Laboratory of Transplantation Immunology

Transplantation immunity, cytokines, stem cells, immunoregulation

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Transplantation of organ or transfer of stem cells 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 the model of immunological reaction to histocompatibility antigens we have 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 and mesenchymal stem cells in the mouse and using them for the repair of damaged corneal epithelium. For the transfer of stem cells we use various types of nanofibre scaffolds, which represent optimal 3D matrices for stem cell growth. 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.

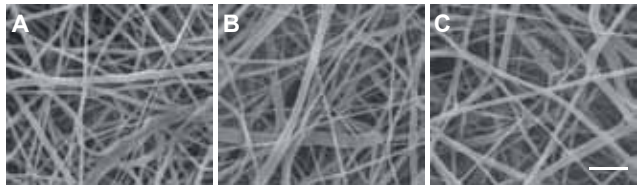

Fig. 1. Scanning electron microscopy of PA6/12 nanofibres used for culturing stem cells. Stability of the structure aqueous solution: before soaking (A) and preservation of the nanofibre architecture after one (B) or two (C) weeks soaking in aqueous solutions. Scale bar: 5 μm.

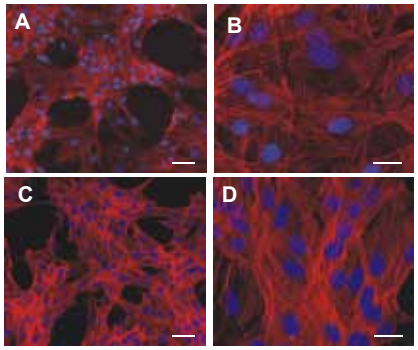

Fig. 2. The morphology of limbal stem cells (LSC) growing on a glass surface or on PA6/12 nanofibres. The cells were cultured for 24 h on poly L-lysine-coated glass inserts in 24-well tissue culture plates or on nanofibres fixed in the inserts and were stained for F-actin with phalloidin (red filaments). The nuclei are blue (DAPI staining). (A) and (B) demonstrate LSC growing on the glass surface at two different magnifications, (C) and (D) show LSC growing on nanofibre scaffolds. Scale bars: A, C – 50 μm, B, D – 20 μm.

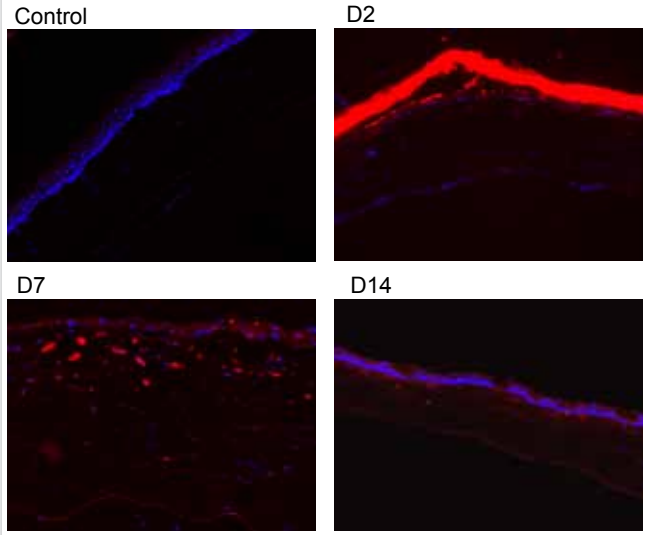

Fig. 3. Detection of PKH26-labelled limbal stem cells (LSC) on the damaged ocular surface after their transfer using nanofibre scaffold. The globes were removed 2, 7 or 14 days after the operation and 7 μm cryosections were prepared. The nuclei were visualized with DAPI. The cryosections were prepared from the control undamaged eye (without labelled cells), (D2) from the eye 2 days after operation (the nanofibre scaffold with labelled LSC is seen as a red lane, corneal epithelium is removed), and from the eyes 7 (D7) and 14 (D14) days after the cell transfer (red stained cells are still present, the corneal epithelium is regenerated). Magnification: 200x.

- FP7 EU, 222509 KINACEPT – Novel anti-inflammatory compounds for autoimmune diseases, 2008-2010, V. Holáň
- GA CR, GD310/08/H077 – Regulation of immunological mechanisms in health and disease: Development of new diagnostic and therapeutic approaches, 2008-2011, V. Holáň
- AS CR, KAN200520804 – Biocompatible nanofibre scaffolds forming novel drug matrices for the application of biologically and pharmacologically active substances, 2008-2012, V. Holáň
- GA CR, GA206/08/0640 – Immunogenetic study of the hybrid zone of the house mouse, 2008-2012, V. Holáň

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