

Postdoctoral Position in immunology (M/F)



The hosting structure

Institut Curie Research Center

Institut Curie is a major player in the research and fight against cancer. It consists of a Hospital group and a Research Center of more than 1000 employees with a strong international representativeness.

The objective of the Research Center is to develop basic research and to use the knowledge produced to improve the diagnosis, prognosis, and therapeutics of cancers as part of the continuum between basic research and innovation serving the patient.

Context

Laboratory

The Stem cell immunity laboratory is a young and dynamic team, created in the Institut Curie in December 2021 within the Immunity and Cancer unit (U932). Because stem cells are key for the maintenance of tissue architecture and integrity, they need to be protected from insults. There is increasing evidence that stem cells implement specific immune mechanisms not found in differentiated cells. The team focuses on identifying and characterising these mechanisms. For example, we recently discovered that stem cells express an antiviral protein called aviD, which specifically targets viral genomes and thwarts infection from RNA viruses such as SARS-CoV-2 (Poirier *et al.*, 2021, Science).

Our current projects focus on:

- understanding and characterising the aviD antiviral response
- assessing if stem cell-specific mechanisms of protection are shared by cancer cells and play a role in cancer growth or immune evasion
- discovering novel stem cell-specific mechanisms of defence

We are looking for a highly motivated postdoc to join the team and study the aviD antiviral response *in vivo*.

The project

In mammalian differentiated cells, viral infection triggers the production of type I and III interferons (IFN), which promote the expression of interferon stimulated genes (ISGs), a broad panel of antiviral effectors (1). This protection conferred by the IFN pathway is however severely compromised in embryonic and adult stem cells, which lack key components of the pathway (2). Despite their IFN unresponsiveness, stem cells are largely resistant to viral infection. This can be attributed in part to the steady-state expression of ISGs (3), as well as the presence of an antiviral protein called aviD, that we recently discovered (4).

aviD is an antiviral isoform of Dicer produced by alternative splicing, that is better able to target and cleave viral RNA compared to canonical Dicer. Using a model of brain organoid infected with Zika virus or SARS-CoV-2, we demonstrated

that aviD protects neural stem cells from RNA viruses by mounting a canonical antiviral RNAi response (4). *In vivo* in mice, aviD expression is enriched in stem cells within tissues, including gut, skin and brain. **This project aims at investigating the role of aviD *in vivo* in protecting stem cells against RNA viruses.**

To do so, we will characterise a recently generated aviD knock-out mouse, with intact Dicer expression. We will infect aviD KO mice and wild type controls with various RNA viruses and monitor signs of pathology and recovery. Using immunofluorescence and confocal microscopy, we will quantify the infection of stem cells and differentiated cells, as well as tissue regeneration. As documented in brain organoids, we expect that loss of aviD *in vivo* will correlate with increased stem cell infection and demise, potentially leading to decreased tissue regeneration and survival. This will be the first characterisation of the aviD antiviral response *in vivo*.

References

1. X. Tan, L. Sun, J. Chen, Z. J. Chen, *Annu. Rev. Microbiol.* **72**, 447–478 (2018).
2. P. V. Maillard, A. G. Veen, E. Z. Poirier, C. Reis e Sousa, *EMBO J.* **38** (2019), doi:10.15252/embj.2018100941.
3. X. Wu *et al.*, *Cell* (2017), doi:10.1016/j.cell.2017.11.018.
4. E. Z. Poirier *et al.*, *Science*. **373**, 231–236 (2021).

Candidate Profile

Training and Skills required

- Training: PhD in virology or immunology will be considered favourably
- Scientific skills: Experience in basic cellular and molecular biology techniques, as well as in mouse experiments.
- Language skills: English

All our opportunities are open to people with disabilities

Contract information

Type of contract: Fixed-term contract.

Starting date: February-April 2022

Duration: two years, with the possibility of extension

Working time: full time

Remuneration: according to the current grids

Benefits: Collective catering, reimbursement of transportation fees up to 70%, supplementary health insurance

Location of the position: Paris

Reference: 2021-11-POSTDOCPOIR932

Contact

Please send your CV, letter of motivation and 2 references, to Enzo Poirier (enzo.poirier@curie.fr)

Publication date: 02/11/2021

Deadline for application: 10/12/2021

*Institut Curie is an inclusive, equal opportunity employer
and is dedicated to the highest standards of research integrity.*