Unravelling Nutrition-Gut Interactions: Integrating Human Gut Organoids with Organ-on-a-Chip Technology

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ABSTRACT

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INTRODUCTION

Human gut organoids, intricate three-dimensional models of human intestinal tissue, have become indispensable tools in the field of biomedical research. These versatile models effectively capture the complexity of the human gut, significantly advancing our understanding of gastrointestinal biology and disorders (Mengxian 2020). Their applications are broad and encompass disease modelling for conditions such as infectious diseases, colorectal cancer, and inflammatory bowel disease (Mengxian 2020). They serve as helpful resources for comprehending disease mechanisms and developing specialized therapies (Kathryn L 2018). Moreover, they play a pivotal role in drug development and discovery, in addition to disease modelling, by offering a precise representation of human physiology for high-throughput drug screening and toxicity assessment (Jun-Hwan 2019). Their utility has also been enhanced through their integration with gut-on-chip technology. These microfluidic systems can dynamically mimic interactions such as peristaltic motions and fluid flow, effectively replicating the gut environment (Shirin 2022). This enhancement significantly augments the physiological relevance of organoid cultures. Gut-on-chip technologies have evolved into valuable tools for elucidating complex host-microbiota interactions and disease modelling. This comprehensive approach contributes to a deeper understanding of gut biology and the substantial impact of microbial communities (Santiago 2018 and Trujillo et al.,2018). The incorporation of human gut organoids with gut-on-chip platforms holds particular significance when investigating microbiome-related disorders (Santiago 2018 and Guo et al., 2023). This combination advances the development of novel microbiota-targeted therapeutics and enhances our understanding of these diseases, ushering in a new era in medical research.

OBJECTIVES

The primary objective of this study is to harness the potential of integrating human organoids within organ-on-a-chip models to investigate nutrition-gut interactions comprehensively. This approach seeks to provide a deeper understanding of complex gastrointestinal diseases, with a particular focus on Environmental Enteric Dysfunction (EED). By utilizing patient-derived human organoids, we aim to demonstrate their capability to replicate human organs' structural architecture and physiological characteristics, thereby offering an unparalleled platform for studying human diseases. Additionally, we will confront the inherent challenges and limitations of this innovative approach, including establishing a suitable microenvironment, standardization protocols, cost-effectiveness considerations, scalability concerns, and managing inherent organoid heterogeneity.

METHODOLOGY

During endoscopy procedures on children under 10 years of age, we collected biopsy specimens, preserving them in ice-cold PBS. These biopsies were treated with a wash buffer containing antibiotics and fungizone to minimize contamination and subsequently rinsed thoroughly. The biopsy tissues were then sequentially agitated with PBS and EDTA solutions, leading to the dissociation of crypts, which could be observed under a microscope. Once approximately 30% of the crypts had dissociated, the biopsies were transferred to a second EDTA tube. Following EDTA treatment, the dissociated crypts were pelleted, embedded in Matrigel within 24-well plates, and supplemented with a growth medium, ensuring efficient crypt isolation and cultivation. After a few days, once the organoids had fully developed, they were cryopreserved in a freezing medium and stored in liquid nitrogen for future processing. These enteroids are intended to be introduced into microfluidic organ-on-a-chip devices, replicating the human physiological environment, particularly that of the gut. Our approach will facilitate real-time monitoring of cellular responses to various nutritional stimuli and microenvironmental changes using advanced imaging and analytical techniques. Additionally, high-throughput screening will be conducted to evaluate the effectiveness of therapeutic interventions for gut-related disorders.

CONCLUSION/RESULTS

The integration of human organoids into organ-on-a-chip models, in conjunction with gut-on-chip platforms, presents a highly promising avenue for advancing our understanding of nutrition-gut interactions. Our initial findings demonstrate the efficacy of this methodology in truly replicating the intricate dynamics of the gastrointestinal tract, enabling dynamic and precisely controlled experiments that bridge the gap between conventional 2D cultures and *in-vivo* studies. Moreover, the integration of high-throughput screening capabilities offers a robust platform for the rapid assessment of potential therapeutic interventions. This groundbreaking approach lays the foundation for personalized medicine applications within the realm of nutrition and gut health, marking the onset of a new era in experimental medicine. Ongoing research in this direction has the potential to revolutionize our comprehension of gastrointestinal physiology and expedite the development of precisely targeted therapeutic strategies for a spectrum of gut-related diseases and disorders. The synergy between human gut organoids and gut-on-a-chip platforms holds great promise for unravelling complex questions in gut biology and advancing healthcare solutions.

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