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Laboratory of Tumour Immunology

Anti-tumour immunotherapy, immunoediting, immunoepigenetics

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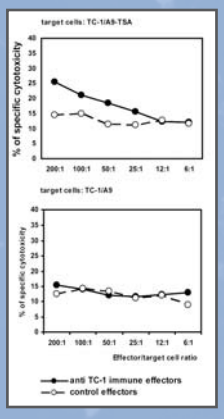

Cytotoxic T lymphocyte-mediated lysis of TC-1/A9 cells after induction of MHC class I surface expression by Trichostatin A.
Spleen cells from mice immunized with irradiated MHC class I-positive TC-1 cells were used in a chromium release microcytotoxicity assay. The targets were TC-1/A9 Tricostatin A (TSA)-treated and untreated TC-1/A9 cells. Control effector cells were spleen cells from non-immune animals. Only TSA-treated TC-1/A9 target cells were significantly lysed with spleen cells from the immune mice. The critical role of cytotoxic T lymphocytes was determined by experiment in which depletion of $CD8^+$ effector cells with a specific antibody blocked the cytotoxic effects.

Research topics

The long-term research programme of the Laboratory is focused on the mechanisms involved in induction and regulation of the anti-tumour immunity. The murine model for tumours associated with human papilloma virus (aetiologic agent of the cervix carcinoma) has been employed in most of our studies. This model has been used for analysis of the missing signals important for effective immune responses and their delivery in the optimal form in order to induce or restore effective anti-tumour responses. Special attention has been paid to the clinically relevant setting of the minimal residual tumour disease treatment after primary tumour resection or chemotherapy. We have investigated mechanisms of immunosupression in the course of the tumour growth, with the final goal to include the blockage of the negative signals into the immunotherapeutic schemes. We have also investigated the mechanisms of the anti-tumour immune responses against tumours mediated by MHC class I-restricted and -unrestricted mechanisms, and immunologic cross-reactivity between tumours of the same aetiology but distinct MHC class I expression.
We have found that epigenetic agents induced expression of genes involved in antigen processing machinery and surface expression of MHC class I molecules on the tumour cells, which consequently became susceptible to the lysis by cytotoxic T lymphocytes.

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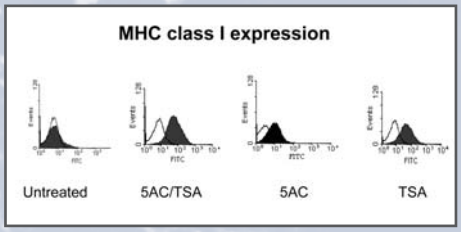
Selected recent papers

1. Indrova M, Bieblova J, Jandlova T, Vonka V, Pajtasz-Piasecka E, Reinis M. Chemotherapy, IL-12 gene therapy and combined adjuvant therapy of HPV 16-associated MHC class I-proficient and -deficient tumours. **Int J Oncol.** 2006;28:253-9
2. Reinis M, Simova J, Bubenik J. Inhibitory effects of unmethylated CpG oligodeoxynucleotides on MHC class I-deficient and -proficient HPV16-associated tumours. **Int J Cancer.** 2006; 118:1836-42
3. Reinis M, Simova J, Indrova M, Bieblova J, Bubenik J. CpG oligodeoxynucleotides are effective in therapy of minimal residual tumour disease after chemotherapy or surgery in a murine model of MHC class I-deficient, HPV16-associated tumours. **Int J Oncol.** 2007;30:1247-51
4. Reinis M, Simova J, Indrova M, Bieblova J, Pribylova H, Moravcova S, Jandlova T, Bubenik J. Immunization with MHC class I-negative but not -positive HPV16-associated tumour cells inhibits growth of MHC class I-negative tumours. **Int J Oncol.** 2007;30:1011-7
5. Manning J, Indrova M, Lubyova B, Pribylova H, Bieblova J, Hejnar J, Simova J, Jandlova T, Bubenik J, Reinis M. Induction of MHC class I molecule cell surface expression and epigenetic activation of antigen-processing machinery components in a murine model for human papilloma virus 16-associated tumours. **Immunology.** Epub Aug 28,2007.



MHC class I expression on MHC class I-deficient TC-1/A9 cells was induced after 5-azacytidine (5-azaC) and Trichostatin A (TSA) treatments, as determined by flow cytometry