

The microbiome in tumor tissue and adjacent mucosa from colorectal cancer patients

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Dysbiosis of bacterial and fungal communities in the bowel has been associated with inflammatory diseases and cancer. Since most of the studies deal with the luminal samples of the gut content, we focused on the microbes closely associated with the mucosa. We collected samples of colorectal cancer tissue and adjacent non-affected mucosa from 125 patients and processed them for sequencing of 16S rRNA and ITS1 genes for bacterial and fungal microbiota profiling, respectively. In the biopsies from CRC patients, we have also investigated relative telomere length (RTL), general and oxidative DNA damage.

We evaluated the relationships among DNA damage, RTL and microbiota/fungi, as analysed in intestinal mucosa and CRC tumors. Tumor-associated microbiota was enriched with potential pathogens, such as genera *Fusobacterium*, *Treponema*, *Campylobacter* and *Selenomonas*, whereas adjacent tissue exhibited increased relative abundance of order Bacteroidales and genera *Blautia*, *Faecalibacterium*, *Odoribacter* and *Dorea*. Tumor tissue was markedly resided by fungal genera *Pseudopithomyces* and *Peniophora*, suggesting environmental origin. Stratification to gastrointestinal tract compartments showed that tumor tissues from the left side of the colon and rectosigmoideum had the highest relative abundance of genus *Fusobacterium* and *Streptococcus*, respectively. Genus *Selenomonas* was significantly and specifically enriched in the tumor tissue from the right side of colon. We found marked positive correlation of genus *Parvimonas* with *Peptostreptococcus* ($r=0.85$, $p=7.6 \times 10^{-15}$), *Campylobacter* ($r=0.82$, $p=4.6 \times 10^{-13}$), *Dialister* ($r=0.55$, $p=4 \times 10^{-5}$) and *Fusobacterium* ($r=0.54$, $p=5.4 \times 10^{-5}$) in adjacent tissue. Whereas we found the only significant difference in RTL between tumors (shorter RTL) and adjacent mucosa, there was no association with either localization or microbial settlement. Interestingly, the levels of both general and oxidative DNA damage were significantly higher in tumor tissues than in adjacent mucosa

Colorectal cancer-associated dysbiotic microbiome differs between colon compartments, and certain genera, such as *Fusobacterium*, *Campylobacter*, *Parvimonas* and *Selenomonas* have potential to improve colorectal cancer detection.