2019-01481 - Post-Doctoral Research Visit F/M PostDoc Campaign 2019: Role of small RNAs in the dialog between host and pathogens

Type de contrat : CDD de la fonction publique
Niveau de diplôme exigé : Thèse ou équivalent
Fonction : Post-Doctorant

**A propos du centre ou de la direction fonctionnelle**
Grenoble Rhône-Alpes Research Center groups together a few less than 800 people in 35 research teams and 9 research support departments.

Staff is localized on 5 campuses in Grenoble and Lyon, in close collaboration with labs, research and higher education institutions in Grenoble and Lyon, but also with the economic players in these areas.

Present in the fields of software, high-performance computing, Internet of things, image and data, but also simulation in oceanography and biology, it participates at the best level of international scientific achievements and collaborations in both Europe and the rest of the world.

**Contexte et atouts du poste**
The topic proposed in this postdoc started being addressed with a partner at the Federal University of Rio Grande do Sul, Porto Alegre, Brazil, namely Prof. Arnaldo Zaha, who is currently part of the LIA Lirio that Erable has with Brazil. It was also in the past part of another project funded by Capes-Cofecub.

**Mission confiée**
The mammalian respiratory tract is inhabited by diverse bacterial species, among which several cause diseases. Pathogenic bacterial infections of the respiratory tract are major causes of morbidity, are difficult to treat, expensive and can be life-threatening [1]. In the veterinary field, they are among the major health problems in the pig farming industry, and among them Mycoplasma hyopneumoniae, agent of swine enzootic pneumonia, and Actinobacillus pleuropneumoniae, agent of porcine pleuropneumonia, as important bacterial pathogens that greatly impact the swine production [2,3].

During infection, host and pathogen undergo significant changes in environmental and physiological conditions, which usually produce responses in both organisms [4]. These host-pathogen interactions induce changes in gene expression, leading to the activation of defense mechanisms in the host and of virulence genes in the pathogen. Small RNAs (sRNAs), especially miRNAs, are known to regulate gene expression in eukaryotes, being able to fine-tune this process [5]. There are several reports of miRNAs being regulated during bacterial infections [4,6]. These miRNAs are involved in the regulation of immune responses in order to eliminate the infection while preserving the organism from deleterious inflammation effects [4]. In addition, sRNAs were also identified in bacteria [7,8] and they might be involved in the crosstalk throughout the course of infection.

Generally, miRNAs bind to target mRNAs in order to change their stability and translation efficiency, leading to degradation, suppression or even up-regulation of the target mRNA levels [4,5]. Interactions between miRNA-mRNA are complex; one single miRNA can target a large number of genes belonging to diverse functional groups. Alternatively, the 3'-UTR of a single mRNA can be targeted by multiple miRNAs [5]. Bacterial sRNAs, on the other hand, work mainly by base pairing with their mRNA targets, regulating their translation or stability [8]. They may be involved in many biological processes, such as stress response, quorum sensing and virulence [8,9]. Besides regulating gene expression in the cells of origin, there are evidences that miRNAs can be transferred to target cells through extracellular vesicles (EVs), such as exosomes, and regulate the expression of these cells [10]. In addition, initial results of the team indicate that in infection of tracheal swine cells with *M. hyopneumoniae*, most differentially expressed (DE) miRNAs were found in the extracellular milieu and in EVs. Moreover, we identified the presence of bacterial sRNAs in the extracellular milieu of the infected host cells. Interestingly, the presence of exogenous sRNAs regulating gene expression was already identified in mammalian cells [11]. Furthermore, there are evidences of sRNAs involved in the communication between hosts and some pathogens, triggering gene silencing in the non-related species [12]. These evidences point to the fact that sRNAs in general may have an essential role in host and pathogen communication during infection.

While there is evidence of the importance of sRNAs in the interaction between host and microbe in the human gut, little is known about their role in the interaction between host and pathogens from the respiratory system. Given the importance of respiratory bacterial infections in the veterinary health, further research on this topic is needed. In this direction, the overall objective of this project is to validate intra- and cross-species targets of host miRNAs and bacterial sRNAs that were shown to be differentially expressed during infection in the respiratory system of swine.

We want to validate targets of eukaryotic DE miRNAs and bacterial sRNAs involved in infection of the respiratory system using sequencing data available from the literature and from our own previous work. We chose the swine host due to the importance of respiratory infections in swine production and our knowledge with this host model. We chose to work with *M. hyopneumoniae* due to our expertise with this pathogen and because this species is the most important pathogen in swine breeding.

**Informations générales**
- Thème/Domaine : Biologie numérique
- Biologie et santé, Sciences de la vie et de la terre (BAP A)
- Ville : Lyon
- Centre Inria : CRI Grenoble - Rhône-Alpes
- Date de prise de fonction souhaitée : 2019-10-01
- Durée de contrat : 1 an, 4 mois
- Date limite pour postuler : 2019-04-28

**Contacts**
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- Recruteur : Sagot Marie-france / mariel-sagot@inria.fr

**A propos d’Inria**
Inria, l’Institut national de recherche dédié aux sciences du numérique, promeut l’excellence scientifique et le transfert pour avoir le plus grand impact. Il emploie 2400 personnes. Ses 200 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3000 scientifiques pour relever les défis des sciences informatiques et mathématiques, souvent à l’interface d’autres disciplines. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 160 start-up. L’Institut s’efforce ainsi de répondre aux enjeux de la transformamtion numérique de la science, de la société et de l’économie.

**L’essentiel pour réussir**
Besides knowledge on the use of bioinformatics tools that were previously developed within the team or that will be developed in parallel, this project requires an expertise in conducting biological experiments. The recruited candidate will interact daily with members of the team who are from mathematics and computer science, and also with another member who has deep expertise in performing experiments. The person will also benefit from an environment, the Laboratoire de Biométrie et Biologie Evolutive of the University of Lyon, that will help with the experimental part, as will the collaborators the team has in Lyon, notably at the Anses, and in Brazil where the work of the team on this topic was initiated in the context of a CNRS LIA (Lirio) and of other projects, funded in particular by Capes-Cofecub.

**Consignes pour postuler**
Starting date: 1st October 2019, duration: 16 months.

Applicants should hold a PhD defended after 1st September 2017.

Applications have to be made on-line on the Inria web site before end of 28th April 2019.

**Sécurité défense**
Ce poste est susceptible d’être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L’autorisation d’accès à une
pleuropneumoniae, on the other hand, was chosen to identify general and species-specific effects of the infection on swine sRNAs. Working with two different bacterial pathogens will help us to identify which effects seem to be specific for determined pathogen and which ones are more general for infections in the respiratory system of swine.

From our previous work, we have data on miRNAs of swine tracheal epithelial cells (NPTr) DE during infection with *M. hyopneumoniae*. These miRNAs were predicted to target genes related to important cell structures, such as cytoskeleton and cilia, as well as genes involved in antioxidant response that are important to protect the cells against H₂O₂ produced by this pathogen [13]. From the literature, we will use datasets of DE miRNAs of swine infected with *A. pleuropneumoniae* [14] to predict and validate miRNA targets in the host and in the bacterial genomes. In addition, we want to validate the predicted targets of sRNAs from *M. hyopneumoniae* [7] and *A. pleuropneumoniae* [15] involved in host-pathogen interactions.

References:


**Principales activités**

Using both the *in silico* methods already developed or that will be developed in parallel in the Erable team, the postdoc will have as main activity to:

- identify targets of eukaryotic differential expressed (DE) miRNAs and bacterial sRNAs involved in infection of the respiratory system using sequencing data available from the literature and from our Erable's previous work;
- experimentally validate the targets identified.

We expect that these two activities will actually be concurrent, the first feeding the second but also vice-versa. The use of *in silico* methods will be done in collaboration with the person responsible for the postdoc (M.-F. Sagot) and with other members of the team with a background in mathematical modelling and algorithm design.

**Compétences**

Technical skills and level required:

- Expertise in conducting biological experiments
- Some knowledge on the use of bioinformatics tools related to the project

Languages: English is required, some knowledge of French would be a plus but is not required

Relational skills: Good relational skills, in particular with researchers from other disciplines

Other values appreciated: Autonomy and determination

**Avantages**

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

**Rémunération**

Gross salary: 2 653 Euros per month.