MAPPING OF GENES, WHICH MODIFY SUSCEPTIBILITY TO *Leishmania major* INFECTION

Leishmania parasites cause complex of diseases that are called leishmaniasis. Symptoms of leishmaniasis range from subclinical to extensive systemic disease with splenomegaly, hepatomegaly, skin lesions, anemia and hyperglobulinemia and in some cases, it can leads to death. It was established that the disease is controlled by many genes, but the basis of variation of symptoms is still unknown. Many of the symptoms observed in human can be studied in mouse model.

The dissection of genetic and functional aspects of susceptibility to infection of *L. major* was performed using two contrasting inbred strains BALB/cHeA (susceptible to infection) and STS/A (resistant to infection) and a set of 20 CcS/Dem recombinant congenic strains. Each of the 20 CcS/Dem strains contains a unique random set of 12.5% genes from the resistant donor strain STS and 87.5% genes from the susceptible background strain BALB/c. The CcS/Dem strains differ in part of STS genome between each other.

I have used F_2 hybrids between the intermediately resistant recombinant congenic strain CcS-9 and the susceptible strain BALB/c. F_2 hybrids were infected by *L. major* and were killed at week 8^{th} after infection. I tested the disease phenotype (including skin lesion size, hepatomegaly, splenomegaly, parasite load in spleen and lymph nodes and levels of IgE, IFNγ, IL-4, IL-10, IL-12 a IL-13 in serum) and genotyped all F_2 hybrids by eighteen microsatellite markers.

I performed linkage analysis between genetic markers and each fenotypic parameter using analysis of variance (ANOVA). I found five loci which control one or more fenotypic parameters. I confirmed position and found new functions of locus *Lmr15* and *Lmr18*, which influence response to *L. major* in strains CcS-16 and CcS-20, respectively, and mapped three novel loci: *Lmr24*, *Lmr25* and *Lmr26*. Future research will be concentrated on finding candidate genes in these loci. The definition of genes controlling response to *L. major* infeciton will permit a better understanding of pathways and genetic diversity underlying the course of disease.

Leishmania major – immune response – genetic control - mouse model – quantitative trait loci (QTL) - linkage analysis