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LABORATORY OF

CELL AND DEVELOPMENTAL BIOLOGY

cancer, haematopoiesis, intestinal stem cells, JAK/STAT signalling, Wnt pathway

In the picture:
1. Vladimír Kořínek | **2.** Linda Berková | **3.** Vítězslav Kříž | **4.** Kateřina Galušková | **5.** Martina Vojtěchová | **6.** Lucie Janečková | **7.** Lucie Láníková | **8.** Olga Babošová | **9.** Monika Horázná | **10.** Eva Šloncová

Not in the picture:
Dušan Hrčkulák | Petra Burešová | Veronika Vilímková

The majority of tissues in the adult organism contain a population of tissue-specific stem cells. The proper maintenance of adult tissues is controlled by various signalling pathways that regulate the balance between the opposing processes of proliferation and differentiation. The scientific goal of our laboratory is to elucidate the molecular mechanisms influencing the behaviour of normal and transformed cells. At present, the laboratory is focused on two research themes:
1. Intestinal stem cells and cancer
Hypermethylated in cancer 1 (HIC1) represents a tumour suppressor gene frequently inactivated by DNA methylation in many types of solid tumours. We have found that the tumour-suppressive function of Hic1 in the colon is related to its inhibitory action on signalling mediated by toll-like receptor 2 (Tlr2) present on tumour cells. In the intestine, Hic1 is mainly expressed in differentiated epithelial cells and its ablation leads to increased Tlr2 production. The absence of Hic1, in a chemical-induced mouse model of carcinogenesis, resulted in larger Tlr2-positive colonic tumours that showed increased proportion of proliferating cells. We also analysed the expression of HIC1 using large datasets of human colorectal polyps and carcinomas and found that high HIC1 production distinguished a specific type of chemotherapy-responsive tumours.
2. Haematopoietic stem cells
We reported the association of gain-of-function germline mutations in Janus kinase 2 (JAK2) with a phenotype-defining mutation in myeloproliferative neoplasm. We proposed that JAK2 germline mutations may provide a clonal advantage, possibly contributing to further genomic alterations in the clone and, eventually, fatal leukemic transformation.

Selected recent papers:

Lanikova L, Babosova O, Swierczek S, Wang L, Wheeler DA, Divoky V, Korinek V, Prchal J T: Coexistence of gain-of-function JAK2 germline mutations with JAK2V617F in polycythemia vera. **Blood 2016** 128(18):2266-2270.

Janeckova L, Kolar M, Svec J, Lanikova L, Pospichalova V, Baloghova N, Vojtechova M, Sloncova E, Strnad H, Korinek V: HIC1 Expression Distinguishes Intestinal Carcinomas Sensitive to Chemotherapy. **Transl Oncol 2016** 9(2):99-107.

Janeckova L, Pospichalova V, Fafilek B, Vojtechova M, Tureckova J, Dobes J, Dubuissez M, Leprince D, Baloghova N, Horazna M, Hlavata A, Stancikova J, Sloncova E, Galuskova K, Strnad H, Korinek V: HIC1 Tumor Suppressor Loss Potentiates TLR2/NF-κB Signaling and Promotes Tissue Damage-Associated Tumorigenesis. **Mol Cancer Res 2015** 13(7):1139-48.


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