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Laboratory of Transplantation Immunology

Transplantation imunity, cytokines, stem cells, immunoregulation

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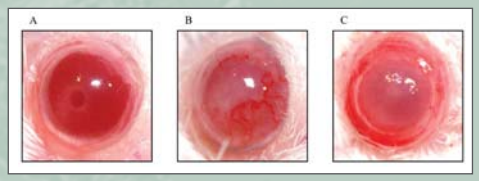
Research topics

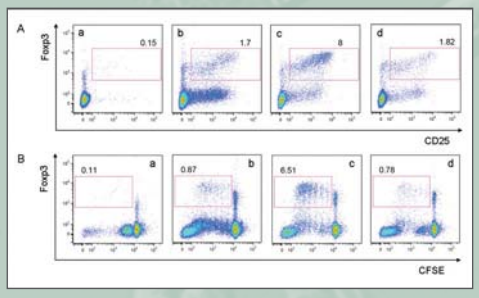
Transplantation of a damaged or non-functional organ often represents the only way to improve or even to rescue life. However, immunological rejection represents the major obstacle to further development of clinical transplantation. Therefore, deep knowledge of molecular and cellular mechanisms of the transplantation reaction is required. Using experimental models of corneal and limbal transplantation in mice we study regulatory mechanisms in the eye and the possibilities to treat corneal injuries by transplantation of limbal stem cells.

Using the model of immunological reaction to histocompatibility antigens we are focused on the study of activation and function of regulatory T cells in transplantation immunity and tolerance. On the model of orthotopic corneal and limbal transplantation we have analysed expression of genes for cytokines and other effector molecules during graft rejection and studied possibilities to prevent rejection of corneal and limbal grafts. Since successful treatment of damaged cornea requires transfer of limbal stem cells, we recently started to isolate, grow and characterize stem cells. We succeeded in isolating limbal stem cells in the mouse and using them for the repair of damaged corneal epithelium.

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, to isolate and transplant stem cells and to propose novel strategies for targeted immunoregulation.



Limbal transplantation in the mouse. A – syngeneic graft, B – allograft, C – xenograft



Induction of CD4⁺CD25⁺Foxp3⁺ regulatory T cells by alloantigens and TGF-β (A) and monitoring of cell proliferation using CSFE (B)

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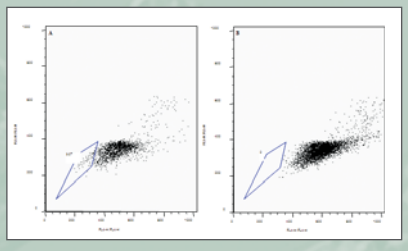
GA AS CR (KAN 200520804), GA CR (GA309/06/0121, GA206/08/0640, GD310/08/H077), 6th FP EC (018094), Ministry of Education, Youth and Sports (Center for Molecular and Cellular Immunology, 1M0506)

Selected recent papers

1. Tavandzi U, Procházka R, Usvald D, Hlučilová J, Vitásková M, Motlík J, Vítová A, Filipec M, Forrester JV, Holáň V. A new model of corneal transplantation in the miniature pig. Efficacy of immunosuppressive treatment. **Transplantation.** 2007;83:1401-1403.
2. Frič J, Marek M, Hrušková V, Holáň V, Forstová J. Cellular and humoral immune responses to chimeric EGFP-pseudocapsids derived from the mouse polyomavirus after their intranasal administration. **Vaccine.** 2008;26:3242-3251.
3. Piálek J, Vyskočilová M, Bímová B, Havelková D, Piálková J, Dufková P, Bencová V, Dureje L, Albrecht T, Hauffe HC, Macholán M, Munclinger P, Storchová R, Zajícová A, Holáň V, Gregorová S, Forejt J. Development of unique house mouse resources suitable for evolutionary studies of speciation. **J Hered.** 2008;99:34-44.
4. Krulová M, Pokorná K, Lenčová A, Zajícová A, Frič J, Filipec M, Forrester JV, Holáň V. A rapid separation of two distinct populations of corneal epithelial cells with limbal stem cell characteristics in the mouse. **Invest Ophthalmol Vis Sci.** 2008;49:3903-3908.



Detection of limbal stem cells as a "side population" based on the ability of stem cells to efflux DNA-binding dye Hoechst 33342 (A) and blocking the efflux by ABCG2 transporter inhibitor verapamil (B)