

MICROBIOME IDENTIFICATION USING SUPER-RESOLUTION DNA MAPPING

Jochem Deen¹, Jia Su², Kristin Grussmayer¹, Arno Bouwens^{1,2}, Rafael Camacho², Adrien Descloux¹, Kris PF Janssen², Johan Hofkens² and Theo Lasser¹

¹ Laboratoire d'optique biomédicale, EPFL, CH-1015 Lausanne, Switzerland

² Molecular imaging and photonics, KU Leuven, BE-3001 Leuven, Belgium

E-mail: Jochem.Deen@epfl.ch , Theo.Lasser@epfl.ch

Key-words: DNA mapping, fluorescent labeling, microbiome, Alzheimer, Super-resolution

An immense number of microbial species live in a symbiotic relationship with their host. The composition of this bacterial community, known as the microbiome, plays an important role in the development of many diseases.(1) Recently, for example, our lab discovered how germ-free mice have a drastic reduction of cerebral Ab amyloid pathology and thus may influence Alzheimer's disease.(2)

Currently, identification of species in the gut microbiome using classical nucleic acid-based techniques proves complicated, as a typical DNA sample contains many different, often very

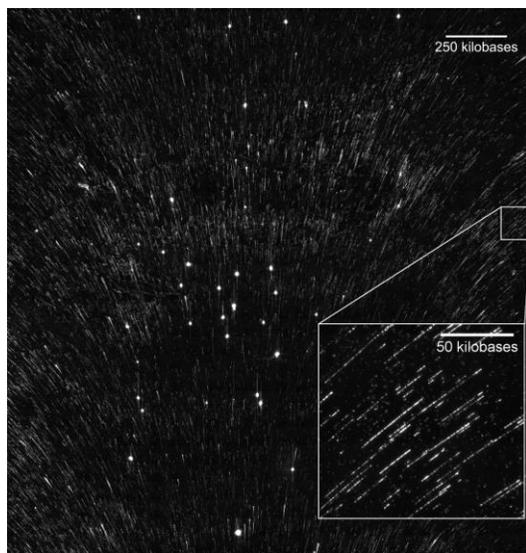


Figure 1 Typical example figure of the labeled DNA

similar, genomes. We developed a novel concept to identify species based on super resolution DNA mapping. In our method, the DNA molecules are sequence specifically labeled with fluorescent dyes using DNA methyltransferases. These enzymes typically possess recognition sequences of 2-6 bases.(3,4) Subsequently, the DNA molecules are stretched on a coverslip using a novel rolling droplet method (5) and imaged on a super-resolved fluorescent microscope (Figure 1). The result is a fluorescent signature varying over the distance of the molecule that is specific to the underlying sequence. This signature can thus be used as a marker for specific sequences, and provides a way to identify genomic regions and thus species and their abundance.

References

- (1) Cho I, Blaser MJ. "The Human Microbiome: at the interface of health and disease" *Nature reviews Genetics*, **13**, 260-270 (2012)
- (2) Harach T, Marungruang N, Dutilleul N, Cheatham V, Mc Coy KD, Neher JJ, Jucker M, Fåk F, Lasser T, Bolmont T. "Reduction of Alzheimer's disease beta-amyloid pathology in the absence of gut microbiota" Submitted and available on *Arxiv.org*, 2015.
- (3) Neely RK, Deen J, Hofkens J, "Optical mapping of DNA: single-molecule-based methods for mapping genomes" *Biopolymers*, **95**, 298-311 (2011)
- (4) Deen J, Vranken C, Leen V, Neely RK, Jansen KPF, Hofkens J, "Methyltransferase directed labeling of biomolecules and its applications" *Angewandte Chemie*. (2016)
- (5) Deen J, Sempels W, De Dier R, Vermant J, Dedecker P, Hofkens J, Neely RK, "Combing of Genomic DNA from Droplets Containing Picograms of Material" *ACS Nano*, **9**, 809-816 (2015)