PATHOGENS AND IMMUNOGENETICS: ANALYSING VIRUS SPECIFICITY AND RISK OF RODENT BORNE EMERGING DISEASES

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Immunogenetics focuses on the study of immune defence genes and on the variability of outcomes generated by genotype-genotype interactions between and within host and parasite species. One of the leading goals of immunogenetics has been to understand the associations of genetics to immune related diseases. The profound influence of the host genetics on resistance to infections has yet been established in numerous animal studies, which mainly concerned human infections such as malaria, HIV and hepatitis. Analysing the fitness consequences of immune gene polymorphisms and the patterns of evolutionary change over time and space is a second step through the understanding of host-parasite interactions. Immunogenetics might hence provide essential information to disentangle the effects of genetic variation and environmental factors on the differences observed in the impact of parasites on individual hosts or populations. Immunogenetics may provide key insight into epidemiology and transmission ecology, and may contribute to the identification of zoonotic potential of previously unidentified agents. Moreover, polymorphism and selective pressure acting on these genes could affect the parasite specificity, and the development of local adaptation. Another potential application of immunogenetics thus concerns the assessment of emergent or re-emergent disease risks in natural populations

In this context, the Major Histocompatibility Complex (MHC) has been extensively studied. It is a central component of the vertebrate immune system. Certain of these genes are among the most polymorphic coding regions of the genomes. There are multiple lines of evidence supporting the idea that this polymorphism is maintained by some form of balancing selection mediated by pathogens and parasites through frequency-dependent selection.

During this talk, we are going to analyse the genetic diversity of two class II MHC genes at different evolutionary scales in voles. First, we will analyse the phylogenetic organisation of allelic forms within three sympatric vole species in search for the existence (or not) of trans-species polymorphism (TSP). Observing TSP would indicate a probable important selective force exerted by shared pathogens. Second, we will search associations between haplotypes and Hantavirus presence in voles of the same species. In this goal, class II MHC

genes are adequate candidates because of their well known role in Puumala Hantavirus infections severity in humans. Finally, we will conclude on the importance of an immunogenetic approach for analysing virus specificity and the risk of emerging diseases.
Our study site is located in the East of France, an endemic area of Hemorrhagic Fever with Renal Syndrome, disease caused by Hantaviruses. In this region, three Arvicoline species were studied: the bank vole *Clethrionomys glareolus* (reservoir of Puumala), the common vole *Microtus arvalis* (reservoir of Tula) and the water vole *Arvicola terrestris* (not yet reservoir of an identified Hantavirus).
1. The two most polymorphic MHC class II genes, namely the exon II of DQA and DRB genes, have been developed for the three vole species in our laboratory. The phylogenetic analysis of the allelic sequences detected at the exon II of the DQA gene revealed extensive trans-species polymorphism within the Arvicoline subfamily although no alleles were shared between species in our data set. This suggests the non-neutral retention of MHC sequences across different genera of voles causing discordance between MHC sequences and species trees. Parasites shared between these Arvicolines could actually be the evolutionary pressure that causes this trans-species polymorphism.
2. Positive associations between one *A. terrestris* DQA haplotype and presence of anti-hantavirus antibodies revealed that this haplotype could be in relation with a higher susceptibility to infections by Hantaviruses. The detection of similar associations in *M. arvalis* and *C. glareolus* are under progress.
In conclusion, we will show how these results highlight the importance of immunogenetics in emerging rodent-born diseases.