Libor Macůrek

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LABORATORY OF

CANCER CELL BIOLOGY

cell cycle, checkpoint, DNA damage response, phosphorylation, phosphatase, tumorigenesis, oncogenic transformation

In the picture:
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Not in the picture:
Zuzana Líčeníková-Hořejší | Gabriela Jeníková | Jan Benada | Tomáš Liďák

Proliferation of cells is essential for keeping organisms alive and healthy, and is accomplished by passing through interphase followed by nuclear division (mitosis) and cellular division (cytokinesis). In response to DNA damage, cells temporarily stop progression through the cell cycle (checkpoint) to prevent transmission of mutations to the progeny. After completion of DNA repair, cells are allowed to re-enter the cell cycle (checkpoint recovery). Radiotherapy and chemotherapy with genotoxic pharmaceuticals represent two commonly used non-surgical strategies in the treatment of human tumours and they both rely on induction of cell death by genotoxic stress. Progression through the cell cycle and cellular responses to DNA damage are tightly controlled by interconnected signalling cascades. Malfunction of cellular checkpoints causes accumulation of mutations and can lead to the genome instability, activation of oncogenes, and eventually to malignant transformation.

In our laboratory we employ cell biology, molecular biology and biochemical approaches to identify the molecular mechanisms that control cellular responses to DNA damage. In particular, we focus on protein phosphatase PPM1D/Wip1, which is an important negative regulator of tumour suppressor p53 and controls termination of the checkpoint. Our work aims to decipher the molecular mechanisms regulating the function of PPM1D/Wip1 in human cells and in mouse models. Using chemical genetics we also evaluate PPM1D/Wip1 as a potential pharmacological target. In addition, we study the mechanisms by which Polo-like kinase 1 modulates DNA repair during mitosis. Finally, we investigate the role of CK2 kinase in folding of the large protein complexes involved in the DNA damage response.

Selected recent papers:

Pechackova S, Burdova K, Benada J, Kleiblova P, Jenikova G, Macurek L: Inhibition of WIP1 phosphatase sensitizes breast cancer cells to genotoxic stress and to MDM2 antagonist nutlin-3. **Oncotarget. 2016**; 7:14458-75.

Benada J, Burdová K, Lidak T, von Morgen P, Macurek L: Polo-like kinase 1 inhibits DNA damage response during mitosis. **Cell Cycle 2015**; 14:219-31.

Benada J, Macurek L: Targeting the Checkpoint to Kill Cancer Cells. **Biomolecules 2015**; 5:1912-37.


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