A two year post-doctoral position at the Bacterial Genome Plasticity Unit

A **2-year postdoctoral position** is available at the **Institut Pasteur** (Paris, France) in the *Bacterial Genome Plasticity Unit*, headed by **Prof. Didier Mazel**, in collaboration with **Dr. Pierre-Alexandre Kaminski**. This project is funded by the **French National Research Agency (ANR)** from 01.10.2025.

Our research focuses on the mechanisms by which certain bacteriophages replicate genomes that deviate from canonical DNA chemistry. A striking example is the complete replacement of adenine by **2-aminoadenine (Z)** in the DNA of several lytic phages, including the *Vibrio* phage **PhiVC8**. This substitution results in the formation of a Z–T base pair with three hydrogen bonds, which increases **DNA thermostability** and alters **DNA structure**. These changes can significantly affect recognition by DNA-binding proteins and influence essential processes like replication, transcription, and recombination.

Despite this chemical divergence from standard Watson–Crick base pairing, these phages replicate efficiently, raising key questions about how their replication machinery has adapted.

Project Overview

The aim of this project is to understand how DNA replication functions in phage PhiVC8, which uses **ZTGC-DNA**, and how it differs from replication of canonical **ATGC-DNA**. Our experimental model is the infection of *Vibrio cholerae* O1 by PhiVC8.

This ANR-funded project is structured around two complementary objectives, pursued in close collaboration between our research group and that of Ludovic Sauguet, in the Laboratory of Structural Dynamics of Macromolecules led by Dr. Marc Delarue, also at the Pasteur Institute.

Objective 1 ZTGC-DNA Replication *In Vivo*
[Led by the recruited postdoc)
We aim to define the gene set responsible for replication of Z-modified DNA in vivo:

- Characterization of known replication genes (primase-polymerase, DNA polymerase, ssDNA-binding protein, helicase)
- Functional exploration of additional genes with unknown roles
- Identification of the **minimal gene set and origin of replication** required for ZTGC replication
- Determination of the specificity of these factors for Z-modified DNA

Objective 2 ZTGC Replication System *In Vitro*
[Led by a postdoc in the group of Dr. Ludovic Sauguet]
This part focuses on reconstituting the ZTGC replication machinery in vitro to:

- Dissect interactions among essential replication proteins and their binding to ZTGC vs. ATGC DNA
- Explore biochemical adaptations to Z-modified DNA
- Evaluate enzyme kinetics, replication fidelity, and uncover novel nucleic acid activities

The two postdoctoral researchers, based respectively in the **Kaminski** and **Sauguet** groups, will **work in close collaboration**, bridging in vivo and in vitro approaches to gain a comprehensive understanding of this unusual replication system.

Candidate Profile

We are seeking a highly motivated candidate with:

- A PhD in molecular biology, microbiology, biochemistry, or related fields
- Expertise in genetic manipulation, molecular cloning, or DNA replication systems
- Strong interest in phage biology, nucleic acid chemistry, and protein-DNA interactions
- Ability to work independently and collaboratively in an interdisciplinary team

Application Instructions

To apply, please send:

- A **cover letter** describing your research interests and motivation
- A detailed **CV**
- **Contact information for two academic referees**

Send applications to: **pierre-alexandre.kaminski@pasteur.fr**