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Role of lymphotoxin beta receptor signaling during B cell mediated protection against Toxoplasma gondii

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Background
The lymphotoxin beta receptor (LT?R) belongs to the TNF receptor superfamily and is essential for the organogenesis of secondary lymphoid organs as well as the coordination of an effective immune response against invading pathogens. LT?R-deficient mice (LT?R$^{-/-}$) exhibit a pleiotropic phenotype with immunological defects that cause increased susceptibility to pathogens such as *Toxoplasma gondii* (*T. gondii*).

T. gondii is an obligate intracellular parasite that causes toxoplasmosis in humans and virtually all warm-blooded animals. LT?R$^{-/-}$ mice infected with *T. gondii* fail to induce a potent immune response in time and succumb to the infection instead of reaching chronic stage. While cell autonomous defense mechanisms and T cell immunity against *T. gondii* have been investigated in the past, the role of B cell mediated protection and LT?R-signalling against this intracellular pathogen is less well understood.

Results and Conclusion
In contrast to WT animals, LT?R$^{-/-}$ mice do not survive acute toxoplasmosis. Passive immunization of WT and LT?R$^{-/-}$ mice with immune serum containing *T. gondii*-specific antibodies led to prolonged survival, but ultimately could not rescue LT?R$^{-/-}$ mice from death. Parasite burdens in spleen, lung, peritoneal exudate but not brain were increased in LT?R$^{-/-}$ compared to WT mice at day 9 post infection, with no significant impact of the transferred immune serum. *T. gondii*-specific IgM and IgG antibodies were almost not detectable in the serum of LT?R$^{-/-}$ compared to WT mice.

In the bone marrow, LT?R$^{-/-}$ mice showed an increased frequency of mature B cells compared to WT mice. Furthermore, plasma cells in LT?R$^{-/-}$ mice expressed predominantly IgM, whereas WT plasma cells expressed IgA. During infection, WT mice showed an almost complete loss of BM B cells which was less pronounced in LT?R$^{-/-}$ animals.

These results illustrate an interesting role of LT?R signalling for the B cell compartment during *T. gondii* infection.