

Unveiling the Hidden Communication of Gut Bacteria to Improve Health

This project focuses on *Bacteroides fragilis* (*B. fragilis*), a gut bacterium that plays a dual role in human health. While most strains of *B. fragilis* help maintain a healthy gut and support the immune system, some harmful strains are linked to serious diseases like inflammatory bowel disease (IBD), colorectal cancer, and infections. The goal of this research is to understand how *B. fragilis* uses tiny molecules called small RNAs (sRNAs) to control its behavior, helping us find new ways to enhance its benefits and reduce its risks.

What Is This Research About?

B. fragilis communicates internally using sRNAs, which act as switches to turn specific genes on or off. These sRNAs help the bacterium adapt to changing conditions in the gut, interact with the immune system, and respond to stress. This project will explore these sRNAs to answer key questions:

- How do they help *B. fragilis* perform its beneficial functions?
- Why do some strains turn harmful under certain conditions?
- Can understanding these mechanisms lead to new treatments?

The research will focus on:

1. **Mapping sRNA Activity:** Creating a detailed map of all the sRNAs in both harmless and harmful strains of *B. fragilis*, especially when they are in gut-like environments.
2. **Understanding How sRNAs Work:** Exploring how these sRNAs interact with the bacterium's genes and proteins to regulate processes like nutrient absorption and immune modulation.
3. **Testing Effects on Health:** Studying how these RNAs influence the bacterium's ability to calm or trigger inflammation, focusing on molecules like IL-10 and TNF- α , which are critical for balancing immune responses.

Why This Research Matters

Gut bacteria are essential for health, influencing digestion, immunity, and even mental well-being. However, when the balance of these microbes is disrupted, it can lead to diseases. Despite its importance, *B. fragilis* is less studied than harmful bacteria like *E. coli*. Understanding how *B. fragilis* uses RNA to control its functions will fill this gap, offering new insights into gut health.

For example, non-harmful *B. fragilis* strains produce beneficial substances like short-chain fatty acids (SCFAs) and a molecule called PSA, which supports immune balance. Harmful strains, like enterotoxigenic *B. fragilis* (ETBF), produce a toxin that damages gut cells, causing inflammation and increasing the risk of cancer. By uncovering the role of sRNAs in these processes, researchers aim to identify ways to suppress harmful activities while preserving the bacterium's benefits.

What Can We Expect from This Work?

The study is expected to produce:

- A comprehensive map of the sRNAs in *B. fragilis*.
- Insights into how these sRNAs regulate the bacterium's functions.
- Evidence of how *B. fragilis* affects the immune system through RNA-based communication.

Ultimately, these findings could lead to innovative therapies for conditions like IBD, gut infections, and colorectal cancer. For example, treatments might target harmful behaviours of *B. fragilis* while preserving its health-promoting activities, improving gut microbiome balance and overall health. By uncovering the hidden language of gut bacteria, this research aims to redefine how we understand and manage gut health, offering hope for better treatments and a deeper appreciation of the microbes that live within us.