

Project 16: The functional role of Tspan2 in anti-infectious immune responses

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Background:

Tetraspanin proteins play important roles in the regulation of cellular processes critical in CNS development and immune defence against pathogens. Either through lateral association within membrane domains or direct binding with interaction partners these proteins are involved in pathogen recognition, proliferation and trafficking of immune cells, and differentiation and proliferation of CNS cells. The tetraspanin family member Tspan2 was originally identified in oligodendrocyte lineage cells but has so far remained ill characterized. In the CNS it has been suggested to mediate immunoregulatory effects based on an increased microglia and astrocyte activation in the absence of inflammatory stimuli found in Tspan2^{-/-} mice. However, a role of Tspan2 in anti-infectious immune responses remain to be elucidated.

Own previous work:

The rationale for the proposed project is based on our following observations in newly generated Tspan2/DTR/EGFP reporter mice and Tspan2^{-/-} mice: (i) All neutrophils, as important cellular components of early innate immunity, express Tspan2 at high levels, (ii) Tspan2^{-/-} neutrophils show reduced ROS production but enhanced migration to inflammatory sites in thioglycollate-induced peritonitis, and (iii) LPS-induced production of proinflammatory cytokines is enhanced in Tspan2^{-/-} mice.

Aim of the project:

Based on our findings we hypothesize that Tspan2 is involved in pathogen recognition, innate immune cell functions, and anti-infectious immune responses. We propose to study the role of Tspan2 in anti-infectious immune responses.

Work program:

In our studies we will determine how Tspan2 expression is regulated during microbial infections and define its functions in pathogen recognition and modulation of effector functions of innate immune cells in host defence. Specifically, Tspan2 involvement neutrophil specific effector functions such as myeloperoxidase and NET production will be analysed as well as the role of Tspan2 in fungal and bacterial infections *in vivo* (*L. monocytogenes*, *C. albicans*). In an explorative mass spectrometry screen, we aim at defining cellular interaction partners of Tspan2.