

7 Summary

Characterization of the scrapie-infection in CD40L-deficient mice

The aim of this study was to clarify the role of CD40-CD40L-interactions in transmissible spongiform encephalopathies (TSEs).

In a mouse model of Alzheimer's disease (AD) the inhibition of CD40L mediated signaling led to a reduced amyloid deposition and neuroinflammation and therefore was suggested as a therapeutic strategy for the treatment of AD. On the other hand, neuroprotective properties of intact CD40-CD40L-interactions were reported, as CD40-deficient neurons proved to be more vulnerable to stress associated with ageing as well as nerve growth factor-beta and serum withdrawal, respectively.

We studied the scrapie infection of CD40L-deficient (CD40L^{-/-}) mice to see whether ablation of the CD40L gene would be beneficial or detrimental in this model of a neurodegenerative amyloidosis. CD40L^{-/-} mice died on average 40 days earlier than wild type controls and exhibited a more pronounced vacuolization of the neuropil, an increased microglia activation, and a higher loss of GABAergic neurons. No differences were observed concerning the deposition of misfolded PrP^{Sc}-amyloid and the activation of astrocytes. The experimental model shows that a deficiency for CD40L is highly detrimental in prion diseases and reinforces the neuroprotective function of intact CD40-CD40L interactions. The stimulation of neuroprotective pathways may represent a possibility to delay the disease onset in prion infections of the central nervous system therapeutically.