Metagenome-wide association study on oral microbiome uncovered markers for rheumatoid arthritis

July 28 2015

Researchers from BGI, Peking Union Medical College Hospital, etc., reported the study on the oral and the gut microbiome in rheumatoid arthritis (RA). The results show that the gut and oral microbiome are involved in the pathophysiology and management of RA and provide indication for developing microbiome-assisted personalized treatments. The latest finding was published online today in *Nature Medicine*.

RA is a debilitating autoimmune disorder affecting tens of millions of people worldwide, while the mortality in the patients increases due to systemic complications. Bacterial infection has long been suggested to relate with RA. However, the identity and functional capacity of the RA-associated bacterial agent(s) have been largely unclear. Disease-modifying antirheumatic drugs (DMARDs) alleviate but do not cure RA, and with possible severe side effects. A comprehensive understanding of the RA-associated microbiome holds promise for new advancement in RA pathophysiology, as well as early diagnosis and precision treatment. In the study, researchers performed metagenomic shotgun sequencing and a metagenome-wide association study (MGWAS) in fecal, dental and salivary samples from RA patients and healthy controls, and observed dysbiosis changes in the gut and oral microbiome partially restored after treatment with DMARDs.

Metagenome-wide association studies (MGWAS) have proved to be a powerful approach to study gut microbiome for type 2 diabetes,

colorectal cancer, etc. This is the first study on dental and saliva microbiomes. The researchers found that, Haemophilus sp. is depleted in RA patients at all three gut and oral sites and negatively correlates with RA auto-antibodies, while Lactobacillus salivarius is over-represented in RA patients at all three sites, especially in the very active cases.

Functional convergence was also observed—the RA gut and oral microbiomes show abnormalities in the redox environment, iron, sulfur, zinc and arginine transport and metabolism, and possible molecular mimicry to RA-related human antigens.

In addition, the study indicates that fecal, dental and salivary microbial markers could all be useful for the diagnosis and management of RA, while the oral microbiome might be more sensitive to DMARD treatment than the gut microbiome. Microbiome-based classifiers that distinguish between RA patients from healthy controls were constructed for all three body sites, and the use of all three body sites further improved accuracy to nearly 100%. The same classifiers were applied to samples after DMARD treatment, and dental samples with low disease activity were often classified as healthy, consistent with clinical relief of periodontitis in RA patients after treatment.

Furthermore, gut and oral microbial markers were identified that possibly distinguish between patients of different disease duration, improvement after DMARDs, and types of DMARDs, although validations in additional cohorts would be necessary.

Xuan Zhang, Project Leader and Professor from Peking Union Medical College Hospital said, the study paves the way for metagenome-wide association study on oral microbiome and gut microbiome. It uncovers the preclinical and clinical phases of RA. Clinical validation would further deepen our understanding of RA. We expect the metagenome-wide association study will actively promote patient stratification, drug

improvement and novel therapeutic target of RA, and lead to the precise diagnosis and treatment.

More information: The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment, DOI: 10.1038/nm.3914

Provided by BGI Shenzhen