Fecal microbiota, serum biomarkers, diet and lifestyle: colorectal cancer risk and prognosis.

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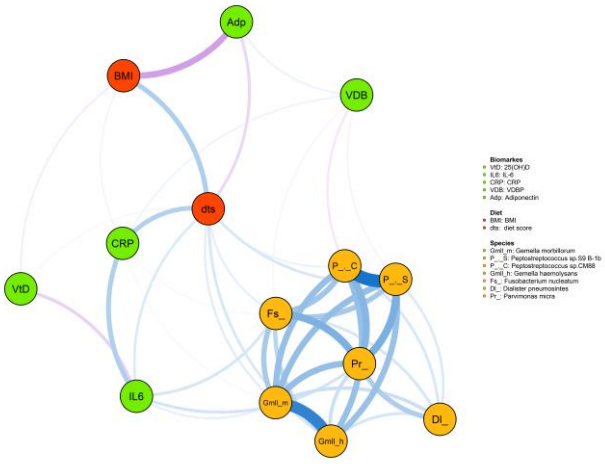
Previous pooled analyses identified reproducible microbiome biomarkers able to predict Colorectal Cancer. Functional analysis of microbiome outlined the important role of diet.
We designed a prospective case-control study of 34 colorectal cancer (CRC) patients and 33 age matched-controls to investigate microbiota composition, circulating biomarkers of inflammation, diet and lifestyle. For metagenomic analysis, genomic bacterial DNA was isolated from feces of CRC patients and healthy donors. The V5-V6 hypervariable regions of 16S rRNA gene were amplified and sequenced.
We found that CRC was associated with high BMI (P=0.02), low physical activity (P =0.006), regular alcohol consumption (P =0.005) and smoking (P=0.005) and a diet poor in fatty fish and rich in carbohydrate (P=0.003) and we built a risk score based on this risk factors. CRC were also significantly more deficient in vitamin D (P=0.04) and had lower adiponectin (P =0.002) and higher markers of inflammation: for high sensitivity C-reactive protein (hs-CRP) and Interleukin-6 (IL-6) respectively P =0.01 and P =0.03.



We found a microbiome signature related to CRC and to a diet poor in fatty fish and rich in carbohydrates.
The markers of inflammation IL-6 and hs-CRP significantly inversely correlated with Vitamin D, positively with BMI and the lifestyle risk score that are inversely associated with adiponectin. The strongest correlation with *F. nucleatum*, and other species associated with CRC microbiome, was found with the risk score and markers of inflammation.
We combined microbiome data with serum biomarkers and lifestyle variables by employing the Data Integration Analysis for Biomarker Discovery (DIABLO). This allowed us to discriminate between the CRC and healthy controls by a block sPLS-DA supervised model. We found that the microbiome dataset contributed the most to the separation between the groups, followed by the serum biomarkers and the lifestyle variables. The diet and BMI were able to identify cases whereas controls were better classified by Vitamin D and adiponectin.
Lastly, several species and families were found associated with lymph-nodes involvement, pT and relapse free survival (Log-rank P=0.03). Multivariable models including *F. nucleatum*, Vitamin D and Adiponectin identify CRC with an area under the ROC curve that patients ranged from 80-90% after cross-validation and reached similar values predicting recurrence. Altogether, this study shows the significant role of microbiota, inflammatory biomarkers, diet and lifestyle with CRC.