Abstract ID: 755 中/ 英文姓名：許雯雅/Hsu, Wen-Ya

Association between host genetic variants and gut microbiota composition in mood disorders

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Background: Mood disturbance is common in the population, and depression ranks high in the global burden of diseases. Growing evidence has shown that microbiota-gut-brain axis plays important roles in host's stress, anxiety, mood and behavior. The heritability of specific bacteria abundance in human was moderate, indicating the need to investigate the impacts of host genetic factors on gut microbiota. Microbiome genome-wide association studies (mGWAS) was recently used to study the interaction between host genetic variants and microbiota composition.

Aims & Objectives: The current study explored associations between genetic variants and gut microbiota among patients with depression in a Taiwanese sample. We also evaluated whether findings in previous mGWAS in European populations can be replicated in our samples.

Methods: We recruited 280 adult patients with mood disorders (143 major depressive disorder and 137 bipolar disorder under depressive episode) in several central and regional hospitals in Taipei. We assessed demographic, clinical and dietary information using interviewed and self-reported questionnaires. Stool samples were collected from all patients without using antibiotic, probiotic, prebiotic, symbiotic or having infections or surgery during the past 2 months. We amplified V3 and V4 regions of the 16S rRNA gene for sequencing and identified microbiota at genus level. Genetic variants were genotyped using Axiom Genome-Wide TWB 2.0 Array Plate from blood samples. We used multivariate linear regression models to analyze microbiota data with relevant covariates adjusted to minimize their influences on the composition of gut microbiota. We then extracted residuals from these models to perform genetic association analysis using additive genetic model.

Results: There were 9 previous mGWAS, which reported in total 133 significant signals between gut microbiota and host genetic variants. Among them, only 1 signal was replicated in 4 out of the 9 studies. However, such signal was not found in our samples. On the other hand, we found a novel association between genus *Bacteroides* and rs859255 (OR = 2. 60, β = -0.95, p-value = 2.63×10^{-8}). Less abundant *Bacteroides* was associated with obesity, high-fat and high-protein diets.[5,6]

Discussion & Conclusion: We identify a significant signal for the association between genus *Bacteroides* and one genetic marker in patients with mood disorders. Future studies to expand sample size and perform replication are warranted to obtain reliable findings in Taiwanese. The discovery of convincing signals between gut microbiota and genetic variants could provide more insights on the mechanisms of mood disturbances.