

LS18-053 - Targeting mucosal biofilms in patients with gastrointestinal disorders

Abstract

Our research project focused on gut biofilms and their contribution to chronic disorders such as Inflammatory Bowel Diseases (IBD, including Ulcerative Colitis and Crohn's Disease) and Irritable Bowel Syndrome (IBS). These disorders affect about 10-15% of the Western population, significantly reducing quality of life and leading to substantial socioeconomic costs.

What are Biofilms?

Biofilms are slimy layers of microorganisms, such as bacteria or fungi, that stick to surfaces. Biofilms provide protection to the microorganisms against a hostile environment. This includes protection against antibiotics and host defence mechanisms, making them difficult to remove.

Biofilms and Gut Health

The human gastrointestinal tract is densely populated with diverse microorganisms, forming the gut microbiota, which plays a critical role in digestion and overall health. While many gut microbes are free-floating, some can form biofilms. Our clinical study involving more than 1,100 patients found a high prevalence of gut biofilms in patients with IBS and IBD, suggesting a significant role for biofilms in these gut diseases. Biofilms were present in 57% of IBS patients and 34% of ulcerative colitis patients, compared to only 6% of healthy individuals.

Impact on IBS and IBD

IBS and IBD cause symptoms like abdominal pain, bloating, inflammation, and irregular bowel movements. Gut biofilms can interfere with gut functions and change the gut microbiota, contributing to these symptoms. Our research revealed that biofilm-positive patients have an imbalanced gut microbiota with reduced diversity, bacterial overgrowth supporting biofilm formation, and a reduced mucous layer that allows close interaction of bacteria with the gut epithelium, which can cause inflammatory responses.

Tying into Societal Challenges

IBS and IBD not only impact individual health but also pose societal challenges, including high healthcare costs, lost work productivity, and reduced quality of life. By focusing on the role of gut biofilms in these diseases, our research addressed a critical gap in understanding and managing these widespread conditions. Improving therapeutic strategies for IBS and IBD could alleviate the personal and economic burdens associated with these diseases, contributing to better public health outcomes.

Therapeutic Approaches

We demonstrated that jet-washing with water during colonoscopy can remove larger biofilms; however, this remains an invasive procedure. Therefore, we established the first patient-derived anti-gut-biofilm drug discovery program worldwide to develop new, less invasive treatments. Inspired by Nature, we pursued antimicrobial peptides from animals that naturally defend against biofilms, including frogs, cows, sheep and marsupials. This led to the discovery of therapeutic

leads capable of potentially inhibiting and eradicating gut biofilms. Medicinal chemistry was employed to enhance the gut stability, biofilm selectivity and safety of these leads towards new oral drug treatments that can prevent and remove gut biofilms without harming the beneficial gut microbiome.

Mid- to Long-Term Applications

Our research directly addressed gut health and could become a game-changer for millions suffering from biofilm-associated IBD and IBS. Understanding and controlling biofilms could further lead to advancements beyond gut health, such as in infectious disease management, medical device safety, and chronic wound care. This is expected to have a substantial impact on reducing healthcare costs and enhancing patient outcomes across multiple medical conditions.

Future Directions

We will continue refining our drug leads and test their effectiveness and safety. Our ultimate aim is to translate these findings into clinical applications to improve the lives of patients suffering from pathogenic biofilms, an unmet need in gut health. We will continue to raise awareness of gut biofilms in IBS and IBD patients, particularly in the medical field and patient communities, so new strategies can be developed to benefit patients affected by these challenging conditions.

Scientific disciplines:

Gastroenterology (40%) | Medicinal Chemistry (30%) | Medical microbiology (30%)

Keywords:

inflammatory bowel diseases (IBD); irritable bowel syndrome (IBS), bacterial gut biofilm, biomarkers, antimicrobial peptides, chemical biology, venom drug discovery, antibiotics, personalised medicine

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Further links to the persons involved and to the project can be found under
<https://www.wwtf.at/jpeto2.brunner.at/funding/programmes/ls/LS18-053/>