HOKKAIDO UNIVERSITY

Title	Studies on programmed death-ligand 1 in equine and swine diseases [an abstract of dissertation and a summary of dissertation review]
Author(s)	Ganbaatar, Otgontuya
Degree Grantor	北海道大学
Degree Name	博士(獣医学)
Dissertation Number	甲第15040号
Issue Date	2022-03-24
Doc URL	https://hdl.handle.net/2115/86021
Rights(URL)	https://creativecommons.org/licenses/by/4.0/
Type	doctoral thesis
File Information	GANBAATAR_Otgontuya_abstract.pdf, 論文内容の要旨

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

学位論文内容の要旨
Abstract of the dissertation

博士の専攻分野の名称：博士（獣医学）　　氏名：ガンバータル　オトゴンツヤ
Name：GANBAATAR OTGONTUYA

学位論文題名
The title of the doctoral dissertation

Studies on programmed death-ligand 1 in equine and swine diseases
（　ウマおよびブタ疾病における PD-L1 に関する研究　）

Programmed death-1 (PD-1) is an immunoinhibitory receptor, which is expressed on T cells. Programmed death ligand 1 (PD-L1) is the ligand of PD-1, and expressed on immune cells, including antigen-presenting cells, and tumor cells. The interaction of PD-1 with PD-L1 induces the functional exhaustion of T cells, which is characterized by the suppression of activation signals mediated by T-cell receptors and the inhibition of effector functions of T cells, including cytokine production and cell proliferation. During chronic infections and tumor formation, the expression level of PD-1 is upregulated by persistent stimulations via antigens and cytokines, and T cells fail to eliminate infected cells and tumor cells. However, the immunological role of the PD-1/PD-L1 pathway remains unclear in chronic diseases of horses and pigs. This study examined the cross-reactivity and blocking effects of anti-bovine PD-L1 monoclonal antibody (mAb) against equine and swine PD-L1. In addition, the expression of PD-L1 were analyzed in swine chronic infections. Furthermore, the immunomodulatory effects by anti-PD-L1 antibodies were evaluated in immune cells of horses and pigs. Nucleotide sequences of swine and equine *PD-1* and *PD-L1* were identified. Additionally, PD-L1 was expressed at the site of infection in pigs affected with PRRS, mycoplasmosis, PCV-2 infection, and proliferative enteropathy. Moreover, PD-L1 blockade with anti-PD-L1 mAb induced IL-2 production in swine PBMCs. These results suggest that the PD-1/PD-L1 pathway could be involved in immunosuppression and that therapeutic antibody against PD-L1 could be a novel option to treat chronic infections

of pigs.

Taken together, the PD-1/PD-L1 pathway is found to be associated with the swine chronic infections. Blockade of the PD-1/PD-L1 pathway is a hopeful therapeutic approach against these chronic diseases in pigs.