Abstracts

HIGH FIBER DIET MODIFIES GUT MICROBIOME, PROPIONATE PRODUCTION, INTRATUMOR IMMUNE RESPONSE AND IS ASSOCIATED WITH OUTCOME IN PATIENTS WITH LUNG CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS

Corentin Richard*, Myriam Berlafauci, Omar El Ouazzani, Khoudia Diop, Antoine Desilets, Julie Malo, Wiam Belkaid, Andréanne Leblanc, Julien Lamontagne, Meriem Messaoudene, Anwilla Ekrief, Bertrand Routy. CRCHUM, Montreal, Canada

Background The gut microbiome plays a key role in immune checkpoint inhibitors (ICI) efficacy and several strategies are currently being investigated to improve microbiome composition. The impact of a specific diet on microbiome modulation and clinical outcomes remains unknown. In this study, we assessed the effects of a high fiber diet on clinical outcomes as well as on microbiome composition, production of fecal metabolites, and intratumor immune infiltration in metastatic non-small cell lung cancer (mNSCLC) patients amenable to ICI.

Methods In this prospective study, 39 chemotherapy-refractory or naive patients with mNSCLC treated with ICI alone or in combination with chemotherapy completed a validated dietary survey. Based on the total fiber intake, patients were divided into high vs low fiber groups (HF vs LF). Objective response rate (ORR), progression-free survival (PFS) and overall survival (OS) were compared between both groups. In addition, fecal and tumor samples were collected prior to ICI initiation. Fecal metagenomic sequencing was performed and fecal short-chain fatty acids (SCFA) were measured by LC-MS/MS. Tumoral transcriptome profiling was performed through RNA sequencing to define differentially expressed pathways.

Results Baseline characteristics were well balanced between both groups, including body mass index (BMI) and PD-L1 status. Median PFS for the HF group was longer compared to the LF group (27.4 vs 12.6 months). Microbiome metagenomic profiling revealed a higher baseline alpha diversity (p=0.048) in the HF group compared to the LF group. Bifidobacteriaceae, Alistipes, and Bacteroides salsae were enriched in the HF group while Fusobacterium was overrepresented in the LF group. SCFA measurement revealed that a high level of propionate correlated with a significantly longer OS (not reached vs 18.4 months, p=0.02) in the entire cohort. Moreover, propionate levels were significantly higher in the HF vs LF group (p=0.02). At the tumor level, RNA sequencing demonstrated a downregulation of DNA repair mechanisms and an upregulation of humoral and adaptive immune responses in the HF group.

Conclusions In this study, we demonstrated that a HF diet in patients with mNSCLC was associated with better clinical outcomes. Importantly, HF was associated with an enrichment of previously reported beneficial gut bacteria. Moreover, propionate correlated with longer OS and was increased in the HF group. This study provides further insights into how the diet can beneficially shift the microbiome composition and intratumor immune responses in patients with mNSCLC treated with ICI and this may lead to novel, dietary-gearered therapeutic avenues in the oncomicrobiome arena.

Ethics Approval The study was approved by CRCHUM Institution’s Ethics Board, approval number 17.035.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0679

680 AUTOMATED ION TORRENT BASED SOLUTION ENABLES ACCURATE GUT MICROBIOME QUANTIFICATION OF BACTERIAL SPECIES RELEVANT TO RESEARCH IN CANCER AND ITS RESPONSE TO IMMUNOTHERAPY


Background A low-cost targeted solution to profiling gut microbial diversity is sequencing of the 16S rRNA gene; however, it is often insufficient to gain species level resolution due to high homology across different bacteria. Therefore, we developed a first-of-its-kind targeted sequencing solution that supplements 16S gene targets, with highly species-specific primers for a cohort of 73 bacteria associated with research in diabetes, cancer and its response to immunotherapy,
gastrointestinal and auto-immune disorders. This assay performs at 100% sensitivity and specificity for the species-level detection (Ion AmpliSeq Microbiome Health Research Kit: www.thermofisher.com/ngsmicrobiome) of these bacteria and is hence better suited for gut microbiome profiling in the context of the above phenotypes, as compared to other existing solutions.

Methods To assess the utility of the panel in cancer immunotherapy research, we sequenced DNA from 15 stool samples from subjects with Non-Small Cell Lung Carcinoma (NSCLC) undergoing immunotherapy, and compared their microbiome profiles to 26 healthy stool samples collected internally. With our post-sequencing workflow on Ion Reporter™, we automatically generate a report with taxonomic classifications, sample diversity metrics through QIIME2 integration, and relative abundance visualizations for bacteria across multiple samples.

Results We identified significant microbiome composition differences between the healthy samples and cancer/treated samples, as evidenced by (i) a clear separation between the two cohorts based on a beta diversity principal coordinate analysis (PCoA) plot, driven by large abundance changes in Clostridium, Lachnoclostridium, Subdoligranulum and Oscillibacter (P < 0.05), (ii) grouping into distinct classes based on overall microbiome profiles (Analysis-of-Similarities ANOSIM P = 0.003), and (iii) differences in abundances of specific bacteria with anti-tumor effects such as F. prausnitzii (P = 0.02).

Conclusions We have created a highly multiplexed, sensitive and specific assay for robust characterization of gut microbiota, with compatibility on both (i) the Ion GeneStudio S5™ with a 48-hr sample-to-result turnaround, and (ii) the new Ion Genexus™ System, a fully integrated platform featuring a hands-off, automated sample-to-report workflow that delivers results in a single day. It enables an efficient and affordable means for conducting extensive analyses of the human microbiome having applications in the study of phenotypic variability, and the potential relationship to disease. For research use only. Not for use in diagnostic procedures.

REFERENCE

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0680