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Butyrate, a postbiotic of intestinal bacteria, affects pancreatic cancer and gemcitabine response in in vitro and in vivo models

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer. The characteristic excessive stromatogenesis accompanying the growth of this tumor is believed to contribute to chemoresistance which, together with drug toxicity, results in poor clinical outcome. An increasing number of studies are showing that gut microbiota and their metabolites are implicated in cancer pathogenesis, progression and response to therapies. In this study we tested butyrate, a product of dietary fibers' bacterial fermentation, whose anticancer and anti-inflammatory functions are known. We provided in vitro evidence that, beside slowing proliferation, butyrate enhanced gemcitabine effectiveness against two human pancreatic cancer cell lines, mainly inducing apoptosis. In addition, we observed that, when administered to a PDAC mouse model, alone or combined with gemcitabine treatment, butyrate markedly reduced the cancer-associated stromatogenesis, preserved intestinal mucosa integrity and

affected fecal microbiota composition by increasing short chain fatty acids producing bacteria and decreasing some pro-inflammatory microorganisms. Furthermore, a biochemical serum analysis showed butyrate to ameliorate some markers of kidney and liver damage, whereas a metabolomics approach revealed a deep modification of lipid metabolism, which may affect tumor progression or response to therapy. Such results support that butyrate supplementation, in addition to conventional therapies, can interfere with pancreatic cancer biology and response to treatment and can alleviate some damages associated to cancer itself or to chemotherapy.

Keywords: Butyrate; Gemcitabine response; Microbiota; Pancreatic cancer.

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