

## PhD fellowship in bioinformatics:

### **Searching for ICEs, Integrative and Conjugative Elements in bacteria: development of a tool for the search and the visualization of ICEs, and impact of these elements in the dissemination of antibiotic resistance genes**

**Background:** Mobile genetic elements play a key role in bacterial genome evolution by enabling gene acquisition through horizontal gene transfer (HGT). Multiplication of bacterial genome sequencing projects provided a remarkable opportunity to explore the pool of bacterial mobile genetic elements ("mobilome"). This shed the light on elements integrated in the chromosome called Integrative and Conjugative Elements (ICEs). These elements are still poorly known although all the very few ICE searches in genomes suggest their high prevalence in bacteria. ICEs encode their own excision, transfer by conjugation and integration. In addition to the genes involved or controlling their mobility, ICEs carry cargo genes, which can provide properties (adaptation, virulence, antibiotic resistance) advantageous for bacterial host. In particular, ICEs are vehicles for antibiotic resistance genes and therefore largely participate to their spreading and to the emergence of multi-resistant pathogenic bacteria. Bacterial genomes also carry another class of very poorly known but probably widespread elements that transfer by conjugation, that also participate actively to the dissemination of antibiotic resistance genes. These elements, called IMEs for "Integrative and Mobilizable Elements", subvert the transfer machinery of co-resident conjugative element to promote their own transfer.

**Position:** A 3 year-doctoral position will be available, starting from October 2017, for a junior scientist with a background in bioinformatics and bacterial genomics. The doctoral project aims at developing a bioinformatic tool dedicated to the search of ICEs and IMEs in bacterial genomes (particularly in Firmicutes, including many pathogens and bacteria from gut microbiota). The objectives are to constitute a pipeline allowing: (i) the automation of the search for ICE including the determination of their boundaries, (ii) the detection of their insertion sites within the chromosome, and (iii) the identification of the functions they encode. The characterization of the genes involved in their transfer will be used to classify ICEs and IMEs. The exploration of the accessory functions they code will allow us to evaluate the impact of ICEs on the adaptation of bacteria to environment. This work is based on exhaustive researches of the ICE and IME in the genomes of streptococci that demonstrate the extreme abundance and variety of these elements (Ambroset *et al.*, 2016; Coluzzi *et al.*, 2017). The objective will be to adapt the current method in order to enlarge it to the search of elements distantly or not related to the ones already identified, such as in *Escherichia*, *Salmonella* or *Vibrio*.

The project will be held in collaboration between the ICE-TeA team, Integrative and Conjugative Elements in Streptococci, of the DynAMic laboratory, Dynamique des génomes et Adaptation Microbienne (Université de Lorraine-INRA UMR1128, <http://dynamic.univ-lorraine.fr/>), and two teams of the INRA MaIAGE unit, Unité Mathématique et Informatique Appliquées du Génome à l'Environnement (INRA UR1404, Jouy-en-Josas, <http://maiage.jouy.inra.fr>): the MIGALE Bioinformatics platform team, <http://migale.jouy.inra.fr>, and the StatInfOmics team, Statistique et Bioinformatique des données Omiques. The successful candidate will be co-supervised by Pr. Nathalie Leblond-Bourget (DynAMic) and Dr. Philippe Bessières (MaIAGE), the applicant will join the ICE-TeA team of DynAMic in

Nancy and will regularly interact with the MaIAGE's teams. This work will also be done in collaboration with the CAPSID team of the LORIA in Nancy, on database developments. Applicants should have a strong interest in bacterial genomics and/or bacterial evolution, and knowledge in Microbiology would be greatly appreciated.

Scientific curiosity, professional conscience, ability for team-work and motivation are of foremost importance. Applicants should send a letter of motivation, CV detailing their computing skills and early experiences in Bioinformatics, and contact information of two references to [nathalie.leblond@univ-lorraine.fr](mailto:nathalie.leblond@univ-lorraine.fr) and to [philippe.bessieres@inra.fr](mailto:philippe.bessieres@inra.fr) (deadline: 25th of August 2017).

#### **Recent articles on ICEs and IMEs from the DynAmic unit:**

1. Dahmane N, Libante V, Charron-Bourgoin F, Guédon E, Guédon G, Leblond-Bourget N, Payot S. (2017). Diversity of integrative and conjugative elements of *Streptococcus salivarius* and their intra- and interspecies transfer. *Appl Environ Microbiol.* 83(13).
2. Coluzzi C, Guédon G, Devignes MD, Ambroset C, Loux V, Lacroix T, Payot S, Leblond-Bourget N (2017). A glimpse into the world of integrative and mobilizable elements in streptococci reveals their unexpected diversity and novel families of mobilization proteins. *Front Microbiol.* 8:443.
3. Ambroset C\*, Coluzzi C\*, Guédon G, Devignes M-D, Loux V, Lacroix T, Payot S, Leblond-Bourget N (2016). New insights into the classification and integration specificity of *Streptococcus* integrative conjugative elements through extensive genome exploration. *Front Microbiol.* 6:1483.
4. Chaffanel F, Charron-Bourgoin F, Libante V, Leblond-Bourget N, Payot S (2015). Resistance genes and genetic elements associated with antibiotic resistance in clinical and commensal isolates of *Streptococcus salivarius*. *Appl Environ Microbiol.* 81: 4155-63.
5. Bellanger X, Payot S, Leblond-Bourget N, Guédon G (2014). Conjugative transfer and the evolution of genomic islands in bacteria. *FEMS Microbiol Rev.* 38(4):720–60.

#### **Recent articles on Microbial Genomics from the MaIAGE unit:**

6. Deutsch SM, Mariadassou M, Nicolas P, Parayre S, Le Guellec R, Chuat V, Peton V, Le Maréchal C, Burati J, Loux V, Briard-Bion V, Jardin J, Plé C, Foligné B, Jan G, Falentin H (2017). Identification of proteins involved in the anti-inflammatory properties of *Propionibacterium freudenreichii* by means of a multi-strain study. *Sci Rep.* 7:46409.
7. Mäder U, Nicolas P, Depke M, Pané-Farré J, Debarbouille M, van der Kooi-Pol MM, Guérin C, Dérozier S, Hiron A, Jarmer H, Leduc A, Michalik S, Reilman E, Schaffer M, Schmidt F, Bessières P, Noirot P, Hecker M, Msadek T, Völker U, van Dijk JM (2016). *Staphylococcus aureus* Transcriptome Architecture: From Laboratory to Infection-Mimicking Conditions. *PLoS Genet.* 12(4):e1005962.
8. Mariadassou M, Pichon S, Ebert D (2015). Microbial ecosystems are dominated by specialist taxa. *Ecol Lett.* 18(9):974-82.
9. Lacroix T, Loux V, Gendrault A, Hoebeke M, Gibrat J-F (2014). Insyght: navigating amongst abundant homologues, synteny and gene functional annotations in bacteria, it's that symbol! *Nucleic Acids Res.* 42(21).