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Revisiting and Re-Considering Containment Discarded Reads from High-Throughput Approaches Aids Host-Microbiota Link in Various Diseases

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Short commentary

Numerous microbial communities reside in the human body, and it is feasible to consider the microbiota that resides in our gastrointestinal tract and other anatomical locations as a component of the environment to which we are continuously exposed at high doses throughout our lifespan [1-5]. However, during the past decade, the advent of meta-genomics, with meta-transcriptomics sequencing and metabolomic approaches along with targeted microbiota 16S rRNA sequencing have documented the diversity and relative abundance of microbes at different anatomical locations in the host body in a cultureindependent manner [3,6-12].

Moreover, previous studies by high-throughput methods showed that significant number of sequencing reads belonging to microbial origin, like microbial reads of Epstein-Barr Virus in stomach adenocarcinoma and Human Papillomavirus in cervical cancer were reported [13,14]. Studying the microbial composition of internal organs and their associations with diseases like cancer remains challenging, due to the difficulty of acquiring clinical biopsies, the highly variable composition of microbial community across host individuals, the majority of these microbes are commensal bacteria, which have been difficult to culture, and the role of the microbiome and bioactive microbiota-derived small molecules associated with induction of pathological changes limiting our understanding until recently. However, diversity shifts in tumor microbiota have been reported in a variety of cancers including cervical, lung, prostate, colorectal, and breast cancer [15]. Also, recent studies have shown that how members of the gut microbiota-gene

interactions and several virulent factors from pathogenic bacteria produce genotoxins which damage or mutate host DNA, are critical drivers for cancer pathogenesis [16-22]. Re-examining high-throughput data may discover distinct microbial signatures in various biospecimens like tissues and blood among and between different cancer types and can, therefore, be mined to increase understanding of host-microbe interactions in both healthy and diseased human tissues. Even, The Cancer Genome Atlas (TCGA) sequencing data of various malignancies can be integrated, reanalysis and offers significant potential to delineate host-microbiota mechanisms [23].

Therefore, re-considering containment reads from highthroughput approaches is crucial for understanding host-microbiota associations in diseases like cancer. These reads, often discarded as contaminants, may provide valuable insights into the intricate interactions between host and microbiota. Revisiting and conversely confirming by 16S rRNA sequencing will increase our understanding] these data can help identify overlooked microbial signatures and uncover their roles in disease mechanisms, progression, and therapeutic responses. By refining bioinformatics pipelines and integrating these reads into analyses, researchers can better characterize the complex hostmicrobiome ecosystem, potentially revealing novel biomarkers and therapeutic targets. This re-evaluation will enhance our understanding of disease etiology, to uncover disease-specific interactions and new mechanisms that contribute to both disease development and gut homeostasis and fosters precision medicine approaches tailored to individual microbiome profiles.

Authors are encouraged to delve into methodologies that enhance the precision of data obtained from high-throughput sequencing by focusing on improving containment read management. Future submissions could explore innovative strategies to refine data cleaning processes, improve sequence alignment, and correct for contaminant artifacts that currently pose challenges in microbiome research. This would not only increase the robustness of findings but also expand our understanding of how microbiota influences cancer and other disease states.

Potential areas of interest include

Developing advanced bioinformatics tools: Authors could focus on creating or optimizing software that better identifies contaminant reads for reanalysis from sequencing data and Comparative analyses of different containment read across various high-throughput platforms.

Integration of multi-omics approaches: Future manuscripts could explore the integration of metagenomics, meta-transcriptomics, and metabolomics to provide a holistic view of host-microbiota interactions, allowing researchers to validate containment reads more effectively.

Linking microbiome containment accuracy with clinical outcomes: Investigations that directly correlate improved containment reads with clinical insights into host-microbiota interactions, particularly in cancer, would be highly valuable. These studies can potentially identify novel microbial markers for diagnosis or targets for therapy. Such studies would provide valuable contributions to the field, offering fresh perspectives on refining data analysis from high-throughput approaches. Insights from these manuscripts could pave the way for developing novel diagnostic and therapeutic strategies that leverage the intricate relationships between the host and its microbiota. The potential of this research lies in its ability to reshape our understanding of how microbiota influences disease progression, therapeutic responses, and overall health.

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