IECs, loss of TM9SF4 impaired epithelial barrier functions by promoting inflammation, elevating ER stress, oxidative stress and consequently contributing to apoptotic deaths. For macrophages, more colonic infiltration of macrophages was observed in TM9SF4 KO mice than in WT mice. Besides, TM9SF4 facilitated clearance of apoptotic cells by colonic macrophages, enhanced monocytes polarization into proinflammatory M1 macrophages while suppressed M2 macrophages polarization in vitro and in vivo.

Conclusions Our studies suggested that TM9SF4 in intestinal epithelial cells and macrophages may act in coordinated ways to exert its anti-inflammatory role in IBD.

IDDF2021-ABS-0065

THE TUMOR IMMUNOLOGICAL CHARACTERIZATIONS OF COLON ADENOCARCINOMA REVEAL CLINICALLY RELEVANT POPULATION-SPECIFIC DIFFERENCES

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Background Immunomodulation has become a topical area of interest in many tumors, being colon adenocarcinoma (COAD), not an exception. Considering the molecular heterogeneity of COADs and their non-immunogenic character, immunotherapy only showed a viable role in a certain subset of COADs. This study aimed to determine immune subtypes (ISs) of COADs for the selection of suitable patients from an extremely heterogeneous population.

Methods Gene expression profiles and corresponding clinical information were collected from TCGA and GEO databases, respectively. Consensus clustering analysis was performed to identify the ISs. Immunogenomics methods were integrated to characterize the immune environment of each IS subtype. Linear discriminant analysis was conducted to establish an immune subtyping characteristic index (ISCI) for IS classification of COADs. Co-expression network analysis was used for detected hub genes. DAVID was used for functional annotation.

Results Based on 17 prognostic immune characteristics, COADs were stratified into three ISs characterized by differential molecular, cellular and clinical features. Patients with the IS1 tumor had immune 'hot' and immunosuppressive phenotype, IS3 tumor had immune 'hot' phenotype, whereas those with the IS2 tumor had immune 'cold' phenotype. Patients with the IS1 tumor had the worst disease-free survival

Abstract IDDF2021-ABS-0065 Figure 1

Abstract IDDF2021-ABS-0065 Figure 2

compared with the other IS types, while those with the IS3 tumor had the best prognosis. Moreover, the proportion of highest adenomatous polyposis coli (APC) mutations in IS2 subtype is significantly higher than that in the IS1 and IS3; the proportion of TP53 mutations in IS1 subtypes were significantly higher than IS2 and IS3; while the proportion of KRAS mutations in IS1 subtypes were significantly lower than IS2 and IS3. IS3 subtype is predicted more sensitive to Cisplatin than other ISs, while IS1 is predicted more sensitive to 5-FU. Furthermore, the ISCI developed based on immune subtypes of COADs revealed immune infiltration degree in individual patients and can be utilized to determine the IS of patients with COAD.

Based on 17 prognostic immune characteristics, COADs were stratified into three ISs. Patients with the IS1 tumor had the worst disease-free survival compared with the other IS types, while those with the IS3 tumor had the best prognosis (IDDF2021-ABS-0065 Figure 1, IDDF2021-ABS-0065 Figure 2, IDDF2021-ABS-0065 Figure 3, IDDF2021-ABS-0065 Figure 4). The proportion of highest adenomatous polyposis coli (APC) mutations in IS2 subtype is significantly higher than that in the IS1 and IS3; the proportion of TP53 mutations in IS1 subtypes were significantly higher than IS2 and IS3; while the proportion of KRAS mutations in IS1 subtypes were significantly lower than IS2 and IS3 (IDDF2021-ABS-0065 Figure 5, IDDF2021-ABS-0065 Figure 6). Moreover, distinct

Abstract IDDF2021-ABS-0065 Figure 3

Abstract IDDF2021-ABS-0065 Figure 4

Abstract IDDF2021-ABS-0065 Figure 5

Abstract IDDF2021-ABS-0065 Figure 6

molecular, cellular and clinical features were observed among different IS tumors: patients with the IS1 tumor had immune 'hot' and immunosuppressive phenotype, IS3 tumor had

immune 'hot' phenotype, whereas those with the IS2 tumor had immune 'cold' phenotype (IDDF2021-ABS-0065 Figure 7, IDDF2021-ABS-0065 Figure 8, IDDF2021-ABS-0065 Figure 9,

Abstract IDDF2021-ABS-0065 Figure 7

Abstract IDDF2021-ABS-0065 Figure 8

Abstract IDDF2021-ABS-0065 Figure 9

Abstract IDDF2021-ABS-0065 Figure 10

IDDF2021-ABS-0065 Figure 10). IS3 subtype is predicted more sensitive to Cisplatin than other ISs, while IS1 is predicted more sensitive to 5-FU (IDDF2021-ABS-0065 Figure 11). Furthermore, the ISCI developed based on immune subtypes of COADs revealed immune infiltration degree in indi-

vidual patient and can be utilized to determine the IS of patients with COAD (IDDF2021-ABS-0065 Figure 12, IDDF2021-ABS-0065 Figure 13). Specifically, high ISCI level is correlated with high CTLA4, PDCD1 and CD274 (PD-L1) expression (IDDF2021-ABS-0065 Figure 14), and the ISCI

Abstract IDDF2021-ABS-0065 Figure 11

Abstract IDDF2021-ABS-0065 Figure 12

Abstract IDDF2021-ABS-0065 Figure 13

Abstract IDDF2021-ABS-0065 Figure 14

Abstract IDDF2021-ABS-0065 Figure 15

level of the partial response (PR)/complete response (CR) group is significantly lower than of stable (SD) and progressive disease (PD) group (IDDF2021-ABS-0065 Figure 15).

Conclusions The immune subtyping and ISCI system are indicative for the prediction of tumor prognosis of COADs. Identification of immune subtypes may facilitate the optimal selection of COAD patients responsive to adequate therapeutic strategies.

IDDF2021-ABS-0066 ANTIOXIDANTS-RICH SUPPLEMENTS INCREASE FAECALIBACTERIUM ABUNDANCE IN GUT MICROBIOTA

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Background Antioxidants are becoming a popular type of dietary supplement. We believe a further understanding of the role of the gut microbiota in the health benefits of antioxidants could be gained from comparing the changes in gut microbiota composition and strain abundances from taking different sources of antioxidants.

Methods We recruited 120 volunteers and randomly divided them into 4 groups of 30 receiving grape seed extract (GSE), berries juice, vitamin E (VE), and amylopectin (placebo). Stool samples were collected at baseline after 3 months of intervention, and after 3 months of washout period for

metagenomic sequencing and analysis. Contig assembly and alignment were done using 4644 reference genomes to calculate relative abundance and annotate KOs for each strain. Associations between intervention, phases, and changes in bacterial relative abundance and functions were evaluated with paired Wilcoxon rank-sum test and McNemar's test for those strains with very low relative abundance.

Results We first analyzed the influence of the placebo vs. the whole antioxidants group. Shannon diversity and richness of the gut microbiota were not significantly different among the phases for both the placebo and the antioxidants group. Forty strains had significantly changed relative abundance in the antioxidants group ($p < 0.05$), among which 13 were Faecalibacterium strains. Intervention-induced changes persisted after the washout period for a small number of strains. Then we investigated the similarities and differences among the three sources of antioxidants. Changes in relative abundances of butyric acid producers were found in both the juice and the VE group, while inflammation, tumor, and insulin resistance-related bacteria Dorea formicigenerans, Fusobacterium nucleatum, and Enterobacter cloacae had lower, lower, and higher relative abundance in the GSE group. Furthermore, Faecalibacterium strains had higher relative abundance in all three groups.

Conclusions Through a long-term intervention study in humans, we found that although the sources of antioxidants did not alter the overall characteristics of the gut microbiota, each of them affected a unique set of bacteria strains, and the SCFA producer Faecalibacterium were increased in all three groups.