THE ROLE OF THE GUT MICROBIOME IN IMMUNOTHERAPY RESPONSE: LESSONS FROM AN URUGUAYAN COHORT

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Abstract

Monoclonal antibodies that target immune checkpoints have revolutionized cancer medicine and therapeutics. Drugs targeting the cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) and the programmed death 1/programmed death ligand 1 (PD-1/PD-L1) axis have transformed the management of a variety of advanced cancers. Recently, a role of the gut microbiome in modulating immunotherapy response has been identified. Human microbiome is highly influenced by environmental factors, the host lifestyle and the geographic region. Efforts to understand the role of the microbiome in cancer immunotherapy on a local scale are needed to incorporate this knowledge in the clinic. We recruited 25 patients (melanoma, renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), and head and neck squamous cell carcinoma (HNSCC)) and we aimed to characterize the microbial population before and after starting immunotherapy. Using shotgun metagenomics and culture based tools we profiled the microbial composition of our uruguayan cohort. Using a healthy cohort as a reference (n = 68) we compared the relative abundance of different microbial populations, gene families and metabolic pathways in both cohorts. The microbial composition of the oncologic cohort differs from that of the healthy control. Our results show higher relative abundance of *Enterococcus faecium* and *Klebsiella pneumoniae* in the gut of oncologic patients as compared to healthy individuals. In addition, data from several studies previously obtained in other parts of the world were used to identify putative microbial biomarkers associated with immunotherapy response. We found no single microbial feature associated with immunotherapy response. Using culture-based techniques, we began the first Uruguayan microbial biobank from the gut microbiome. We speculate that these results can be used in the future to fuel the development of new clinical interventions.