Hosts are under evolutionary pressure to be able to fight infections, whereas infectious organisms are under selection to evade host immune system. This paradigm predicts co-evolution of host immune systems and their targets in pathogens, with both parties in a need for continuous adaptation in order to keep up with the opponent – a dynamics described as a Red Queen process after the character in Lewis Carroll's Through The Looking-Glass who tells Alice "It takes all the running you can do, to keep in the same place". Such co-evolution may have important consequences for several crucial evolutionary processes the maintenance of sex, sexual selection, speciation and evolution of virulence. Yet, demonstrating that co-evolution is actually occurring requires knowledge of interacting genes in both hosts and parasites. This condition is fulfilled for Lime-disease agent, the spirochete *Borrelia* and its mammal hosts.

Mammalian complement system, an important part of innate immune system, and microorganismal proteins downregulating its function have recently emerged as an excellent candidates to study host-parasite co-evolutionary dynamics at the level of genes. *Borrelia* is a prominent example of bacteria using a range of strategies of complement evasion. As a result of intense research driven by a role of *Borrelia burgdorferi sensu lato* as an agent of epidemiologically important Lyme disease, interactions between vertebrate complement system and evasion molecules produced by *Borellia* are now well understood. This provides an excellent, but as yet underused, potential for evolutionary biologists to study host-parasite coevolution at the level of genes. Within the proposed project, complement factor H (CFH), preventing complement system from attacking host's own cells, and OspE proteins of *Borrelia* which highjack CFH to evade complement, will be studied. By testing if spirochete OspE genes are adapted to infect local host CFG genotypes we hope to provide a textbook example of host-parasite co-evolution at the level of molecules. Another pair of genes we intend to study are host major histocompatibility complex (MHC) genes, and their target in inciting adaptive immune response, *Borrelia* OspC proteins, necessary for the spirochete infection success.

Furthermore, we will use the CFH/OspE system to investigate the potential of host-parasite co-evolution to lead to speciation. Our preliminary data indicate that bank vole populations in regions colonized by from two different glacial refugia (Carpathian and Eastern) are dominated by different variants of CFH genes, which contrasts with many other genes in the genome. We will test the hypothesis that co-evolution between OspE and CFH caused emergence of a barrier to CFH gene flow in a zone of secondary contact between vole clades which originated from different glacial refugia. This barrier can be either due to adaptation of CFH genes to deal with local Borrelia strains or CFH-associated autoimmunity problems in hybrids. Both scenarios will be tested in the proposed project.

Finally, we intend to test whether changes in species ranges, eg. due to environment changes, facilitate evolution of supervirulent pathogens. This may occur if hosts are less likely to raise immune response against pathogens they have not coevolved with, or if genetic exchange between parasite strains leads to increased virulence. Both scenarios will be tested using *Borrelia*-vole system.