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LABORATORY OF

GENOME INTEGRITY

DNA damage response, carcinogenesis, inflammation, ageing, RecQ helicases, R-loops, gold nanoparticles

In the picture:
1. Zdeněk Hodný | **2. Jiří Bártek** | **3.** Filip Havel | **4.** Miroslav Přibyl | **5.** Jana Dobrovolná | **6.** Terezie Imrichová | **7.** Pavla Vašicová | **8.** Barbora Šalovská | **9.** Václav Urban | **10.** Martéta Vančurová | **11.** Barbora Boleslavská | **12.** Zuzana Naščáková | **13.** Blanka Mrázková

Our research is centred on cellular responses to damaged DNA (termed DNA damage response). Cells with unhealed DNA damage are mostly prevented from cell division due to activated cell cycle checkpoints; however, following unscheduled cell division, unrepaired breaks result in chromosomal instability with accompanying changes in gene dosage – the driving force of malignant transformation. We focus on 1) mechanisms of cellular response to persistent irreparable DNA damage lesions manifested as irreversible cell cycle arrest (cellular senescence); 2) mechanisms of radioresistance and chemoresistance of cancer cells; 3) role of DNA damage-induced expression of cytokines in paracrine signalling, cancer microenvironment and cell reprogramming; 4) DNA transactions mediated by RecQ DNA helicases, key players in the maintenance of genomic stability; 5) mechanisms resolving collisions between replication and transcription machineries and associated RNA:DNA hybrids referred to as R-loops; and 6) impact of the above mechanisms on cancer and ageing with the aim to find new therapeutic approaches, such as thermotherapy using targeted gold nanoparticles. Recently, we have identified the mechanism of IFNγ-induced senescence and the role of senescent cells in tumour promotion. We have described development of a stem cell-like phenotype of cancer cells in response to genotoxic stress and examined pro-survival signalling pathways responsible for radio- and chemo-resistance of cancer cells.

Selected recent papers:

Urban V, Dobrovolna J, Hühn D, Fryzelkova J, Bartek J, Janscak P: (2016) RECQ5 helicase promotes resolution of conflicts between replication and transcription in human cells. **J. Cell Biol.** 214(4), 401-15.

Burdova K, Mihaljevic B, Sturzenegger A, Chappidi N, Janscak P: (2015) The Mismatch-Binding Factor MutSβ Can Mediate ATR Activation in Response to DNA Double-Strand Breaks. **Mol. Cell** 59(4), 603-14.

Kyjacova, L., S. Hubackova, K. Krejcikova, R. Strauss, H. Hanzlikova, R. Dzijak, T. Imrichova, J. Simova, M. Reinis, J. Bartek, Z. Hodny: 2015. Radiotherapy-induced plasticity of prostate cancer mobilizes stem-like non-adherent, Erk signaling-dependent cells. **Cell Death Differ.** 22:898-911.

Hubackova, S., A. Kucerova, G. Michlits, L. Kyjacova, M. Reinis, O. Korolov, J. Bartek, and Z. Hodny: 2015. IFN[gamma] induces oxidative stress, DNA damage and tumor cell senescence via TGF[beta]/SMAD signaling-dependent induction of Nox4 and suppression of ANT2. **Oncogene.** 35:1236-1249.


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