

## Colon cancer: a bacterium which obstructs chemotherapy

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*A study reports that a bacterium called *Fusobacterium nucleatum* helps colon cancer cells to resist chemotherapy medications and contributes to cancer recurrence.*

### CHEMORESISTANCE: THE IMPORTANCE OF THE CELLULAR ENVIRONMENT

The **resistance** of cancer cells to chemotherapy medications remains one of the principal barriers to cancer treatment and a major cause of the mortality linked to this disease. The cancer cells have an incredible ability to adapt to the presence of these medications, for example by producing certain proteins which expel the medications outside the cells, thus preventing them from causing damage, or else by deleting certain genes which usually force the cell to kill itself (apoptosis) when the medication manages to succeed in entering the cell

The microenvironment present in the proximity of the cancer cells also plays a very important role in the acquisition of this chemoresistance. For example, the cellular damage caused by chemotherapy provokes the recruitment of certain immune cells (macrophages) which secrete different growth factors that can favour the survival of tumor cells. Studies have also documented that certain cells of the bone marrow, specialized in suppression of the immune response, are activated following chemotherapy. The large-scale arrival of these suppressive cells in the proximity of the tumor creates a molecular shield which reduces the anti-cancer immunity and thus permits the cancer to survive the chemotherapeutic medicines.

### PROCANCEROUS BACTERIA

The microenvironment of the cells which line the intestinal mucosa contains another factor which cannot be ignored: the hundreds of billions of bacteria which reside within the digestive system, principally within the colon. Some recent studies suggest that the intestinal microbiome could participate in the development of colorectal cancer; analysis of stool samples from colon cancer patients shows a disequilibrium in the intestinal microbiome composition, with important increases in the bacterial species which generate inflammatory molecules. One of these bacteria, *Fusobacterium nucleatum*, seems to be particularly important because it is present in



significant quantities near the cancerous cells of the colon and its abundance is directly correlated with the stage of the tumor. Currently available data suggest that the bacterium does not cause cancer *per se*, but that the pro-inflammatory conditions which it provokes ensures that cells which have acquired a cancerous mutation will profit, thanks to this bacterium, from a microclimate that is favorable for their progression to a mature cancer.

### BACTERIAL BOOST

Results recently published in the very prestigious journal *Cell* indicate that *F. nucleatum* can also play an important role underlying disease recurrence in patients treated for colorectal cancer<sup>1</sup>. By analyzing the bacterial composition of cancerous tissues removed from patients who had been diagnosed with colorectal cancer, the researchers originally noted that the levels of *F. nucleatum* were much higher in tissues from patients who had cancer recurrence and that the presence of this bacterium was correlated with both the aggressiveness of the cancer and with poor prognosis. A more powerful analysis revealed that the bacterium activated autophagy in the cancerous cells, which permitted them to recycle molecules and to thus avoid the unleashing of cellular death by apoptosis, which is normally provoked by chemotherapy.

This discovery could have important repercussions for the treatment of colorectal cancer. For one thing, measuring the levels of *F. nucleatum* in patients treated by chemotherapy could improve the medical care of patients by rapidly identifying those who are at greater risk of recurrence. In addition, the importance of this bacterium in the resistance to chemotherapeutic agents allows us to consider whether a neutralizing antibiotic for this bacterial species could improve the effectiveness of current treatments. One more victory in our battle against cancer!

<sup>(1)</sup> Yu T et al. *Fusobacterium nucleatum* promotes chemoresistance to colorectal cancer by modulating autophagy. *Cell* 2017;170:548-563.