Abstract

Toll-like receptors (TLRs) are one of the key and presumably also evolutionary most original components of animal immune system. As Pattern recognition receptors they form the first line of innate immune defence against various pathogens. The proper receptor binding of pathogenic ligands is crucial for their correct recognition and for subsequent triggering of an appropriate immune response. Because there exists a direct interaction between the receptor surface and the pathogenic ligand, host-pathogen coevolution on molecular level can be predicted. Thus, through variability of their ligands, TLRs are exposed to extensive selective pressures that may be detected on both genetic and protein levels. Surprisingly, the variability we revealed in birds is even higher than previously expected based on the reports from other vertebrates, mainly mammals. In my doctoral thesis I summarise the results of my contribution to the avian TLR research. We were the first who experimentally verify the absence of functional TLR5 in several avian species and duplication of TLR7 in others. We finally resolved the origin of duplication in TLR1 and in TLR2 family. An important part of my research project focused on the prediction of potentially functionally important positions in TLRs. We have outlined an investigation strategy universally applicable to any coding genes. Moreover, we found that some of the positively selected positions importantly affect the surface charge distribution. In passerine birds, we also attempted to find ecological factors determining the adaptive evolution in TLRs. However, this attempt was unsuccessful. Besides that, our methodological research improved the knowledge of the molecular background of the PHA-skin swelling test used for assessing the inflammatory responsiveness related to the TLR function. Since further research is highly needed to test the real functional effect of the TLR genetic variation, at the end of this thesis I outline several possible future directions.

Key words:

adaptive evolution, birds, gene duplication, gene expression, host-pathogen coevolution, inflammation, protein structure, pseudogenisation, selection, surface electrostatic potencial, TLRs