

Fusobacterium nucleatum promotes autophagy-mediated chemoresistance in patients with colorectal cancer

Subject Code: H16

With the support by the National Natural Science Foundation of China, a collaborative study by the research groups led by Prof. Fang Jingyuan (房静远) from the Division of Gastroenterology and Hepatology, RenJi Hospital, School of Medicine, Shanghai Jiao Tong University and Prof. Weiping Zou from the Department of Surgery, University of Michigan School of Medicine, demonstrated the gut microbiota may modulate chemotherapeutic efficacy, and *Fusobacterium* (*F.*) *nucleatum* abundance has been linked to a shorter survival in patients with colorectal cancer, which was published in *Cell* (2017, 170: 548–563).

Gut microbiota are linked to chronic inflammation and carcinogenesis. Chemotherapy failure is the major cause of recurrence and poor prognosis in colorectal cancer patients.

Their group investigated the effects of *F. nucleatum* on chemotherapy. *F. nucleatum* was present at higher levels in tissue from patients with recurrent colorectal cancer compared with non-recurrent colorectal cancer and adjacent normal tissue. Furthermore, the amount of *F. nucleatum* was an independent predictor of colorectal cancer aggressiveness and could predict recurrence. RNA-sequencing of colon cancer cells cocultured with *F. nucleatum* showed an enrichment of genes involved in autophagy, and coculturing colorectal cancer cells with *F. nucleatum* induced autophagy, which was associated with chemoresistance. Mechanistically, *F. nucleatum* targeted TLR4 and MYD88 innate immune signaling and specific microRNAs to activate the autophagy pathway and alter colorectal cancer chemotherapeutic response. Thus, *F. nucleatum* orchestrates a molecular network of the Toll-like receptor, microRNAs, and autophagy to clinically, biologically, and mechanistically control colorectal cancer chemoresistance. Measuring and targeting *F. nucleatum* and its associated pathway will yield valuable insight into clinical management and may ameliorate colorectal cancer patient outcomes.

Their findings indicate that *F. nucleatum* may promote chemoresistance in patients with colorectal cancer, suggest that anti-*F. nucleatum* therapies may potentially prevent chemoresistance in patients with colorectal cancer.

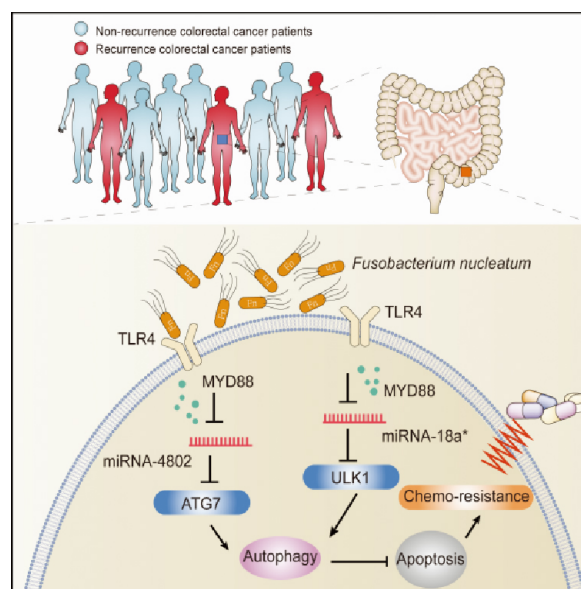


Figure *F. nucleatum* promote chemoresistance in colorectal cancer patients.