microbial fermentation of dietary fibers in human cancer. *Frontiers in Nutrition*, *10*, 1243390–1243390

Metabolic inflammation



MICROBIOME MEDICS



https://www.frontiersin.org/articles/10.3389/fmed.2020.585744/full

The ten hallmarks of cancer

- Sustained proliferation
- Insensitivity to antigrowth signals
- Evasion of apoptosis
- Limitless replicative potential
- Sustained angiogenesis
- Ability to metastasize
- Reprogramming of energy metabolism
- Avoidance of immune destruction
- Tumour-promoting inflammation
- Genome instability and mutation

Cancer loves sugar

- Cancer cells ingest sugar at almost 50 x faster than healthy cells
- 80% of human cancers driven by effects of glucose and insulin
- Aggressiveness of cancers determined by glucose consumption
- All sugar consumption can reduce immune cell function for up to 5hours
- Average UK adult consumes 700g sugar per week (almost 4 x recommendation)
- 20% cancer patients are diabetic

The warberg effect

- The Warburg effect is a key feature of cancer cell metabolism and rapid proliferation. It involves the conversion of glucose to lactate, even when oxygen is present, and the inhibition of pyruvate from entering mitochondria. This process produces ATP efficiently and supports cell proliferation
- ATP production through damaged cancer cell mitochondria can be >100 times faster than in healthy cells.

Solutions

- Starve cancer cells
- Enhance the gut microbiome
- individual gut microbes matter

MICROBIOME MEDICS

How do we starve a cancer cell?

Cut out sugar

Ketogenic diets

challenges

- Difficulty in adherence to ketogenic diet
- Interpretation of diet
- Cachexia in cancer
- Long term data lacking
- Different responses with different cancers

Enhancing the gut microbiome

- >30 different varieties of plants per week
- Fibre fibre fibre…..
- Fermented food daily
- Cut out UPF
- Organic vs non organic
- Nature is best
- Sleep
- Exercise
- Stress management

MICROBIOME MEDICS

What is the best diet for gut health?

WFPB

Prebiotic: a substrate that is selectively utilized by host microorganisms conferring a health benefit.

(e.g., chicory, Jerusalem artichoke, garlic, onions, leeks)

Polyphenols : compounds found in plant foods >8000 identified to date

(e.g., blueberries, strawberries , blackberries, coffee , green & black tea)

Tomova A, Bukovsky I, Rembert E, Yonas W, Alwarith J, Barnard ND, et al. The Effects of Vegetarian and Vegan Diets on Gut Microbiota. Front Nutr. 2019;6:47.

Individual microbes matter

- Akkermansia and melanoma
- Faecalibacterium Prauznitsi and breast cancer
- Lactobacillus Reuteri and colon cancer
- Cancer microbiomes
- Immunotherapy, chemotherapy and gut microbes

Summary

- Cancer and Diabetes are both METABOLIC DISEASES
- Microbiome dysbiosis is central to both conditions
- Modern diet and lifestyle integral to both conditions
- Low carb, ketogenic and microbiome enhancing diets can help
- Prevention is best

References

- Mechanisms linking the gut microbiome and glucose metabolism. Krisma M. Utzschneider et al; J. Clin Endocrin and Metabolism 2016; Vol 101 (4); p1445-1454
- Camilleri M. Human Intestinal Barrier: Effects of Stressors, Diet, Prebiotics, and Probiotics. Clin Transl Gastroenterol. 2021 Jan;12(1):e00308
- Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. BMJ. 2018 Jun;361:k2179.
- Diabetes and the Gut Microbiota; Yue Xi & Peng-Fei Xu; World J. Diabetes; 2021 Oct 15; 12(10): 1693-1703
- Association of diabetes and microbiome- an update. Suhila S. Al-Jamaal; Saudi J. of Biolojical Sci; 28; 2021; 4446-4465
- Baquero F, Nombela C. The microbiome as a human organ. Vol. 18 Suppl 4, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. England; 2012. p. 2–4.
- Berg G, Rybakova D, Fischer D, Cernava T, Vergès M-CC, Charles T, et al. Microbiome definition re-visited: old concepts and new challenges. Microbiome [Internet]. 2020;8(1):103.
- Probiotics in Cancer. Lu Ke et al; Frontiers in Oncology 2021; 11: 638148
- Gut Microbiota and cancer: from pathogenesis to therapy, Silvia Vivarelli et al; Cancers 2019; Vol 11 (1); p 38
- Ou, Carbonero, F., Zoetendal, E. G., DeLany, J. P., Wang, M., Newton, K., Gaskins, H. R., & O'Keefe, S. J. (2013). Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. The American Journal of Clinical Nutrition, 98(1), 111–120. https://doi.org/10.3945/ajcn.112.056689
- Cancer and the microbiome– influences of the commensal microbiota on cancer, immune response and immunotherapy. Vyara Matson et al; Gastroenterology 2021; 160: 600-613
- Pancreatic cancer and gut microbiome related aspects: a comprehensive review and dietary recommendations. Bartosz Kamil Sobocki et al; Nutrients 2021;13(12), 4425
- The skin and gut microbiome and its role in dermatologic conditions. Microorganisms 2019 Nov; 7(11):550
- An unexpected link: the role of mammary and gut microbiota on breast cancer development and management (review). Daniella Toumazi; Oncology reports 2021; 45;5
- Chen D, Wu J, Jin D, Wang B, Cao H. Fecal microbiota transplantation in cancer management: Current status and perspectives. Int J cancer. 2019 Oct;145(8):2021–31.
- de Martel C, Ferlay J, Franceschi S, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol 2017; 13: 607–615
- The metabolic approach to cancer, N Winters and J Higgins Kelley; 2017

BSLM Learning Academy

The Fundamentals of Gut Microbiome Science

Learn the fundamentals of Gut Microbiome Science in an easy-to-understand format, which includes practical information on how to use this knowledge in clinical practice.

BRINGING YOU A WORLD-CLASS LEARNING PACKAGE

EVIDENCE BASED

FLEXIBLE AND SELF-PACED

PEER-REVIEWED

MICROBIOME MEDICS PODCAST

Listen on Spotify, Apple & Google Podcasts

SCAN TO FIND OUT MORE

www.courses.bslm.org.uk