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BIOCEV

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In the picture:
1. Nikol Baloghová | **2.** Jiří Švec | **3.** Tomáš Liďák | **4.** Lukáš Čermák | **5. Vladimír Kořínek**

Not in the picture:
Klára Klimešová

LABORATORY OF

CANCER BIOLOGY

mass spectrometry, protein stability, protein-protein interaction, ubiquitin proteasome system

The principal goal of the laboratory established in 2015 is to understand the molecular complexity of cancer formation starting from initial stages through to metastasis. In more detail, we are elucidating the role of proteasome-dependent protein degradation in various intracellular processes. Under physiologic conditions, the Ubiquitin Proteasome System (UPS) is required for precise temporal and spatial expression of a diverse repertoire of proteins. UPS is involved in the cell cycle, differentiation, or stress and immune response. The ubiquitination process is achieved via triggering an enzymatic cascade in which the ubiquitin moiety is activated by covalent linkage to E1 – the ubiquitin-activating enzyme, and transferred to E2 – the ubiquitin-conjugating enzyme. In the final step, E3 ubiquitin ligases mediate transfer of ubiquitin to the lysine residues in protein substrates, which mark them for degradation. Importantly, some ubiquitin ligases are deregulated in a wide range of disorders including cancer. In addition, many ubiquitin ligases are "orphan" since they have not yet been "paired" with specific substrate(s). Our aim is to identify substrates for selected orphan ligases. We utilize a broad spectrum of molecular biology and biochemical techniques; nevertheless, our main experimental tool is mass spectrometry analysis of ubiquitin ligase-associated proteins. In addition, to reveal biological functions of selected ligases, we employ gene editing in human cells and mice. Subsequently, the resulting cellular and mouse models are assayed to discover the involvement of the studied genes/proteins in the cell cycle control, DNA damage repair, cell migration, and invasiveness.

Selected recent papers:

Stancikova J, Krausova M, Kolar M, Fafilek B, Svec J, Sedlacek R, Neroldova M, Dobes J, Horazna M, Janeckova L, Vojtechova M, Oliverius M, Jirsa M, Korinek V: NKD1 marks intestinal and liver tumors linked to aberrant Wnt signaling. **Cellular Signalling** 27 (2): 245-56, 2015.

Hayakawa Y, Ariyama H, Stancikova J, Sakitani K, Asfaha S, Renz B W, Dubeykovskaya Z A, Shibata W, Wang H, Westphalen C B, Chen X, Takemoto Y, Kim W, Khurana S S, Tailor Y, Nagar K, Tomita H, Hara A, Sepulveda A R, Setlik W, Gershon M D, Saha S, Ding L, Shen Z, Fox J G, Friedman R A, Konieczny S F, Worthley D L, Korinek V, Wang T C: Mist1 Expressing Gastric Stem Cells Maintain the Normal and Neoplastic Gastric Epithelium and Are Supported by a Perivascular Stem Cell Niche. **Cancer Cell** 28: 1–15, 2015.

Janeckova L, Fafilek F, Krausova M, Horazna M, Vojtechova M, Alberich-Jorda M, Sloncova E, Galuskova K, Sedlacek R, Anderova M, Korinek V: Wnt signaling inhibition deprives small intestinal stem cells of clonogenic capacity. **Genesis** 54:101-14. 2016.


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23