The capacity of tumour cell populations to escape from antitumour immunity in the course of tumour development represents a serious obstacle to the development of effective anti-tumour immunotherapy or vaccination. In our laboratory, we are mainly focused on selected reversible processes, such as MHC class I deficiency or altered expression of co-stimulatory/ inhibitory molecules, by which tumour cells can escape from specific immune responses. In last several years, we have been interested in epigenetic mechanisms underlying reversible MHC class I downregulation on tumour cells, as well as in the design of immunotherapy/vaccination that would be effective against MHC class I-deficient tumours. Using murine models for MHC class I-deficient tumours (e.g. cervical carcinoma, prostate cancer), in which the MHC class I expression could be restored by cytokines, we have documented association of the MHC class I cell surface expression and DNA methylation of the regulatory regions of the antigen-presenting machinery genes. We have also found that DNA methyltransferase inhibitors induced expression of the genes involved in antigen-processing machinery and surface expression of MHC class I molecules on tumour cells, as well as of selected co-stimulatory and inhibitory molecules. In vivo experiments documented the efficacy of immunotherapy of MHC class I-deficient tumours combined with administration of 5-azacytidine, a DNA methyltransferase inhibitor. Our results also suggest an important role of the DNA methylation in the interferon-γ-induced expression of antigen-presenting machinery genes. We are also interested in epigenetic mechanisms underlying regulation of genes encoding antigen-presentation machinery genes, as well as co-stimulatory/inhibitory genes in antigen-presenting or regulatory immunocytes. Besides DNA methyltransferase inhibitors, we have investigated other immunomodulatory chemotherapeutics, such as cyclophosphamide, especially in terms of the impacts of immunomodulatory molecule expression on tumour cells. Further, our areas of interest are populations of immunoregulatory cells and their dynamics and function in the course of chemotherapy. Recently, we have characterized in detail the immunosuppressive character of myeloid-derived suppressor cells induced by cyclophosphamide administration in mice. In our projects we have been interested in experimental anti-tumour immunotherapy and vaccines, with a special attention paid to the minimal residual tumour disease treatment. We have used cell and gene therapy approaches and dendritic cell-based vaccines, as well as genetically modified tumour cells producing cytokines (especially IL-12-producing cells) for vaccination and immunotherapy optimization.

From the left:
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Veronika Hrušková / Diploma Student • Anna Žlabová / Diploma Student (until 2012) • Prof Jan Bubeník, MD, DSc (until 2011)