BUTYRATE-PRODUCING BACTERIA AMELIORATE CRC TUMORIGENESIS THROUGH MODULATION OF IMMUNE RESPONSES

BUTYRAT-PRODUZIERENDE BAKTERIEN VERBESSERN DIE TUMORGENESE VON DARMKREBS DURCH MODULATION VON IMMUNREAKTIONEN

LUBOR BORSIG
Institute of Physiology
University of Zurich

MICHAEL SCHARL
Department of Gastroenterology and Hepatology
University Hospital Zurich

KEYWORDS - INTESTINAL MICROBIOTA, COLORECTAL CANCER, MELANOMA, BUTYRATE-PRODUCING BACTERIA, MICROBIOTA THERAPY

SCHLAGWÖRTER – INTESTINALE MIKROBIOTA, DICKDARMKREBS, MELANOM, BUTYRAT-PRODUZIERENDE BAKTERIEN, MIKROBIOTA-THERAPIE

SUMMARY

Recent data demonstrate that cancer patients feature an altered intestinal microbiota composition that causatively might contribute to cancer pathogenesis and affect responses to anti-tumor therapy in colorectal carcinoma (CRC) and melanoma patients. Several studies showed a major structural imbalance of the intestinal microbiota in CRC patients towards a reduction of butyrate producers and an increase of opportunistic pathogens. This is of great interest, since we have recently demonstrated that oral administration of a mix of four butyrate producers is able to ameliorate the onset of colon tumors in mouse models in vivo via modulating the intestinal/intratumoral immune cell composition.

Based on that knowledge, our overall hypothesis is that targeted transplantation of a specific and well-defined intestinal microbiota consortium consisting of four butyrate producers induces immune cell infiltration into tumors and a distinct immune composition within the tumors turning them immunogenic. We aim to identify a novel microbiota-based therapeutic approach for the treatment of cancer. We plan (1) to study the functional role of butyrate producing bacteria in mouse models of CRC and (2) to investigate their immune effects.

To achieve those goals, we will use well-defined mouse as well as a broad number of biosamples from CRC and melanoma patients. We will study the effects of butyrate-producing bacteria on development of colorectal tumors in vivo. We will use colon tumor (MC38 cecum injection and APCmin/cdx2CRE ERT mice) mouse models and orally administer the butyrate producers in a preventive and a therapeutic setting and study whether the bacteria affect tumor development. We will investigate whether butyrate-producing bacteria affect immune responses in tumors from mice and in CRC patient specimens.

We will translate our findings into the human setting and study the connection between certain bacteria and immune cell compositions in human samples. We will define the mechanism how the intestinal microbiota modulates immune and therapy responses in CRC patients and specifically identify a “responder” microbiome in CRC patients. Within this project we will elucidate whether a targeted microbiota therapy using four butyrate-producers might be a promising approach for personalized cancer therapy as a precision medicine approach in humans by modulating the immune system. If successful, the proposed project might have a tremendous impact on how we treat cancer patients.