Immune phenotyping of beta-2-microglobulin knockout pigs

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There is increasing interest in pigs as a donor species for xenotransplantation. Beta-2-microglobulin (B2M) is pivotal for the expression of class I major histocompatibility complex (MHC I) molecules, which are important inducers of tissue rejection in the recipient. Moreover, MHC I and the closely related CD1 molecule family are central players in antigen presentation and regulation of T cell development. B2M deficiency results in severe consequences, but its impact on the porcine immune system is widely unknown. Therefore, we investigated leukocyte subpopulations from peripheral blood with a focus on MHC I- and CD1-restricted adaptive T cells. In contrast to age-matched controls, B2M knockout pigs displayed a prominent leukopenia with a substantial loss of cytotoxic CD8+ T cells in favor of CD4+ helper T cells. CD4+/CD8+ memory/effector T cells were not affected. Moreover, we detected an increased frequency of gamma/delta T cells, which showed enhanced activation over time in knockout animals, evidenced by increased CD8 expression. B2M knockout resulted in a complete loss of invariant Natural Killer T cells, but no changes in NK cell frequency. Taken together, we characterized the immune phenotype of B2M knockout pigs, allowing insights into the immune development in pigs and new approaches for xenotransplantation.

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