

Mechanisms of signal transduction by leukocyte surface receptors and transmembrane adaptor proteins

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Abstract

The central role in the initiation and maintenance of the adaptive immune response is played by interaction of T cells with antigen presenting cells. Upon recognition of peptide-loaded MHC glycoproteins on the surface of antigen presenting cells by specific T cell, immunological synapse is formed and signaling events are initiated in both cells involved. The signal propagation is regulated by various molecules that can have positive or negative function, or even both, depending on specific circumstances. In this work we focused our attention on three topics all encompassing processes of signal propagation or regulation. First, we extended our understanding of the signaling processes taking place in the immunological synapse by the discovery of a new transmembrane adaptor protein SCIMP expressed on antigen presenting cells. Detailed study of this protein demonstrated that it is a positive regulator of MHCII signaling. Next two projects were focused on T cells. We described the role of another transmembrane adaptor protein termed PRR7 in the regulation of apoptosis and T cell receptor (TCR) mediated signaling in T cells. Finally, we provided evidence that in human T cells CD148 phosphatase can have both activatory and inhibitory effect on T cell receptor signaling.

Presented thesis consists of three publications :

1. Draber P, Vonkova I, Stepanek O, Hrdinka M, Kucova M, Skopcova T, Otahal P, Angelisova P, Horejsi V, Yeung M, Weiss A, Brdicka T. 2011. **SCIMP: transmembrane adaptor protein involved in MHCII signaling**. *Moll Cell Biol* [published ahead of print on 19 September 2011, doi:10.1128/MCB.05817-11]
2. Hrdinka M, Draber P, Stepanek O, Ormsby T, Otahal P, Angelisova P, Brdicka T, Paces J, Horejsi V, Drbal K. 2011. **PRR7 is a transmembrane adaptor protein expressed in activated T cells involved in regulation of T cell receptor signaling and apoptosis**. *J Biol Chem* 286: 19617-29

3. Stepanek O, Kalina T, Draber P, Skopcova T, Svojgr K, Angelisova P, Horejsi V, Weiss A, Brdicka T. 2011. **Regulation of Src family kinases involved in T cell receptor signaling by protein-tyrosine phosphatase CD148.** *J Biol Chem* 286: 22101-12