Bruce-GenoProt

PROJECT SUMMARY

Brucellosis is a debilitating and incapacitating bacterial disease that affects all livestock species and wildlife. Despite the fact that the disease has been eradicated from many countries, it still causes public health concerns and economic losses in animal productions, particularly in the Mediterranean countries. In the last few years, brucellosis has reemerged as a new challenge with new foci of disease, both in humans and animals. Brucellae have been isolated from wildlife, carrier hosts and non-classical hosts. However, little information is available on the role of environment and wildlife in transmission and dissemination of the infection. Moreover, the risk for livestock and humans infection concerning wildlife and carrier hosts' contact and environmental contamination cannot be assessed. Tackling this disease will improve animal health and productivity and bolsters the economies. Several aspects of its biology, host/pathogen interaction and virulence mechanisms are not understood yet. To explain its epidemiology, virulence mechanisms and host specificity, a better understanding of **Omics (genomics, transcriptomics, proteomics and metabolomics)** of brucellae will be needed. To date, few multicenter projects have been conducted on genomics and proteomics of *Brucella* and this kind of approach is paramount to tackle this dangerous disease.

Thus, the main objectives of the current project are to assess the role of environment and wildlife in transmission and dissemination of brucellosis, development of a cgMLST scheme for epidemiological investigation, as well as to unravel several enigmatic aspects of *Brucella* utilizing various proteogenomics and transcriptomics approaches. A representative number of *B. abortus* and *B. melitensis* strains collected from different host reservoirs (cattle, buffaloes, sheep, goats, camels, and wildlife) will be investigated by whole genomic sequencing and complete proteomic analysis. A comprehensive evaluation of the differences in genomes of *B. abortus* and *B. melitensis* isolated from different hosts using NGS technology will help to understand the genetic code of the entire organism, as well as it will provide an overview of the unique virulence and host related genes in each species. Pan-proteomic analysis of the same set of isolates will be applied to understand the consequences of regulatory processes on the protein composition of the microbe. Culturing and growth of strains from different hosts under stress conditions will be evaluated by transcriptomics, genomics and proteomics. Experimental infection of cell lines originating from cows and sheep (bovine and sheep trophoblast cells) with *B. abortus* and *B. melitensis* will be carried out, and the outcomes will be assessed by RNA sequencing, WGS and proteomics technologies. We expect to develop a cgMLST scheme useful for epidemiological investigations and for tracing back the sources of brucellosis at least in domestic ruminants (sheep, goats, cattle, water buffaloes and camels) living in the participating countries. On the other hand, we want to carry out a detailed characterization of *B. melitensis* and *B. abortus* pan-proteome and genome that will further extend current knowledge on *Brucella* biology, host-pathogen interaction, virulence mechanisms and host specifity.

All results achieved will be used to understand several ambiguous aspects of brucellosis, as well as applied to improve indirect diagnosis by developing a novel serological test. Besides, results obtained will serve scientific bases for the development of promising recombinant vaccine candidates and protein antigens for diagnosis. The data obtained from the WGS and proteomics analysis will help to explore the secret behind host specificity and host/pathogen interaction phenomena, as well as to explore the undiscovered virulence mechanisms. This will help to unravel the unknown mechanisms of infection and develop strategies to hinder the spillover of the diseases.