**ANGERS UNIVERSITY**

Junior Contract Researcher
Post-doctoral contract in public law

Category : A

## Presentation of the University of Angers

In the heart of a region recognized for its quality of life, the University of Angers, the 3rd largest employer in the region, offers an environment conducive to the development of its staff and students. The UA is a multidisciplinary university, welcoming more than 26000 students spread over 3 campuses and 2 relocated campuses (in Cholet and Saumur). It has 8 components (5 UFR, 1 IUT, 1 internal engineering school and 1 internal business and management school), and 31 federative research units and structures. Thanks to the many innovative projects it carries out and its openness to the world, the AU allows everyone to evolve in a stimulating environment. Its annual budget is €156 million (including €123 million in payroll). The UA has 1167 teachers and teacher-researchers, 917 administrative and technical staff and nearly 2000 individual contractors and is looking for involved and daring actors. You recognize yourself in this job offer ? Join us !

## Contract features:

**Starting date :** early 2025 (date to be confirmed)
**Contract duration** : one year (renewable for one year)
**Work quota :** 100%
**Monthly wage :** 3461 gross
**Location :** Angers University, Assigned to the MitoVasc laboratory (Mitolab team) and located at the Center for Research in Cancer and Immunology (CRCI2NA).

## Name of research project : **MITIMMUNE**

## Description of the research project in which the research activities entrusted to the officer take place:

**Therapeutic Strategies Targeting Mitochondrial Dysfunction and Inflammation in Mitochondrial Diseases**

Mitochondrial diseases are severe and debilitating conditions, with largely unknown pathophysiology. This lack of understanding represents a major obstacle to the development of specific therapies. It is therefore crucial to make concerted efforts to better understand their pathophysiology.

Since mitochondria are involved in a multitude of molecular processes, the clinical manifestations of mitochondrial diseases are diverse, including metabolic abnormalities and chronic inflammation, as observed in the Ndufs4-/- mouse model replicating Leigh syndrome (LS) (Simon et al., 2021). This model exhibits ataxia, blindness, growth retardation, and lethargy, leading to premature death at around 8 weeks of age (Kruse et al., 2008). Chronic inflammation can disrupt tissue homeostasis, particularly by impairing mitochondrial functions (Lopez-Amada et al., 2006; Horssen et al., 2019; Marchi et al., 2023). However, inflammation as a potential therapeutic target in mitochondrial diseases has so far been little explored.

The primary goal of our project is to identify strategies that combine restoring mitochondrial functions with reducing chronic inflammation. Our central hypothesis is that anti-inflammatory strategies, whether based on nutritional/metabolic interventions such as the ketogenic diet or on immunotherapy, could normalize mitochondrial functions, and vice versa. This hypothesis is supported by preliminary results showing that specific nutrients or an interleukin-1 receptor antagonist (IL-1Ra) can normalize mitochondrial functions.

**Provisional project schedule:** Project duration 2 years: 2024/12/01 - 2026/11/30

## Expected results :

- **Identification of Key Pathways Involved in the Mitochondrial Disease Process (Genes/Metabolites/Cytokines)**
N=4 (September 2025)
- **Identification of LEAD Compounds**
(Identification of compounds with a desirable LEAD profile based on efficacy, mechanism, and risk assessment) using in vitro models, N=2 (December 2025).
- **Identification of Key Biomarkers**
(Identification of markers associated with the disease profile), N=2 (December 2025).
- **In Vivo Evaluation of Compounds and Metabolic Strategies**
Using selected evaluation criteria in murine models of Complex I dysfunction, N=3 (September 2026).

## Definition of research activities and tasks to be accomplished:

- **Molecular and Functional Characterization of Patient-Derived Cells with Complex I Deficiency and MELAS**
a. Characterization of mutated cells using an integrated approach combining metabolomics and gene expression profiling.
b. Characterization of inflammatory secretomes in mutated cells.
- **Development of Strategies to Correct Mitochondrial Deficiencies and Reduce Inflammation In Vitro, While Identifying Novel Robust Biomarkers for Mitochondrial Diseases**
a. Analysis of the ability of ketone bodies to restore mitochondrial function and reduce inflammation.
b. Validation of IL-1β inhibition to mitigate inflammation associated with mitochondrial dysfunction.
- **In Vivo Validation of Nutritional and Immune Strategies Using the Ndufs4-/- Mouse Model of Complex I Deficiency**
a. Impact of the ketogenic diet (KD) on mitochondrial function and inflammation.
b. Impact of IL-1β neutralization on mitochondrial function and systemic inflammation.
c. Impact of combining KD with IL-1 receptor antagonist (IL-1Ra) on mitochondrial function and inflammation.

## Expected skills :

Knowledge :

- Specific Equipment
- Molecular Biology: Applied methodology (general knowledge)
- Biochemistry: Applied methodology (general knowledge)
- Cell Biology**:** Applied methodology (general knowledge)

Know-how:

- Knowledge of Primary and Secondary Cell Culture
- Familiarity with Hygiene and Safety Guidelines
- Proficiency in Experimental Tools Related to Mitochondrial Metabolism and Dynamics

Soft skills:

- Teamwork Orientation
- Strong Communication Skills, Availability, and Attentiveness
- Analytical Reasoning Ability
- Creativity and Innovation

## Qualifications

**PHD degree of less than 3 years**
Specialty : Biochemistry, Molecular and Cellular Biology

**Recruitment procedures and contact :**

**You must submit your CV, cover letter and doctoral degree** by mail at : vincent.procaccio@univ-angers.fr **copy to : recrutement@univ-angers.fr**

**Deadline for applications**: **2024/01/20**
**This job description is available until the closing date for applications.**
**On that date, it will no longer be available on the website.**

**If needed, your contact for any further information:**
**Vincent PROCACCIO**, **02 41 35 78 54** or vincent.procaccio@univ-angers.fr