

## **Dietary fat content is crucial to modulate tumor-related gut integrity and circulating microbiome in colorectal cancer**

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### **Background:** (max 50 words)

In colorectal cancer (CRC), a correct diet could be crucial to contain tumor-related dysbiosis and gut damage. We investigated the effect of different dietary fat content on changes in the circulating microbiota as a result of gut dysbiosis and altered mucosa permeability in a CRC mouse model (AOM/DSS) and patients.

### **Methods and Results:** (max 100 words)

CRC-mice fed a standard, high-fat (HFD) or low-fat (LFD) diet were sacrificed at early and late time points. Glycobiology, histochemical analysis, and quantification of specific permeability markers showed that HFD-fed CRC-mice colon was highly inflamed, with a prevalence of carboxylated-acidic glycans and a reduction of mucus-secreting cells in the glandular crypts, thus affecting the mucosa permeability. After circulating microbiome quantification by ddPCR, distinct bacterial taxa were identified through 16SrRNA sequencing in association with different diets and CRC stages, most of which are commonly associated with the gastrointestinal/oral tract. Preclinical data were validated in 43 CRC patients subjected to dietary questionnaires.

### **Conclusions and Significance:** (max 50 words)

Our translational study showed that circulating microbial load and composition during CRC development are influenced by different dietary fat content and may be related to an alteration of gut permeability and the inflammation induction. These findings could be relevant to improve therapeutic approaches and to set-up novel non-invasive CRC screening.

**Keywords:** colorectal cancer, microbiome, diet, gut permeability, circulating biomarkers

**References:** (max 5 relevant references from the Authors in the following format:

*full authors list, title, year, journal, vol.: pages)*

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