Synthesis of modified tRNA to explore biological targets: application to the study of Fem transferase in Bacteria

Prof. **Mélanie ÉTHÈVE-QUELQUEJEU**

Équipe *Chimie et Biologie, Nucléos(t)ides et Immunologie pour la Thérapie*,
LCBPT *Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques*,
UMR 8601 CNRS, Université Paris-Descartes

In addition to their role in protein synthesis aminoacyl-tRNAs (aa-tRNA) participate in various metabolic pathways as a source of ester-activated amino acids in bacteria. In order to explore the role of aa-tRNA in the biosynthesis of the peptidoglygan, a major component of the cell wall of bacteria, we develop versatile methods for the synthesis of modified aa-tRNA. We report here the synthesis of stable analogues of aa-tRNA, fluoro-tRNA and peptidyl-RNA. These novel analogues of RNAs have been developed using two strategies. The first strategy involves an enzymatic ligation by T4 RNA ligase and the second strategy is base on the solid phase synthesis and the click chemistry. One peptidyl-RNA conjugates was found to inhibit the non-ribosomal $FemX_{Wv}$ aminoacyl-transferase with an IC_{50} of 90 ±9 pM; and one was used to successfully obtain the crystallographic structure of $FemX_{Wv}$ in Complex with the Peptidyl-RNA.

These modified tRNAs are interesting tools to investigate in the field of RNA biology.

(la conférence sera donnée en français)