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Functional gene mapping, leishmaniasis, atopy



Research topics

The laboratory is dealing with two main topics:

- Mapping and functional analysis of genes that control resistance to infection
- Genetic and environmental influence on atopy

We study the genetic regulation of interaction between the immune system and the infectious agent in leishmaniasis. The disease is caused by protozoan parasites of genus *Leishmania* that multiply in macrophages. Different species of *Leishmania* induce different symptoms, but even the patients infected by the same species develop different clinical manifestations. Many phenomena observed in human leishmaniasis can be investigated in *Leishmania major* infection in mouse. Our work is aimed at identification and functional analysis of genes influencing the course of *L. major* infection in mouse. Our approach uses a combination of genetic dissection with screening of a large set of immunological and clinical parameters of the disease. We found that *Lmr* (*Leishmania major response*) gene effects on disease symptoms were organ-specific and heterogeneous. Thus, these studies revealed a network-like complexity of the combined effects of multiple functionally diverse QTLs (quantitative trait loci).

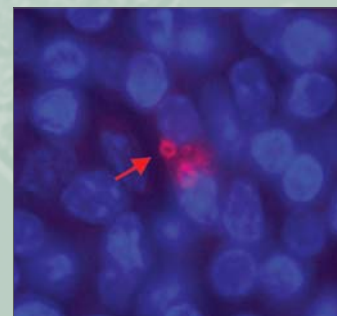
Interestingly, six of nine *Lmr* that influence serum IgE level after *Leishmania major* infection were mapped in the regions homologous with the human chromosomal segments that control total serum IgE in human atopic diseases. Genetic analysis in the mouse can therefore help identify in these regions the unknown genes that control atopic response in humans.

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Selected recent papers

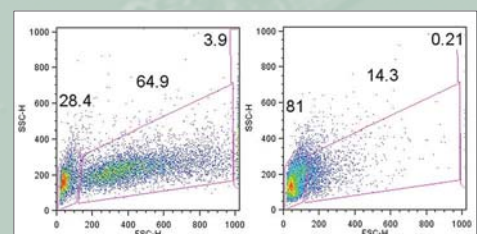
1. Gusareva ES, Bragina EJ, Deeva EV, Kazakevich NV, Puzyrev VP, Ogorodova LM, Lipoldová M. Cat is a major allergen in patients with asthma from west Siberia, Russia. **Allergy**. 2006;61:509-510.
2. Havelková H, Badalová J, Svobodová M, Vojtišková J, Kurey I, Vladimirov V, Demant P, Lipoldová M. Genetics of susceptibility to leishmaniasis in mice: four novel loci and functional heterogeneity of gene effects. **Genes Immun**. 2006;7:220-233.
3. Lipoldová M, Demant P. Genetic susceptibility to infectious disease: lessons from mouse models of leishmaniasis. **Nat Rev Genet**. 2006;7:294-305.
4. Gusareva ES, Ogorodova LM, Chernyak BA, Lipoldová M. Relationship between total and specific IgE in patients with asthma from Siberia. **J Allergy Clin Immunol**. 2008;121:781.



Leishmania tropica



Cutaneous leishmaniasis



Flow cytometry analysis of different growth forms of *Leishmania major* promastigotes

Left. Third day of cultivation (logarithmic phase of growth). Left frame – procyclics, central frame – nectomonades, right frame – other forms

Right. Seventh day of cultivation (stationary phase of growth). Left frame – metacyclics and haptomonades, central frame – nectomonades, right frame – other forms