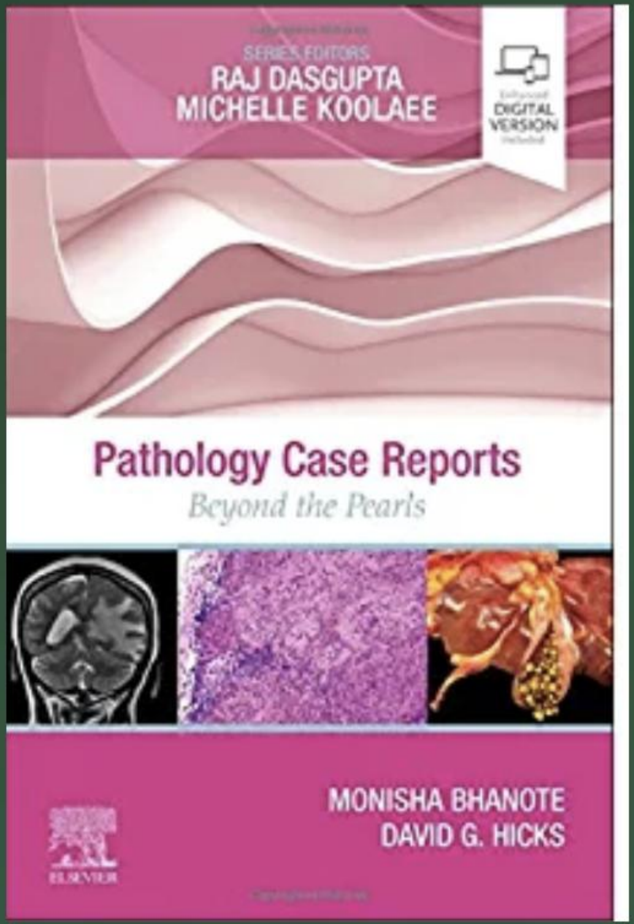
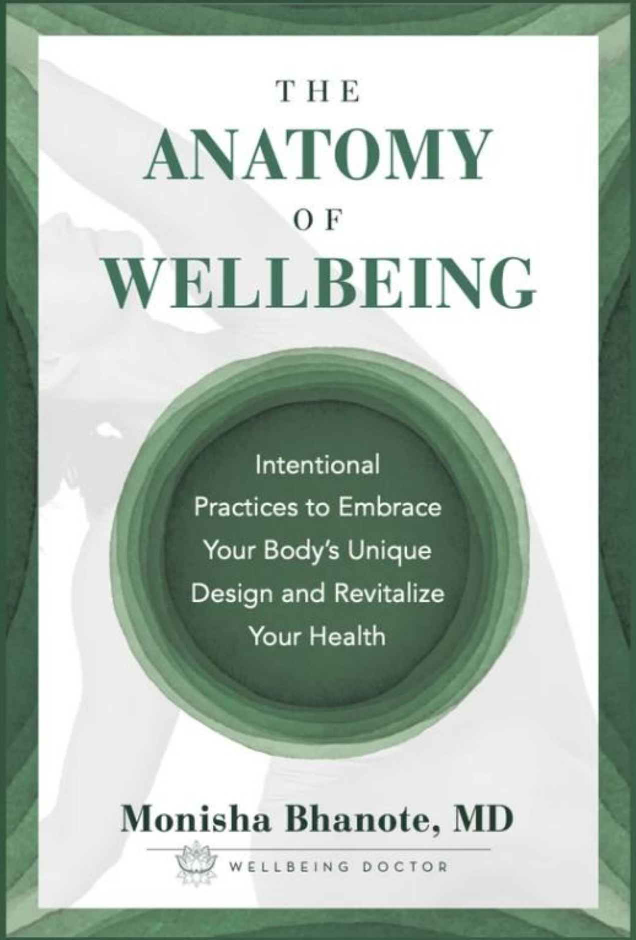
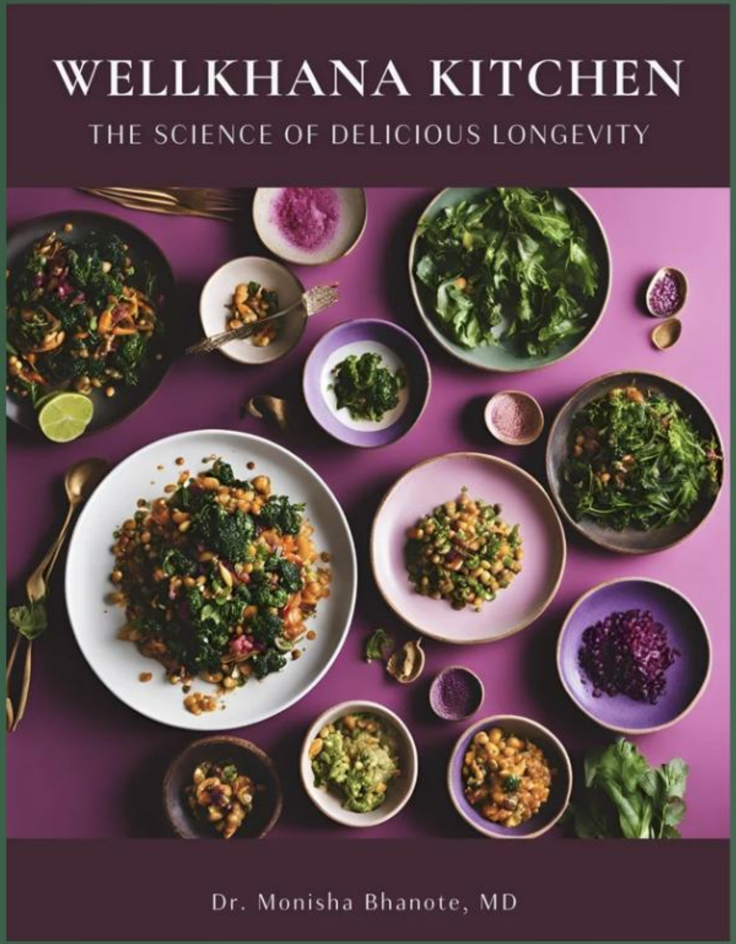
BOOKS BY DR.BHANOTE







INTEGRATED PERSONALIZED MEDICINE CONGRESS · WESTMINSTER, LONDON

The Gut Dysbiosis–Cancer Axis

Emerging Mechanisms Linking Microbial Imbalance to Oncogenesis

DR. MONISHA BHANOTE, MD, ABOIM, FCAP, ACCM

MEET YOUR SPEAKER

QUINTUPLE BOARD CERTIFIED

- ☑ Anatomic Pathology
- ☑ Integrative Medicine
- ☑ Clinical Pathology
- ☑ Culinary Medicine
- ☑ Cytopathology

THE HOLISTIC HORIZON
(Integrative & Lifestyle Medicine)

Culinary Medicine Specialist

Certified through **The Goldring** Center at Tulane University for evidence-based nutrition.

THE DIAGNOSTIC CORE
(Pathology & Oncology)

The Cellular Perspective

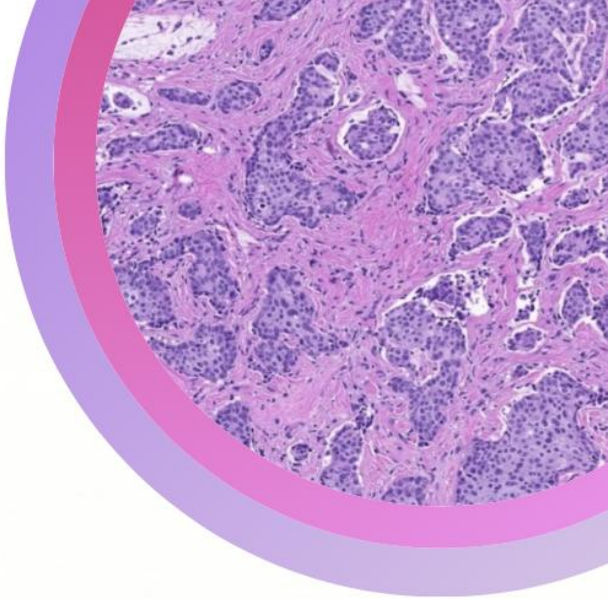
Utilizing cytopathology to analyze disease at the microscopic and cellular levels.

Anatomic Pathology, Clinical Pathology, and Cytopathology

Expertise from NYU and Weill Cornell.

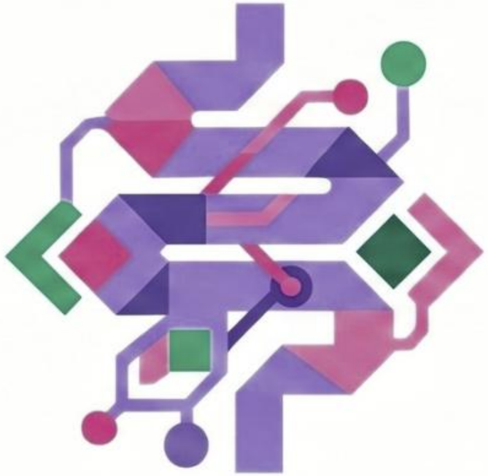
MONISHA BHANOTE, MD, ABOIM, FCAP, ACCM, YMTS

Learning Objectives



01 Analyze Mechanisms of Oncogenesis

Understand how gut dysblosis drives cancer through inflammation, barrier dysfunction, and the production of genotoxins.



02 Map Immune Communication Pathways

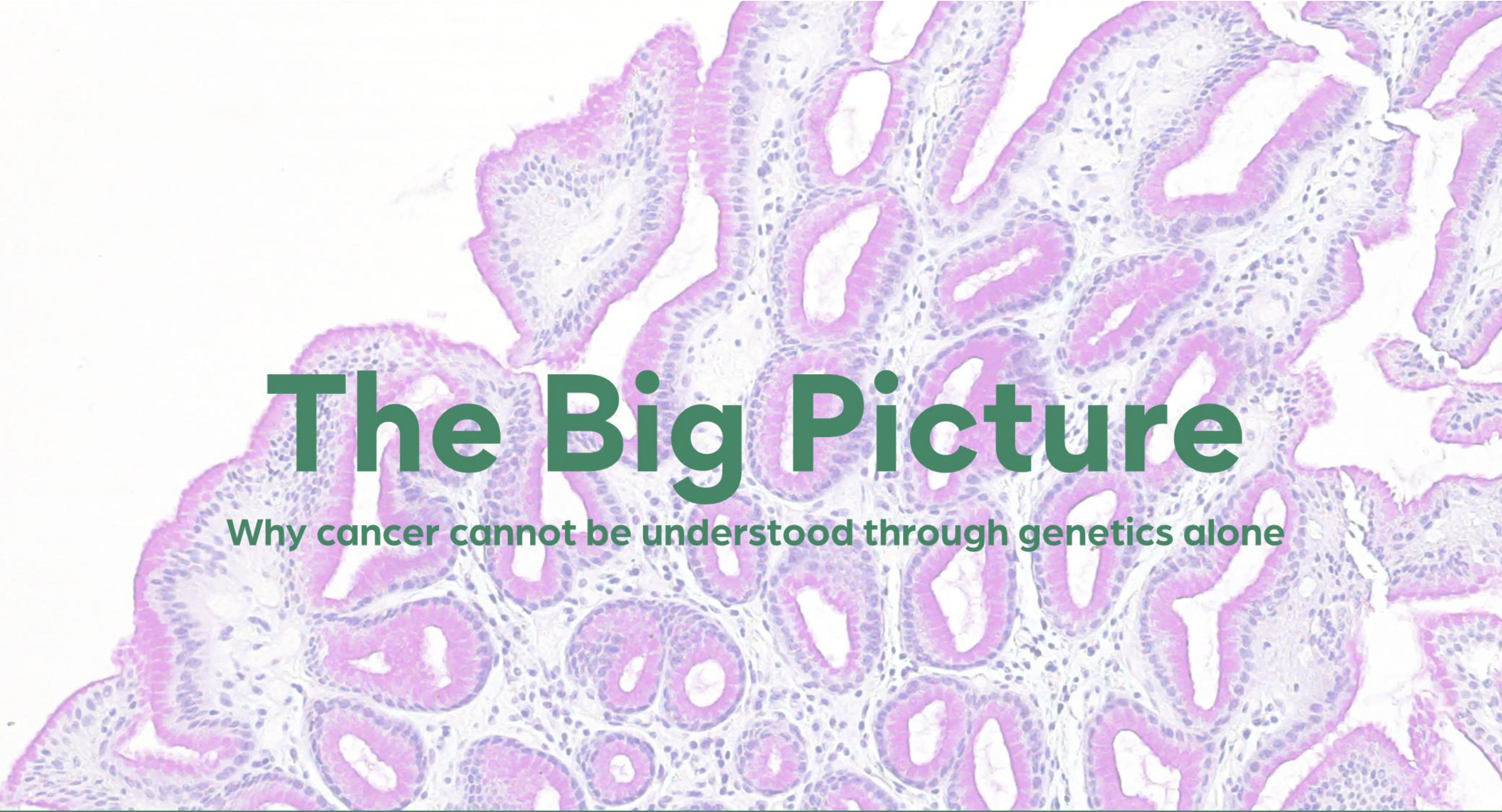
Describe microbial-host immune pathways that influence the formation of the tumor micro-environment and drive cancer progression.

03 Identify Resilience Strategies

Leverage evidence-based lifestyle and dietary interventions that support microbial resilience and mitigate cancer-promoting dysbiosis.

04 Implement Actionable Frameworks

Translate emerging microbiome science into clinical, personalized, and integrative oncology frameworks for patient practice.



The Big Picture

Why cancer cannot be understood through genetics alone

Rethinking What Drives Cancer

'THE ENVIRONMENTAL MAJORITY'

90–95%

OF CANCER CASES

The vast majority of cancer cases have their roots in environment and lifestyle factors.

PRIMARY EXTERNAL DRIVERS

- Diet
- Behavior
- Various Exposures
- The Microbiome

'THE GENETIC MINORITY'

5–10%

OF CANCER CASES

Only a small fraction of all cancer cases are attributable to genetic defects, specifically sumatic and germline mutations.

'THE EMERGING FRONTIER'

HOST-MICROBIOME INTERACTION

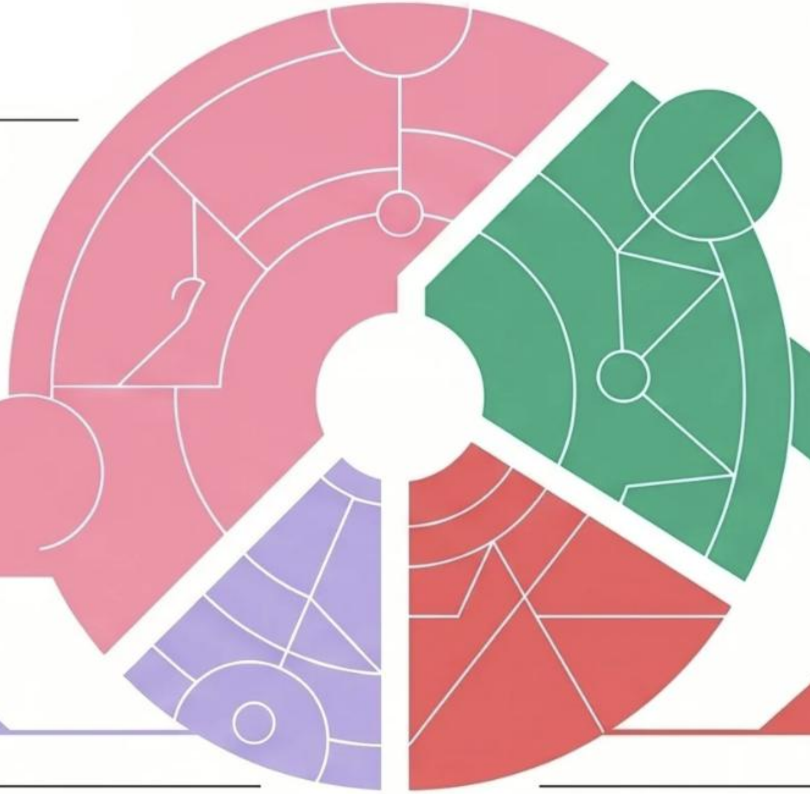
This represents a critical but still emerging area of study where the cellular environment actively shapes cancer risk.

Anand et al., Pharm Res 2008 · Bautista et al., npj Biofilms Microbiomes 2026

An Organ We Cannot See

~10–100 TRILLION

Microorganisms The human body hosts a massive community of symbiotic microorganisms that function as an "invisible organ."



MICROBIOTA VS. MICROBIOME

MICROBIOTA
Refers to the physical organisms.

MICROBIOME
Refers to their collective genomes and metabolic output.

THE 4 DOMINANT PHYLA

FIRMICUTES (60–80%)
The most prevalent phylum within the human microbial community.

ACTINOBACTERIA (2.5–5%)
A smaller but consistent component of the microbial landscape.

BACTEROIDETES (15–25%)
The second most dominant group, making up a significant portion of the gut ecosystem.

PROTEOBACTERIA (1–10%)
A phylum with variable presence, typically representing a minority of the total population.

CORE BIOLOGICAL FUNCTIONS

NUTRIENT SYNTHESIS & DIGESTION
Microorganisms play a direct role in breaking down compounds and synthesizing essential nutrients.

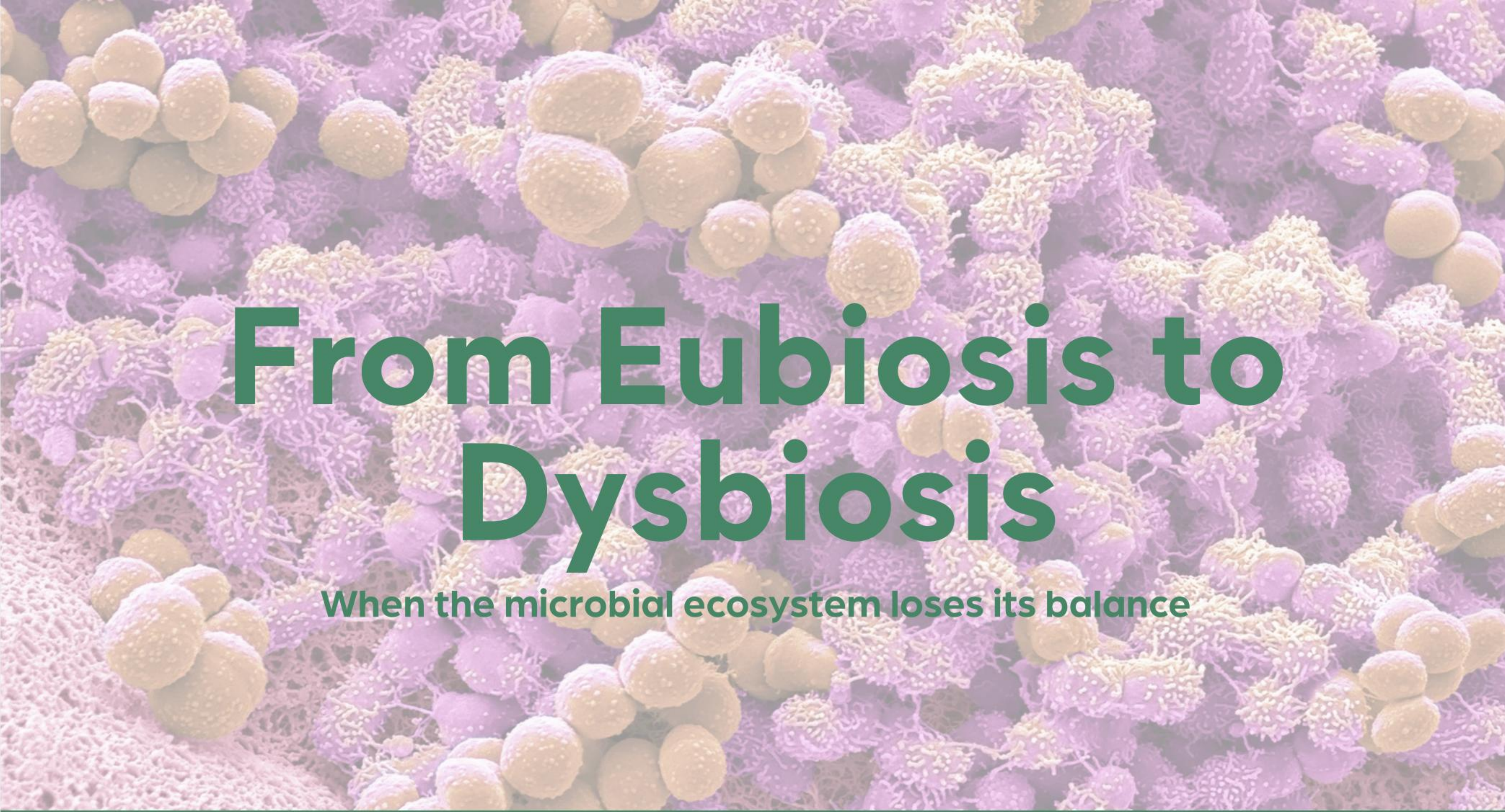
IMMUNE SYSTEM EDUCATION & REGULATION
The microbiome is critical for training the immune system to distinguish between friend and foe.

METABOLIC REGULATION & SIGNALING
Microbial activity influences metabolic pathways and systemic signaling throughout the body.

INTESTINAL BARRIER MAINTENANCE
The microbiota helps preserve the structural integrity of the gut lining.

NEUROTRANSMITTER & HORMONE MODULATION
The "invisible organ" impacts the brain and endocrine system by modulating chemical messengers.

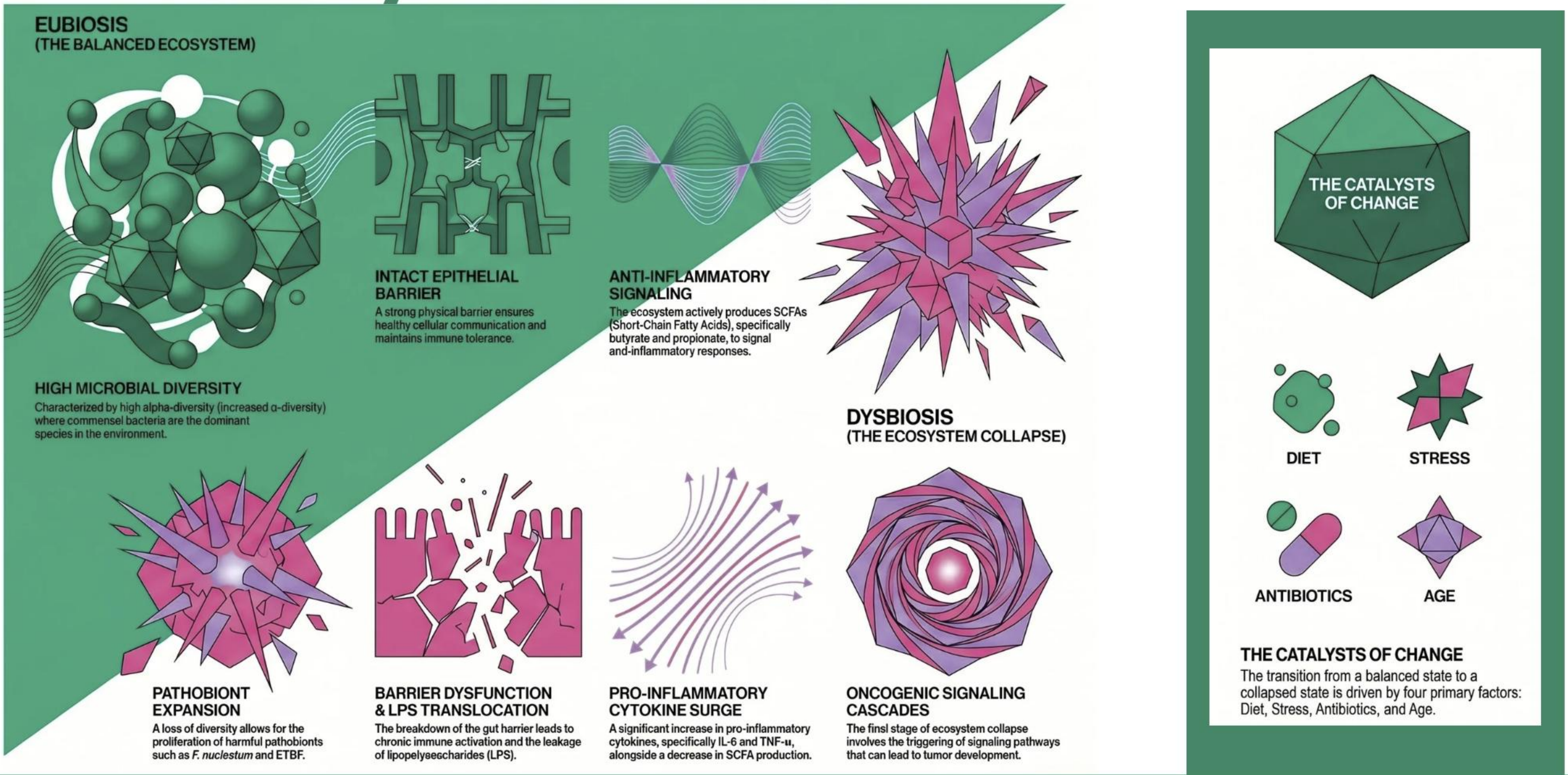
Ağagündüz et al., Front Pharmacol 2023 · Ursell et al., Nutr Rev 2012



From Eubiosis to Dysbiosis

When the microbial ecosystem loses its balance

The Ecosystem Within



Carding et al., Microb Ecol Health Dis 2015 · Bautista et al., npj Biofilms Microbiomes 2026

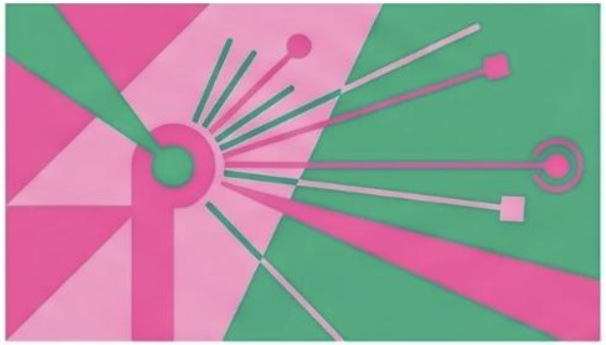
How Microbes Drive Oncogenesis

Six mechanistic pathways from dysbiosis to cancer

Six Pathways: From Dysbiosis to Oncogenesis

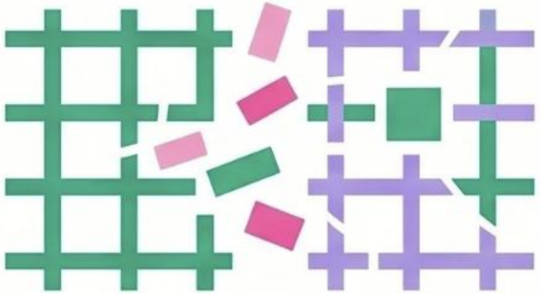
1. Chronic Inflammation

Driven by key pro-inflammatory mediators including NF-κB, IL-6, and TNF-α, which foster a tumor-promoting environment.



4. Microbial Metabolites

Impacted by the presence and balance of specific substances such as Butyrate, Bile acids, and Indoles.

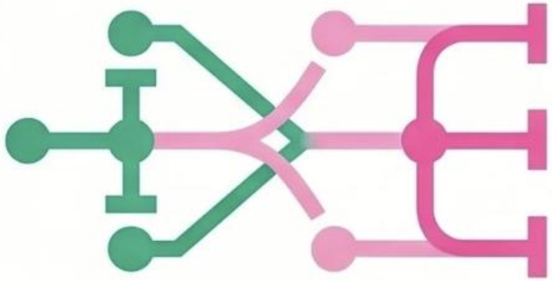


2. Barrier Dysfunction

Characterized by "leaky gut" and the translocation of Lipopolysaccharides (LPS) across the intestinal lining into systemic circulation.

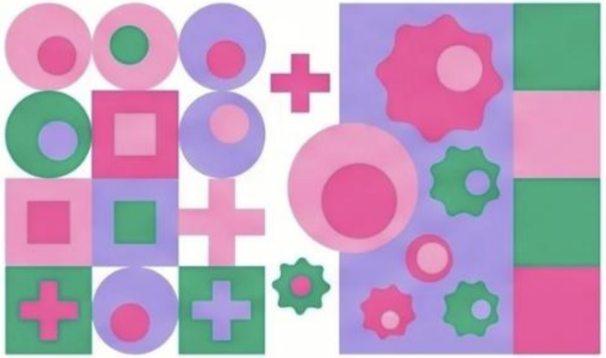
5. Metabolic Reprogramming

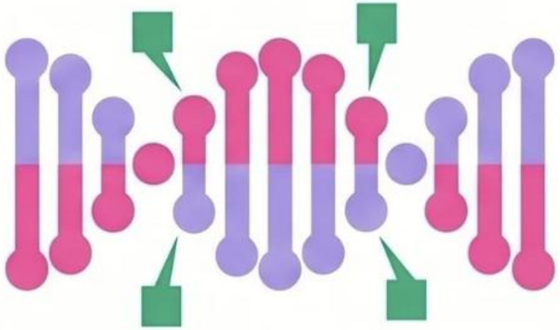
Marked by systemic metabolic shifts, specifically involving Insulin-like Growth Factor 1 (IGF-1) and the development of insulin resistance.



3. Immune Dysregulation

Involves the alteration of the Tumor Microenvironment (TME) through the activity of Regulatory T cells (Tregs) and Myeloid-Derived Suppressor Cells (MDSCs).



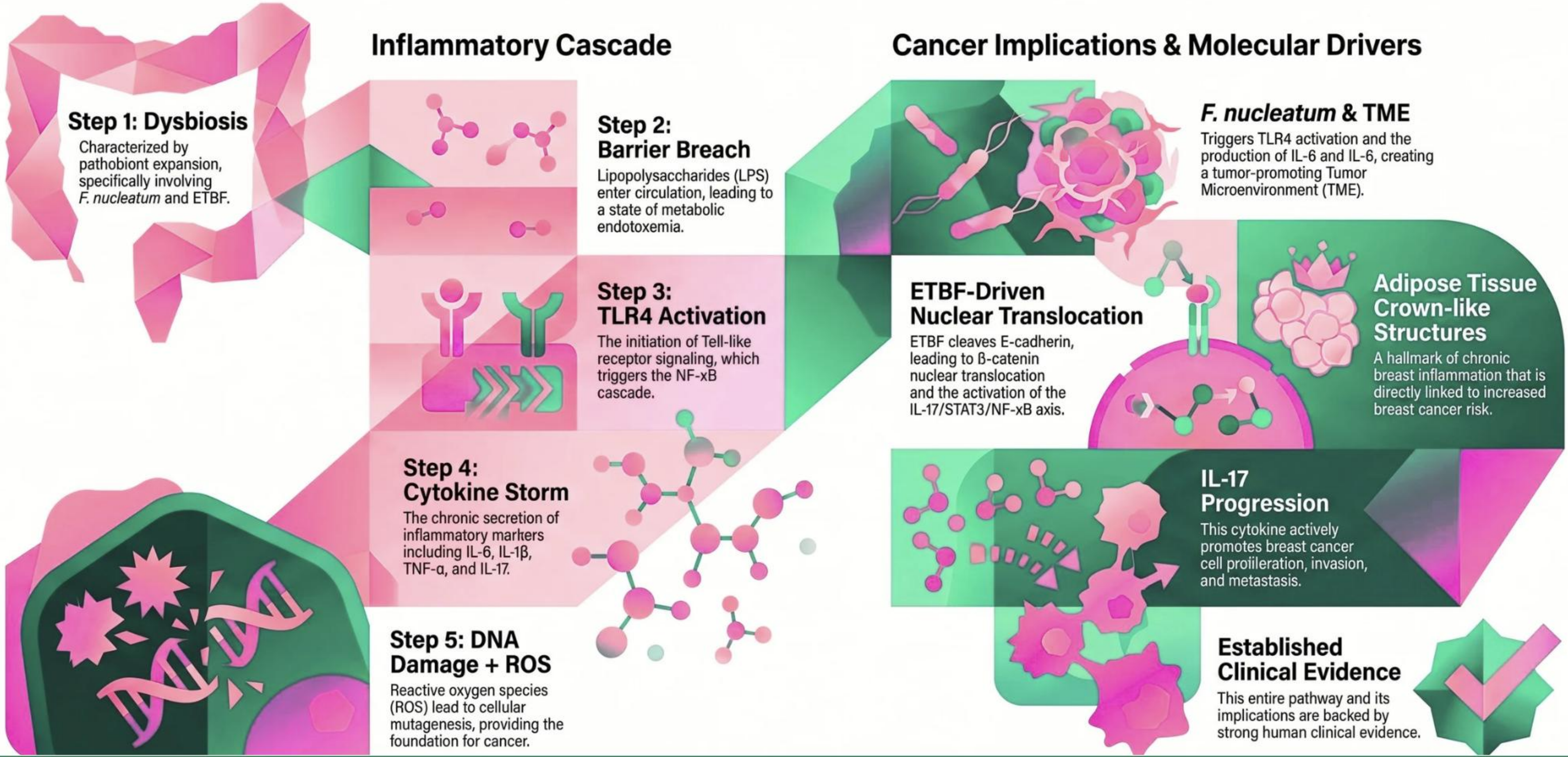


6. Epigenetic Modification

Direct alterations to gene expression through mechanisms such as Histone modification and DNA methylation.

Bautista et al., npj Biofilms Microbiomes 2026 · Ağagündüz et al., Front Pharmacol 2023

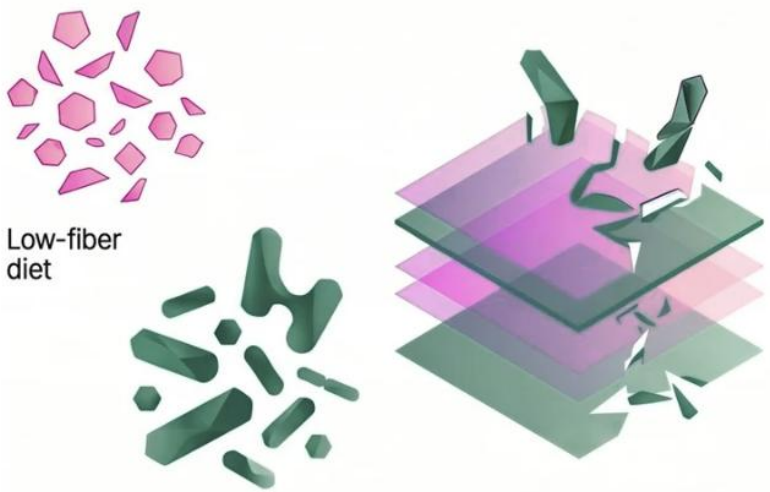
Pathway 1: The Inflammatory Cascade



Wu et al., Nat Med 2009 · Danforth, Cancers 2021 · Crusz & Balkwill, Nat Rev Clin Oncol 2015

Pathway 2: Barrier Dysfunction

PHASE 1: MICROBIAL & MUCOSAL SHIFTS



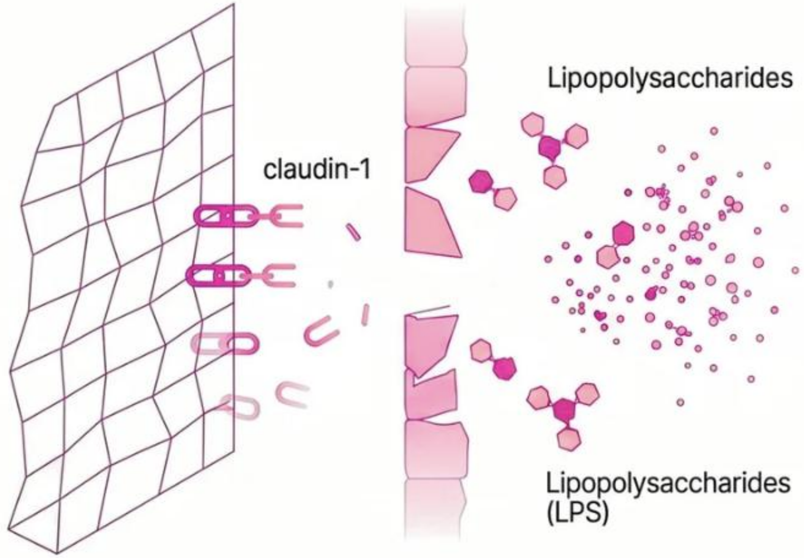
Dietary Trigger and Microbial Decline

A low-fiber diet leads to a measurable decrease in butyrate-producing bacteria, which are essential for gut health.

Mucus Layer Degradation

The bacteria *Akkermansia* and *Bacteroides caccae* actively degrade the protective mucus layer of the intestine.

PHASE 2: STRUCTURAL FAILURE & TRANSLOCATION



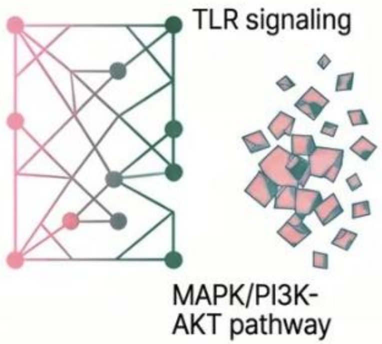
Disruption of Tight Junction Proteins

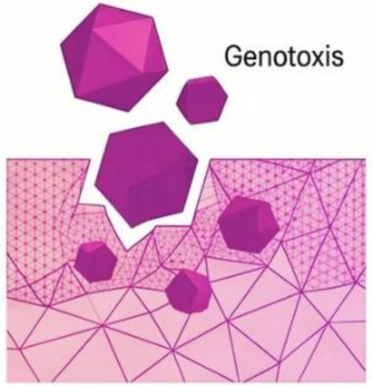
The intestinal barrier loses integrity as claudin-1 levels decrease, disrupting the proteins that hold cells together.

LPS Translocation

Lipopolysaccharides (LPS) move across the compromised barrier, resulting in metabolic endotoxemia.

PHASE 3: CELLULAR RESPONSE & CLINICAL RISK





Proliferation Signaling Cascades

Activates ias leads TLR signaling activates the MAPK/PI3K-AKT pathway, which directly stimulates cell proliferation.

Host Tissue Exposure

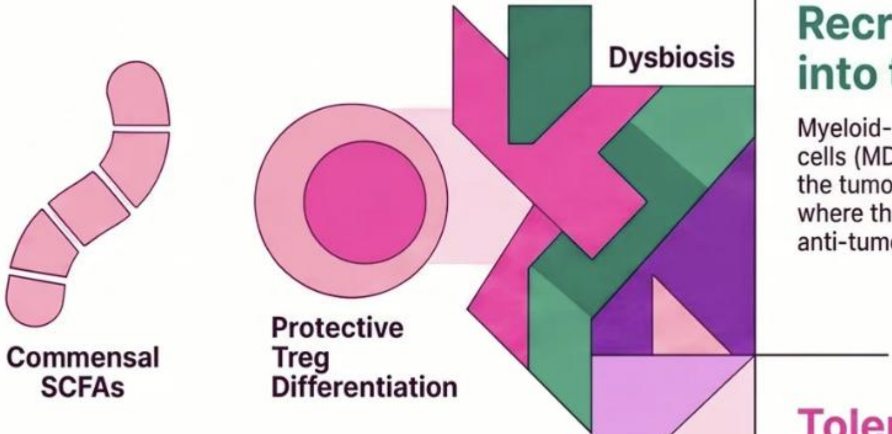
Harmful genotoxins gain direct access to the host tissue due to the breach in the barrier.

Gur et al., Immunity 2015 · Furusawa et al., Nature 2013 · Bautista et al., npj Biofilms Microbiomes 2026

Pathway 3: Immune Dysregulation

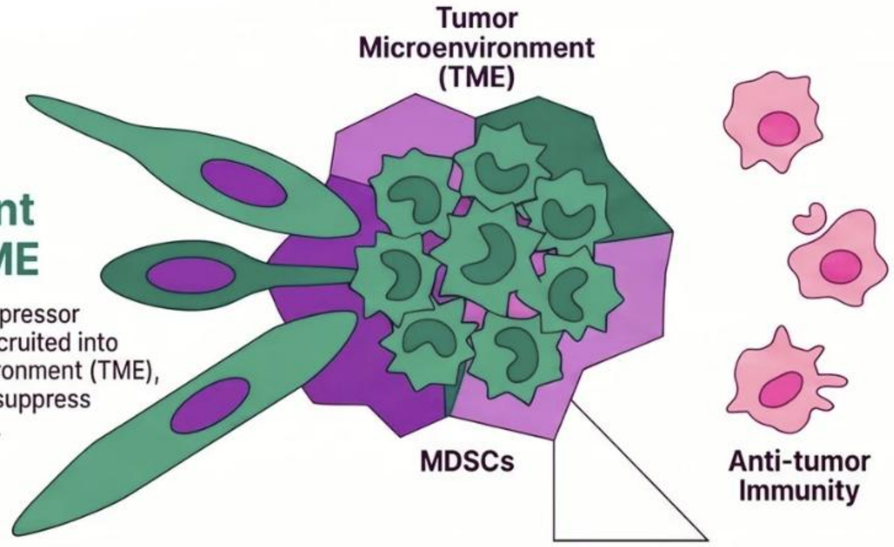
Treg Subversion via Dysbiosis

While commensal Short-Chain Fatty Acids (SCFAs) normally drive protective Treg differentiation, dysbiosis blocks this response, removing a key immune safeguard.



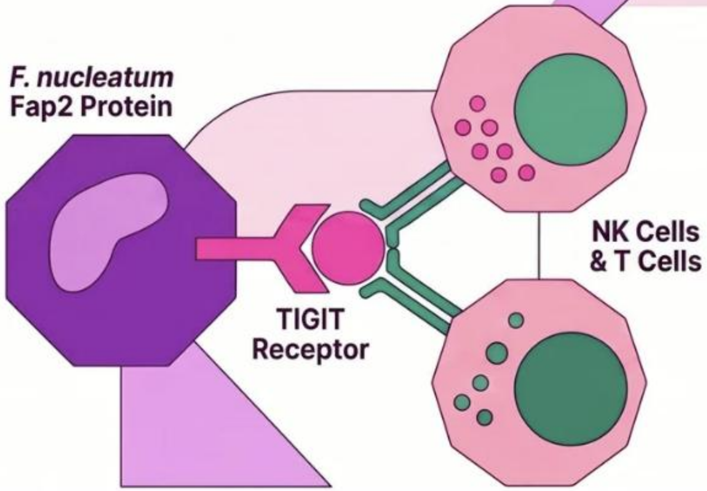
MDSC Recruitment into the TME

Myeloid-derived suppressor cells (MDSCs) are recruited into the tumor microenvironment (TME), where they actively suppress anti-tumor immunity.



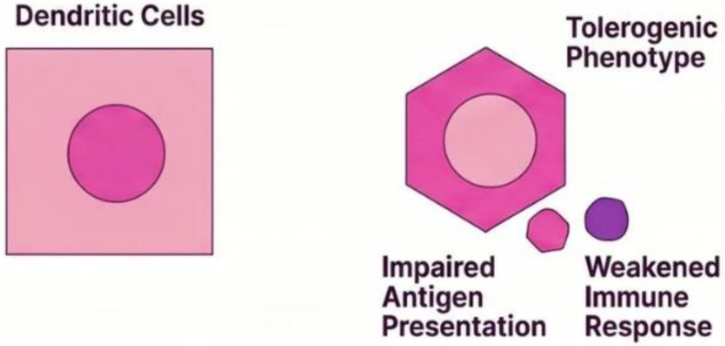
NK Cell Evasion via Fap2/TIGIT

The *F. nucleatum* Fap2 protein binds to the TIGIT receptor, which inhibits the attack capabilities of both NK cells and T cells.



Tolerogenic Dendritic Cell Polarization

Dendritic cells are polarized toward a tolerogenic phenotype, resulting in impaired antigen presentation and a weakened immune response.



Gur et al., Immunity 2015 · Furusawa et al., Nature 2013 · Bautista et al., npj Biofilms Microbiomes 2026

Pathway 4: Microbial Metabolites

PROTECTIVE FUNCTIONS

Short-Chain Fatty Acids (SCFAs)

Provide essential protective functions like fueling cells and regulating immunity, but can become dysbiotic drivers of disease under specific dietary or bacterial conditions.

Secondary Bile Acids

LCA reduces cancer prollibration.

DYSBIOTIC DRIVERS

Short-Chain Fatty Acids (SCFAs)

are lost during fiber-depleted diets.

Secondary Bile Acids

whereas excess DCA triggers DNA damage and carcinogenesis.

Emerging Chemical Signals

Indoles & Indolimines

Tryptophan-derived metabolites that regulate immunity.

Formate

Supports nucleotide synthesis at low levels.

	Source/ Origin	Clinical Status
Indoles & Indolimines	Tryptophan-derived	Emerging
Formate	One-carbon matabolite	Emerging
Secondary Bile Acids	Microbially converted	Dual Role

Indoles & Indolimines

or, if IBD-derived, produce genotoxic effects.

Formate

but exacerbates colorectal cancer progression when elevated.

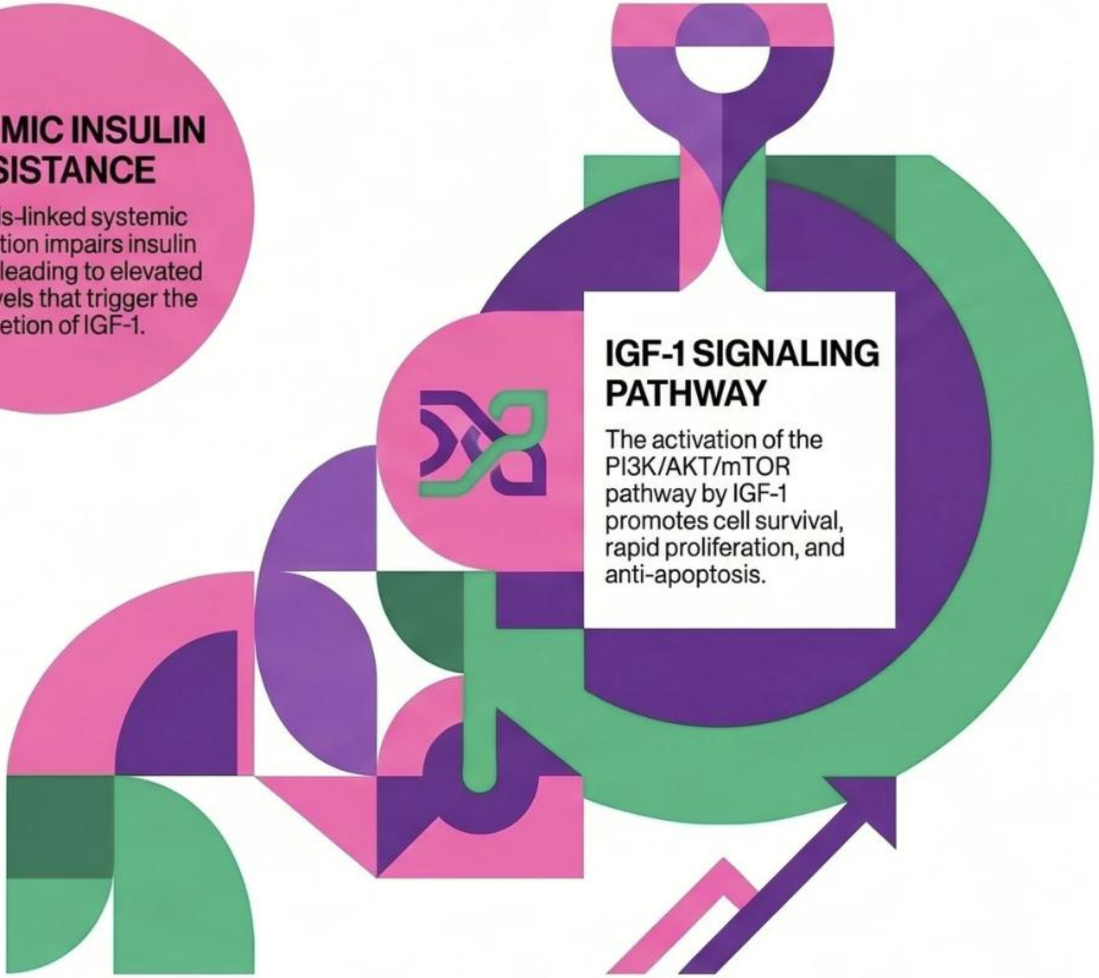
Cao et al., Science 2022 · Ternes et al., Nat Metab 2022 · Mikó et al., BBA 2018 · Donohoe et al., Cancer Discov 2014

Pathway 5: Metabolic Reprogramming

HORMONAL & GROWTH SIGNALING

SYSTEMIC INSULIN RESISTANCE

Dysbiosis-linked systemic inflammation impairs insulin signaling, leading to elevated insulin levels that trigger the secretion of IGF-1.



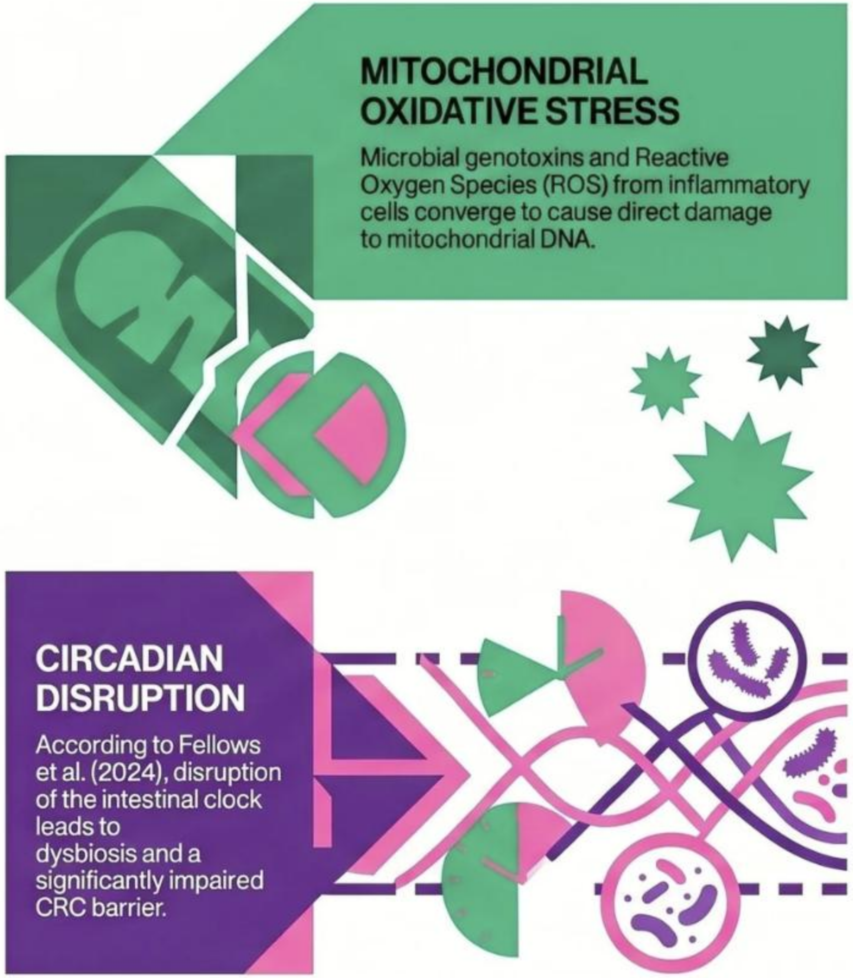
IGF-1 SIGNALING PATHWAY

The activation of the PI3K/AKT/mTOR pathway by IGF-1 promotes cell survival, rapid proliferation, and anti-apoptosis.

CELLULAR STRESS & STRUCTURAL INTEGRITY

MITOCHONDRIAL OXIDATIVE STRESS

Microbial genotoxins and Reactive Oxygen Species (ROS) from inflammatory cells converge to cause direct damage to mitochondrial DNA.



CIRCADIAN DISRUPTION

According to Fellows et al. (2024), disruption of the intestinal clock leads to dysbiosis and a significantly impaired CRC barrier.

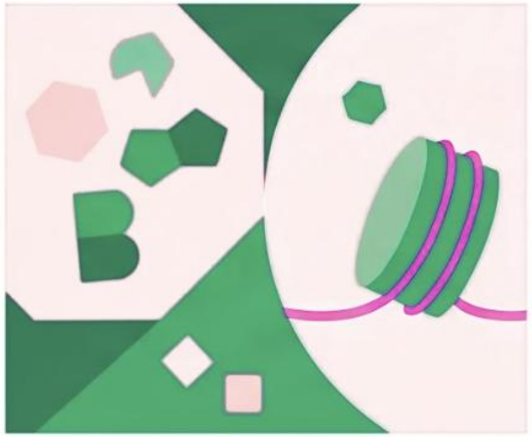
Fellows et al., Sci Adv 2024 · Cao et al., Gastroenterology 2021 · Yang et al., mSystems 2024

Pathway 6: Epigenetic Modification

Chromatin & Histone Modification

Butyrate-Driven HDAC Inhibition

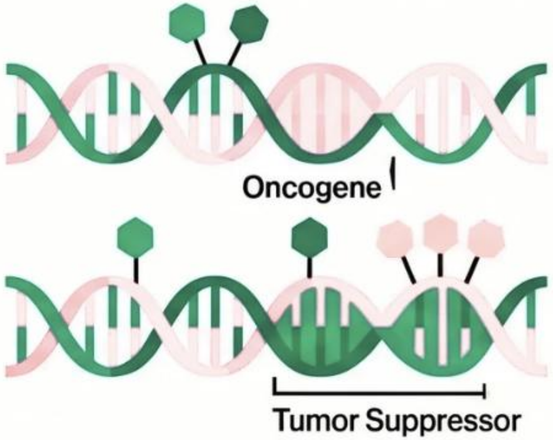
Butyrate inhibits Histone Deacetylases (HDACs), which alters chromatin accessibility to reactivate tumor suppressor genes, creating a protective cellular context.



Essential Methyl Donors

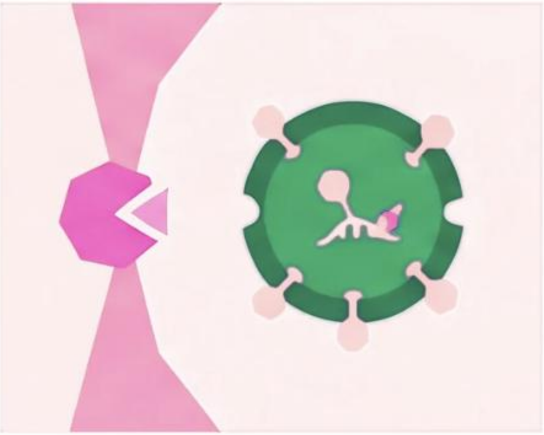
Microbial-derived folate and B vitamins serve as critical methyl donors for histone modification; however, state of dysbiosis can deplete these essential substrates.

Gene & RNA Regulation



Targeted DNA Methylation

Microbial metabolites exert influence over DNA methylation patterns specifically at oncogene and tumor suppressor loci, dictating gene silencing or activation.



miRNA Dysregulation by ETBF

ETBF (*Enterotoxigenic Bacteroides fragilis*) inhibits exosome-packaged miR-149-3p, a pathway that triggers intestinal inflammation and subsequent malignancy.

Fellows et al., Sci Adv 2024 · Cao et al., Gastroenterology 2021 · Yang et al., mSystems 2024

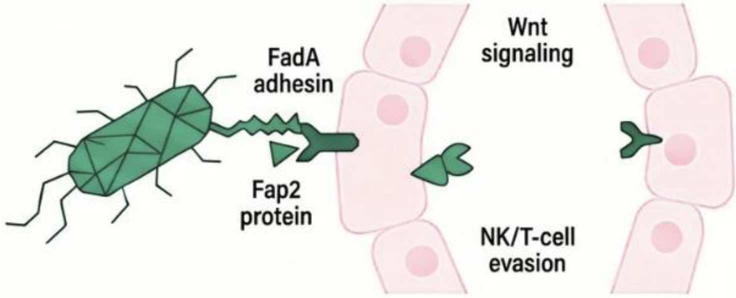
Cancer-Specific Evidence

Colorectal Cancer · Breast Cancer · Pancreatic Cancer

Pathological Drivers of Colorectal Cancer

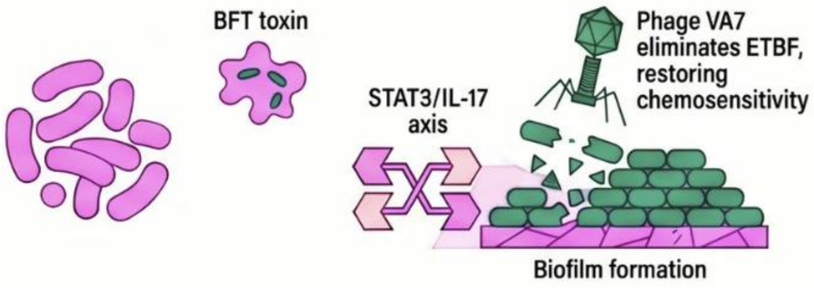
ESTABLISHED MICROBIAL DRIVERS

Fusobacterium nucleatum: A Driver of Evasion and Resistance

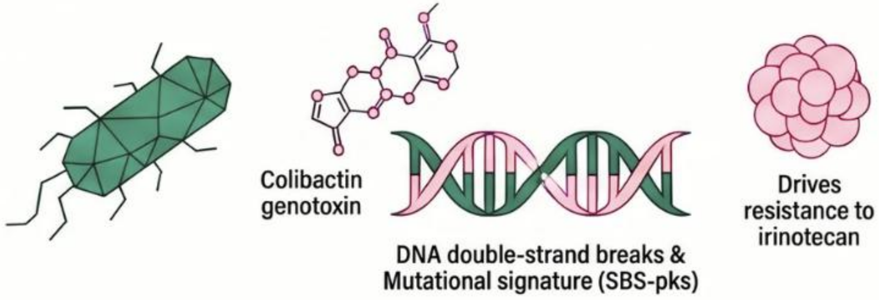


Uses FadA adhesin to activate Wnt signaling and Fap2 protein to evade NK/T-cells, ultimately promoting chemoresistance via autophagy and predicting a worse clinical prognosis.

Enterotoxigenic *Bacteroides fragilis* (ETBF): Toxin-Mediated Inflammation



Secretes BFT toxin to trigger the STAT3/IL-17 axis and biofiim formation; notably, phage VA7 has been shown to eliminate ETBF and restore chemosensitivity.

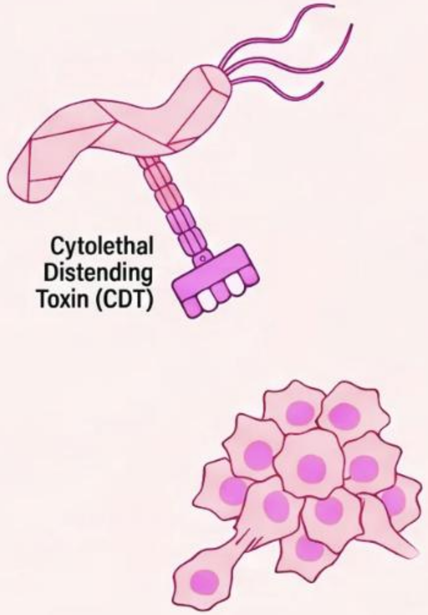


pks+ Escherichia coli: The Genotoxic Catalyst

Produces colibactin genotoxin which causes DNA double-strand breaks, leaving a distinct mutational signature (SBS-pks) in tumors and driving resistance to irinotecan.

EMERGING PATHOGENS

Campylobacter jejuni: Promoting Metastasis

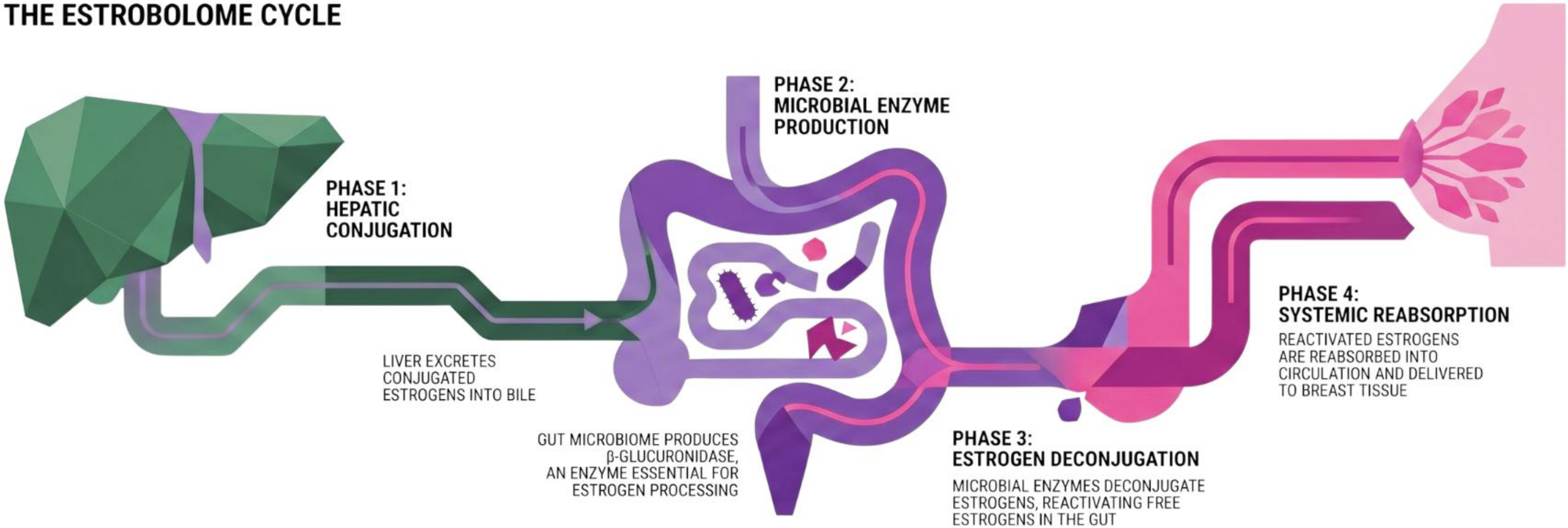


Emerging research indicates that its Cytolethal Distending Toxin (CDT) acts as a significant promoter of colorectal cancer metastasis.

Rubinstein et al., Cell Host Microbe 2013 · Pleguezuelos-Manzano et al., Nature 2020 · Ding et al., Cell Host Microbe 2025

Microbial Estrogen Metabolism and Breast Cancer

THE ESTROBOLOME CYCLE



CLINICAL RELEVANCE & EVIDENCE

β-GLUCURONIDASE DYSBIOSIS

Imbalances in enzyme production clovate shouloting estrogen tevels, promoting ER+ (Estrogen Receptor positive) breast cancer growth

CAUSALITY VS. CORRELATION

Compelling mechanism, but causal inik between estrobaltime and breast cancer not yet established in humans; currently, only correlution data exists

α-DIVERSITY CONTESTED

Studies on microbial diversity (α-diversity) show modlicting results—some decrease, some increase—varying by cancer subtype and menopausal status

CDK4/6i TREATMENT RESPONSE

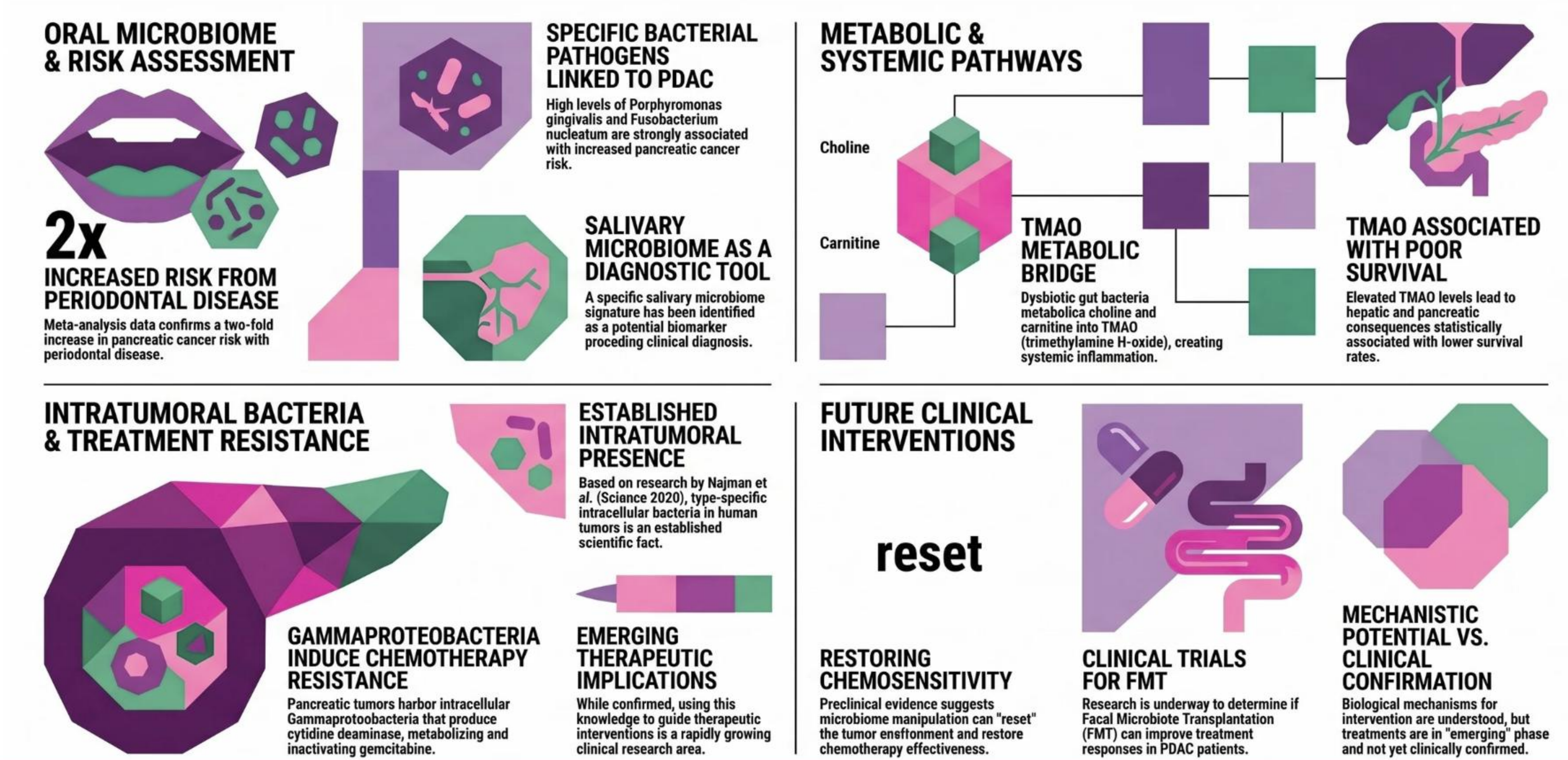
Recent research (Schettini et al., 2020) suggests gut intcrobiute composition can predict response to COKAIR inhibitors in matastatic breast cancer patients

TRASTUZUMAB EFFICACY

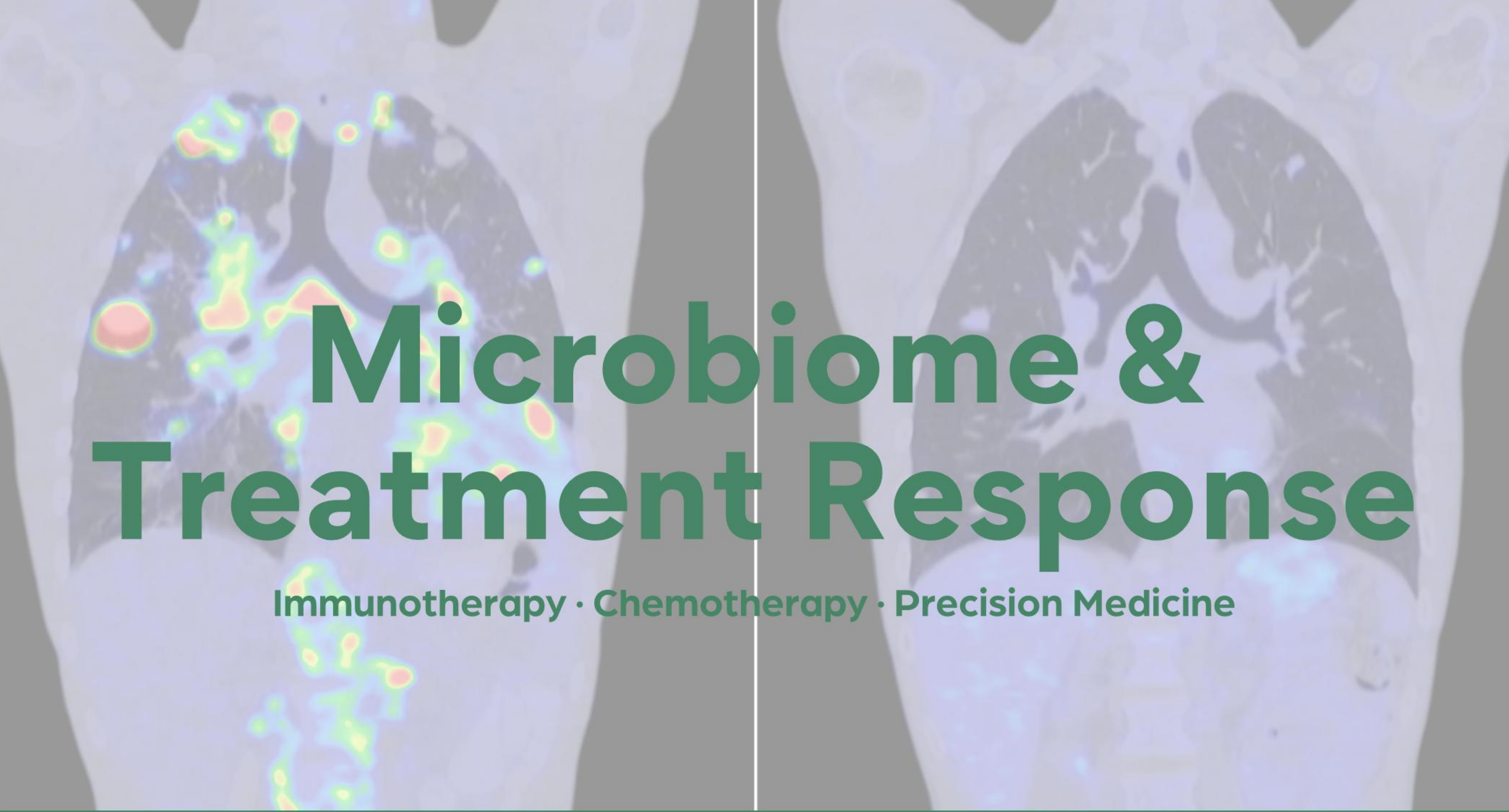
Research (DI studiea et al., 2021) indicates gut intcrobiuts modulates the officacy of Trastuzumab in HER2+ breast cancer cases

Rubinstein et al., Cell Host Microbe 2013 · Pleguezuelos-Manzano et al., Nature 2020 · Ding et al., Cell Host Microbe 2025

Pancreatic Cancer: The Intratumoral Microbiome Frontier



Nejman et al., Science 2020 · Bautista et al., npj Biofilms Microbiomes 2026



Microbiome & Treatment Response

Immunotherapy · Chemotherapy · Precision Medicine

Gut Microbiome: A Critical Determinant of Cancer Treatment Success

Predictive Bacterial Signatures

Akkermansia muciniphila Predicts NSCLC Response

The presence of intestinal *Akkermansia muciniphila* is a clinical predictor for positive responses to PD-1 blockade in patients with advanced non-small-cell long cancer.

Ruminococcaceae Enrichment in Melanoma

A gut microbiome enriched with Ruminococcaceae correlates strongly with anti-tumor responses in patients undergoing PD-1 blockade for melanoma.

Faecalibacterium prausnitzii & Immunotherapy

Responders to Anti-PD-1 immunotherapy typically exhibit higher levels of Faecalibacterium preusnitzii compared to non-responders.

Routy et al., Science 2018 · Gopalakrishnan et al., Science 2018 · Davar et al., Science 2021 · Derosa et al., Nat Med 2022

Gut Microbiome: A Critical Determinant of Cancer Treatment Success

Diversity as a Success Metric

High Diversity vs. Bacteroidetes-Dominance

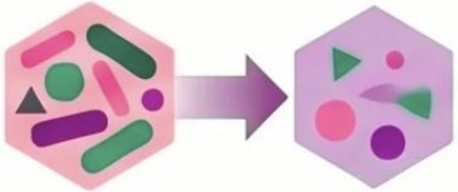
High diversity is a key predictor of treatment success, while non-responders often exhibit Bacteroidetes-dominant profiles.

Microbial Conditioning in Breast Cancer

The therapeutic efficacy of trastusumab in HER2+ breast cancer is conditioned by gut microbiota, with diversity serving as a primary treatment predictor.

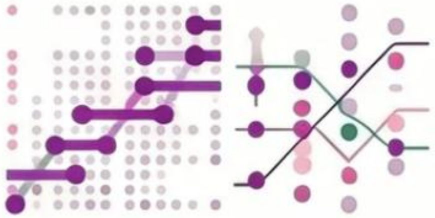
Advanced Diagnostics & Interventions

FMT Overcomes Treatment Resistance



- In a clinical study of 15 melanoma patients resistent to PD-1 therapy, 3 achieved a partial response after receiving a Fecal Microbiota Transpiant (FMT) from successful responders.

GOMS: The Next-Gen Biomarker



Gut OncoMicrobiome Signatures (GOMS) are proposed as a sophisticated diagnostic tool for stratifying patients for cancer immunotherapy based on their microbial profile.

Routy et al., Science 2018 · Gopalakrishnan et al., Science 2018 · Davar et al., Science 2021 · Derosa et al., Nat Med 2022

Integrative & Lifestyle Applications

Evidence-based strategies to support microbial resilience

Supporting Microbial Resilience: Dietary Diversity & Fiber

DIETARY BENCHMARKS FOR DIVERSITY

30+ PLANT SPECIES PER WEEK

Consuming this variety of piants is the primary driver for increasing microbial diversity.

SUPPORTED MICROBIAL RESILIENCE

Diversity in plant intake creates a robust and stable internal ecosystem.

BIOLOGICAL IMPACT & OUTCOMES

SCFA PRODUCTION VIA FIBER

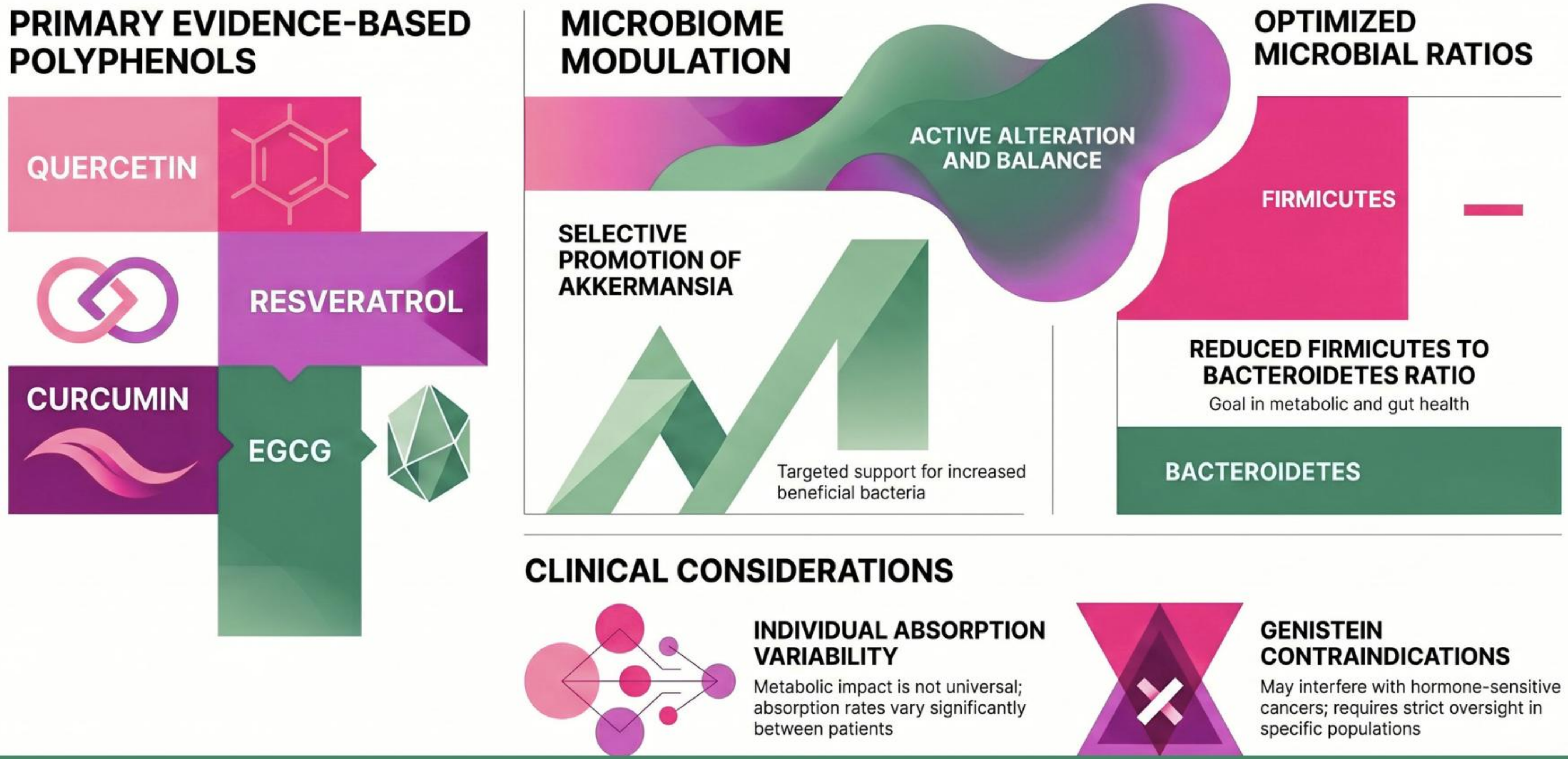
Dietary fiber intake is the essential precursor for short-chain fatty acid production.

RAPID RISK MARKER REDUCTION

Studies show CRC risk markers can change in just 14 days following dietary shifts.

O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

Supporting Microbial Resilience: The Role of Polyphenols



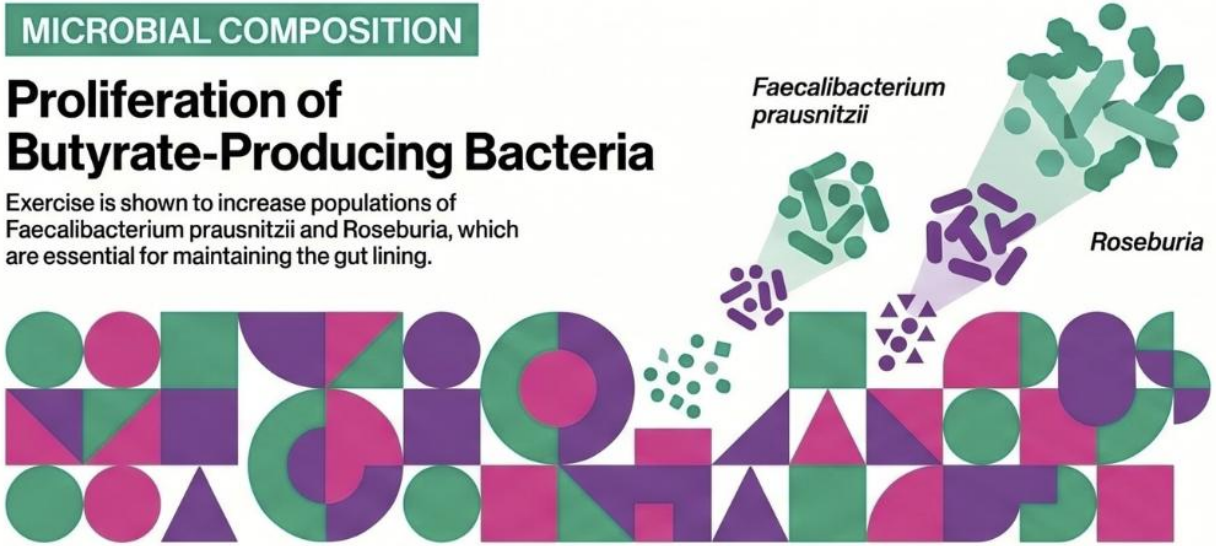
O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

Supporting Microbial Resilience: The Impact of Physical Activity

MICROBIAL COMPOSITION

Proliferation of Butyrate-Producing Bacteria

Exercise is shown to increase populations of Faecalibacterium prausnitzii and Roseburia, which are essential for maintaining the gut lining.



PHYSIOLOGICAL IMPACT

Reduced Systemic Inflammation

Regular physical activity helps lower markers of inflammation throughout the body, supporting a more resilient immune environment.

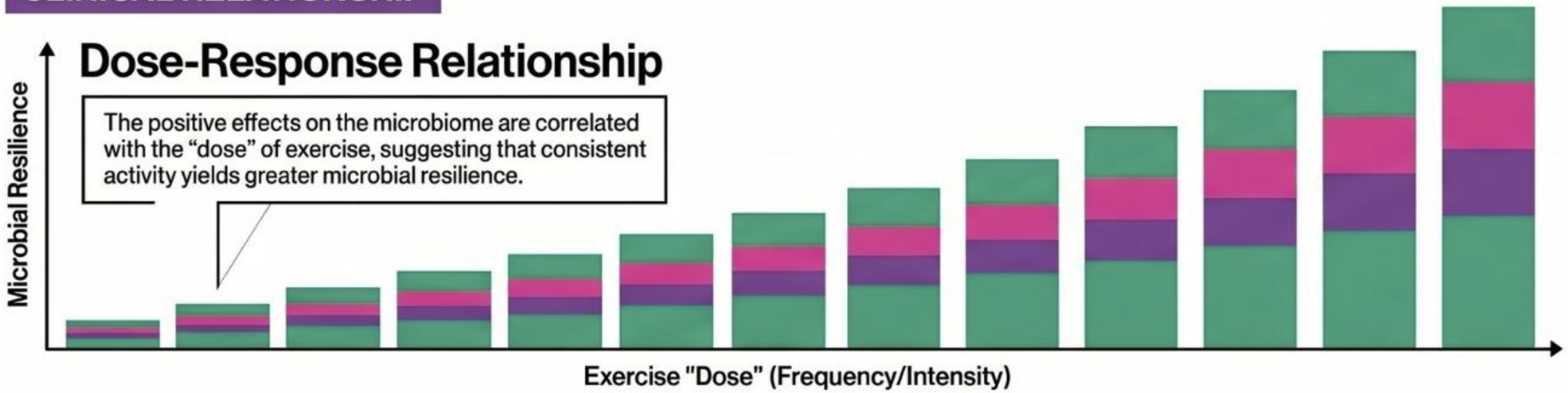
Improved Intestinal Transit Time

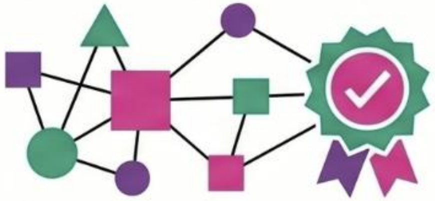
Exercise aids the mechanical movement of the digestive tract, ensuring efficient waste removal and nutrient processing.

CLINICAL RELATIONSHIP

Dose-Response Relationship

The positive effects on the microbiome are correlated with the "dose" of exercise, suggesting that consistent activity yields greater microbial resilience.





Evidence-Based Strategy

The link between physical activity and microbial health is categorized as a "supported" intervention for improving biological resilience.

O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

Sleep, the Clock, and Gut Resilience

THE DISRUPTION CASCADE

Intestinal Clock Disruption

Irregular sleep patterns interrupt the natural rhythm of the intestinal environment.

Microbial Dysbiosis

Clock disruption leads to an imbalance in gut bacteria, known as dysbiosis.

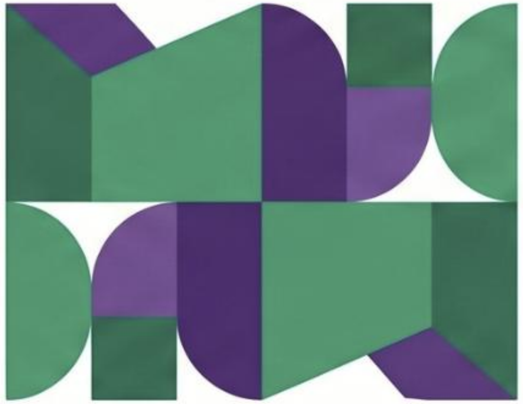
Impaired CRC Barrier

This microbial imbalance weakens the colorectal barrier, reducing the gut's natural defenses.

RISK & RESILIENCE

Increased Colorectal Cancer Risk

Night shift workers show altered microbiome composition and higher colorectal cancer rates.



Sleep Regularity Matters

Consistent sleep-wake cycles are an evidence-based strategy for supporting microbial resilience.

O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

Stress & Microbial Resilience: The Gut-Brain Connection

Chronic Stress Trigger

Psychological stress initiates the release of corticotropin-releasing factors throughout the body.

Altered Gut Function

Stress-induced factors lead to measurable changes in gut motility and increased intestinal permeability.

Stress Reduction Intervention

Targeted stress reduction is a promising method for stabilizing the gut-brain-microbiome interaction.

HPA Axis Disruption

The HPA axis mediates interactions that can result in stress-induced microbial dysblosis.

Microbial Resilience

Evidence-based strategies designed to protect the microblome from environmental and psychological stressors.

O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

Microbial Resilience: Emerging Environmental Exposures

Emerging evidence identifies specific environmental exposures—ranging from clinical interventions to pollution—that actively disrupt the gut microbiome. Understanding these drivers is essential for developing evidence-based strategies to support long-term microbial resilience.

CLINICAL & DIETARY DRIVERS

REPEATED ANTIBIOTIC USE

Identified as the strongest clinical driver of gut dysbiosis, requiring critical stewardship.

PROCESSED FOOD ADDITIVES

Specific emulsifiers are known to disrupt the mucosal microbiome.

ENVIRONMENTAL IMPACT

AIR POLLUTION CORRELATION

Exposure to air pollution is significantly associated with altered gut composition.

MICROBIAL RESILIENCE

The capacity of the microbiome to maintain or regain stability despite environmental stressors.

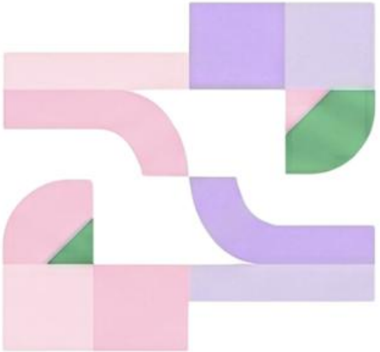
O'Keefe et al., Nat Commun 2015 · Fellows et al., Sci Adv 2024 · Donohoe et al., Cancer Discov 2014

The Evolution of Precision Microbiome Medicine

NOW: GOMS BIOMARKERS

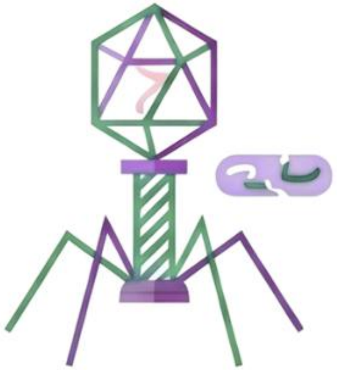
Gut OncoMicrobiome Signatures serve as predictive biomarkers for immunotherapy response stratification.

NEAR: NEXT-GEN FMT PROTOCOLS



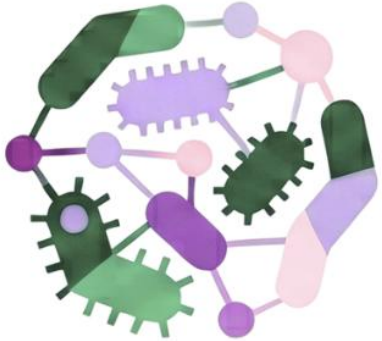
Refined fecal microbiota transplants are being tested to overcome immunotherapy resistance.

EMERGING: PHAGE THERAPY



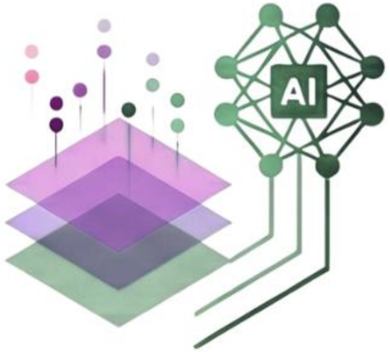
Bacteriophages are used to eliminate specific bacteria and restore chemosensitivity.

HORIZON: ENGINEERED MICROBIAL CONSORTIA



Synthetic biology creates precision-designed bacterial communities targeting specific oncogenic pathways.

FUTURE: AI + MULTI-OMICS INTEGRATION



Machine learning integrates microbiome data for individualized cancer risk prediction and prevention.

Thomas et al., Nat Rev Clin Oncol 2023 · Davar et al., Science 2021 · Ding et al., Cell Host Microbe 2025

The Cellular Health Perspective

FROM THE PATHOLOGIST'S LENS

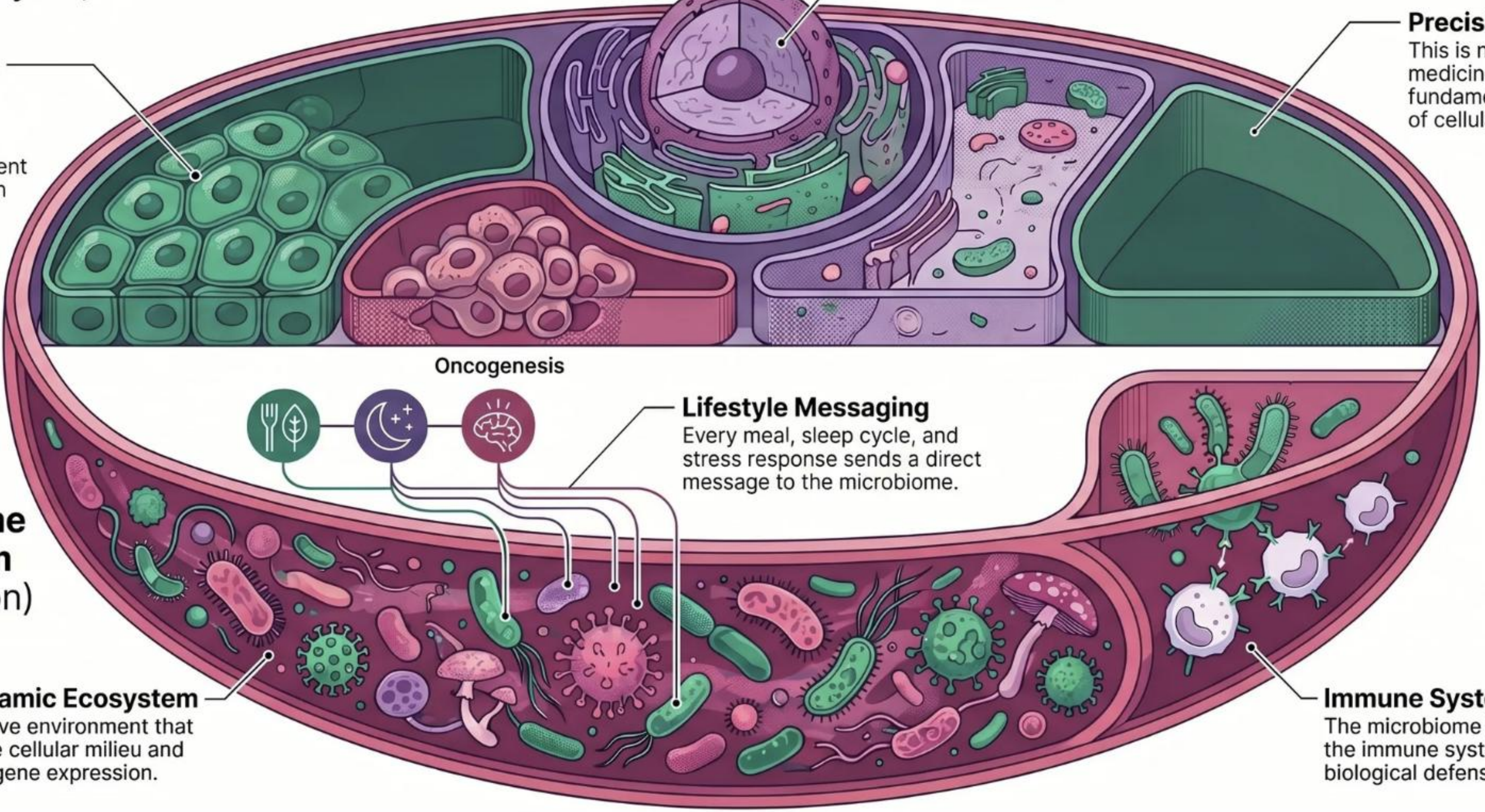
The Cellular Health Perspective

Cellular Architecture & Outcomes
(Internal Layers)

Resilience vs. Oncogenesis
The microbiome determines if the cellular environment tips toward health or disease.

Pre-Diagnostic Architecture
Cellular changes occur long before a clinical diagnosis is ever made.

Precision Biology
This is not alternative medicine; It is the fundamental science of cellular care.



Lifestyle Messaging
Every meal, sleep cycle, and stress response sends a direct message to the microbiome.

The Microbiome Ecosystem
(Foundation)

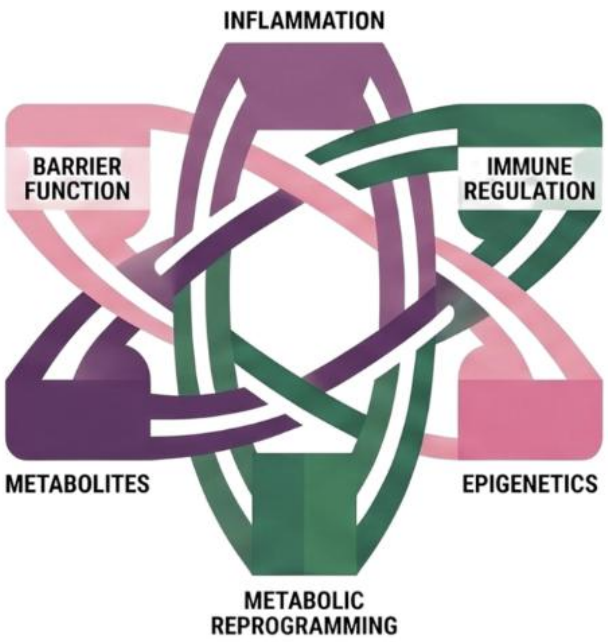
The Dynamic Ecosystem
A responsive environment that shapes the cellular milieu and regulates gene expression.

Immune System Training
The microbiome actively trains the immune system to maintain biological defense.

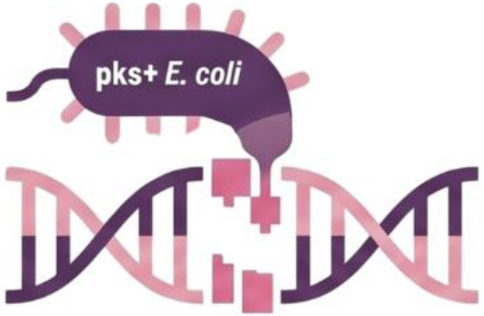
The Gut Microbiome: Clinical Takeaways

MECHANISTIC PATHWAYS & DISEASE LINKS

A Dynamic Organ with 6 Pathways



PATHOGENIC DRIVERS OF CANCER



Specific pathogens like *pks+ E. coli* produce colibactin, which physically writes mutations into human DNA.

THE ESTROBOLOME CONNECTION

Provides a mechanistic link between gut health and estrogen-sensitive cancers.

THE FUTURE OF CLINICAL INTERVENTION

PRECISION MEDICINE FRONTIERS

FMT, phage therapy, and next-gen probiotics are emerging as targets to improve immunotherapy response.

LIFESTYLE AS A CLINICAL INTERVENTION

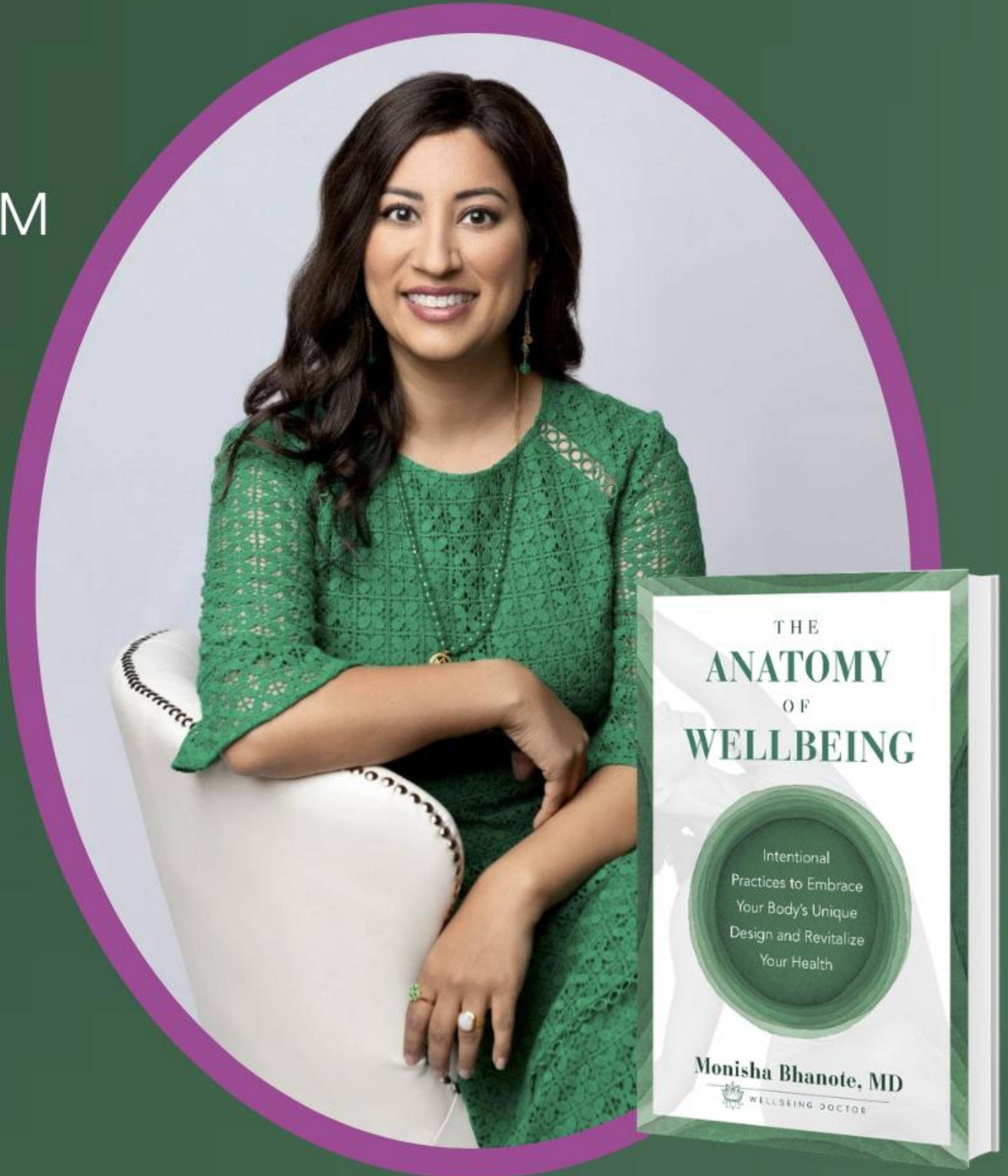
Diet, fiber, sleep, movement, and stress reduction function as direct microbiome interventions.

“Every Encounter Matters”

Patients deserve a microbiome conversation at every clinical encounter.

THANK YOU

DR. MONISHA BHANOTE, MD, FCAP, ABOIM



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