EAAS 2: Microbiome in allergic diseases

Microbiome in Different Endotype of CRSwNP

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Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory disease with high prevalence in the worldwide. CRSwNP could be classified into two distinct immunohistological subtypes based on the observed eosinophil infiltration: eosinophilic CRSwNP (ECRSwNP) and noneosinophilic CRSwNP(nonECRSwNP). The two subtypes are characterized by different TH type inflammation: ECRSwNP is pronounced as TH2-skewed whereas nonECRSwNP is characterized by a TH1 or TH17 milieu. It is well established that microbes and their metabolite could be crucial to the pathogenesis of CRSwNP. Whether TH inflammation bias possesses the distinguished microbial colonization in nasal sinus has not been fully elucidated.

Objective: To describe the relationship between the airway microbiome and patterns of nasal mucosal inflammation types in steroid-free subjects with CRSwNP and healthy controls (HCs).

Methods: One hundred and fourteen swabs were collected under the nasal endoscope from middle nasal meatus for three groups of subjects, including 31 from ECRSwNP, 49 from nonECRSwNP, and 34 from HCs. Bacterial DNA was extracted and amplified using specific primers for Illumina HiSeq PE250 sequencing 16S rRNA V3-V4 region. ECRSwNP and nonECRSwNP were identified by infiltrated eosinophils cell proportions in nasal polyps submucosa through immunohistological(IHC) staining. Sinus microbiome diversity was assessed by α and β diversity. Relative abundance and composition difference of microbiome were illustrated and compared in ECRSwNP, nonECRSwNP and HCs at each level, including phylum, class, order, family and genus levels. A total of 23 clinical indexes were collected and the correlation between the microbiome and the clinical indexes were identified.

Results: Both α and β diversity of the microbiome in HCs were significantly lower than in either ECRSwNP or nonECRSwNP (both $P<0.01$). There was no significant difference in both α and β diversity

of the microbiome between the two subtypes of CRSwNP. In each level, an altered bacterial abundance profile was observed. In phylum level, HCs host more *Bacteroidetes* (HCs VS. ECRSwNP, *P*=0.004; HCs VS. nonECRSwNP, *P*<0.001) but less *Proteobacteria* (Both *P*<0.001) compared to either ECRSwNP or nonECRSwNP. For the two subtypes, *Verrucomicrobia* (*P*=0.013) and *Candidatus Saccharibacteria* (*P*=0.011) were significantly higher in ECRSwNP compared to nonECRSwNP. In genus level, HCs host significantly higher *Prevotella*(HCs VS. ECRSwNP, *P*<0.001; HCs VS. nonECRSwNP, *P*=0.026), *Bacteroides* (HCs VS. ECRSwNP, *P*=0. 0.02; HCs VS. nonECRSwNP, *P*<0.001) and *Clostridium XlVa* (Both *P*<0.001), lower *Neisseria* (HCs VS. ECRSwNP, *P*<0.001; HCs VS. nonECRSwNP, *P*=0.035) compared to ECRSwNP and nonECRSwNP. For the two subtypes, *Neisseria* (*P*=0.035), *Veillonella*(*P*=0.012), *Bifidobacterium*(*P*=0.015), *Porphyromonas*(*P*=0.034), *Actinomyces*(*P*=0.023), *Akkermansia* (*P*=0.018) were significantly higher while *Corynebacterium* (*P*=0.01) was lower in ECRSwNP compared to nonECRSwNP. Furthermore, *Verrucomicrobia* (*P*=0.044,R=0.223) and *Akkermansiagenera* (*P*=0.047, R=0.220) were positively correlated with eosinophils infiltration. *Corynebacterium* was positively correlated with the percentage of peripheral blood neutrophil (*P*=0.016, *R*=0.265) and negatively correlated with the percentage of peripheral blood eosinophil(*P*=0.030, *R*=-0.238). Escherichia was negatively correlated with the neutrophil infiltration (*P*=0.045, *R*=-0.222).

Conclusions: Patients with CRSwNP have an altered sinus microbiome. The microbial colonization of ECRSwNP is significantly different from nonECRSwNP. Certain bacterial colonization is associated with the clinical symptom. Further research was needed to understand the role of microbiome in different inflammation phenotypes of CRSwNP and guild clinical medication.

Keywords: CRSwNP, 16s rRNA, microbiome

*These authors contributed equally to this work.