Influenza “D” virus: which host range for this novel pathogen?

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Cross-species transmission of pathogens from the animal reservoir to domestic species and ultimately to humans constitutes a major risk for animal or human health. Recent studies in the USA and our preliminary work in France have identified a new Genus tentatively named Influenzavirus D within the *Orthomyxoviridae* family. The novel virus was shown to infect swine and cattle and to efficiently replicate and transmit in ferrets, the animal model of choice for the study of influenza in human, suggesting that humans could be infected. Our project aims at assessing the emergence threat associated with influenza D viruses’ circulation. We will screen samples from different animal species (wild and domestic) for the presence of influenza D virus and antibodies against the novel virus to assess the host range of the pathogen. Our field samples originate from France and from Africa.

Keywords: influenza D virus, host range, serology, molecular biology

Molecular epidemiology of infectious bronchitis viruses in Morocco

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Within the framework of our collaboration with the Institut Agronomique et Vétérinaire Hassan II in Rabat, Morocco, we study the circulation and evolution of avian coronaviruses in Morocco. In Africa, very little is known on avian viruses, their circulation, evolution and spread. The aim of the internship is to understand putative virus exchanges between wild and domestic birds and between geographic areas. We will work on Moroccan field samples, screen them for infectious bronchitis virus by RT-PCR, isolate virus in embryonnated eggs, and carry out a molecular characterization of the strains (partial or full genome sequencing, phylogenetic analyses). Our findings will be compared with available data available from Europe and North Africa.

Keywords: avian respiratory virus, avian coronavirus, Morocco, molecular epidemiology

FlyScreen project
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Facing increasing needs to feed human populations requires, more than ever, enhancing quantity, quality, safety and security of agricultural products, and, at the same time, to reduce environmental contamination. Thus, in livestock production, it is required to control blood-feeding flies such as tabanids and stable flies which are responsible of huge annual economic losses, stress, loss of appetite and energy, immunosuppression and mechanical transmission of viruses, bacteria and parasites. Control of hematophagous flies is most often neglected or occasional, is expensive, of low efficacy and meets increasing chemo-resistance problems. Moreover, residues contamination of animal products and environment is unacceptable, especially for organic farming.
Tsetse fly control using insecticide impregnated targets proved to be efficient in Africa, because tsetse flies have low prolificacy and are very sensitive to insecticides. Unfortunately this does not apply to otherhematophagous flies such as Tabanids (> 4000 species present in all types of environments and climates).
Moreover, Stomoxys species (one species is cosmopolite) which are highly prolific, may develop early chemo-resistance to insecticides.

FlyScreen project aims at the development and optimization of efficient, low cost and low or non-polluting methods for the control of hematophagous insects. It will consist in: (i) designing and optimizing specific color baited attractant screens/traps (excluding pollinators); (ii) developing and evaluating in laboratory conditions various toxic systems including: growth hormones or insecticides incorporation into polymers (slow release), single or combined, UV and water-protection (iii) evaluating and validating these screens in semi-liberty and field conditions to measure efficacy and environmental safety; and (iv) promoting lowcost, low-polluting, and possibly insecticide-free control methods.
FlyScreen project will be carried out in partnership by UMR17/InterTryp (CIRAD-bios), UMR1225/ IHAP (National Veterinary School of Toulouse ; ENVT), UMR 5175/CEFE UPVM (University Paul-Valery, Montpellier) and Kasetsart University (Bangkok, Thailand)

The intern will help in the third objective of the project (evaluation of screens in the campus of the National Veterinary School of Toulouse and in farms located in the vicinity of the city)

Development of an integrative approach to evaluate the human fœtal internal exposure to bisphenol S

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Xenobiotic exposure of the foetus during critical windows of development have repeatedly been suggested to be involved in the onset of a variety of biological effects later in life, even when exposure occurs at low doses. In particular, impaired regulation of steroid hormones contributes to the development and progression of several major diseases. The bisphenol S (BPS) is widely used as a substitute for bisphenol A. Its estrogenic properties are similar to that of Bisphenol A and the toxicity data for fetal exposure are, to date, non-existent. So, to not reproduce another controversy about BPS, the development of methods able to predict the extent of human fetal internal exposure to BPS is critical to determine if the substitution of bisphenol A by the BPS is an acceptable alternative in terms of human health risk.

Our project aims to determine the toxicokinetic parameters of BPS on integrative physiological models and to develop a modeling approach able to predict, in humans, the fetal internal exposure to the active form of BPS. On the chronically catheterized pregnant sheep model, we have shown that BPS cross the placental barrier and is metabolized by the feto-placental unit into BPS-glucuronide, which is inactive. This main metabolite is not able to pass through the placenta and is trapped into the fetal compartment. We have shown also that BPS glucuronide is reactivated into BPS by hydrolysis, leading to a persistence of BPS into fetal compartment. For extrapolating data from the ovine model to humans, it is necessary to determine specific mechanistic data on human model.

In that context, the project of the study will focus on the detailed mechanism of BPS and BPS glucuronide placental transfer on an ex vivo model of human perfused placenta.

These data will be implemented to a physiologically based toxicocinetic model to predict the human fetal exposure from the external maternal exposure. As fetal period represents a critical BPA exposure window, such integrative toxicockinetic approach will provide new insights for human health risk assessment.

Potential roles of stable fly *Stomoxys calcictrans* and *Aedes albopictus* as vectors of the Lumpy skin disease (LSD)

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is a poxviral disease affecting cattle. It is of primary economic importance and notifiable for the world organization for animal health (OIE). LSD is widely distributed in many African countries where it is considered endemic. Since 1989, LSD spread on an unusually large scale affecting Middle Eastern countries, Turkey, Kazakhstan, Azerbaijan, Russia, but also European countries. Indeed, since 2015 where the first outbreak was reported in Greece, LSD expanded uninterruptedly to new territories with ongoing outbreaks still arising in Greece, Macedonia, Albania, Bulgaria, Montenegro and Serbia (2016, OIE, WAHID).

Previous studies demonstrated a potential role of certain hematophagous arthropod vectors (stable flies, mosquitoes, and certain tick species) in the transmission of the virus. The stable fly *Stomoxys calcitrans* is indeed considered as the most likely candidate to play a role in the epidemiology of the LSD. However a formal demonstration of its role in the transmission of LSDV has not been made yet. The mosquito *Aedes aegypti* has been reported once to transmit LSDV in cattle under experimental conditions (Chihota et al., 2001). However no data are available on the potential vectorial role of *Aedes albopictus* now widely settled in Europe. In this context, the Parasitology and Virology teams of the National Veterinary School of Toulouse, France will focus on the cosmopolitan stable fly *Stomoxys calcictrans* and on the invasive mosquito species *Aedes albopictus* to ascertain their potential roles as vectors of the LSDV. These investigations are conceivable as these two species of insects are maintained under laboratory colonies in the National Veterinary School of Toulouse.

These investigations will have the folllowing objectives: i/ to confirm the transmission of LSDV by *S. calcitrans* using an in vitro model and to investigate its possible transmission by *Aedes albopictus*, ii/ to assess the virus titer threshold still enabling a transmission in vitro by these two vectors, iii/ to determine the virus lifespan in its vectors, iv/ to ascertain the maximal delayed transmission after a contaminated blood-meal.

During his internship the student will actively take part of the experiments: he will participate to the experimental infection of the insects with the LSD virus, and will learn how to dissect the insects to isolate the mouthparts, and abdominal parts to further analyze them using molecular tools, so as to look for the presence of the virus.

Modulation of the innate immune response by changes in the cellular lipid composition Romain Volmer

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Diet or stress-induced changes in the lipid composition of cellular membranes have been shown to correlate with low-grade inflammation contributing to morbidity in a number of diseases, including morbid obesity, by mechanisms that remain poorly understood. The goal of this project is to test the hypothesis that changes in the cellular lipid composition modulate toll-like receptor signalling by regulating the oligomerization state of toll-like receptors. The student will perform state of the art cellular and in vitro assays.