Influence of microbiota on the effectiveness of immunotherapeutic drugs in the treatment of metastatic solid tumors

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Tumor cells use immune checkpoint pathways to evade the host's immune system. The use of immune checkpoint inhibitors can suppress this signal. This type of therapy can be an effective strategy for the treatment of patients with solid metastatic tumors. However, the outcome of immunotherapy is difficult to predict and it is ineffective for many patients. Gut microbiota is shown to be one of factors leading to the success of therapy.

In this study we used reads of 16S rDNA obtained from 71 cancer patients. To assess the taxonomic diversity we used two different pipelines: dada2 and Qiime2. As a result of dada2 workflow, ASV were obtained, analyzed using the phyloseq package and normalized with the Deseq2. Qiime2 output is an OTU table, the data of which is already normalized. We performed alpha-diversity analysis based on the Shannon diversity index and beta-diversity analysis using Bray-Curtis distance, Jaccard index, UniFrac and rarecurve. Profiling of predictive gut microbiota was analyzed by using three different types of linear regression, and random forest methods. The dependent variables in these models were the presence or absence of progress and type of objective response.

As a result we found that the microbiota of patients with different types of response to therapy does not differ in either the alpha or beta diversity of the community. The use of machine learning methods allowed us to build a model that can predict the treatment outcome. Analysis of the most influential predictors of the model reveals about 5 taxa for which correlations with the success of therapy are already known. However, the list of predictors is not reproducible when using a different set of methods.