Analysis of micro-evolutionary changes in a host genome in response to multiple viral infections in wild animals

The increasing scale of human mediated environmental change raises concerns regarding the appearance of new infectious diseases, as a result of either changing climate or human activity. To better understand the effect of these new diseases on wild populations, it is crucial to comprehend the genetic mechanisms underlying fast adaptation in wild organisms to their changing environment. Although various theoretical models of this process exist, robust empirical data from wild populations is still lacking to corroborate them. Ideally, theoretical models should be tested using genomic data from DNA samples obtained when populations were exposed to a novel pathogen.

However, it is challenging to obtain such materials, because collecting DNA samples representing changes in a population during a sufficiently long period is very difficult, particularly for highly mobile, elusive animals. This project will take advantage of a sample archive of the Mediterranean population of striped dolphins (*Stenella coeruleoalba)* to quantify genome-wide genetic variation changes during 20 years, using cutting edge genomic technologies. The archive contains samples from nearly every year from a 20 year period, during which striped dolphins have experienced repeated outbreaks of morbillivirus, a lethal virus related to human measles and canine distemper virus.

Preliminary results for two immune system genes suggest increasing adaptation of the host's population to the pathogen over the time studied. This host-pathogen system therefore represents an unprecedented natural model for the study of pathogen adaptation in wild animal populations. Because morbillivirus infection is usually associated with other opportunistic infections (such as *Toxoplasma*), a more comprehensive analysis of immune system genes across the whole genome is necessary to understand the host adaptation process to new pathogens.

For this purpose, we will sequence all currently known immune system related genes, which will allow a direct comparison between the genetic changes observed during 20 years and their potential role in enhancing resistance to the virus. For a comparison, variation at genome regions without any function will also be determined, using a technique that generates sequences of small DNA regions randomly sampled from across the entire genome. These data will allow assessing the influence of other potential genetic factors, such as decline in genetic diversity due to inbreeding.

This project is technically challenging, but offers a significant advance in our understanding of molecular adaptation mechanisms, not possible to achieve without the long-term comprehensive sampling from this wild population. The proposed study will allow validation of theoretical models using data from a natural host-pathogen system, and thus contribute to the improvement and refinement of such models. Because new infectious diseases are commonly transmitted between wildlife and domestic animals, the results of the proposed project may also stimulate further research on the effects of new infectious diseases on endangered wild species and on domestic animal health.