Establishment of oral carnitine challenge test for clinical assessment of TMAO production capacity from diet-gut microbiota-host interactions in human body

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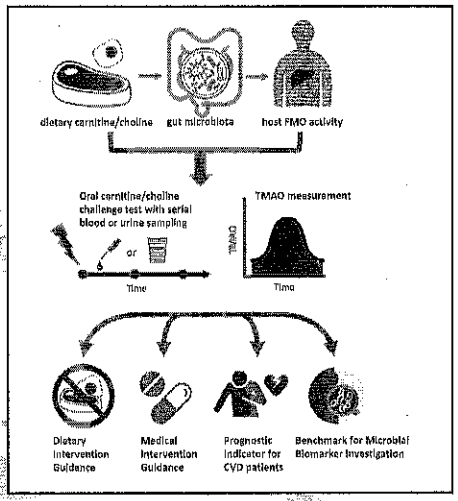

Market Needs:

We proposed the "Oral Carnitine Challenge Test" as a novel tool in accessing the function of human gut microbiota for the clinical application. This technique is capable of identifying TMAO production capacity in different subjects, and through which we can access the subject's risk of cardiovascular disease from their gut microbiota. The test can also serve as a dietary guidance and pharmaceutical instruction as well as a benchmark for the investigation of TMAO-relevant microbial biomarkers.

Our Technology:

The gut microorganism-derived metabolite, trimethylamine N-oxide (TMAO) plays an important role in cardiovascular disease (CVD). In recent studies, the measurement of fasting plasma TMAO was shown to be a prognostic factor in CVD patients. However, because of its efficient renal clearance and fluctuation property, the plasma TMAO level may not be a representative indicator to access individual TMAO production capacity. Here we established a clinically applicable oral carnitine challenge test (OCCT) to functionally represent TMAO synthesis capacity from diet-gut microbiota-host interactions by using a pharmacokinetic study and a validation cohort comprised of subjects with different eating habits (omnivorous and vegetarian). We sequenced 16S rDNA from fecal samples of 57 volunteers to profile gut microbial composition. In addition, the OCCT survey of each volunteer was integrated with gut microbiome sequencing, host genotyping, dietary frequency, and serum biochemistry test. The results suggested that the OCCT exhibit a much better efficacy than fasting plasma TMAO to determine the functional phenotype of TMAO synthesis capacity of the gut microbiota. The TMAO-associated taxa found in human gut microbiota were consistent with previous studies of mouse model. The TMAO-producing phenotypes were also reproduced in germ-free mice via fecal microbiota transplantation. Besides, our results showed that fecal *CntA* gene quantification and *CntA*-containing bacteria abundance were not associated with TMAO synthesis capacity, suggesting that other key player genes were involved with the TMAO formation in the human gut microbiome. Finally, we demonstrated that urine TMAO exhibit a strong positive correlation with plasma TMAO ($r = 0.90$, $p<0.0001$) at the same times and improved the feasibility of OCCT. Accordingly, we proposed the OCCT as a functional measurement for individual TMAO-producing ability and it may serve as a potential protocol in cardiovascular risk assessment as well as dietary and pharmacological intervention. This study may also provide a reference for the functional measurement of synthesis capacity of other gut microorganism-derived metabolites, such as short chain fatty acids, secondary bile acids, and indoxyl sulfate.

Strength: Instead of just doing commercial gut microbiome sequencing in the market, the OCCT aims to exam the function of TMAO producing ability from the gut microbiota. The OCCT also exhibited better predictive value of gut microbiota functional phenotypes as compared to fasting plasma TMAO measurement.

Competing Products: NA

Intellectual Properties: R.O.C. patent: 108128635; PCT In progress

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