operational taxonomic unit (OUT) analysis using 16S rRNA gene sequencing were performed. The richness of microbial diversity within subject (alpha diversity) was scaled via Shannon entropy. The dissimilarity between microbial community composition was calculated using Bray-Curtis distance as a scale, and differences between groups (beta diversity) were tested by permutation multivariate analysis of variance (PERMANOVA). In addition, UniFrac distance calculated in consideration of the distance on the phylogenetic tree were performed.

Results: Median age 70 y.o., % Female 58.8 %. Among RA and non-RA subjects, not alpha diversity but beta diversity was statistically significance (p=0.022, small in RA). In RA subjects, both alpha and beta diversity is small (p<0.0001), especially significant in ACPA positive RA (Figure 1). Amongt RA subjects, presence of HLA-DRB1*SE did not show the difference but the tendency of being small of alpha diversity (p=0.29).

Conclusion: Our study has suggested for the first time the association of oral microbiota alteration with the presence of ACPA and HLA-DRB1*SE. Oral dysbiosis may reflect the immunological status of patients with RA.

References:

Disclosure of Interests: None declared

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ORAL DYSBIOSIS REFLECTS THE IMMUNOLOGICAL ALTERATION OF RA REGARDING TO ACPA AND HLA DRB1*SE; NAGASAKI ISLAND STUDY

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Background: Anti-citrullinated protein antibody (ACPA) production is observed in several organs even prior to the onset of rheumatoid arthritis (RA), and oral mucosa is considered to be one of the important tissues. The presence of HLA-DRB1*SE closely associates with ACPA production. Saliva is considered to reflect the oral microbiota including periodontal disease. Alteration of oral microbiota of RA becomes to be normalized by DMARDs treatment, however, the interaction of HLA-DRB1*SE, ACPA and oral microbiota of RA patients remains to be elucidated.

Objectives: The Nagasaki Island Study, which had started in 2014 collaborating with Goto City, is intended for research of the preclinical stage of RA, including ACPA/HLA genotype screening and ultrasound and magnetic resonance imaging examinations in high-risk subjects. Using the samples accumulated in this cohort, we have tried to investigate the difference of oral microbiota among RA patients and healthy subjects regarding to ACPA and HLA-DRB1*SE.

Methods: Blood and salivary samples were obtained from 4276 subjects out of 4276 who have participated in the Nagasaki Island Study from 2016 to 2018. ACPA positivity was 1.7 % in total. Some of RA patients resided in Goto City participated in the Nagasaki Island Study. At this point, we selected 291 subjects, who were ACPA positive non-RA healthy subjects (n=22) and patients with RA (n=33, 11 subjects were ACPA positive and 22 ACPA negative respectively) as the case, age and gender matched ACPA negative non-RA healthy subjects (n=236) as the control. ACPA was measured by an enzyme-linked immunosorbent assay, and HLA genotyping was quantified by next-generation sequencing (Ref.1). The

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