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Transplantation immunity, cytokines, immunoregulation

## Research topics

Immunological rejection represents the major obstacle for further development of clinical transplantation. Therefore, the insight into the cellular and molecular mechanisms of immunological reaction and the search for possibilities to manipulate with the immune response are the main tasks of the group.

Using the model of skin grafting in mice we characterized the role of nitric oxide produced by graft-infiltrating macrophages after allo- or xenotransplantation. Recent research is focused on the study of activation and function of regulatory T cells in transplantation immunity and tolerance. Using the model of orthotopic corneal transplantation we have analysed expression of genes for cytokines and other effector molecules during graft rejection and studied possibilities to prevent rejection of corneal grafts.

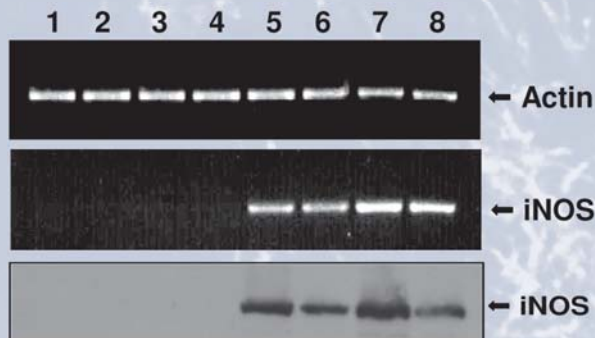
Well-established methods for monitoring the immune response enabled us, in co-operation with other laboratories, to study cytokine response in various experimental models of immunoregulation. The ultimate goal of our research is to get insights into the mechanisms of specific immune response and to propose and test novel strategies for targeted immunoregulation.

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### Selected recent papers

- Holář V, Pindjácová J, Krulová M, Neuwirth A, Zajícová A, Frič J. Production of nitric oxide during graft rejection is regulated by the Th1/Th2 balance, the arginase activity and L-arginine metabolism. *Transplantation*. 2006;81:1708-1715.
- Holář V. Corneal stromal cells selectively inhibit the production of certain anti-inflammatory cytokines. *Expert Rev Clin Immunol*. 2006;2:101-108.
- Havelková H, Holář V, Kárník I, Lipoldová M. Mouse model for analysis of non-MHC genes influencing allogeneic response: recombinant congenic strains of OcB/Dem series that carry identical H-2 locus. *Central Eur J Biol*. 2006;1:16-28.
- Kubera M, Roman A, Basta-Kaim A, Budziszewska B, Zajícová A, Holan V, Rogoz Z, Skuza G, Leskiewicz M, Regulska M, Joglek G, Nowak G, Lason W. Effect of acute and repeated treatment with mirtazapine on the immunity of noradrenaline transporter knockout C57BL/6J mice. *Pharmacol Biochem Behaviour*. 2006;85:813-819.
- Tavandzi U, Procházka R, Usvald D, Hlučilová J, Vításková M, Motlík J, Vítová A, Filipec M, Forrester JV, Holář V. A new model of corneal transplantation in the miniature pig. Efficacy of immunosuppressive treatment. *Transplantation*. 2007;83:1401-1403.



Expression of gene for iNOS and production of iNOS protein in normal mouse skin (1,2), syngeneic skin graft (3,4), rejected allograft (5,6) and rejected xenograft (7,8).



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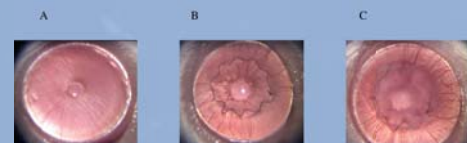
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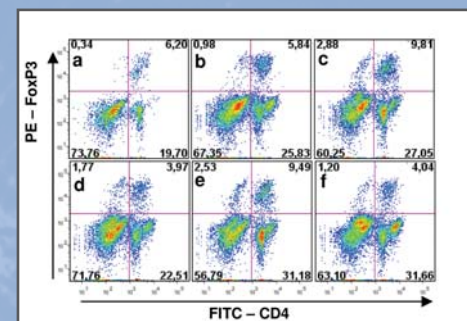
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Orthotopic corneal transplantation in mice. A – healthy mouse eye, B – surviving corneal allografts, C – rejected corneal allografts.



Flow cytometry analysis of mouse spleen cells expressing Foxp3, a marker of regulatory T cells.