Changes of microbiome profile during nivolumab treatment in NSCLC patients.

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Abstract

Background:
Immune Checkpoint Inhibitors (ICIs) are improving the survival of cancer patients, however only the 20-30% of treated patients present long term benefits. Hence in the context of multiple treatment possibilities, the identification of predictive markers of response and toxicity is a challenging approach for drug selection in order to obtain the best clinical benefit. The changes occurring in the microbiota composition has been proposed as a mechanism potentially influencing the response and the toxicity to immunotherapy.

Methods:
The microbiome composition was studied in an age-matched control-case study of 11 patients affected by non-small cell lung cancer (NSCLC) treated with Nivolumab versus 11 healthy controls (CTRLs). The stool samples of NSCLC patients were collected at cycle 1, 3 and 5. The microbiome analysis was performed by targeted-metagenomics of the 16S rRNA locus (V3-V4 region) on an Illumina MiSeq Platform. Non-parametrical statistical analyses were performed to assess microbial OTUs distribution and a- and b-diversity indexes were computed to describe the microbial ecology

Results:
Microbiota meta-taxonomy was described for the NSCLC patients versus CTRLs and at each time-course of the Nivolumab treatment (C1-C5). In NSCLC patients Rikenellaceae, Prevotella, Streptococcus, Lactobacillus (p < 0.05), Bacteroides plebeius, Oscillospira, Enterobacteriaceae (p < 0.05) appeared increased compared to CTRLs. Not responders had Ruminococcus bromii, Dialister, Sutterella more abundant than responder patients to therapy (p < 0.05). Slightly increased in responders appeared Akkermansia muciniphila, Bifidobacterium longum and Faecalibacterium prausnitzii (p < 0.05). Propionibacterium acnes, Veillonella, Staphylococcus aureus, Peptostreptococcus appeared significantly over-expressed, while Clostridium perfringens was significantly reduced at the C1 compared to the C3 time-point of the treatment.

Conclusions:
Nivolumab seems to influence the microbiome composition during treatment. Moreover our data confirm significant role of specific gut microbiota bacteria in influencing cancer development and response to immunotherapy.

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