LABORATORY OF

CANCER BIOLOGY

Ubiquitin ligase, cell cycle, stress, mouse model, cancer

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Protein degradation via the proteasome-ubiquitin system (UPS) plays a crucial role in cellular homeostasis. Defects in this system are often associated with pathologic states such as cancer or developmental abnormalities. E3-ubiquitin ligases are responsible for substrate recognition and subsequent degradation. Despite this fact, many of them have not been paired with any specific substrate yet. In our projects, we focused on Cullin-dependent ubiquitin ligases. To discover novel substrates of these multisubunit enzymes, we perform state-of-art affinity purification of protein complexes associated with these enzymes. Detailed biochemical analysis of the interaction between potential substrates and ubiquitin ligases helps us to reveal novel mechanisms of substrate recognition and signalling pathways involved in cellular growth, survival and stress response. Besides the cancer cell line environment, we aspire to confirm novel roles of selected ubiquitin ligases in a physiologic context. In collaboration with the Czech Centre for Phenogenomics (CCP), we are developing mouse models of their deficiency and dysregulation.

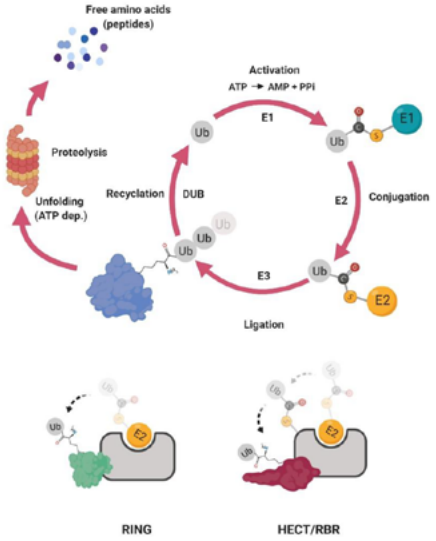


Figure 1. UPS system

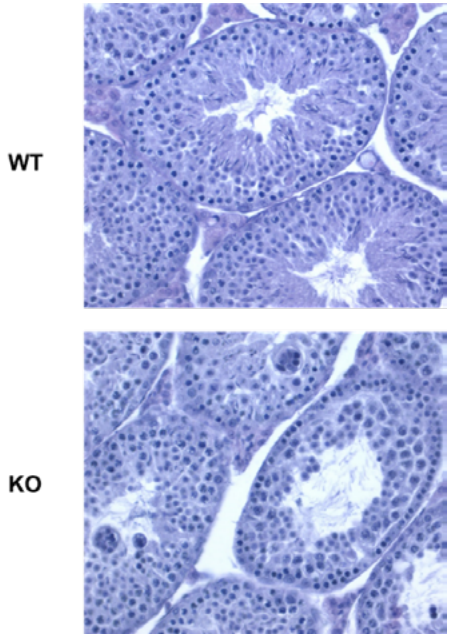


Figure 2. Inactivation of E3 ubiquitin ligase in the mouse model and its effect on spermatogenesis

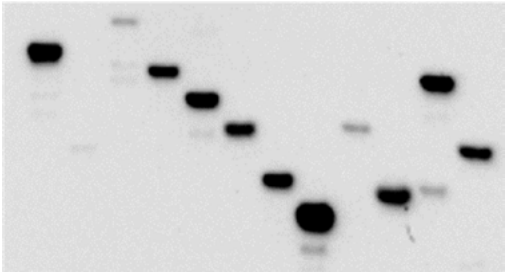
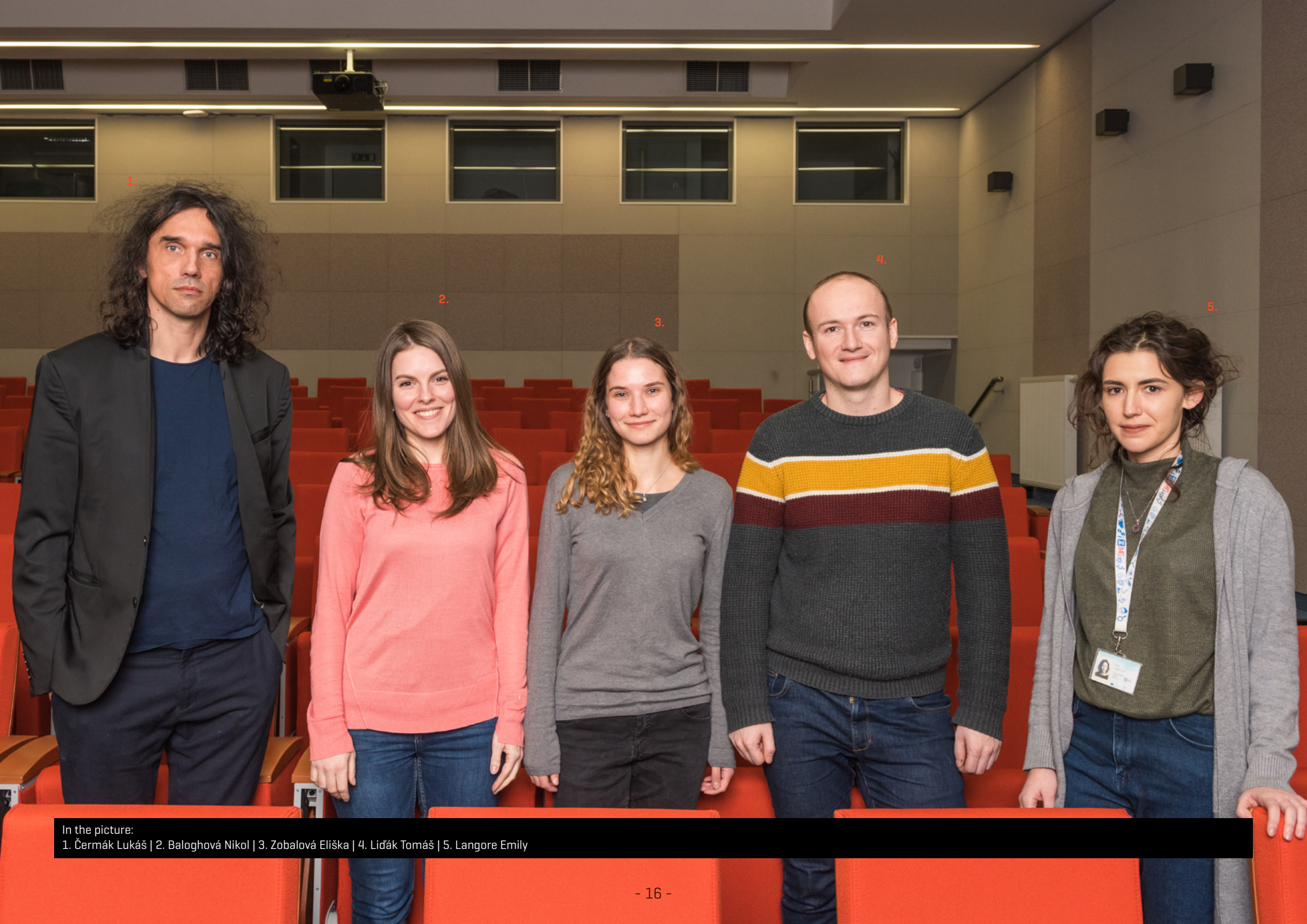


Figure 3.: Expression of various E3 ubiquitin ligases isolated for mass-spectrometry analysis of their potential substrates

Selected publications:

1. Baloghova N, Lidak T, Cermak L* (2019) Ubiquitin ligases involved in the regulation of Wnt, TGF-β, and Notch signaling pathways and their roles in mouse development and homeostasis. Genes. 2019 Oct 16;10(10)
2. Horn M, Geisen C, Cermak L, Becker B, Nakamura S, Klein C, Pagano M, Antebi A. DRE-1/FBXO11-dependent degradation of BLMP-1/BLIMP-1 governs C. elegans developmental timing and maturation. Developmental Cell. 2014 Mar 31;28(6):697-710
3. Duan S, Cermak L, Pagan JK, Rossi M, Martinengo C, di Celle PF, Chapuy B, Shipp M, Chiarle R, Pagano M (2012) FBXO11 targets BCL6 for degradation and is inactivated in diffuse large B-cell lymphomas. Nature. 2011 Nov 23



In the picture:
1. Čermák Lukáš | 2. Baloghová Nikol | 3. Zobalová Eliška | 4. Liďák Tomáš | 5. Langore Emily