The Impact of Microbiome on Diagnostic and Therapeutic Theranostics in Gastroentero-pancreatic Neuroendocrine Tumors (GEP-NETs)

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Abstract

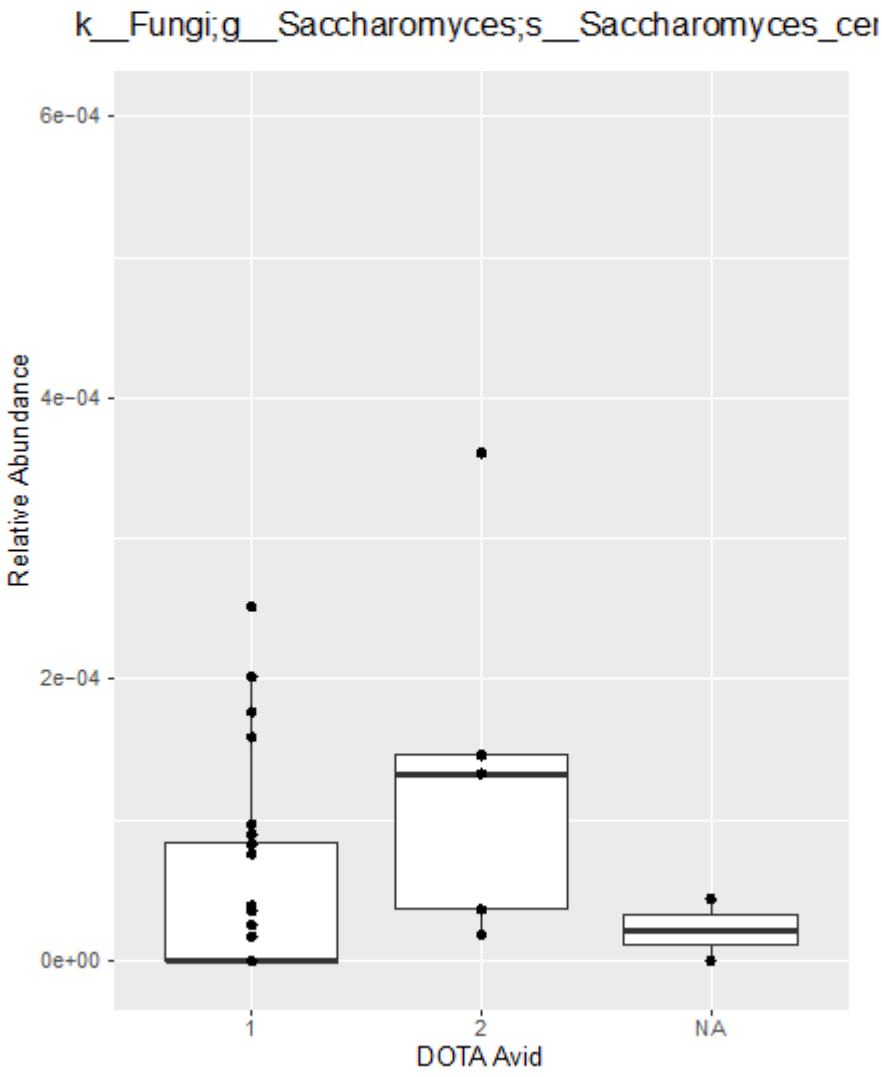
Background: Gut microbiome balance has a key role in human health and is linked to a variety of diseases, including cancer. In this study, we analyzed the impact of gut microbiome (both fungal and bacterial species) alterations on PET-Gallium 68 (PET-Ga68) avidity and PRRT (Peptide Receptor Radionuclide Therapy) response in patients with metastatic gastroenteropancreatic neuroendocrine neoplasms (GEP-NETs).

Methods: Oral and fecal samples were collected and matched with healthy control samples using linear regression models. After control confounding factors (Age, sex, race, previous therapies, and somatostatin expression for PRRT response), differences in microbiome profiles between those who have PET-Ga68 avid versus non-avid imaging studies, and between responders versus non-responders to PRRT were performed. All tests are two-sided and *P*-values ≤ 0.05 were considered statistically significant.

Results: Gut samples of 31 patients (11 males, 20 females, median age 65 years) with metastatic GEP-NETs (24 small bowel, and 7 pancreatic) were analyzed. All patients had baseline PET-Ga68 and 16 patients who were refractory to somatostatin analogues (SSAs) received PRRT in the second line setting. Our data showed that patients who had weak or didn't express somatostatin on PET-Ga68 had significant relative increase in abundance of fungi (notably Saccharomyces and Taphrinaceae species) compared to those who had strong homogenous somatostatin expression (p=0.05 and 0.09 respectively), (Figure 1A, B). Regarding PRRT, patients who either progressed during treatment or within 3 months of last therapy had significantly enriched fungi (mainly Candida species), (p=0.03) compared to responders who had more bacterial species (Aggregatibacter Segnis) (p=0.05), (Figure 2A, B).

Conclusions: This is the first study to analyze the correlation between microbiome environment with somatostatin expression and PRRT response in patients with GEP-NETs. There were significant differences supporting the role of the gut microbiome in GEP-NETs and need to be validated in future clinical trials.

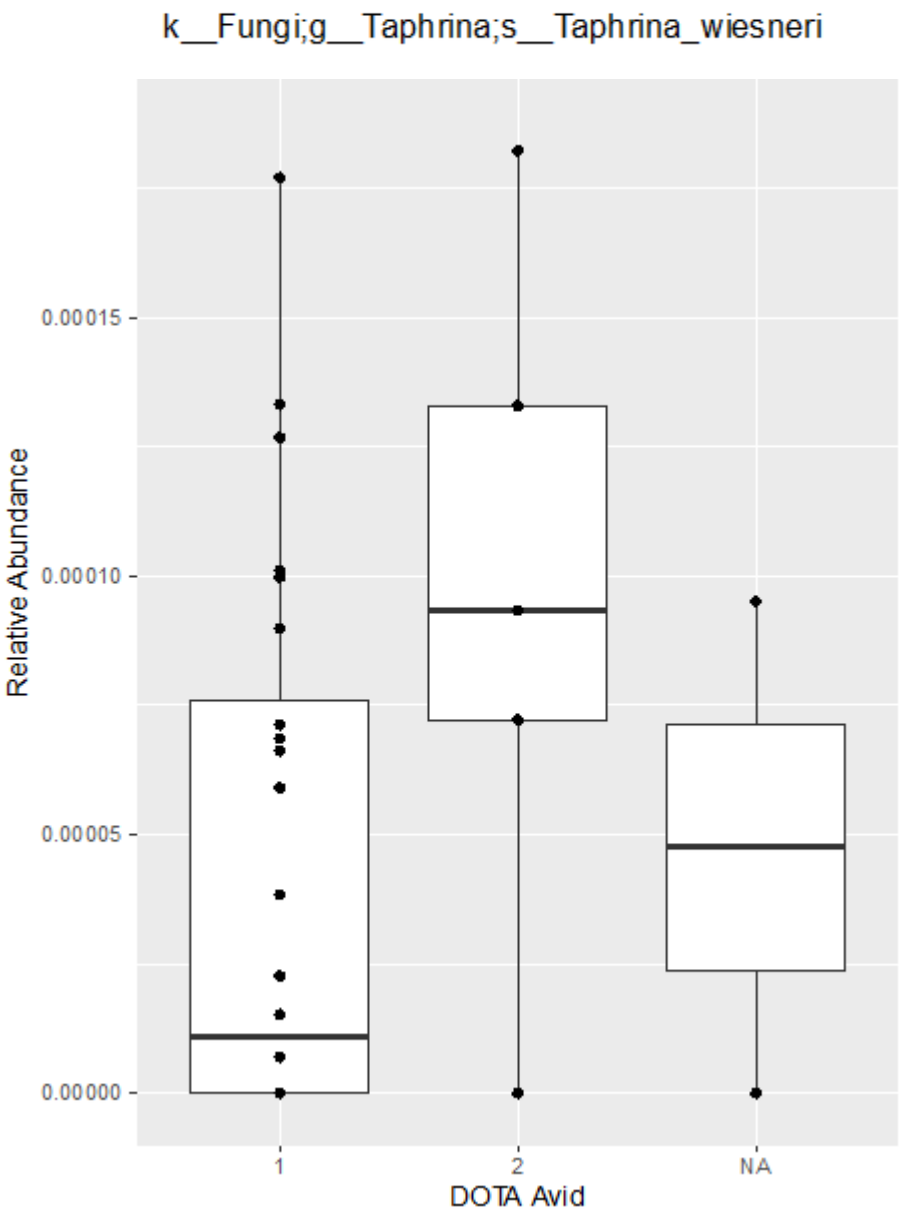
Figure.1



1: PET-Ga68 avid

2: PET-Ga68 non-avid

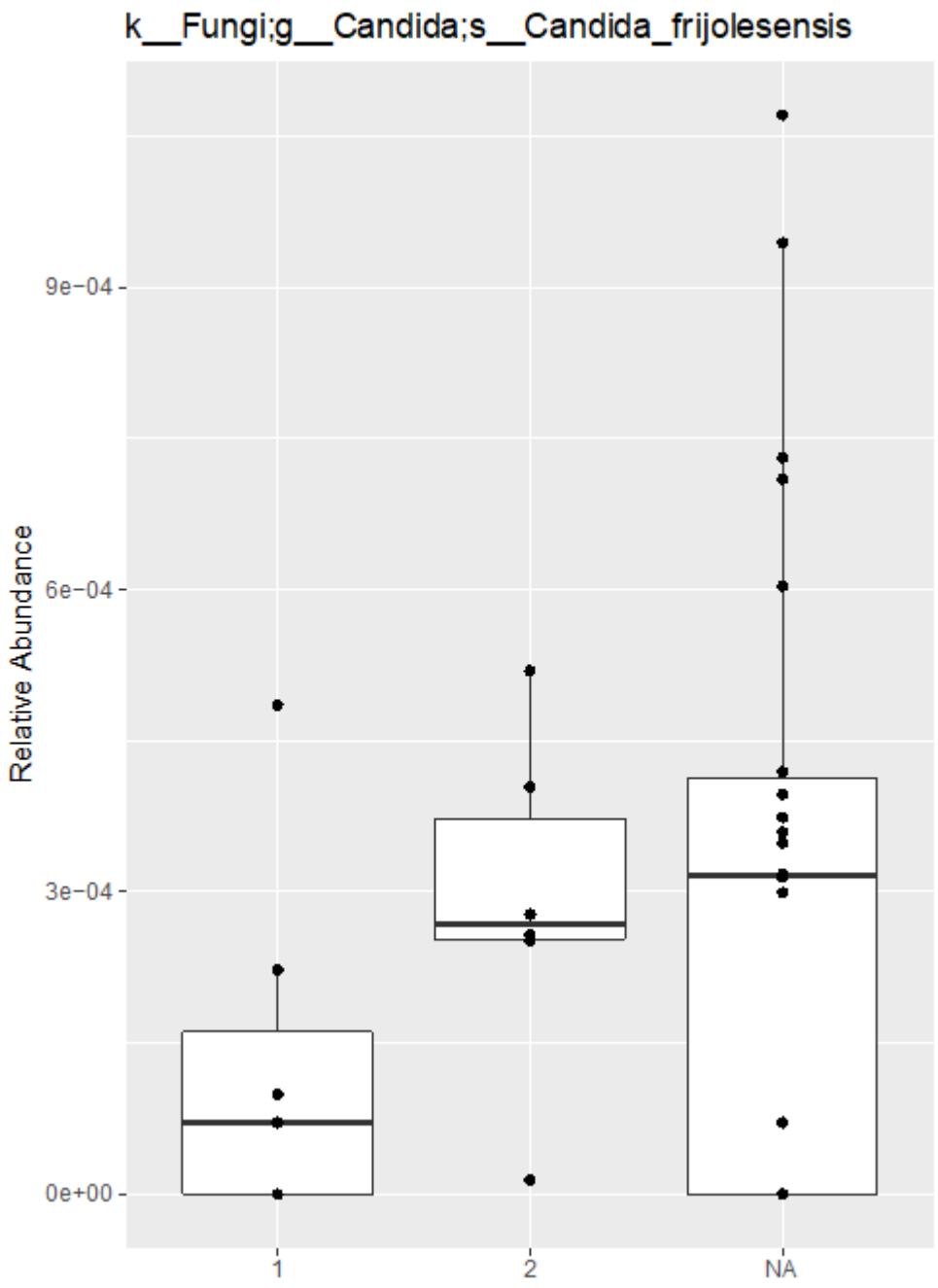
Figure.1.B



1: PET-Ga68 avid

2: PET-Ga68 non-avid

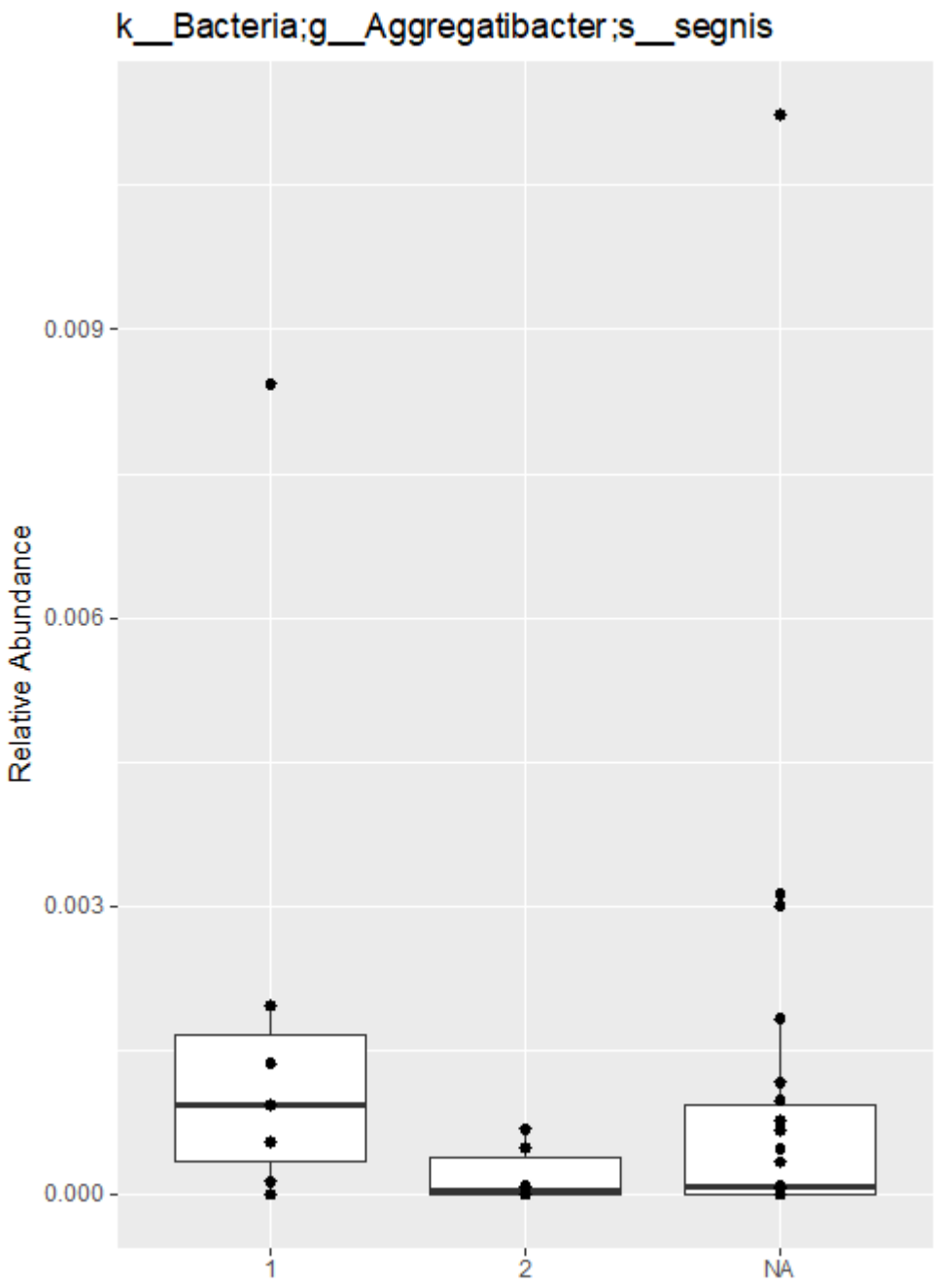
Figure.2.A



1: PRRT responders

2: PRRT non-responders

Figure.2.B



1: PRRT responders

2: PRRT non-responders