

#167 - STRUCTURE OF THE COMMENSAL MICROBIOTA OF THE STOMACH EVOLVES DURING THE *H. PYLORI*-ASSOCIATED PRENEOPLASTIC CASCADE LEADING TO GASTRIC CANCER

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INTRODUCTION: *H. pylori* infection with non-atrophic gastritis (NAG) is considered the beginning of a distinct histological stage progression to gastric cancer (GC). The role of gastric microbiota in the progression to GC is poorly understood. **OBJECTIVE:** Determine the microbial diversity, composition and associated metabolic pathways at each stage of the progression to GC. **METHODS:** We obtained gastric antrum biopsies and classified premalignant stages using OLGA score (based on Sydney protocol). Microbiota diversity was determined using 16S rRNA bacterial gene sequencing. Alpha diversity index and compositional structure were determined at each stage, specific bacterial taxa contributions and PICRUST2 functional analysis were performed. **RESULTS:** 98 patients from the PREVECAN cohort were recruited into the study. Alpha diversity (Shannon index) is higher in non-infected subjects regardless of stage displaying an inverse correlation between *H. pylori* abundance and diversity. Bacterial community structure in *H. pylori* infection with NAG differed significantly from the structure in normal and non-infected NAG ($p=0.004$). Further, the microbiota in *H. pylori*-associated NAG differed significantly from that in atrophic gastritis (AG) ($p=0.006$), gastric intestinal metaplasia (GIM) ($p=0.004$) and GC ($p=0.004$). Abundance of *Streptococcus* and *Prevotella* were significantly increased in GA and GIM. GC harbored a distinct profile of bacteria with the presence of *Lactobacillus* and *Limosilactobacillus*. *H. pylori*-positive patients display differences in biosynthesis, degradation and energy metabolism pathways and a specific clade in several GC patients showed variation in co-factor, nucleotide, amino acid and tetrapyrrole biosynthesis pathways. **CONCLUSIONS:** As *H. pylori* is lost during the premalignant stage progression to GC, the commensal microbiota becomes more diverse and distinct biosynthetic pathways evolve. Specific genera of bacteria are significantly more represented in the different stages suggesting specific profiles associated with GC progression.

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