


PHD POSITION OT-21883

# PhD – THE ROLE OF METAL IONS DURING HOST-PATHOGEN INTERACTIONS

 37380 Nouzilly

## INRAE presentation

The French National Research Institute for Agriculture, Food, and Environment (INRAE) is a major player in research and innovation. It is a community of 12,000 people with 272 research, experimental research, and support units located in 18 regional centres throughout France. Internationally, INRAE is among the top research organisations in the agricultural and food sciences, plant and animal sciences, as well as in ecology and environmental science. It is the world's leading research organisation specialising in agriculture, food and the environment. INRAE's goal is to be a key player in the transitions necessary to address major global challenges. Faced with a growing world population, climate change, resource scarcity, and declining biodiversity, the Institute has a major role to play in building solutions and supporting the necessary acceleration of agricultural, food and environmental transitions.

## Work environment, missions and activities

You will join the **MiMoSa** (Microbiota, Monogastrics and *Salmonella*) team which consists of experts in *Salmonella* pathogenicity and host-pathogen interactions. The position is available for 36 months.

**Background and project description:** *Salmonella* is a major source of zoonotic infection, mainly through food contamination linked to eggs and meat from chicken and pork (1). In the host, these infections lead to the recruitment and the activation of macrophages: one of the first immune cells to fight bacterial infections that use a broad arsenal to contain and eliminate pathogens (2). Unfortunately, *Salmonella* has evolved to survive in host cells. It can remain quiescent in macrophages and use them as a reservoir and as a protection against antibiotics. Thus, it is paramount to identify new pathways that we could modulate to enhance the macrophage antimicrobial response. We have recently characterised a new antimicrobial response in macrophages linked to nutritional immunity that employs metal ions (e.g zinc) toxication and/or starvation to eradicate bacterial infection (3-5). The mechanism still needs to be fully characterised in order to modulate and enhance this antibacterial response.

**Objectives:** During this project, you will 1) identify the list of critical genes that allow *Salmonella* to resist and escape zinc toxicity in the host cell; 2) characterise how the zinc-dependent antimicrobial response is driven in the host (in particular in chickens); 3) and contribute to the development of new tools to study zinc toxicity in host cells. The aim of this thesis is therefore to gain a better understanding of this mechanism linked to zinc toxicity and to improve the innate immunity of livestock and humans.

**You will be responsible for:**

- Identifying the critical genes in the zinc resistance and escape mechanism, using RNA-seq, Tn-Seq analysis and live confocal imaging.
- Characterising the zinc response in different cell types and host species - in particular in chicken, a known asymptomatic carrier of *Salmonella*.
- Participating to the identification of potential inhibitors for host zinc transporters to help modulate the host antimicrobial response.

**You will be supervised by:**

- Ronan Kapetanovic, PhD, DR (he/him) – Expert in host-pathogen interaction, macrophages, antimicrobial response
- Isabelle Virlogeux-Payant, PhD, DR (she/her) – Expert in bacteriology and the virulence mechanisms of *Salmonella*, especially the mechanisms of their interaction with host cells.

**References:**

1. Coburn B, Grassl GA, Finlay BB: **Salmonella, the host and disease: a brief review.** *Immunol Cell Biol* 2007, **85**(2):112–118.
2. Stocks CJ, Schembri MA, Sweet MJ, Kapetanovic R: **For when bacterial infections persist: Toll-like receptor-inducible direct antimicrobial pathways in macrophages.** *J Leukoc Biol* 2018, **103**(1):35–51.
3. von Pein JB, Stocks CJ, Schembri MA, Kapetanovic R, Sweet MJ: **An alloy of zinc and innate immunity: Galvanising host defence against infection.** *Cell Microbiol* 2021, **23**(1):e13268.
4. Kapetanovic R, Bokil NJ, Achard ME, Ong CL, Peters KM, Stocks CJ, Phan MD, Monteleone M, Schroder K, Irvine KM *et al*: **Salmonella employs multiple mechanisms to subvert the TLR-inducible zinc-mediated antimicrobial response of human macrophages.** *FASEB J* 2016, **30**(5):1901–1912.
5. Stocks CJ, Phan MD, Achard MES, Nhu NTK, Condon ND, Gawthorne JA, Lo AW, Peters KM, McEwan AG, Kapetanovic R *et al*: **Uropathogenic Escherichia coli employs both evasion and resistance to subvert innate immune-mediated zinc toxicity for dissemination.** *Proc Natl Acad Sci U S A* 2019, **116**(13):6341–6350.

# Training and skills

**Master's degree/Engineering degree**

- **Recommended training:** Master 2 (Bac +5) in Immunology or Bacteriology
- **Appreciated experience:** Previous work in BSL2 with pathogen(s), skills in bacteriology and cell culture, experience in bioinformatics would be a plus, ability to work successfully in a collaborative and inclusive environment.
- **Skills sought:** curious, assiduous, ability to set up and perform well designed experiments, good presentation skills.

# INRAE's life quality

By joining our teams, you benefit from (depending on the type of contract and its duration):

- up to 30 days of annual leave + 15 days "Reduction of Working Time" (for a full time);
- parenting support: CESU childcare, leisure services;
- skills development systems: training, career advise;
- social support: advice and listening, social assistance and loans;
- holiday and leisure services: holiday vouchers, accommodation at preferential rates;
- sports and cultural activities;
- collective catering.

## How to apply

Send in a combined PDF with a motivation letter stating why you are interested to join the MiMoSa research team and this research project (max 2 pages), a CV, your Master transcript and 2 referent names and their emails.

By e-mail: [ronan.kapetanovic@inrae.fr](mailto:ronan.kapetanovic@inrae.fr)


### OFFER REFERENCE

- **Contract:** PhD position
- **Duration:** 36
- **Beginning:** 01/10/2024
- **Remuneration:** 2100 €
- **Reference:** OT-21883
- **Deadline:** 31/05/2024



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### CONTACT

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**LIVING IN FRANCE AND WORKING AT INRAE**  
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