P11 & FP - **Gemcitabine chemotherapy shapes microbiota promoting pro-inflammatory state of pancreatic cancer xenografted mice.**

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Background: Pancreatic ductal adenocarcinoma (PDAC) represents the fourth cause of cancer-related death.
Objective: We aimed to evaluate whether gemcitabine treatment shapes the gut microbiota in a model of PDAC xenografted mice.
Methodology: Pancreatic cancer xenograft mice were subjected to gemcitabine injection once per week for three weeks to assess the tumor volume as compared to control mice injected with normal saline solution. The composition of fecal microbiota, the activation of NF-kB pathway in cancer tissues and the serum metabolomics were further analyzed.
Results: Gemcitabine considerably decreases the proportion of Gram- positive Firmicutes (from about 39 to 17%) and the Gram- negative Bacteroidetes (from 38 to 17%) which are the two dominant phyla in the gut of tumor-bearing control mice. This downshift was replaced by an increase of Proteobacteria (Escherichia coli and Aeromonas hydrophila) from 15 up to 32% and Verrucomicrobia (Akkermansia muciniphila) from 5 to 33% in the gut of drug-receiving mice. An overall increase in inflammation-associated bacteria was observed upon gemcitabine. Consistently, activation of the NF-kB canonical pathway was found in cancer tissues from gemcitabine-treated mice. Serum metabolomics revealed a significant decrease of the purine compounds inosine and xanthine, and a decreasing trend for their metabolically-related molecule hypoxanthine.
Conclusions / Implications for practice: Understanding chemotherapy side effects may explain the lack of activity or the chemoresistant processes and it may help to set up strategies to improve the effectiveness of therapy.

References

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