The major histocompatibility complex of reindeer

I. Olsaker and K.H. Røed.

Department of Animal Genetics, The Norwegian College of Veterinary Medicine and National Veterinary Institute, P.O. Box 8156 Dep., N-0033 Oslo 1, Norway.

Abstract: The major histocompatibility complex (MHC) is a system of closely linked genes showing an extremely high degree of polymorphism. These genes are major elements in the government of specific immune reactions. Consequently they may represent a genetic marker system well suited to investigate variability in selective pressure from disease agents on different populations. On this background we have started investigation of the MHC complex in reindeer *(Rangifer tarandus* L). The MHC complex consist of polymorphic regions as well as regions conserved during evolution which should allow the use of cross-species reagents. We have shown that human MHC gene probes hybridize with genomic DNA from reindeer, and thus can be used as a tool in reindeer MHC research. By RFLP (restriction fragment length polymorphism) analysis using these probes we have also been able to show polymorphism in MHC related genes from reindeer.

Key words: *Rangifer*, MHC, RFLP

Rangifer, Special Issue No. 3, 1990: 369-372

Introduction

The Major Histocompatibility Complex (MHC) is a family of related, highly polymorphic and closely linked genes occupying one chromosomal region. These genes encode different classes of cell-surface glycoproteins. The glycoproteins are involved in cell - cell interactions and functions as major elements in the government of specific immune reactions.

Class I proteins occur on the surface of nearly all cell types and function as restricting elements in the process of eliminating virus infected and foreign cells. Class II proteins are expressed on specialized cells involved in regulation of the humoral and cellular response against foreign antigens. The number of genes for class I and class II polypeptides shows variation both between and within species. Moreover individual MHC genes contains regions conserved during evolution as well as highly polymorphic domain. The degree of polymorphism varies with the species, the population and the locus.

The conserved regions makes reagents such as antibodies and DNA- probes developed for typing of MHC genes in one particular species, potentially useful for MHC typing in other species as well.

The properties and peculiarities of the Major Histocompatibility Complex in different species are reviewed in Klein (1986) and Klein & Figueroa (1986).

The polymorphism of MHC genes in a given species might reflect the diversity of respective environmental pathogens. MHC may thus represent a genetic marker system well suited to investigate variability in selective pressure from disease agents on different populations.

On this background we have started investigation of the MHC in reindeer. Reindeer mainly live under natural environmental conditions. In Scandinavia numerous different populations exist both as semi-domestic and wild animals. The amount of differentiation and the evolution of the different populations are unknown. Studies on the pattern of genetic variability of the MHC of reindeer (tentatively called RaLA - Rangifer Leucocyte Antigens) might provide information regarding evolution of the different reindeer populations.

Here we describe the results of using a human class II ß MHC gene probe in restriction fragment length polymorphism (RFLP) studies on reindeer genomic DNA.

Materials and methods

Genomic DNA was isolated from 26 semi-domestic reindeer from Norway. Some of the animals were related (dam/offspring).

The DNA was digested with restriction endonucleases at 37°C over night. The digests were separated in 0.7 % agarose gels and blotted onto Gene Screen Plus filters (NEN - Du Pont) by alkaline capillary transfer. Hybridization (at 42°C with formamide) and washing was performed according to the filter producers manual.

Cloned DNA from a human class II gene was used as probe: The DQ ß probe was isolated as the 672bp Ava I fragment from the cDNA clone pII-ß-1 (Larhammar et al. 1982). The fragment was isolated by preparative agarose gel electrophoresis followed by extraction with GeneClean (BIO 101) and radiolabelled with α ($^{-32}$ p) dCTP by multiprime DNA labelling (Amersham).

Results and discussion

The tested probe from the human MHC class II gene did hybridize to reindeer DNA showing that this DNA contains MHC class II related gene sequences.

14 different RFLP-phenotypes were revealed among the tested animals. Fig. 1 shows some of these phenotypes. This indicates the existence of at least 4 different variants of DQß related genes in reindeer. Offspring always had bands in common with their mothers. The family material was however to small to allow assignment of distinct bands belonging to specific alleles.

RFLP studies with human MHC gene probes have revealed highly polymorphic MHC gene loci in other animals such as cattle, sheep, horses, pigs, squirrels etc. (Vaiman & Chardon, 1986; Wettstein & States, 1986 a,b; Sigurdardôttir, Lundén & Andersson, 1988). For some of these animals the RFLP patterns were shown to be associated with serologically determined MHC types (Vaiman & Chardon, 1986). Our RFLP results from reindeer conform with the results from other animals and strongly indicates the existence of MHC genes in reindeer.

Confirmation of this can be achieved in different ways. One is to isolate the tentative RaLA gene fragments, perform sequencing and compare the results with known MHC gene sequence data. Further mapping of genes in a RaLA complex can be done by chromosome walking. Another method for confirmation involves studies of cell reactions in mixed lymphocyte cell cultures. Genes in the Major Histocompatibility Complex are related to disease resistance and susceptibility. The high amount of variation revealed in reindeer MHC genes suggests these genes as useful disease related genetic markers in studies of reindeer populations.

Lately there has been a lot of speculation con-

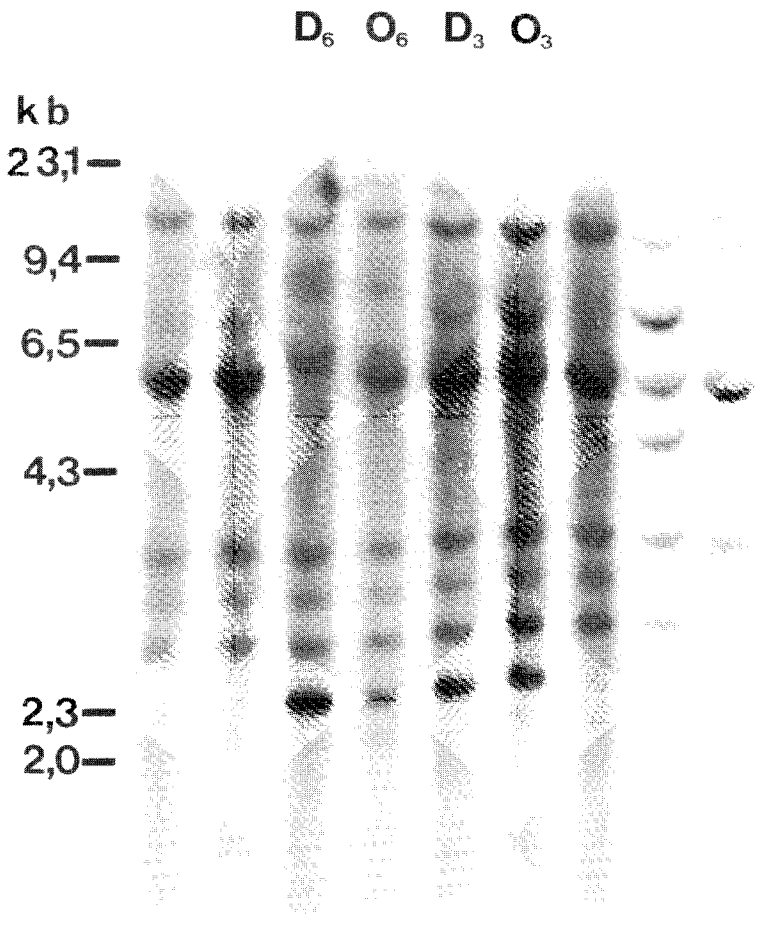

Fig. 1. EcoRI digested DNA from reindeer hybridized to a human DQ ß probe. D:dam. O:offspring

cerning the evolution of the high degree of polymorphism in the MHC. There is a large genetic distance between different alleles and a large number of alleles within most of the investigated species. Generally it has been assumed that these differences accumulated after speciation. Recent reports indicate that a large part of the MHC polymorphism pre-dates speciation and is passed from species to species (McConnell *et al.* 1988, Figueroa, Günther & Klein, 1988; Lawlor *et al.* 1988). Reinder populations live under natural environmental conditions. Investigations of reindeer MHC therefore have considerable interest in the light of MHC evolution as well.

Further analysis of tentative MHC genes in reindeer including more family material and animals from differens populations are under way.

References

Figueroa, F., Günther, E. and **Klein, J.** 1988. MHC polymorphism predating speciation. *Nature* 335:265-267.

Klein, J. 1986. Natural History of the Major Histocompability Complex. John Wiley and Son, New York.

Klein, J. and **Figueroa, F.** 1986. Evolution of the Major Histocompatibility Complex. - *CRC Critical Reviews in Immunology* 6:295-386.

Larhammar D., Schenning L., Gustafsson K., Wiman K., Claesson L., Rask L. and Peterson P. A. 1982. Complete amino acid sequence of an HLA-DR antigen-like ß chain as predicted from the nucleotide sequence: Similarities with immunoglobulins and HLA-A, -B, and -C antigens. — *Proc. Natl. Acad. Sci. USA* 79:3687-3691.

Lawlor, D. A., Ward, F. E., Ennis, P. D., Jackson, A. P. and Parham, P. 1988. HLA-A and B polymorphism predate the divergence of humans and chimpanzees. - *Nature* 335:268-271.

McConnell, T. J., Talbot, W. S., McIndoe, R. A. and Wakeland, E. K. 1988. The origin of MHC class II gene polymorphism within the genus *Mus*. - *Nature* 332:651-654.

Sigurdardôttir, S., Lundén, A. and Andersson, L. 1988. Restriction fragment lenght polymorphism of DQ and DR class II genes of the bovine major histocompatibility complex. - *Animal Genetics* 19:133-150.

Vaiman, M. and Chardon P. 1986. DNA polymorphism in the major histocompatibility complex of man and various farm animals. — *Animal Genetics* 17:113-133.

Wettstein, P. J. and States, J. S. 1986a. The Major Histocompatibility Complex of Tassel-Eared Squirrels. I. Genetic Diversity Associated with Kaibab Squirrels. - *Immunogenetics* 24:230-241.

Wettstein, P. J. and States, J. S. 1986b. The Major Histocompatibility Complex of Tassel-Eared Squirrels. II. Genetic Diversity Associated with Abert Squirrels. - *Immunogenetics* 24:242-250.