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Review

The vaginal and gastrointestinal microbiomes in gynecologic cancers: A review of applications in etiology, symptoms and treatment

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HIGHLIGHTS

- Dysbiotic gut and vaginal microbiota may be implicated in carcinogenesis, therapy-related side effects and treatment outcomes in gynecologic cancers.
- Changes in the microbiome following chemotherapy and radiation may impact patient quality of life and/or treatment outcomes.
- Further research is needed to determine optimal composition, function and efficacy of probiotics in reinstating mucosal homeostasis and barrier function.

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ABSTRACT

The human microbiome is the collection of microorganisms in the body that exist in a mutualistic relationship with the host. Recent studies indicate that perturbations in the microbiome may be implicated in a number of diseases, including cancer. More specifically, changes in the gut and vaginal microbiomes may be associated with a variety of gynecologic cancers, including cervical cancer, uterine cancer, and ovarian cancer. Current research and gaps in knowledge regarding the association between the gut and vaginal microbiomes and the development, progression, and treatment of gynecologic cancers are reviewed here. In addition, the potential use of probiotics to manage symptoms of these gynecologic cancers is discussed. A better understanding of how the microbiome composition is altered at these sites and its interaction with the host may aid in prevention, optimization of current therapies, development of new therapeutic agents and/or dosing regimens, and possibly limit the side effects associated with cancer treatment.

Contents

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1. Introduction

The human microbiome is the aggregate of microorganisms that reside in the body's mucosal surfaces [1]. These microbes help perform essential functions that include nutrient absorption, establishing/regulating the immune system, and protecting against pathogenic insults. These microbiota also occupy critical niches to prevent pathogen invasion. While these microbial communities populate all mucosal surfaces, the composition of each community varies from site to site within the body depending upon a myriad of host-derived factors (Fig. 1). These factors include available nutrients (e.g. diet), hormone levels, host genetics, race and age [1–3]. This core human microbiome can also be altered by cancer and cancer treatment, which may result in the variable human microbiome as depicted in Fig. 1.

Our knowledge of the human microbiome and its implications in health and disease has grown exponentially in recent years, largely due to advancements in sequencing technology and the establishment of the several international consortia to characterize and understand the role of the human microbiome in health and multiple types of diseases. The most common sequencing methods to characterize the microbiome are pyrosequencing and 16S ribosomal RNA (rRNA) sequencing [4]. The latter method relies on the identification f hypervariable regions in the 16S rRNA gene, which are unique from species to species. This method is advantageous because ribosomes and rRNA are present in all cells, and rRNA sequences are highly conserved. This method can also facilitate the identification of new or lesser-known bacterial species [5].

These sequencing methods have been used to characterize diverse microbial ecosystems, including the human microbiome. A healthy gastrointestinal (GI) microbiome is typically populated by five major bacterial phyla: *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, and *Fusobacteria*. These bacteria make up approximately 90% of the total microbiota in the gut (Fig. 2), although the relative abundance of GI microbiota may vary throughout the host's lifespan [6]. In contrast, a healthy vaginal microbiome is typically populated by members of the *Firmicutes* phylum (Fig. 2),dominated by *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus iners*, and *Lactobacillus jensenii* [1]. Similar to GI microbiota, the relative abundance of each of these bacteria may change over time [1].

The sequencing and characterization of GI microbiota have greatly expanded our understanding of how the human microbiome impacts the overall health of the host. For example, the GI microbiome supports functions that include immune system development, digestion, fat metabolism, epithelial homeostasis, enteric nerve regulation, and

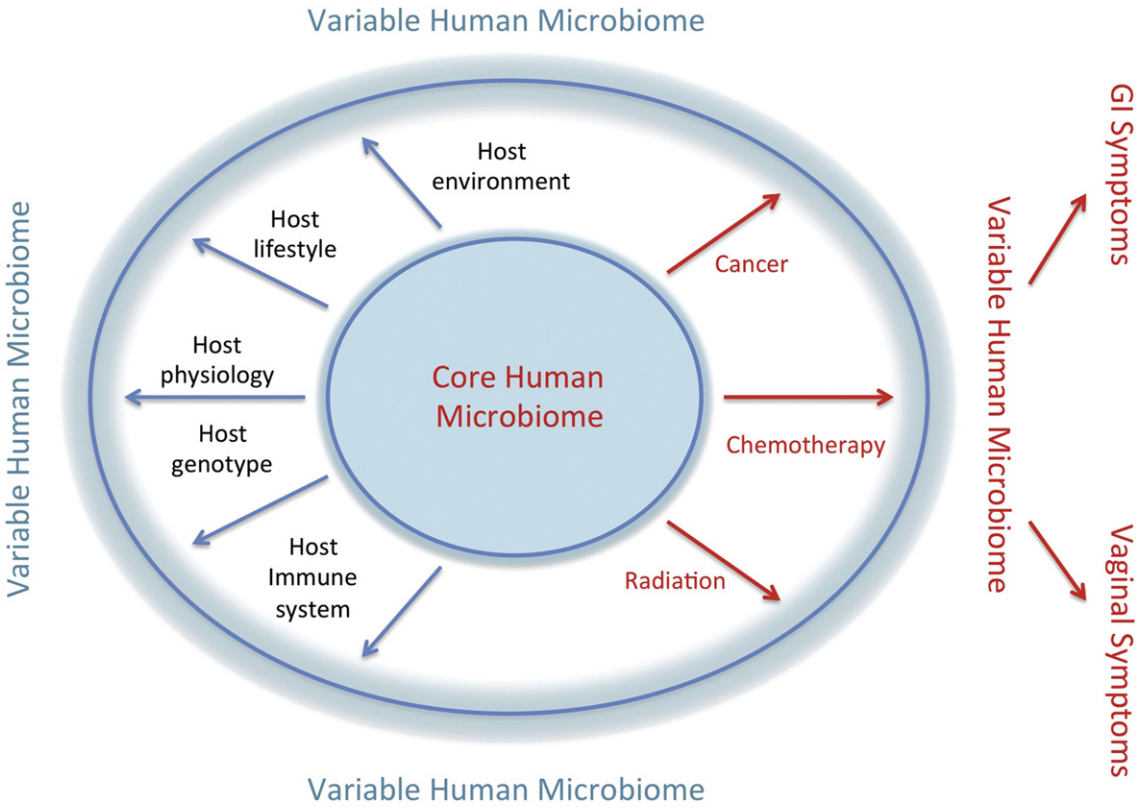

Fig. 1. The core human microbiome is variable, depending on a myriad of factors. These factors (blue) include host environment, lifestyle, physiology, genotype, and immune system. Other conditions (red) that can impact the microbiome composition include cancer, chemotherapy, and radiation treatment, all of which can contribute to GI and vaginal symptoms in cancer patients.