**Methanogenesis and Pyl-system of human gut archaea (*Methanomassiliicoccales)*: comparative multi -omics analysis**

**Supervisor :** J-F Brugère (MCU-HDR) J-Francois.Brugere@uca.fr

**UMR CNRS 6023 Laboratoire Microorganismes : Génome et Environnement, Clermont Université (T. Sime-Ngando)**

*Methanomassilicoccales* (MMC) or 7th methanogenic order are an euryarchaeal group characterized by a strong dichotomy which occurred during evolution (environmental vs host-associated species) and by an original methanogenesis (hydrogenotrophs using C1- compounds as finale electron acceptors). Anaerobic metabolism of trimethylamine (TMA) is of interest for human health purposes (notably cardiovascular disease prevention by archaebiotics and derived forms) and requires synthesis and encoding of the 22nd amino-acid pyrrolysine (Pyl), *i.e*. the Pyl-system. Only two MMC species are grown as pure culture, one of the two being an obligatory gut commensal. Genomic data from the human-associated MMC indicate an original Pyl-system with a probable genetic code evolution and an expansion of Pyl-encoding and use. Transcriptomics (RNAseq), ribosome profiling (Riboseq) and proteomics are currently performed.

The PhD position will combine bioinformatics analyses, wet lab experiments and biological validation, notably using site-directed mutagenesis in a bacterial heterologous model of the Pyl-system. Studies will aim at determining to which extent Pyl amino-acid is used in proteins of commensal species, together with mechanisms that underlie such a genetic code evolution and translation of a usual non-sense codon.

- Borrel G *et al* (2017) Genomics and metagenomics of trimethylamine-utilizing Archaea in the human gut microbiome. *ISME J.* 11(9):2059-2074.

- Brugère JF *et al* (2018). Pyrrolysine in archaea: a 22nd amino acid encoded through a genetic code expansion. *Emerg. Top. Life Sci.*, *2*(4), 607-618.