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ANALYSIS OF BLOOD MICROBIOME BY HIGHLY SENSITIVE 16S METAGENOMIC SEQUENCING: A NEW TOOL FOR DIAGNOSIS

Lelouvier B[1], Servant F[1], Delobel P[2, 3] and Amar J[1, 4]

[1]Vaiomer SAS, Labege, France
[2]CHU de Toulouse, Service des Maladies Infectieuses et Tropicales, Toulouse, France
[3]INSERM, Toulouse, France
[4]CHU de Toulouse, Rangueil Hospital, Toulouse, France

Diagnosis and treatment of bloodstream infection (BSI) and tissue infections will greatly benefit from sensitive and exhaustive molecular methods to detect bacterial DNA in blood, such as quantitative PCR (qPCR) and 16S metagenomics sequencing. Such approaches were already studied with the aim of reducing the turnaround time and increasing the sensitivity of the microbiota detection in suspected BSI. However, this type of molecular diagnosis is greatly complicated by the presence of human DNA and PCR inhibitors in blood and tissue, as well as bacterial DNA contaminants present in the environment, reagents and consumables, which dramatically hamper the signal to noise ratio of qPCR and sequencing pipelines. In the course of our investigations into the role of tissue microbiota in cardiometabolic diseases we developed specific optimized pipelines of qPCR and 16S targeted metagenomic sequencing to analyze blood and tissue bacterial DNA, despite the technical difficulties associated with this sample types. Using these molecular tools we have demonstrated the existence of a highly diversified blood microbiome in healthy human donors and shown the association between changes in the blood microbiome and liver fibrosis in obese patients. These assays were primarily designed to analyze bacterial DNA in blood and tissue of healthy donors and patients with no infectious disease, and therefore their signal to noise ratios are really high. Indeed, we demonstrated that they are also capable of detecting culture negative polymicrobial BSI and bone infection in patients at early stages of the infection.

Recent Publications

1. Lelouvier B, Servant F, Delobel P, Courtney M, Elbaz M and Amar J (2017) Identification by highly sensitive 16S metagenomic sequencing of an unusual case of polymicrobial bacteremia. *J Infect*; 75(3):278-280. doi: 10.1016/j.jinf.2017.05.005.

2. Paisse S, Valle C, Servant F, Courtney M, Burcelin R, Amar J and Lelouvier B (2016) Comprehensive description of blood microbiome from healthy donors assessed by 16S targeted metagenomic sequencing. *Transfusion*; 56(5):1138-47. doi: 10.1111/trf.13477.

3. Lelouvier B, Servant F, Païssé S, Brunet A-C, Benyahya S, Serino M, Valle C, Ortiz MR, Puig J, Courtney M, Federici M, Fernández-Real J-M, Burcelin R and Amar J (2016) Changes in blood microbiota profiles associated with liver fibrosis in obese patients: A pilot analysis. *Hepatology* ; 64(6):2015-2027. doi: 10.1002/hep.28829

4.Lluch J, Servant F, Païssé S, Valle C, Valière S, Kuchly C, Vilchez G, Donnadieu C, Courtney M, Burcelin R, Amar J, Bouchez O and Lelouvier B (2015) The Characterization of Novel Tissue Microbiota Using an Optimized 16S Metagenomic Sequencing Pipeline. *PLoS One*;10(11):e0142334.doi:0.1371/journal.pone.0142334

5. Pindjakova J, Sartini C, Lo Re O, Rappa F, Coupe B, Lelouvier B, Pazienza V, and Vinciguerra M (2017) Gut Dysbiosis and Adaptive Immune Response in Diet-induced Obesity vs. Systemic Inflammation. *Front Microbiol*;8:1157.doi:10.3389/fmicb.2017.0115

Biography

Lelouvier B received his PhD in Cellular and Molecular Neurobiology from the University Pierre et Marie Curie, Paris VI, France, in 2007. After a Postdoctoral fellowship at the National Institutes of Health (USA), he joined Vaiomer in 2012. As Cellular and Molecular biology Group Leader and Head of Biomarkers Discovery, he with his group developed the molecular tools (16S qPCR and 16S metagenomics sequencing) to study specifically the blood and tissue microbiomes, before becoming Chief Scientific Officer of Vaiomer in 2016. The study of tissue and blood microbiota allows Vaiomer to link intestinal dysbiosis and tissular inflammation for the development of biomarkers and therapeutics in the fields of cardiometabolic diseases, neurodegenerative disorders and bacterial infection.

benjamin.lelouvier@vaiomer.com