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A Short Communication: Dynamic Cell-Microbiome Crosstalk in Health

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ABSTRACT

Cells constantly engage with diverse microbial populations that inhabit the human body, collectively known as the microbiome. These microorganisms, including bacteria, viruses, and fungi, interact dynamically with host cells, influencing tissue behavior, metabolic processes, and immune regulation. This review discusses the multifaceted interactions between cells and microbiomes, highlighting the molecular signals, metabolic exchanges, and regulatory feedback loops that sustain tissue integrity and promote repair. We also explore the role of microbial metabolites in stem cell regulation, inflammatory modulation, and neuronal activity, emphasizing the significance of microbial balance for cellular homeostasis. The integration of these insights has implications for regenerative medicine, tissue engineering, and the development of microbiome-informed therapeutic strategies.

Keywords

Microbiome
Host cells
Tissue homeostasis
Stem cells
Metabolism
Inflammation
Regenerative medicine

INTRODUCTION

The human body hosts trillions of microorganisms, forming complex communities collectively referred to as the microbiome. These microbial populations inhabit various niches, including the skin, gastrointestinal tract, oral cavity, respiratory system, and urogenital tract, each with unique environmental conditions that influence microbial composition and activity [1,2]. Far from passive residents, these microbes engage in constant bidirectional communication with host cells, shaping cellular behavior and functional outcomes. The dynamic interplay between cells and microbial populations is essential for tissue stability, immune regulation, metabolic homeostasis, and overall health.

Host cells sense microbial signals through a range of mechanisms, including pattern recognition receptors, metabolic sensors, and epigenetic regulators. In response, cells modify local environments by secreting signaling molecules, antimicrobial peptides, or nutrients that influence microbial growth and composition. This reciprocal communication forms a feedback loop that maintains a delicate equilibrium between microbial diversity and host tissue function [3,4].

Cellular Responses to Microbial Signals

Epithelial cells, which line barrier tissues such as the gut and respiratory tract, are central players in mediating microbial interactions. These cells integrate signals from microbial metabolites, structural components, and secreted proteins to modulate barrier integrity, immune activation, and repair processes [5]. For instance, short-chain fatty acids (SCFAs) such as butyrate, acetate, and propionate, produced by commensal bacteria, serve as energy substrates for epithelial cells and regulate gene expression via histone modification and epigenetic mechanisms [6]. Butyrate, in particular, promotes epithelial proliferation and differentiation, contributing to the maintenance of gut barrier function.

Macrophages and dendritic cells also respond to microbial cues, adjusting their activation state and cytokine production. These cells not only neutralize pathogens but also convey microbial information to adaptive immune cells, promoting tailored immune responses while preventing excessive tissue damage [7,8]. The coordination between innate immune cells and epithelial barriers illustrates how microbial populations influence both immediate and long-term tissue health.

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Microbial Influence on Stem and Progenitor Cells

Microbial signals extend beyond mature differentiated cells, affecting stem and progenitor cell populations. In high-turnover tissues such as the intestinal lining, microbial metabolites regulate stem cell renewal and differentiation. SCFAs, microbial-derived amino acids, and secondary bile acids can modulate the proliferation rate and fate decisions of stem cells, thereby impacting tissue regeneration and resilience [9]. In addition, microbiome interactions influence stem cell niches by modulating extracellular matrix composition and local signaling networks, creating an environment conducive to tissue repair and functional homeostasis.

Inflammatory Modulation by Microbiomes

Immune regulation represents another dimension of cell-microbiome interactions. Specific microbial populations produce anti-inflammatory molecules that dampen excessive immune activation, thereby protecting tissues from chronic inflammatory damage [10]. Conversely, dysbiosis—an imbalance in microbial communities—can trigger pro-inflammatory pathways, leading to altered cellular proliferation, increased oxidative stress, and impaired tissue repair (Table 1). For example, changes in gut microbial composition have been associated with epithelial barrier dysfunction and systemic inflammatory responses, emphasizing the importance of balanced microbial populations for immune homeostasis [11,12].

Neuronal Interactions and Systemic Implications

Microbial metabolites also influence neuronal function and tissue-level signaling. Signals from the gut microbiome, including neurotransmitter precursors and SCFAs, can affect gut-brain communication, neurochemical signaling, and

Table 1: Examples of Key Microbial Metabolites and Their Cellular Effects.

Microbial Metabolite	Source Microbe	Cellular Target	Biological Effect
Butyrate	Clostridia spp.	Epithelial cells, stem cells	Energy substrate, histone modification, promotes differentiation
Acetate	Bacteroides spp.	Immune cells, epithelium	Regulates inflammatory cytokines, supports barrier integrity
Propionate	Firmicutes	Hepatocytes, immune cells	Modulates gluconeogenesis, suppresses inflammation
Secondary bile acids	Gut microbiota	Stem cell niches	Influences proliferation and differentiation
Indole derivatives	Lactobacillus spp.	Intestinal epithelium	Enhances barrier function, regulates xenobiotic metabolism

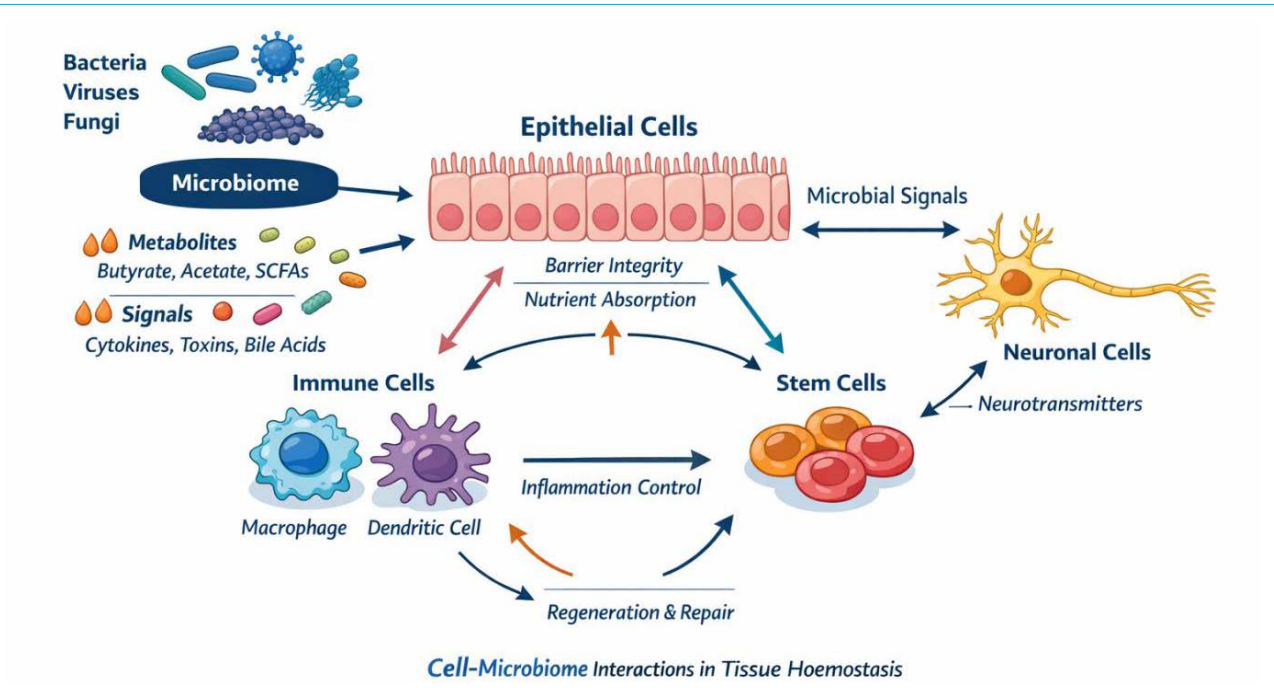

Figure 1: Overview of Cellular and Microbial Interactions in Tissue Homeostasis.

behavioral responses. Neuronal cells integrate microbial cues to modulate motility, secretion, and systemic physiological processes. This cross-talk exemplifies how microbial populations extend their influence beyond local tissue environments, participating in broader regulatory networks across multiple organ systems [13,14].

Applications in Tissue Engineering and Regenerative Medicine

Understanding cell-microbiome interactions has practical implications for tissue engineering and regenerative medicine. Incorporating microbial signals into in vitro culture systems can enhance stem cell proliferation, guide differentiation (Figure 1), and improve functional integration of engineered tissues [15]. By mimicking the natural microbial microenvironment, researchers can create more physiologically relevant tissue constructs with improved stability and regenerative potential.

Microbiome Dysbiosis and Cellular Dysfunction

Disruptions in microbial composition can profoundly affect cellular homeostasis. Dysbiosis may compromise barrier function, increase susceptibility to infection, and provoke chronic inflammation. Studies demonstrate that specific bacterial strains regulate gene expression in epithelial cells, modulate stem cell proliferation, and influence immune responses. Viral and fungal community members contribute additional regulatory signals, although their roles are less extensively characterized. The cumulative effect of microbial imbalance underscores the importance of maintaining a healthy microbiome for tissue stability and repair [16].

CONCLUSION

The intricate network of interactions between cells and microbial communities underpins tissue homeostasis, immune regulation, and cellular regeneration. Microbial metabolites, signaling molecules, and direct cellular interactions collectively shape cell behavior, supporting barrier integrity, stem cell renewal, and immune balance. Dysbiosis disrupts these networks, highlighting the importance of microbial equilibrium for maintaining tissue function. Integrating microbial cues into regenerative strategies and engineered tissue constructs offers promising avenues for enhancing tissue repair and resilience. Future research should focus on characterizing underexplored microbial signals and their systemic effects to leverage these interactions for therapeutic benefit.

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