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LABORATORY OF IMMUNOBIOLOGY

central and peripheral tolerance, TLRs in embryonic haematopoiesis, T-cell signalling

In the picture:

1. Ondřej Ballek | 2. Jan Dobeš |
3. Tomáš Brabec | 4. Matouš
Vobořil | 5. **Dominik Filipp** |
6. Martina Dobešová | 7. Adela
Fellnerová | 8. Jana Balounová |
9. Iva Šplichalová

Not in the picture:

Ilona Chlubnová

The main goal of our research is to elucidate the mechanism(s) guiding the process of central and peripheral immune tolerance. We investigate the role of innate immune receptors (IIRs) expressed on medullary thymic epithelial cells (mTECs) in the modification of these mechanisms. Our data showed that the set of effector molecules produced by mTECs upon IIR stimulation is quite distinct from that produced by other cells of the immune system, and thus provide evidence for a so far uncharacterized role of IIRs expressed on tolerance-inducing mTECs. We have also characterized a novel subset of functionally distinct lymph node cells with the capacity to delete self-reactive CD8+ and CD4+ T cells or mediate conversion of the latter into Tregs.

We are also very interested in the expression pattern and function of Toll-like receptors (TLRs) during the early mammalian embryogenesis. TLR2 seems to be a suitable surface marker for tracking the earliest haematopoietic progenitors in a precirculation embryo. Our newly generated transgenic mice, which enable us to perform genetic lineage tracing experiments, showed that these early TLR2-expressing progenitors contribute not only to primitive, but also to definitive haematopoiesis.

We continue in our effort to understand the biochemical events leading to the activation of T cells. We have identified several proteins involved in the regulation of Lck redistribution via linking this process to the cytoskeletal network.

Selected recent papers:

[Ballek O, Valečka J, Dobešová M, Broučková A, Manning J, Řehulka P, Stulík J, Filipp D](#): TCR triggering induces the formation of Lck-RACK1-actinin-1 multiprotein network affecting Lck redistribution. **Front. Immunol.** **2016** 7: 449.

[Dobeš J, Newwirth A, Dobešová M, Vobořil M, Balounová J, Ballek O, Lebl J, Meloni A, Krohn K, Kluger N, Ranki A, Filipp D](#): Gastrointestinal Autoimmunity Associated with Loss of Central Tolerance to Enteric α -Defensins. **Gastroenterology** **2015** 149(1):139-150.

[Ballek O, Valečka J, Manning J, Filipp D](#): The pool of preactivated Lck in the initiation of T-cell signaling: a critical re-evaluation of the Lck standby model. **Immunol Cell Biol.** **2015** 93: 384-395.

