


Chapter 5

Insights on the Role of the Microbiome in Influencing Cancer Risk: How Ecological Exposures Affect Microbiome in Influencing Cancer Risk


Joyjyoti Das

 <https://orcid.org/0000-0001-6238-7667>
Adamas University, Kolkata, India

Bandana Padhan

Adamas University, Kolkata, India


Anjali Sadhukhan

 <https://orcid.org/0009-0004-1540-2480>
Adamas University, Kolkata, India


Ritika Halder

Adamas University, Kolkata, India

Swetashree Purohit

 <https://orcid.org/0000-0002-2738-0782>
C.V. Raman Global University, India

Tania Aich

 <https://orcid.org/0009-0005-9203-6223>
Adamas University, Kolkata, India

ABSTRACT

The microbiome refers to the complex community of microorganisms dwelling in and on the human body. Especially, the gut microbiota is involved in modulating a host of crucial physiological processes such as immunity development, anabolism, and nutrient uptake. Diverse ecological exposures ranging from environmental pollutants to dietary components and infectious agents may influence the microbiome to either promote carcinogenesis by inducing chronic inflammation and producing toxic metabolites or exert anticancer effects by boosting the host immune response. This chapter accounts for the various exposomes and their role in influencing microbiome-mediated cancer risk, the mechanisms involved, and the various novel

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strategies that are being established by researchers for cancer prevention, early detection, and therapeutic interventions via the microbiome-alteration route. The role of advanced technologies such as metagenomics and NGS in enhancing the understanding of the microbiome-carcinogenesis crosstalk has also been discussed with the hope of fostering research in this domain.

1. INTRODUCTION

The human gut microbiota, a complex ecosystem of microorganisms, plays a fundamental role in human health by influencing various physiological processes, including digestion, immune system regulation, metabolic functions, and even mood and cognitive function (Hickman et al. 2024). Factors like diet, lifestyle, and antibiotic use significantly shape its composition, highlighting the importance of gut-friendly habits for overall well-being. The gut microbiota consists of a diverse community of microorganisms, including bacteria, viruses, fungi, and archaea. Furthermore, the gut microbiome supports immune system regulation by defending against harmful infections and promoting beneficial immune responses (Su and Liu 2021). Several factors can influence the diversity and stability of the gut microbiota, including diet, antibiotic use, stress, and lifestyle choices. Diet is a primary driver, with high-fat diets associated with reduced bacterial diversity and increased intestinal permeability (Hasan and Yang 2019). Antibiotic use can also disrupt the gut microbiota, leading to imbalances clinically termed as “Dysbiosis”, while stress and mental health issues are linked to reduced diversity and altered microbiome composition. Geographical location, genetics, and other lifestyle factors also contribute to the variations in gut microbiota composition among individuals (Ren et al. 2023).

Cancer cases worldwide are soaring high, with an estimated 20 million new cases reported in 2022 and predictions of over 35 million by 2050, primarily driven by population growth, aging, and lifestyle risk factors such as tobacco, alcohol, and obesity (Bray et al. 2024). Traditional treatments such as surgery, radiotherapy, and chemotherapy primarily target cancer epithelial cells but do not sufficiently address the tumor microenvironment and its complex interactions, which play a crucial role in cancer progression (Charmsaz et al. 2019). More importantly, the gut microbiota modulates responses to major anticancer therapies offering opportunities to improve therapeutic outcomes (Zhao et al. 2023a).

Gut dysbiosis, characterized by a less stable, diverse, and more pathogenic microbiota, contributes to pathological conditions, impacting cancer development and treatment. The disruption of the intestinal mucosal barrier may allow gut microbes to become intratumoral microbes, directly impacting cancer development (Zhao et

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