

Cancer and Diabetes

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Objectives

Relationship
between Cancer
and Diabetes

Underlying
Mechansims

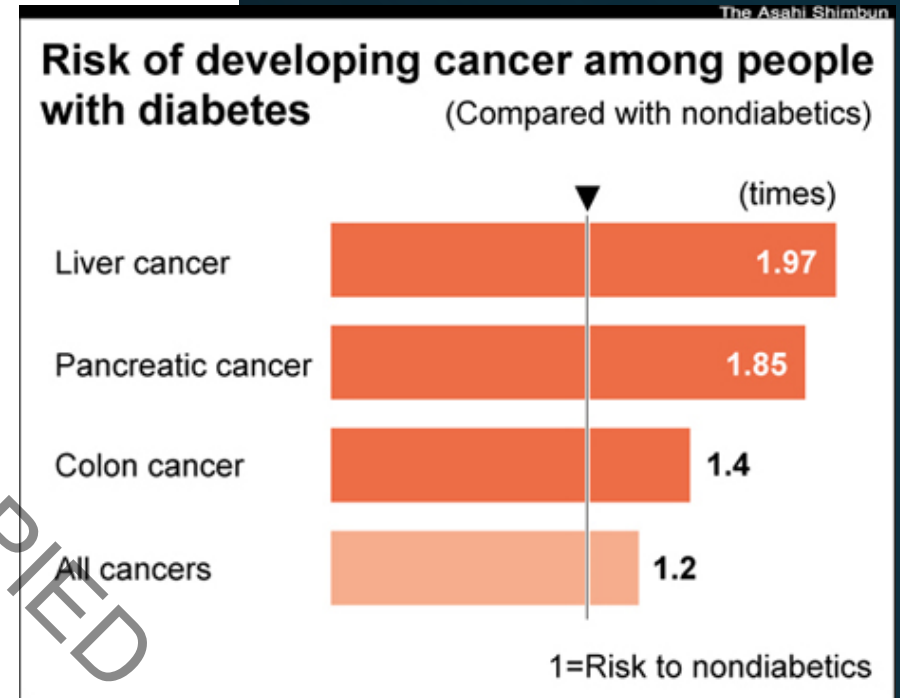
Impact of Cancer
Treatments on
Diabetes

Diabetes and Cancer: A Closer Look

Bidirectional relationship

1 in 5 (20%) patients with cancer have diabetes

Inverse relationship between Diabetes and Prostate cancer



Hyperglycaemia and Cancer



ASSOCIATED WITH WORSE SURVIVAL AND HIGHER RISK OF RECURRENCE



SOME STUDIES SUGGEST IT MAY ATTENUATE THE EFFICACY OF CHEMOTHERAPY



HIGHER RISK OF INFECTION, DELAYED WOUND HEALING AND HOSPITALISATION



OPTIMAL GLYCAEMIC CONTROL CAN IMPROVE CANCER OUTCOMES

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Pancreatic Ca – Cause AND Consequence?

Complex Relationship – 50-80% of patients have T2DM/impaired glucose tolerance at time of diagnosis

Compelling evidence of bidirectional relationship

- Risk of Cancer negatively associated with T2DM duration.
- Worsening glycaemic control often observed in months before diagnosis

Diabetes could be early clue for detection of pancreatic cancer. Consider if:

- New onset diabetes without metabolic syndrome / obesity
- Increasing HbA1c with weight loss
- Unexplained worsening of longstanding pre-existing T2DM

Underlying Mechanisms

Shared Risk Factors

Metabolic dysfunction

- Hyperglycaemia
- Hyperinsulinaemia

Inflammation and
oxidative stress

Cancer Treatments

Cancer Treatments: Chemotherapy

Hyperglycaemia occurs in 10-30% of patients

- Direct effects: Damage to Pancreas, Increased cortisol
- Indirect effects: Weight gain, fatigue, physical inactivity

Can also cause Hypoglycaemia

- Vomiting, diarrhea and anorexia

In practice

- Patients on insulin can have first cycle in hospital
- Patients need to know how to check their blood sugars and ketones
- Seek advice if BGs >10 and unwell or <4 on more than one occasion

Cancer Treatments: Glucocorticoids

Uses: Cancer therapy, nausea, pain, appetite, reduce inflammation

Mechanism: Increased gluconeogenesis and decreased insulin sensitivity

Glucocorticoid induced Hyperglycaemia rates as high as 30-50%

At risk?

- already at risk (FHx, obesity, PCOS, ethnic minorities)
- impaired glucose tolerance
- previous hyperglycaemia on steroid therapy
- On concurrent chemotherapy known to cause hyperglycaemia

Glucocorticoids: Practical Advice

Check baseline HbA1c and plasma glucose when starting steroid therapy

Glycaemic target level is 6-10 mmol/L, allowing a range of 6-12 mmol/L

Educate patients in symptoms of hyperglycaemia

Consider commencing gliclazide 40 mg if raised blood glucose ≥ 12 mmol/L (on 2 occasions) in the absence of contraindications

If blood glucose is ≥ 20 mmol/L or suggestive symptoms, rule out DKA/HHS

Cancer Treatments: Radiotherapy

Rise in blood sugars can occur during and after treatment

Intra-abdominal RTx can be directly toxic to pancreas

Side effects

- Diarrhoea & Vomiting
- Oesophagitis / Difficulty Swallowing

Remember Sick Day Rules

End of Life Care: Principles



Ensure that effective symptom control is provided during the dying stage



Tailor glucose-lowering therapy and minimise diabetes-related adverse treatment effects



Avoid metabolic de-compensation and diabetes related emergencies:



Avoid foot complications and pressure sores in frail, bed-bound individuals with diabetes



Provide an appropriate level of intervention according to stage of illness, symptom profile, and respect for dignity

End of Life: In Practice

- Glycaemic Target 6-15 mmol/L
- Deintensify diabetes medications
- Rationalise other medications – statins, ACEi, Aspirin

Summary

- 1 in 5 cancer patients have diabetes
- Hyperglycaemia can indicate pancreatic cancer
- Chemotherapy can cause hyperglycaemia due to steroids
- In steroid induced hyperglycaemia commence gliclazide 40 mg
- Chemotherapy can cause hypoglycaemia due to nausea anorexia D&V
- Radiotherapy can cause hyperglycaemia
- EOLcare stop non essential medication
- EOLcare simplify Diabetes medication eg O.D. Insulin



MICROBIOME MEDICS

Diabetes, Cancer and the Gut Microbiome

Dr Sheena Fraser

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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



What makes an unhealthy gut microbiome?

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



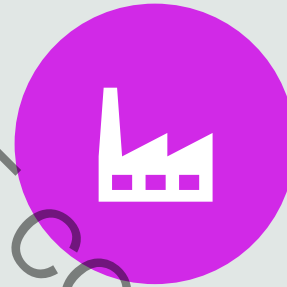


MICROBIOME MEDICS

Function of gut microbiome



PROTECTION FROM
PATHOGENS



METABOLITE
FACTORIES



IMMUNE
DEVELOPMENT &
FUNCTION



DRUG METABOLISM

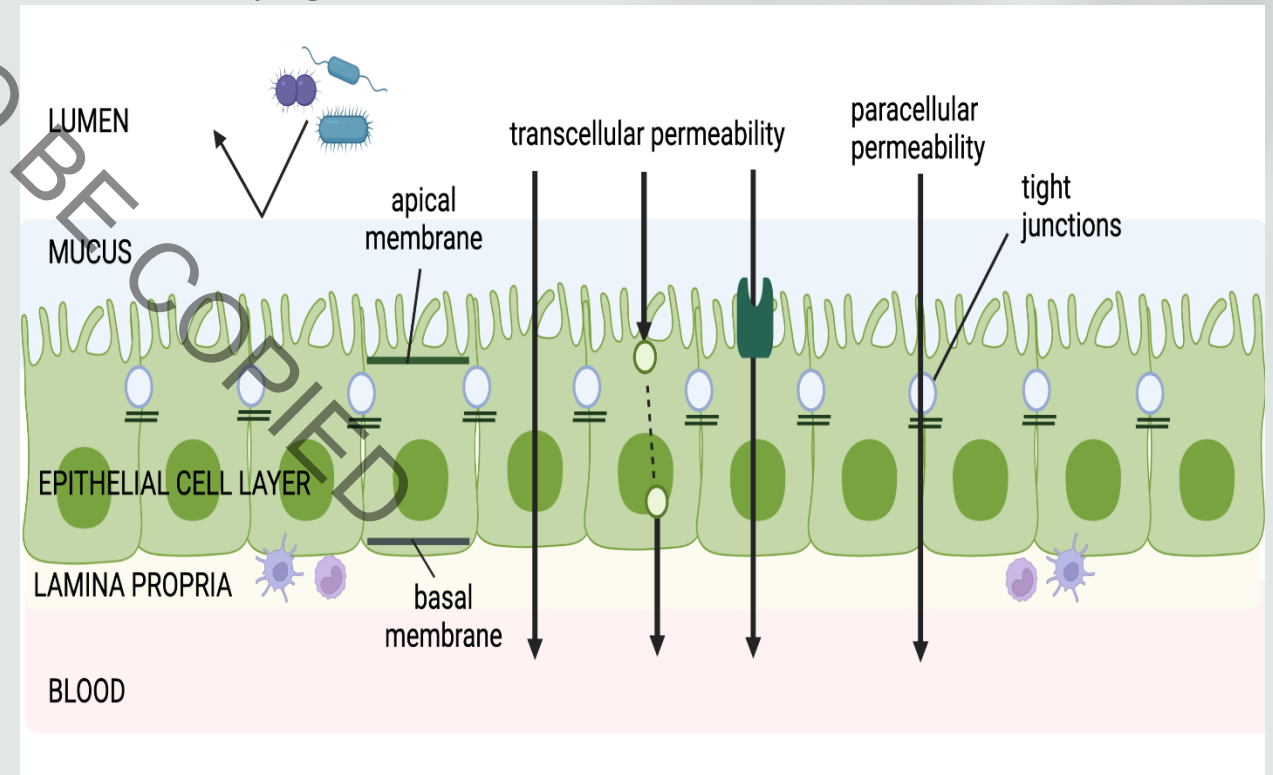
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GM protective Mechanisms include:

- 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”

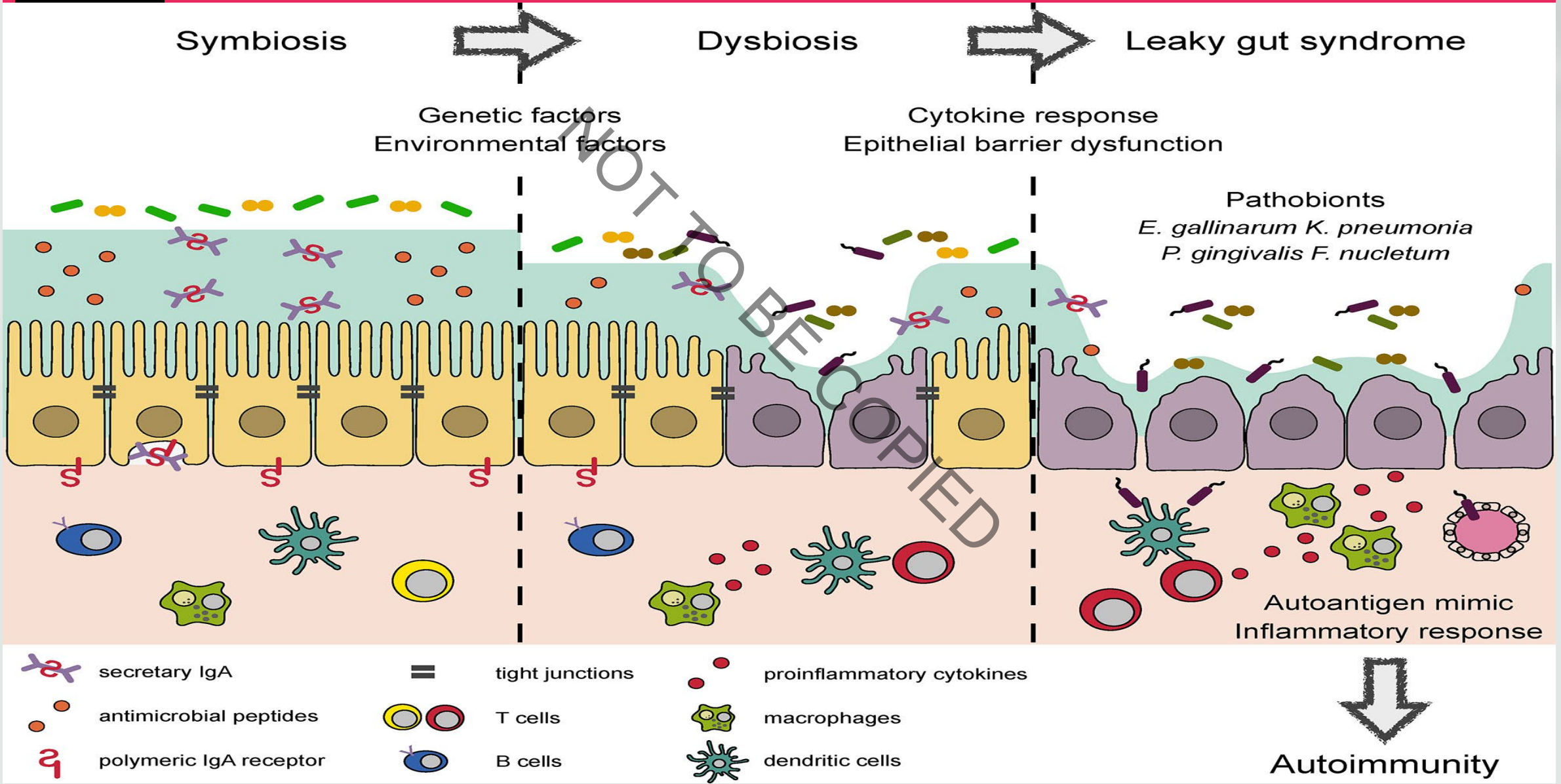


Camilleri M. Human Intestinal Barrier: Effects of Stressors, Diet, Prebiotics, and Probiotics. Clin Transl Gastroenterol. 2021 Jan;12(1):e00308.



Increased Intestinal Permeability (aka 'Leaky Gut')

Gut')



Lipopolysaccharide (LPS)

Derived from pathogenic gram negative bacteria

Product of bacterial wall

creates inflammation

Leaks into blood stream via “leaky gut” creating inflammation elsewhere in body

High levels found in patients with obesity, metabolic syndrome and T2DM



What are Short Chain Fatty Acids ?



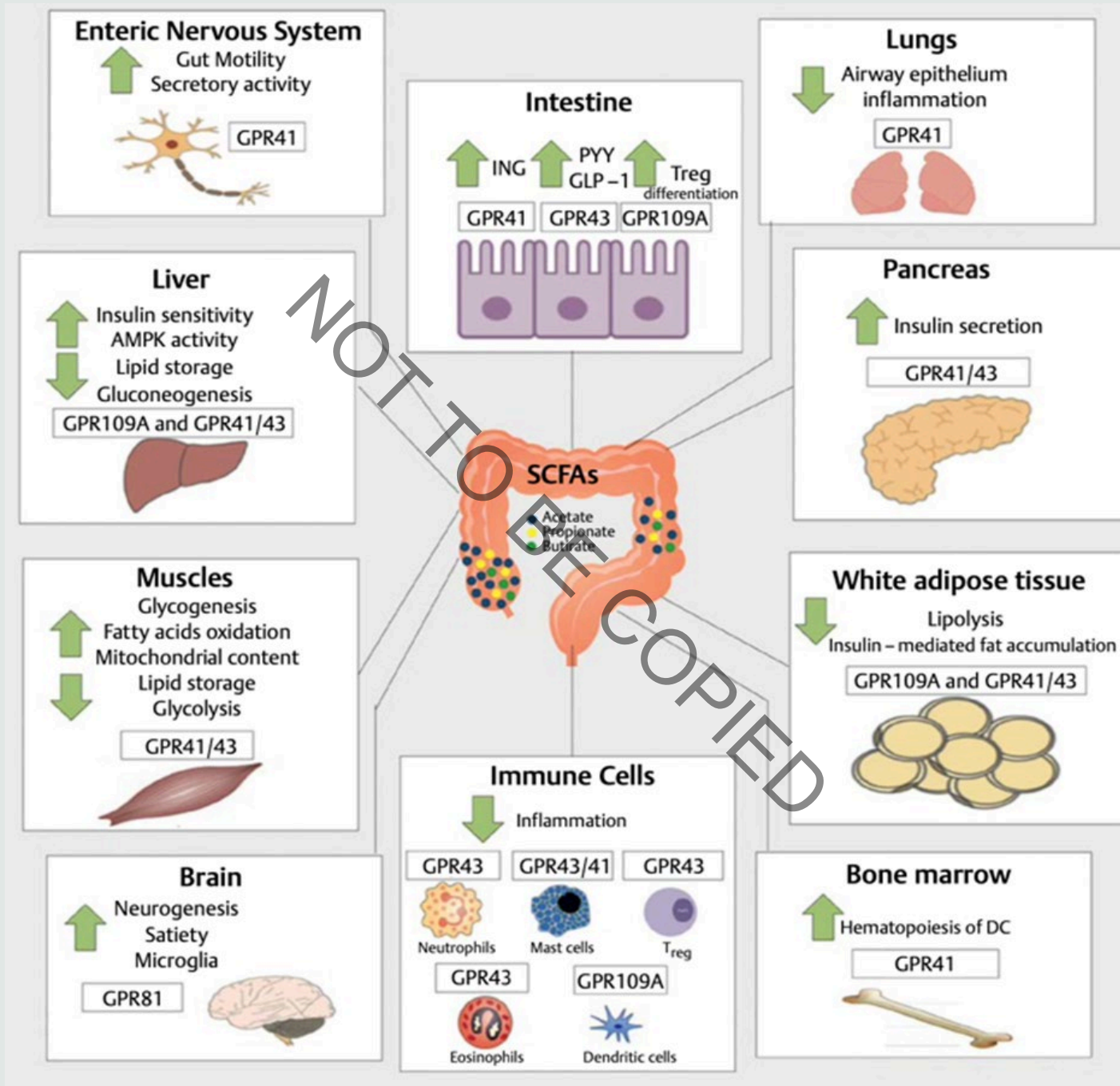
Fibre

Fermentation

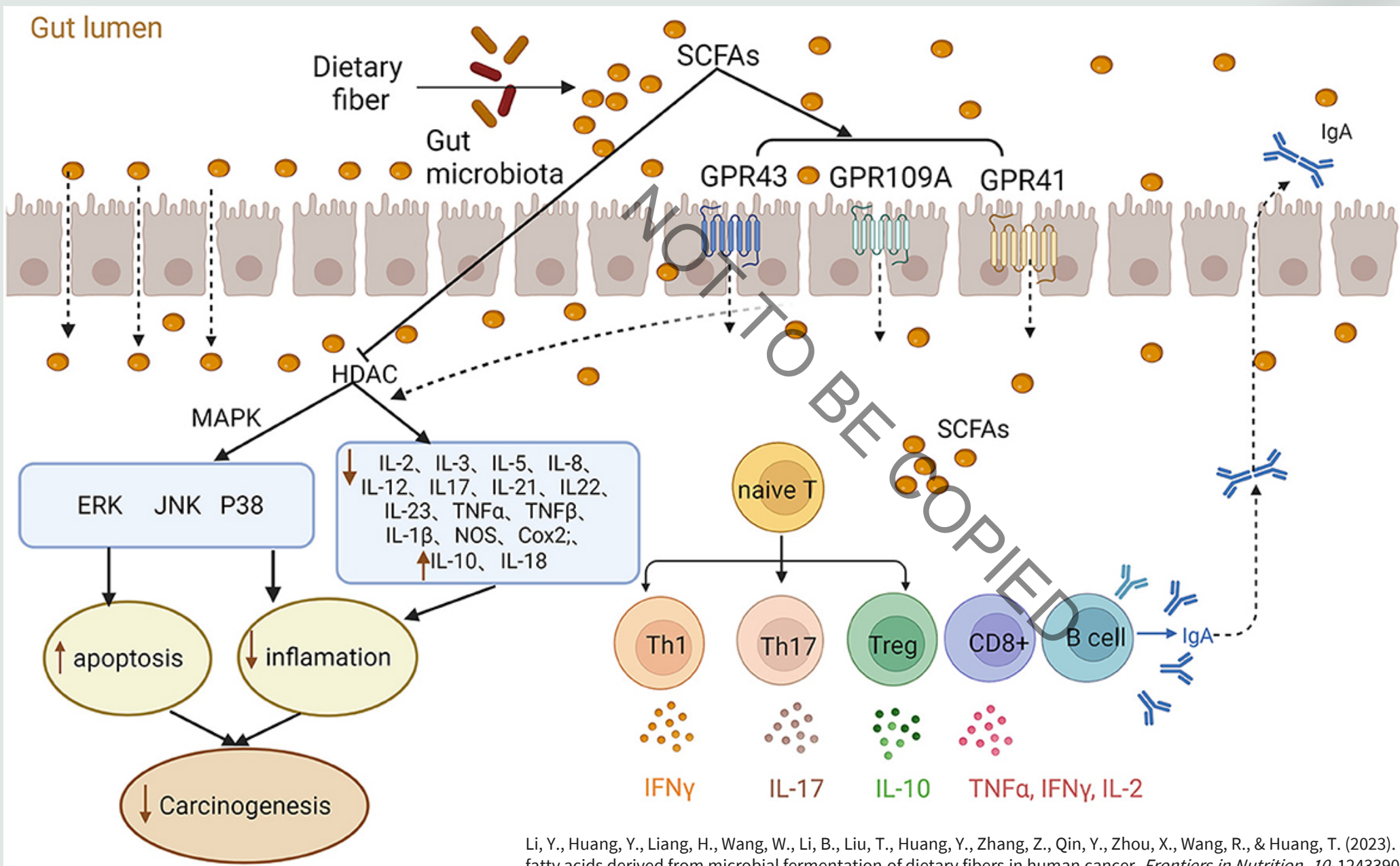
- SCFAs are microbial metabolites (butyrate, acetate, propionate)

SCFAs bind receptors

- SCFAs bind to specific SCFA receptors

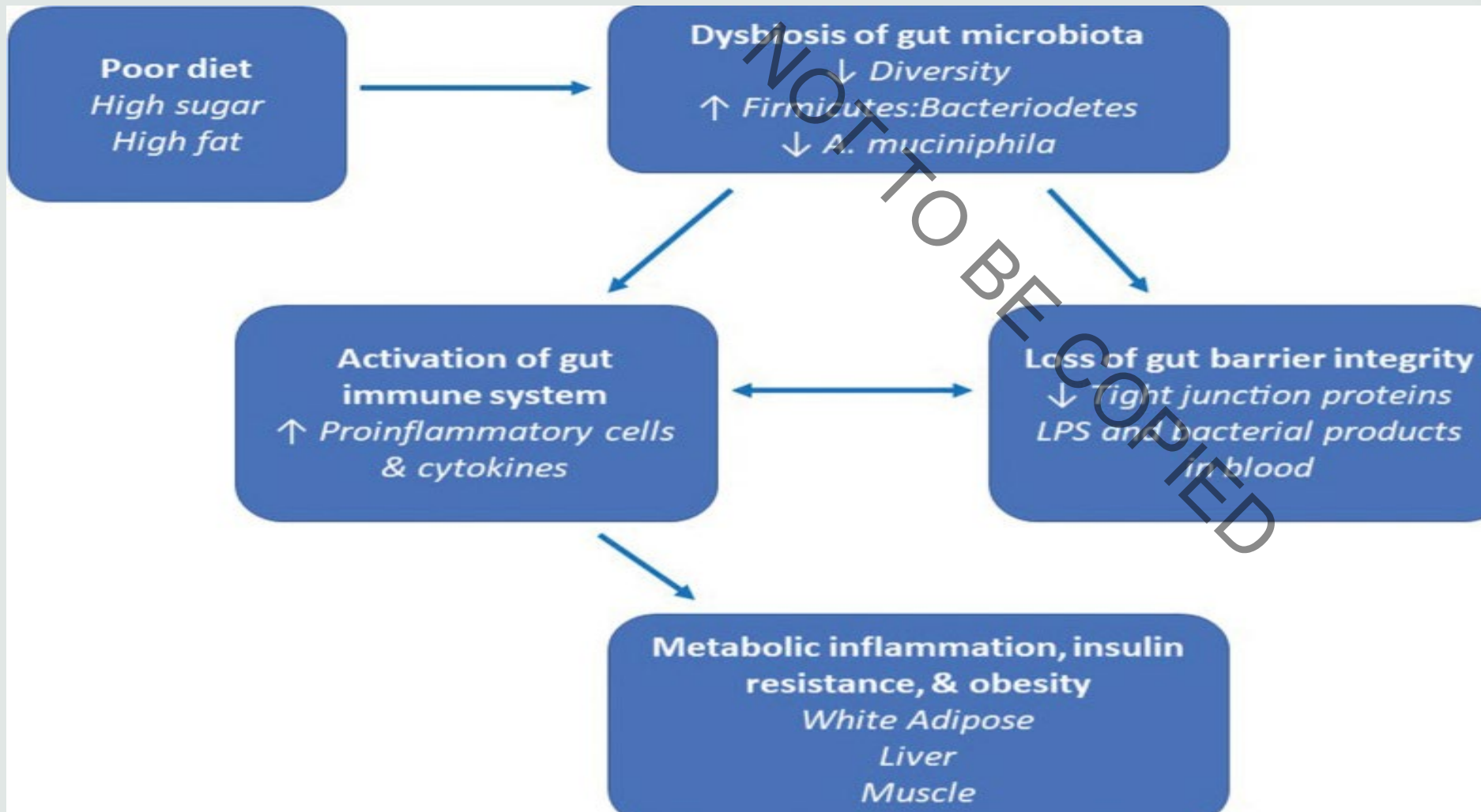


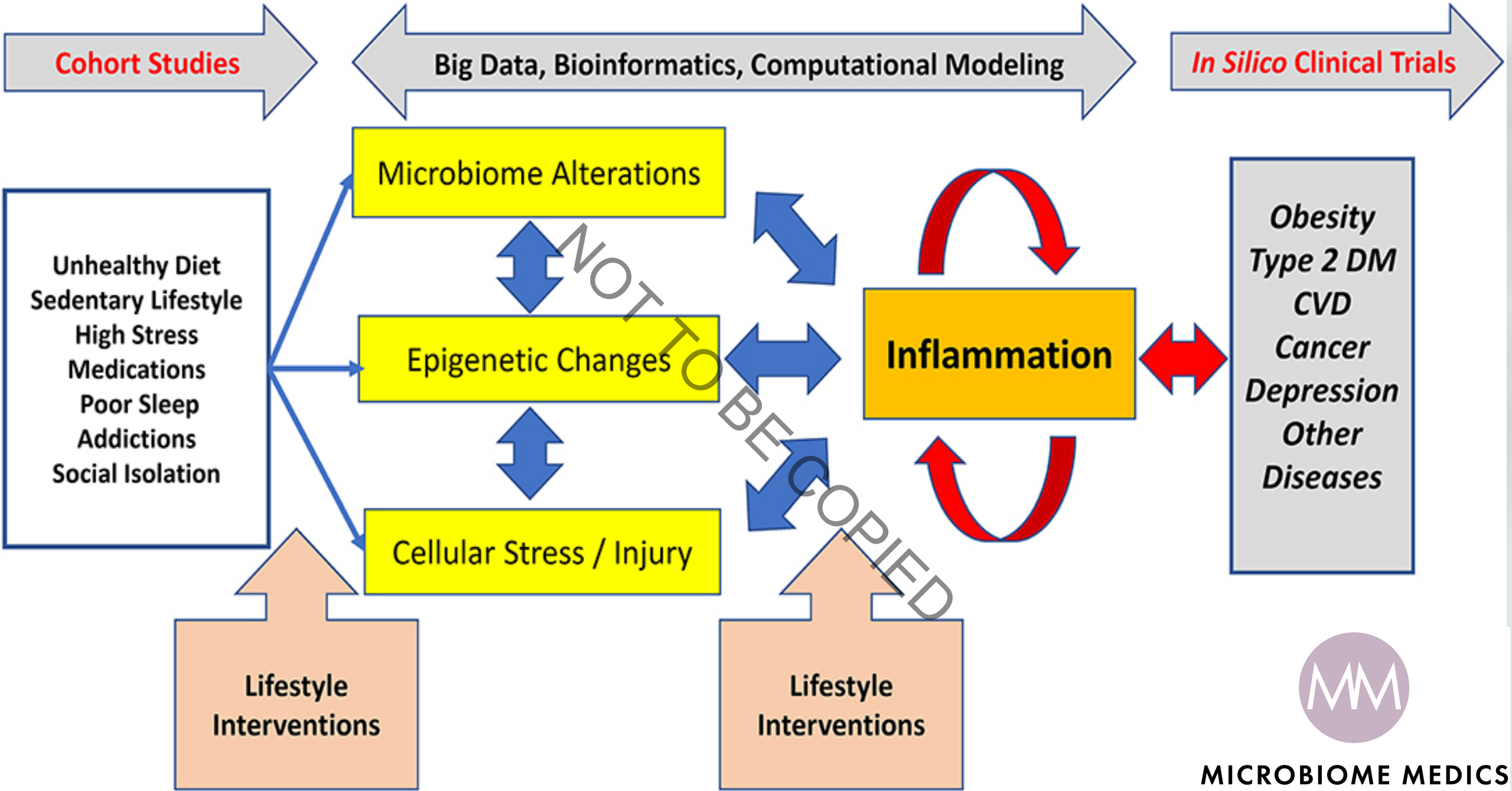
SCFA's



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

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

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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 5 hours
- Average UK adult consumes 700g sugar per week (almost 4 x recommendation)
- 20% cancer patients are diabetic

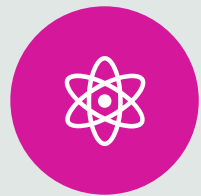


The warberg effect

- 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.



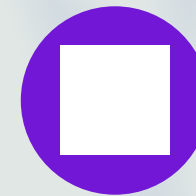
Solutions



Starve cancer cells



Enhance the gut microbiome



individual gut microbes matter



How do we starve a cancer cell?

Cut out
sugar

Ke to g e n i c
d i e t s

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



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



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