The role of the gut microbiota in the pathogenesis of plasma cell dyscrasias

Aim of the project

That project aims to search for differences in the gut microbiota of patients with neoplasms derived from plasma cells in the different stages of their development – from preneoplastic to symptomatic. The composition and functional potential of the gut microbiota will be compared with the gene expression profile of white blood cells, particularly pro-inflammatory genes.

Study description

The stool and blood samples will be collected at the time of diagnosis from patients with different stages of plasma cell dyscrasias (monoclonal gammopathy of undetermined significance, smoldering multiple myeloma, and symptomatic multiple myeloma). Additionally, the same biological material will be collected from regular healthy microbiota donors in the gut microbiota bank - Human Biome Institute – who will constitute the control group. The stool samples will be characterized regarding the microflora composition and its functional potential using the next-generation sequencing (NGS) in the *shotgun sequencing* method. In the NGS method, the blood samples (isolated white blood cells) will be assessed based on their gene expression profile (mainly immune-related genes) with transcriptomics.

Why is this project important?

The gut microbiota constitutes all the organisms living within the gut, such as bacteria, viruses, fungi, and eucaryotes. In recent years, science provided much evidence on the role of these organisms in human health and disease. The first findings show that not only does the gut microbiota changes because of administered treatment, but it is also significant for the initiation of the disease.

Plasma cell dyscrasias are a group of diseases derived from plasma cells, which are mature B cells that produce antibodies. The most common disease in that group is multiple myeloma. The pathway leading from the normal plasma cells to neoplastic type is a continuum – from the most benign forms (monoclonal gammopathy of undetermined significance) to more malignant (smoldering multiple myeloma) and finally to the symptomatic multiple myeloma. The symptoms of the disease result from the neoplastic clone of plasma cells producing the one type of antibody or only its part in significant amounts. We know that apart from the genetic changes, the environmental factors, although not fully elucidated so far, play a role in developing the disease.

One of the biggest human immune system centers is the intestinal lymphoid system, in which approximately 70% of all immunocompetent cells reside. This is the site where the stimulation between the microbes and the immune system conditioning the immune system's pro or anti-inflammatory "mode" occurs. Insights show that at least in part of patients, the loss of diversified gut microbiota and overgrowth of one species of bacteria leads to "mirroring" that process in the plasma cells which can initiate the neoplastic process. That has not been yet thoroughly researched. Elucidating the role of the gut microbiota on the neoplastic processes, particularly regarding the neoplasm directly deriving from the immune system, has got the fundamental meaning for understanding the development of oncological diseases and the impact of the gut microbiota on the continuum of changes leading to the cells' transformation.

Expected results

We hypothesize that the gut microbiota's changed composition and the functional potential impact the development of the immune system's pro-inflammatory "mode", resulting in the initiation and propagation of neoplastic processes in the example of a continuum of the diseases constituting plasma cell dyscrasias. Therefore, we expect a lowering of the gut microbiota biodiversity, changes in the species composition with the elimination of microorganisms having an anti-inflammatory character, accumulation of antibiotic-resistant genes, and abnormal metabolic pathways in the patients diagnosed with plasma cell dyscrasias compared with healthy counterparts. Furthermore, the quantitative and qualitative collection of differences in mentioned parameters along with the progression of the disease is expected.