HOKKAIDO UNIVERSITY

Title	Laboratory of Infectious Diseases (An Introduction of the four Departments composing the Graduate Scholl of Veterinary Medicine, Hokkaido University (2))
Author(s)	ONUMA, Misao; SUGIMOTO, Chihiro; OHASHI, Kazuhiko
Citation	Japanese Journal of Veterinary Research, 45(3), 172-173
Issue Date	1997-11-28
Doc URL	http://hdl.handle.net/2115/2605
Type	bulletin (article)
File Information	KJ00002398565.pdf

Instructions for use

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Jpn. J. Vet. Res. **45**(3): 172–173 (1997)

Laboratory of Infectious Diseases

Professor: Misao Onuma
Associate Professor: Chihiro Sugimoto
Instructor: Kazuhiko Ohashi

The goal of the research in this laboratory is to establish protection methodology, for example development of vaccines, against infectious agents such as bacteria, viruses and protozoa. For this purpose, pathogenesis of these agents and host immune responses are studied at the levels of individual animals, cells and molecules. The research efforts thus focus on 1) identification of factors involved in the pathogenesis of infectious agents, 2) clarification of host immune responses against these pathogens, and 3) experimental development of effective vaccines against infectious diseases.

The main ongoing research projects by the staff, graduate and undergraduate students, and visiting researchers in international collaboration with other laboratories are as follows:

1. Studies on bovine and equine piroplasmosis: Molecular and antigenic studies on *Theileria sergenti/buffeli/orientalis* group parasites have revealed that the field isolates collected from Japan, Korea, China, and other Asian countries contain at least two genotypically different parasites. This study has been expanded to molecular epidemiology of benign *Theileria* species in domestic and wild animal species. This phylogenetic study will clalify evolution of host-parasite relationships.

Recombinant and synthetic peptide-based vaccine against bovine piroplasmosis are also being developed. The tick vector control method is a possible alternative method of controlling tick-borne diseases. cDNAs for protein antigens secreted from *Haemaphysalis* tick salivary glands have been characterized. *T. parva* genome project is also in progress in collaboration with International Livestock Research Institute, Nairobi, Kenya. For development of ELISA as the diagnosis of equine piroplasmosis, recombinant antigens of *B. equi* and *B. caballi* expressed in *Escherichia coli* are now being validated.

2. Pathogenesis and protection of bovine retrovirus infections: Bovine leukemia virus (BLV) causes lymphomatous disorders in cattle. Works has been done to define host immune responses against viral proteins such as envelope and tax proteins, and epitope mapping analysis identified several immunodominant epitopes in these proteins for either humoral and cell-mediated immunity. Studies to examine the protective effects of peptide vaccines, recombinant vaccines using baculovirus or vaccinia virus expression systems, and naked DNA vaccines against BLV infection are in progress.

The pathogenesis of bovine immunodeficiency-like virus (BIV) remains unclear. The survey in the seroprevalence of BIV in Japan is in progress and found that quite many cattle are infected with BIV in Hokkaido. An attempt is being made to isolate BIV and to establish cell culture system for BIV replication to study the antigenic and molecular characteristics of BIV.

3. Pathogenesis of Marek's disease virus (MDV) and protection mechanism by MD vaccines: To clarify the mechanisms by which the virus causes diseases, we have analyzed kinetic changes of $CD4^+$ T cells, target for transformation by MDV. Our works showed that MDV causes both transformation and apoptosis of $CD4^+$ T cells, suggesting that genes involved in the regulation of apoptosis would be key factors for the molecular mechanism of transformation. Thus, we are now investigating changes in expression of apoptosis-related genes including p53 and *bcl*-2 family members to determine how $CD4^+$ T cells choose to undergo either transformation or apoptosis. The protection mechanism by MD vaccines have not been fully understood though anti-tumor rather than anti-virus

activity contribute to the protection. To determine the roles of T cell subsets in the protection mechanism, T cell subset-deficient chickens, established by thymectomy and injection of anti-T cell marker monoclonal antibodies, are being used to measure the protection efficacy of MD vaccines.

4. Roles of cytokines in immunity against infectious diseases : cytokines represent major factors in the development of immune responses. Strategies in the development of vaccines need to consider the balance of the Th-1/Th-2 they induce. The changes in the cytokine profiles after infection with various agents has been monitored in order to clarify the relationship between disease progression and balances in the cytokine profiles. In addition, production of recombinant interleukin 12 and its use as an adjuvant for peptide vaccines to induce cell-mediated immunity are now in progress.

5. Application of plant biotechnology for cytokine production : Recombinant cytokines are currently used for treatment of viral diseases and cancer in human, but the use of recombinant products are very limited in veterinary medicine mainly because of their expensiveness. Production of recombinant products in plants will be suitable for cytokine production at industrial level. In collaboration with plant molecular biologists, transgenic potato producing animal cytokines has been developed. Plant viral vector system is also being validated.

References

1) Hirai N. et al. 1996. Detection of antibodies against bovine immunodeficiency-like virus in daily cattle in Hokkaido. *J. Vet. Med. Sci.*, 58 : 455–457.
2) Hirai, N. et al. 1996. Immunomodurative effects of bovine immunodefficiency-like virus (BIV)-infection and mixed infection of BIV and bovine leukemia virus on sheep. *Jpn. J. Vet. Res.* 44 : 153–163.
3) Kabeya H. et al. 1996. An effective peptide vaccine to eliminate bovine leukemia virus (BLV) infected cells in carrier sheep. *Vaccine*, 14 : 1118–1122.
4) Kubota, S. et al. 1996. Analysis of immunodominant piroplasm surface antigen alleles in mixed populations of *Theileria sergenti* and *T. buffeli*. *Int. J. Parasitol.*, 26 : 741–747.
5) Kubota, S. et al. 1996. Population dynamics of *Theileria sergenti* in persistently infected cattle and vector ticks analysed by a polymerase chain reaction. *Parasitology*, 112 : 437–442
6) Morimura, T. et al. 1996. Apoptosis and CD8-down-regulation in the thymus of chickens infected with Marek's disease virus. *Arch. Virol.*, 141 : 2243–2249.
7) Yamamoto, H. et al. 1996. Characterization of extrathymic T cells of chickens. *Vet. Immunol. Immunopathol.* 49 : 375–386.