Changes in the microbiome during treatment with chemo-immunotherapy in patients diagnosed with pancreatic ductal adenocarcinoma: A prospective study.

Background: Pancreatic ductal adenocarcinoma (PDAC) is the most common neoplastic disease of the pancreas. Chemotherapy is the standard first-line treatment for PDAC, however, recent research has identified that bacteria in the human gut microbiome may influence patient response to chemotherapy. These bacteria are also present in faeces, and are thought to be representative of the bacteria in the pancreatic ductal system. Preliminary studies have shown patients with advanced PDAC demonstrate lower levels of Firmicutes bacteria, and higher levels of Proteobacteria, compared to patients with less advanced PDAC. Additionally, studies have confirmed bacteria belonging to the Firmicutes phylum possess several anti-cancer properties that can improve patient treatment response. Furthermore, Gammaproteobacteria, which belong to the Proteobacteria phylum, have been shown to attenuate gemcitabine efficacy and worsen patient treatment outcomes.

Aim: This study aimed to prospectively investigate the effect of anti-cancer treatment on the human gut microbiome.

Method: This study involved 14 individuals with locally advanced PDAC. Participants received various combinations of Gemcitabine and Nab-Paclitaxel (chemotherapy), and durvalumab (immunotherapy). Gut microbial profiling was completed on patient stool samples taken at baseline (before treatment) and 12 weeks into their treatment using PacBio HiFi full-length 16S rRNA sequencing.

Results: 16S rRNA sequencing identified that after 12 weeks of treatment, 9/14 patients demonstrated an increase in the relative abundance of Firmicutes, with 8 of these patients receiving chemotherapy and immunotherapy. Of the 5 patients who presented with a decrease in their abundance of Firmicutes, 4 patients showed a decrease of less than 10%. Additionally, 9/14 patients also demonstrated a decrease in their relative abundance of Proteobacteria, with 8 of these patients receiving both chemotherapy and immunotherapy. 5 patients showed an increase in their level of Proteobacteria, 4 of which displayed an increase of less than 10%. 7/14 participants showed both an increase in their abundance of Firmicutes and a decrease in Proteobacteria.

Conclusion: This study revealed co-administration of chemotherapy and immunotherapy has a potential beneficial effect on the human gut microbiome through an increase in Firmicutes, and a decrease in Proteobacteria. Manipulation of the microbiome may have the potential to improve patient response to treatment.

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Presenting Author Biography:
Andrew trained in Liverpool, UK, and became a Fellow of the Royal Australian College of Physicians in 1993. He established palliative care services at Sir Charles Gardiner and SJG Hospitals in Perth. In 2006, he transitioned to medical oncology, now leading the Department of Medical Oncology at SJG Subiaco. His expertise includes gastrointestinal and gynaecological cancers, and he is an active researcher in international clinical trials, focusing on pancreatic, lung, and ovarian cancers.

Additional Information:
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