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LABORATORY OF

LEUKOCYTE SIGNALLING

leukocyte signalling, membrane adaptor proteins, autoinflammation, immune responses of myeloid cells

In the picture:

1. Daniela Glatzová | 2. Šimon Borna | 3. Aleš Drobek | 4. Matej Fabišik | 5. **Tomáš Brdička** | 6. Tereza Skopcová | 7. Jarmila Králová

The Laboratory of Leukocyte Signalling is studying the molecular mechanisms of signal transduction downstream of various leukocyte surface receptors. Our interest has recently been focused on the membrane adaptor proteins and on the roles of these proteins in the regulation of leukocyte signalling and in leukocyte-driven pathologies. In the past several years we have been analysing several so far poorly characterized members of this family. Perhaps the most interesting is PSTPIP2. Its deficiency in mice results in an autoinflammatory disorder characterized by sterile inflammation of the bones and skin. It is similar to a human disease known as chronic recurrent multifocal osteomyelitis. We have described interactions of PSTPIP2 with negative regulators of cellular signalling Csk and SHIP1 and now are exploring further molecular mechanisms of how this protein controls inflammation. Additional projects include studies of transmembrane adaptor SCIMP in dendritic cells, which we identified as a positive regulator of signal transduction via the receptor for pathogenic fungi Dectin-1. We are also working on characterization of transmembrane adaptor LST1/A, a potential negative regulator of macrophage and osteoclast signalling, and transmembrane adaptor OPAL1, which is aberrantly expressed in childhood leukaemias and regulates activity of an important bone marrow homing receptor, CXCR4, in leukemic cells as well as in myeloid progenitors.

Selected recent papers:

Drobek A, Králová J, Skopcová T, Kucová M, Novák P, Angelisová P, Otáhal P, Alberich-Jorda M, Brdička T: PSTPIP2, a Protein Associated with Autoinflammatory Disease, Interacts with Inhibitory Enzymes SHIP1 and Csk., **J Immunol.** **2015** Oct 1;195(7):3416-26.

Králová J, Fabišik M, Pokorná J, Skopcová T, Malissen B, Brdička T: The Transmembrane Adaptor Protein SCIMP Facilitates Sustained Dectin-1 Signaling in Dendritic Cells, **J Biol Chem.** **2016** Aug 5;291(32):16530-40.

Chum T, Glatzová D, Kvičalová Z, Malinský J, Brdička T, Cebecauer M: The role of palmitoylation and transmembrane domain in sorting of transmembrane adaptor proteins, **J Cell Sci.** **2016** Jan 1;129(1):95-107.

