The gut microbiome is a complex ecosystem of microorganisms that predominantly colonize the large intestine. It is estimated that the human gut microbiome contains up to 100 trillion microorganisms - outnumbering human body cells. Their total mass can reach up to 2 kilograms, and their collective genome contains over 100 times more genes than the human genome. The microbiome consists primarily of bacteria, but also includes smaller populations of fungi, archaea, viruses, and protozoa. Each person harbors a unique microbial composition that begins to form at birth and usually stabilizes by the age of three.

Recent advances in microbiome research have highlighted its crucial role in both health and disease. Disturbances in microbial composition, known as dysbiosis, have been linked to the development of numerous chronic diseases. Growing evidence suggests that the microbiome may be involved in the pathogenesis of conditions such as Alzheimer's disease, Parkinson's disease, autism, diabetes, obesity, and depression. Recently, particular attention has been given to the role of dysbiosis in the development of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). These are chronic autoimmune conditions of the gastrointestinal tract, characterized by alternating periods of remission and flare-ups. Although they have been recognized for over a century, their exact causes and mechanisms remain largely unknown. Given the observed dysbiosis in IBD patients, it has been hypothesized that these diseases result from interactions between genetic predisposition, immune dysfunction, and an imbalanced gut microbiome. These factors may lead to an overactive immune response against intestinal microbes, triggering chronic inflammation of the intestinal mucosa.

Multiple clinical observations support this theory: improvements in patients following probiotic treatment, relapse after gastrointestinal infections or food poisoning, absence of inflammation in germ-free laboratory animals, and remission induced by fecal microbiota transplantation from healthy donors. However, most studies to date have focused primarily on bacteria and fungi, largely overlooking other important groups such as viruses and archaea. Additionally, there is a lack of data on how specific genetic variants influence microbiome composition and immune responses. Another challenge is that some patients do not respond to modern biological therapies, and the reasons for this resistance are still unclear.

The aim of the present project is to address these knowledge gaps through a comprehensive analysis of the gut microbiome - including bacteria, fungi, archaea, and viruses in adult patients with Crohn's disease and ulcerative colitis. The study will employ advanced molecular biology techniques, such as Nanopore sequencing and next-generation sequencing (NGS). Importantly, microbiological data will be integrated with genetic and immunological analyses. This integrative approach will help explain the complex interactions between the microbiome, host genetics, and the immune system in IBD pathogenesis, and will also shed light on their impact on the effectiveness of biological therapies, which are the standard of care for moderate to severe disease. A key goal is to determine whether a patient's microbial, genetic, and immune profile can predict their response to treatment.

The project will answer fundamental questions about IBD pathogenesis:

- Which microorganisms (including viruses, archaea, fungi, and bacteria) colonize the gut of IBD patients, and how does their composition differ from that of healthy individuals?
- Does the presence of specific microorganisms trigger the release of characteristic pro-inflammatory cytokines?
- Do certain genetic variants modulate immune responses and influence microbiome composition, disrupting the balance between host and microbes?
- How do these complex interactions affect the development of inflammation and the patient's response or resistance to biological therapy?

This project stands out due to its innovative and comprehensive approach to studying IBD. It not only integrates microbiological, genetic, and immunological analyses, but also includes the full spectrum of gut microorganisms, such as viruses and archaea, that have so far been largely overlooked in IBD research. The findings may form the foundation for developing personalized treatment strategies, improving therapeutic outcomes, and enhancing the quality of life for patients.