Genomic and metagenomic approaches for sustainable management of cyathostomins in horses

Hosting units:

- INRA/U. de Tours, UMR1282 Infectiologie et Santé Publique
- INRA/IFCE, UMR1313 Génétique Animale et Biologie Intégrative
- Parasite genomics team, The Wellcome Trust Sanger Institute

Context

Grazing horses are infected by a wide variety of gastro-intestinal strongyles, encompassing large strongyles (*Strongylus vulgaris*) or small strongyles (cyathostomins). *S. vulgaris* is the most pathogenic species and a frequent cause of colic but has been maintained under low prevalence thanks to anthelmintics. On the contrary, cyathostomin can infect up to 100% of horses and are responsible for growth retardation, weight loss, and a so-called larval cyathostominosis due to the emergence "*en-masse*" of encysted larvae from the colic mucosa where they reside. Without treatment such condition can lead to the death of infected horses in at least 30% of cases. Parasite control is therefore required but prevalence of anthelmintic-resistant populations threatens the sustainability of this approach. A recent survey in French farms and riding-schools demonstrated the generalized failure of fenbendazole but the high efficacy of ivermectin treatment. Pyrantel had an in-between status with lowering efficacy being reported. Three different strategies can be proposed to maintain the sustainability of anthelmintics in horses.

First, it is of primary importance to understand the genetic architecture underpinning pyrantel resistance in worm populations to monitor and foresee drug resistance emergence. This requires the building of genomic resources for most prevalent and most abundant cyathostomin species.

Second, a better understanding of the interactions between digestive microbiota and nematode community (10 to 20 species within a single horse) is required for both diagnostic purpose and the identification of putative bacterial species with anthelmintic activity.

Project outline

A first objective will consist in the building of reference genome for the three most prevalent and abundant cyathostomin species, *i.e. Cylicocyclus nassatus, Cylicostephanus longibursatus* and *Cyathostomuum catinatum*. Worm material will be sequenced by a combination of MinION, 10x Genomics and Illumina technologies. After genome assembly and annotation, comparative genomics approaches will be applied to gain a better knowledge of worm biology and a drug repurposing approach will be attempted through an *in-silico* screening.

Building upon the newly assembled and annotated genomes, the population genetic structure of these species will be investigated from a set of worms collected in Europe (France, Poland) and the USA. The genetics of pyrantel resistance will be investigated by a pool-sequencing approach contrasting pyrantel-resistant and pyrantel-susceptible isolates from French stud farms.

A third objective will be dedicated to the characterization of biotic interactions between gastrointestinal microbiota and parasitic communities. This should provide innovative biomarker of infection and will unravel interactions between parasitic and bacterial communities that could further the identification of bacterial anthelmintic compounds.

Essential skills

- Msc in quantitative genetics, population genetics, biostatistics or bioinformatics;
- Proficiency in R, Shell, Python/Perl under a unix environment;
- Fluent spoken and written English;

Ideal skills

- Education in agronomical/veterinary sciences or ecology;
- Previous wet lab experience (helminthology diagnostics, molecular biology)
- Knowledge in computational biology
- Experience with NGS data
- Proven experience of problem solving
- Ability to work independently, under a fast-pace environment and to deliver results to various stakeholders

Other information

The student will be based in Tours (37) and Jouy-en-Josas (78), with a three to six-month stay at the Wellcome Trust Sanger Institute.
Contract duration: 3 years
Estimated annual gross salary: 21240 euros
Target start date: October, 2018.

Please include a covering letter addressed to Dr Guillaume Sallé, Guillaume.Salle@inra.fr and CV with your application, along with one reference letter.

Applications will be reviewed on an ongoing basis until a candidate is found suitable for the job.