LABORATORY OF

SIGNAL TRANSDUCTION

Plasma membrane signalosome, immunoreceptor signalling, mast cells, ORM family proteins, tetraspanins

Petr Dráber

more information

e-mail

Our laboratory is focused on understanding the molecular mechanisms governing signal transduction from the plasma membrane receptors to the cytoplasm. High-affinity immunoglobulin E receptor (FcεRI), cKIT, and G protein-coupled receptors (GPCRs) are plasma membrane receptors involved in the degranulation and/or chemotaxis of mast cells, potent immune modulators of the tissue microenvironment. Within minutes of antigen-mediated activation, mast cells release a variety of preformed biologically active compounds, followed by a wave of mediator synthesis and secretion. Increasing evidence suggests an intricate network of inhibitory and activating receptors, specific signalling pathways, and adaptor proteins whose overall signalling balance governs the mast cell responsiveness to particular stimuli. In our recent studies, we focused on understanding the role of plasma membrane signalosomes and selected cytoplasmic proteins during mast cell activation through FcεRI, cKit, and GPCRs. To reach our goal, we used various techniques of molecular biology, immunology, immunochemistry, and immunohistochemistry. Our principal approach lies in production of cells or animals with increased or reduced expression of selected genes and comparison of their properties with wild-type cells or wild-type animals. We found and described new functions of the members of ORM family proteins, tetraspanins, transmembrane adaptor protein PAG, and cytoskeletal protein 4.1R in mast cell activation. Our studies are aimed to deepen the knowledge of the cellular and molecular mechanisms involved in allergic and inflammatory diseases. Our long-term goal is to contribute to the development of new, more potent, anti-allergic and anti-inflammatory drugs.

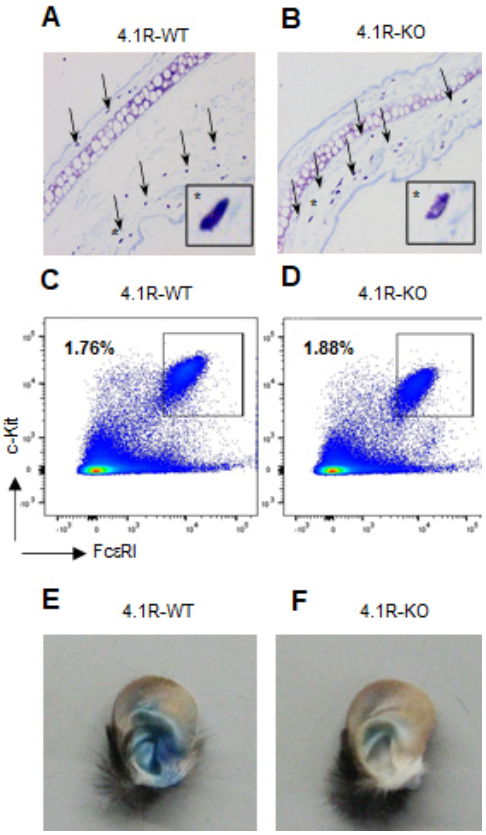

Figure 1. Comparison of wild-type (WT) mice and mice with 4.1R knockout (KO). Although both WT and 4.1R-KO mice express the comparable amount of mast cells in ear tissue (A, B) and peritoneum (C, D), 4.1R-KO mice exhibit reduced passive cutaneous anaphylaxis. Details in Draberova et al., Front. Immunol., 2019.

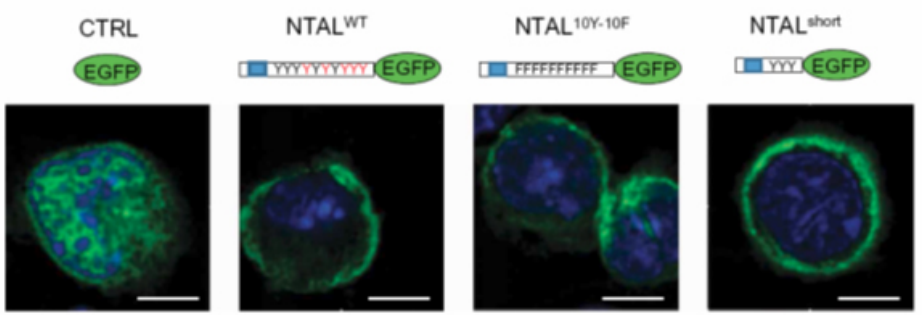

Figure 2. Various vectors used to determine the role of NTAL adaptor protein in prostaglandin E 2 - mediated chemotaxis and localization of the constructs in NTAL knockout bone marrow-derived mast cells. Details in Halova et al., Sci. Signal. 2018. Immunol., 2019.

Selected publications:

1. Draberova L*, Draberova H, Potuckova L, Halova I, Bambouskova M, Mohandas N, Draber P* (2019) Cytoskeletal protein 4.1R is a positive regulator of the FcεRI signaling and chemotaxis in mast cells. *Front* Immunol, doi: 10.3389/fimmu.2019.03068.
2. Halova I*, Bambouskova M, Draberova L, Bugajev V, Draber P* (2018) The transmembrane adaptor protein NTAL limits mast cell chemotaxis toward prostaglandin E_2. *Sci Signal*, **11**:eaao4354.
3. Potuckova L, Draberova L, Halova I, Paulenda T, Draber P* (2018) Positive and negative regulatory roles of C-terminal Src kinase (CSK) in FcεRI-mediated mast cell activation, independent of the transmembrane adaptor PAG/CSK-binding protein. *Front Immunol*, **9**:1771.
4. Halova I, Ronnberg E, Draberova L, Vliagoftis H, Nilsson GP, Draber P* (2018) Changing the threshold-signals and mechanisms of mast cell priming. *Immunol Rev*, **282**:73-86.
5. Bulfone-Paus S, Nilsson G, Draber P, Blank U, Levi-Schaffer F* (2017) Positive and negative signals in mast cell activation. *Trends Immunol*, **38**:657-667.

In the picture: 1. Dráber Petr | 2. Utekal Pavol | 3. Redčenko Oleksij | 4. Mrkáček Michal | 5. Bugajev Viktor | 6. Hálová Ivana | 7. Vávrová Petra | 8. Tůmová Magda | 9. Franková Daniela | 10. Demková Lívia | 11. Dráberová Lubica