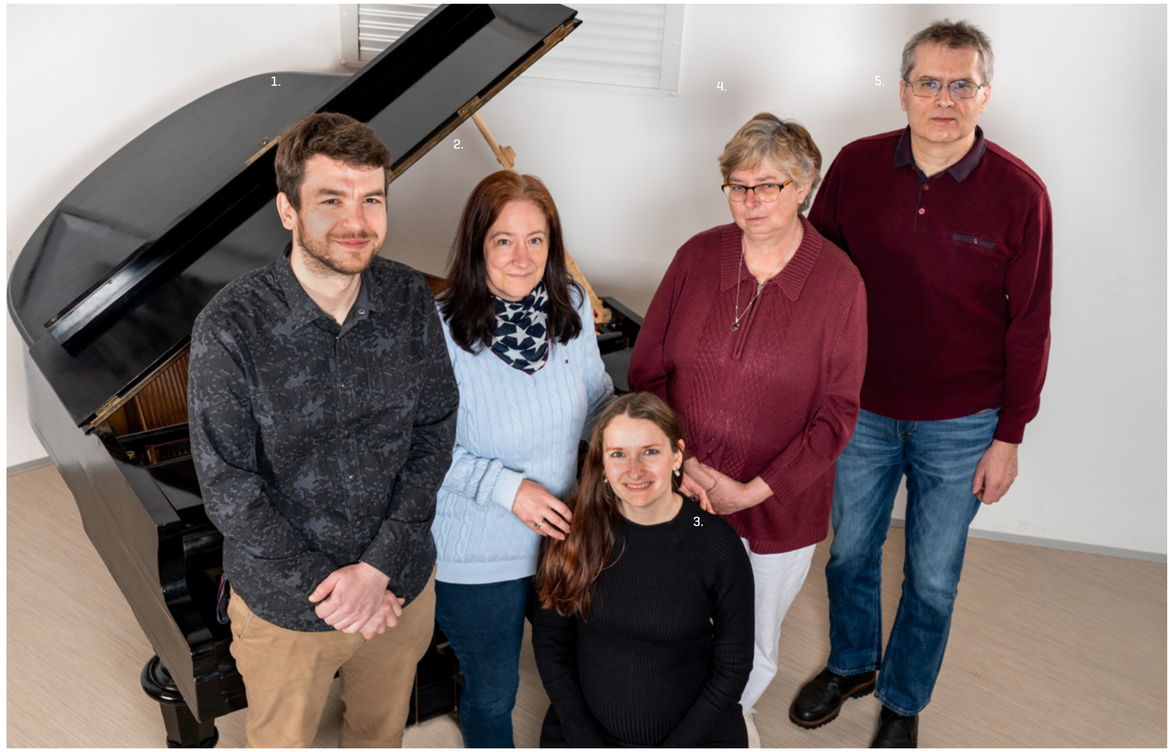
LABORATORY OF

IMMUNOLOGICAL AND TUMOUR MODELS

Experimental cancer therapy, tumour immunology, murine models, JAK/STAT signalling, cellular senescence

Milan Reiniš



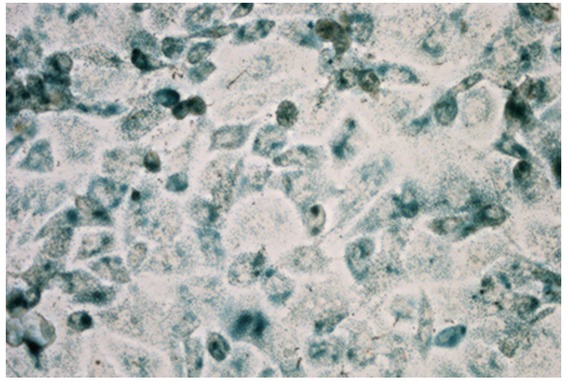
In the picture: 1. Novotný Ondřej | 2. Mikyšková Romana | 3. Sapega Olena | 4. Turečková Renáta | 5. Reiniš Milan

Our long-term research interest lies in interactions between tumour cells and the immune system, as well as the impacts of anti-tumour chemo- and immunotherapies on these interactions. We have been focused on the mechanisms by which tumour cells can escape from immune responses, such as MHC class I downregulation on tumour cells or mechanisms of the immune suppression development in the tumour microenvironment.

At present, we concentrate on the impacts of genotoxic stress and cellular senescence induction by chemotherapeutic agents or cytokines on the crosstalk between tumour cells and the immune system. Cellular senescence represents an important barrier against cancer development. However, the presence of senescent cells, or cells in a genotoxic stress in general, can influence wthe microenvironment in different ways, and it can also have detrimental effects on the tumour growth and anti-tumour immunity.

JAK/STAT signalling pathways play important roles in the processes mentioned above. Recently, we have concentrated on the role of STAT1 in cellular stress/senescence induction. Further, we suppose that STAT3 signalling pathway inhibition can be an important tool for elimination of the negative effects of chemotherapy, and it can also increase its efficacy and eliminate immune suppression. Therefore, we study novel and existing STAT3 inhibitors and their potential clinical usage in murine preclinical models.

In collaboration with several partners, we test novel immune and chemotherapeutic approaches, using syngeneic murine models. We use tumours induced by syngeneic tumour cell transplantation, as well as transgenic mice as orthotopic models that develop spontaneous tumours. We also employ experimental models for minimal residual tumour disease after surgery or chemotherapy. Indeed, we are open to more future collaborations and contract research.



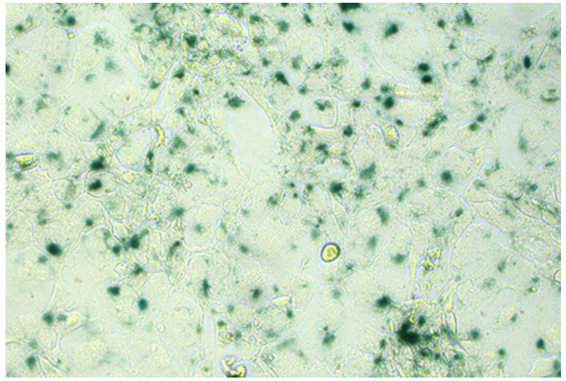


Image of senescent cells stained with b-galactosidase

Selected publications:

1. Mikyskova R, Sapega O, Psotka M, Novotny O, Hodny Z, Balintová S, Malinak D, Svobodova J, Andrys R, Rysanek D, Musilek K, Reinis M*. STAT3 inhibitor Stattic and its analogues inhibit STAT3 phosphorylation and modulate cytokine secretion in senescent tumor cells. Mol Med Rep Accepted.
2. Koncošová M, Rumlová M, Mikyšková R, Reiniš M, Zelenka J, Ruml T, Kirakci K*, Lang K: Avenue to X-ray-induced photodynamic therapy of prostatic carcinoma with octahedral molybdenum cluster nanoparticles. J Mater Chem B 2022 10:3303-3310.
3. Grusanovic S, Danek P, Kuzmina M, Adamcova MK, Burocziova M, Mikyskova R, Vanickova K, Kosanovic S, Pokorna J, Reinis M, Brdicka T, Alberich-Jorda M*. Chronic inflammation decreases HSC fitness by activating the druggable Jak/Stat3 signaling pathway. EMBO Rep 2023 24(1):e54729.
4. Oleksak P, Psotka M, Vancurova M, Sapega O, Bieblova J, Reinis M, Rysanek D, Mikyskova R, Chalupova K, Malinak D, Svobodova J, Andrys R, Rehulkova H, Skopek V, Ngoc Lam P, Bartek J, Hodny Z*, Musilek K*. Design, synthesis, and in vitro evaluation of BP-1-102 analogs with modified hydrophobic fragments for STAT3 inhibition. J Enzyme Inhib Med Chem 2021 36(1):410-424.
5. Truxova I, Kasikova L, Salek C, Hensler M, Lysak D, Holicek P, Bilkova P, Holubova M, Chen X, Mikyskova R, Reinis M, Kovar M, Tomalova B, Kline JP, Galluzzi L, Spisek R, Fucikova J*. Calreticulin exposure on malignant blasts correlates with improved natural killer cell-mediated cytotoxicity in acute myeloid leukemia patients. Haematologica. 2020 105(7):1868-1878.