

Brief Note

Low diversity of the major histocompatibility complex class II DRA gene in domestic goats (*Capra hircus*) in Southern China

L.P. Chen^{1*}, G.X. E¹, Y.J. Zhao¹, R.S. Na¹, Z.Q. Zhao¹, J.H. Zhang¹, Y.H. Ma², Y.W. Sun¹, T. Zhong³, H.P. Zhang³ and Y.F. Huang^{1*}

¹College of Animal Science and Technology,
Chongqing Key Laboratory of Forage and Herbivores,
Chongqing Engineering Research Centre for Herbivores Resource Protection and Utilization, Southwest University, Chongqing, China
²Key Laboratory of Farm Animal Genetic Resources and Utilization of Ministry of Agriculture, Institute of Animal Science,
Chinese Academy of Agricultural Sciences, Beijing, China
³Farm Animal Genetic Resources Exploration and Innovation Key Laboratory of Sichuan Province, Sichuan Agricultural University, Chengdu, Sichuan, China

*These authors contributed equally to this study. Corresponding author: Y.F. Huang E-mail: H67738337@swu.edu.cn

Genet. Mol. Res. 14 (2): 6925-6928 (2015) Received January 6, 2015 Accepted May 25, 2015 Published June 18, 2015 DOI http://dx.doi.org/10.4238/2015.June.18.35

ABSTRACT. DRA encodes the alpha chain of the DR heterodimer, is closely linked to DRB and is considered almost monomorphic in major histocompatibility complex region. In this study, we identified the exon 2 of DRA to evaluate the immunogenetic diversity of Chinese south indigenous goat. Two single nucleotide polymorphisms in an

Genetics and Molecular Research 14 (2): 6925-6928 (2015)

untranslated region and one synonymous substitution in coding region were identified. These data suggest that high immunodiversity in native Chinese population.

Key words: Major histocompatibility complex; DRA; Domestic goat; *Capra hircus*

INTRODUCTION

The major histocompatibility complex (MHC) plays an important role in the adaptive immune response of vertebrates (Trowsdale, 1993). The DRA locus, which encodes the alpha chain of the DR heterodimer, is closely linked to DRB and is considered almost monomorphic (Ballingall et al., 2010). It exhibits low diversity in artiodactyl species (Sena et al., 2003; Sun et al., 2014), including its exon 2 (Sena et al., 2003; Zhou et al., 2007; Shafer et al., 2012). Therefore, investigating the diversity of the 2nd exon in the DRA of domestic goat breeds would help in understanding the specific evolutionary mechanism of the DRA gene, and realize the full breeding potential of Chinese goats.

MATERIAL AND METHODS

DNA samples were obtained from 247 individuals of 12 domestic goat breeds in southern China (Table 1). Screening for polymorphisms was performed by direct polymerase chain reaction (PCR) product sequencing in both directions. The primers and PCR protocol employed for the DRA exon 2 were the same as those used by Shafer et al. (2012). Linkage disequilibrium (LD) between loci within each population was analyzed by Genepop (Rousset, 2008). The heterozygosity (H_E and H_O) and polymorphism information content (PIC) were estimated using Microsatellite Toolkit (Park, 2001).

RESULTS

The total length of the aligned sequences was 303 bp, which included two singlenucleotide polymorphisms, the locations of which were based on AB008755: MI, C > T at 2373 bp on the 2nd intron, and one synonymous substitution (MII) in positions C > T (p.Ala) at 2169 bp on the 2nd exon. In all of the populations studied, the MII site exhibited extremely low diversity ($H_0 = 0.057$, $H_E = 0.0685$, and PIC = 0.0631) in comparison to the MI site ($H_E =$ 0.471, $H_0 = 0.405$, and PIC = 0.3525). We found unlinkage between MI and MII in all of the populations studied (Table 1).

DISCUSSION

Comparative analysis of the results obtained in our experiments revealed minimal diversity in exon 2 of the DRA gene. It seems to be highly conserved for residues that form the peptide-binding site region in the domestic goat, which is consistent with the fact that the gene is highly conserved in all of the mammalian species studied (Shafer et al., 2012; Sun et

Genetics and Molecular Research 14 (2): 6925-6928 (2015)

| | Location | | | | | IW | | | | | | ШМ | | | P (LD) |
|-------------|--|-------------------|--|--|--|--|--|--|--|--|--|---|---|---|---|
| | | | Ŭ | notyp | e | | Diversity | | ľ | ienoty | pe | Г | Diversity | | |
| Breed type | Longitude | Latitude | cc | ΤT | CT | H_0 | $H_{\rm E}$ | PIC | cc | TT | CT | H_0 | $H_{\rm E}$ | PIC | |
| Cultivation | 29°17'N# | 108°09'E | 5 | 9 | 2 | 0.368 | 0.508 | 0.372 | 17 | 0 | - | 0.0526 | 0.0526 | 0.0499 | 0.26203 |
| Indigenous | 29°59'N# | $106^{\circ}14'E$ | 7 | S | 10 | 0.476 | 0.511 | 0.374 | 21 | 0 | - | 0.0476 | 0.0476 | 0.0454 | 1.00000 |
| Indigenous | 29°21'N | $104^{\circ}46'E$ | 4 | 13 | 9 | 0.130 | 0.507 | 0.3731 | 23 | 0 | 0 | 0 | 0 | 0 | |
| Indigenous | 29°24'N# | 105°27'E | 5 | × | 11 | 0.458 | 0.503 | 0.3711 | 22 | | - | 0.0417 | 0.1197 | 0.1103 | 0.795840 |
| Indigenous | 28°21'N | 118°15'E | ŝ | × | 6 | 0.450 | 0.481 | 0.3589 | 20 | 0 | 0 | 0 | 0 | 0 | |
| Indigenous | 28°02'N | $114^{\circ}08'E$ | - | 14 | 5 | 0.300 | 0.328 | 0.2688 | 20 | 0 | 0 | 0 | 0 | 0 | |
| Indigenous | 29°59'N# | 106°14'E | ŝ | 9 | 14 | 0.609 | 0.502 | 0.3707 | 20 | 0 | ŝ | 0.1304 | 0.1246 | 0.1145 | 0.395840 |
| Cultivation | 30°23'N | 104°31'E | 0 | 16 | 10 | 0.357 | 0.382 | 0.3047 | 26 | 0 | 0 | 0.0714 | 0.0701 | 0.0665 | 1.000000 |
| Indigenous | 28°02'N | 102°53'E | с | = | 12 | 0.500 | 0.449 | 0.3432 | 23 | 0 | с | 0.0769 | 0.0754 | 0.0712 | 0.317710 |
| Cultivation | 32°20'N# | 106°49'E | 5 | L- | 4 | 0.250 | 0.508 | 0.3711 | 15 | 0 | - | 0.0625 | 0.0625 | 0.0587 | 1.000000 |
| Indigenous | 32°53'N | 101°46'E | 5 | ~ | 14 | 0.556 | 0.498 | 0.3695 | 22 | | 4 | 0.1481 | 0.2013 | 0.178 | 0.423670 |
| I | | | 43 | 102 | 102 | 0.405 | 0.471 | 0.3525 | 229 | 0 | 16 | 0.0574 | 0.0685 | 0.0631 | 0.913429 |
| 1 | Breed type Cultivation Indigenous Indigenous Indigenous Indigenous Cultivation Indigenous Cultivation Indigenous Cultivation Indigenous | | Longitude 1 29°17'N" 1 29°57'N" 1 29°57'N 1 29°21'N 1 29°22'N 1 28°02'N 1 28°02'N 1 28°02'N 1 28°02'N 1 30°23'N 1 32°53'N 1 | Longitude Latitude CC 29°17N" 108°09'E 5 29°59N" 106°14'E 7 29°59N" 106°14'E 7 29°21'N 104°46'E 4 29°21N 104°46'E 7 29°21'N 104°46'E 5 29°21'N 104°46'E 5 29°27N 104°46'E 5 28°02'N 118°15'E 3 28°02'N 104°31'E 2 30°23'N 102°57'E 3 32°25'N 100°40'E 5 32°53'N 101°40'E 5 32°53'N 101°40'E 5 32°53'N 101°40'E 5 | Longitude Latitude CC 29°17N" 108°09'E 5 29°59N" 106°14'E 7 29°59N" 106°14'E 7 29°21'N 104°46'E 4 29°21N 104°46'E 7 29°21'N 104°46'E 5 29°21'N 104°46'E 5 29°27N 104°46'E 5 28°02'N 118°15'E 3 28°02'N 104°31'E 2 30°23'N 102°57'E 3 32°25'N 100°40'E 5 32°53'N 101°40'E 5 32°53'N 101°40'E 5 32°53'N 101°40'E 5 | Longitude Latitude CC TT 29°17N# 108°09'E 5 6 29°21N 108°14'E 7 5 29°21N 108°14'E 7 5 29°21N 108°14'E 7 5 29°21N 108°24'E 4 13 29°21N 108°27'E 5 8 28°21N 118°25'E 3 8 28°21N 118°25'E 3 8 29°59N# 108°25'E 3 8 29°59N* 108°25'E 3 8 29°59N* 108°25'E 3 8 30°23'N 102°55'E 3 8 30°23'N 102°55'E 3 7 32°55'N 101°46'E 5 7 | $\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$ | Conotype Longitude Lantude CC TT CT H_0 29°17N [#] 108°09'E 5 6 7 0.368 29°27N [#] 106°14'E 7 5 10 0.476 29°27N [#] 106°14'E 7 5 10 0.476 29°24N [#] 106°14'E 7 5 10 0.476 29°24N [#] 108°27'E 5 8 1 0.458 28°21'N 118°15'E 5 8 9 0.450 28°27N 118°15'E 3 6 14 5 0.300 29°25'N [#] 106°14'E 3 6 14 0.609 337 29°27'N 102°31'E 2 16 0 337 2000' 29°27'N 102°31'E 3 11 12 0.500 29°27'N 102°49'E 7 4 0.550 32°55'N | Liversity Longitude Latitude CC TT CT H_0 $H_{\rm E}$ 29°17N* 108°09'E 5 6 7 0.368 0.508 0 29°59N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°54'N* 108°14'E 7 5 10 0.476 0.501 0 29°54'N* 118°15'E 5 8 1 0.450 0.503 0 28°02'N 118°15'E 3 6 14 5 0.300 0.328 0 29°55'N* 108°14'E 3 6 14 5 0.300 0.322 0 29°25'N 104°31'E 2 1 1 2 0.500 0.449 0 <tr< td=""><td>JUNCESTING Longitude Latitude CC TT CT H_{o} H_{E} PIC CC 29°17N* 108°09'E 5 6 7 0.368 0.372 17 CC 29°59N* 106°14'E 7 5 10 0.476 0.511 0.372 17 29°59N* 108°14'E 7 5 10 0.476 0.511 0.374 21 29°21'N 104°46'E 4 13 6 0.130 0.507 0.3711 22 29°24'N* 108°72'E 5 8 1 0.450 0.533 0.3711 22 29°25'N 118°15'E 5 8 1 0.450 0.563 0.3707 20 29°25'N 104°31'E 2 1 0.557 0.388 20 23 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27</td><td>JUNCESTING Longitude Latitude CC TT CT H_{o} H_{E} PIC CC 29°17N* 108°09'E 5 6 7 0.368 0.372 17 CC 29°59N* 106°14'E 7 5 10 0.476 0.511 0.372 17 29°59N* 108°14'E 7 5 10 0.476 0.511 0.374 21 29°21'N 104°46'E 4 13 6 0.130 0.507 0.3711 22 29°24'N* 108°72'E 5 8 1 0.450 0.533 0.3711 22 29°25'N 118°15'E 5 8 1 0.450 0.563 0.3707 20 29°25'N 104°31'E 2 1 0.557 0.388 20 23 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27</td><td>Liversity Longitude Latitude CC TT CT H_0 $H_{\rm E}$ 29°17N* 108°09'E 5 6 7 0.368 0.508 0 29°59N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°54'N* 108°14'E 7 5 10 0.476 0.501 0 29°54'N* 118°15'E 5 8 1 0.450 0.503 0 28°02'N 118°15'E 3 6 14 5 0.300 0.328 0 29°55'N* 108°14'E 3 6 14 5 0.300 0.322 0 29°25'N 104°31'E 2 1 1 2 0.500 0.449 0 <tr< td=""><td>$\begin{array}{ c c c c c c c c c c c c c c c c c c c$</td><td>Genotype Diversity Genotype Longitude Latitude CC TT CT H₀ H_E PIC CC TT CT H₀ H₀</td><td>Genotype Diversity Genotype Diversity Cenotype Diversity Comotype Diversity 29°59N* 106°14E 7 5 10 0.373 23 0</td></tr<></td></tr<> | JUNCESTING Longitude Latitude CC TT CT H_{o} H_{E} PIC CC 29°17N* 108°09'E 5 6 7 0.368 0.372 17 CC 29°59N* 106°14'E 7 5 10 0.476 0.511 0.372 17 29°59N* 108°14'E 7 5 10 0.476 0.511 0.374 21 29°21'N 104°46'E 4 13 6 0.130 0.507 0.3711 22 29°24'N* 108°72'E 5 8 1 0.450 0.533 0.3711 22 29°25'N 118°15'E 5 8 1 0.450 0.563 0.3707 20 29°25'N 104°31'E 2 1 0.557 0.388 20 23 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 | JUNCESTING Longitude Latitude CC TT CT H_{o} H_{E} PIC CC 29°17N* 108°09'E 5 6 7 0.368 0.372 17 CC 29°59N* 106°14'E 7 5 10 0.476 0.511 0.372 17 29°59N* 108°14'E 7 5 10 0.476 0.511 0.374 21 29°21'N 104°46'E 4 13 6 0.130 0.507 0.3711 22 29°24'N* 108°72'E 5 8 1 0.450 0.533 0.3711 22 29°25'N 118°15'E 5 8 1 0.450 0.563 0.3707 20 29°25'N 104°31'E 2 1 0.557 0.388 20 23 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 23°27 | Liversity Longitude Latitude CC TT CT H_0 $H_{\rm E}$ 29°17N* 108°09'E 5 6 7 0.368 0.508 0 29°59N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°59'N* 108°14'E 7 5 10 0.476 0.511 0 29°54'N* 108°14'E 7 5 10 0.476 0.501 0 29°54'N* 118°15'E 5 8 1 0.450 0.503 0 28°02'N 118°15'E 3 6 14 5 0.300 0.328 0 29°55'N* 108°14'E 3 6 14 5 0.300 0.322 0 29°25'N 104°31'E 2 1 1 2 0.500 0.449 0 <tr< td=""><td>$\begin{array}{ c c c c c c c c c c c c c c c c c c c$</td><td>Genotype Diversity Genotype Longitude Latitude CC TT CT H₀ H_E PIC CC TT CT H₀ H₀</td><td>Genotype Diversity Genotype Diversity Cenotype Diversity Comotype Diversity 29°59N* 106°14E 7 5 10 0.373 23 0</td></tr<> | $ \begin{array}{ c c c c c c c c c c c c c c c c c c c$ | Genotype Diversity Genotype Longitude Latitude CC TT CT H ₀ H _E PIC CC TT CT H ₀ | Genotype Diversity Genotype Diversity Cenotype Diversity Comotype Diversity 29°59N* 106°14E 7 5 10 0.373 23 0 |

| 0/0624.0 | 0.913429 | l between National |
|--------------------|---------------|--|
| 0.1 / Q | 0.0631 | uilibrium ie China |
| 6102.0 | 0.0685 | ge disequate the second s |
| 0.1481 0.2015 | 0.0574 0.0685 | or linkag h referei |
| 4 | 16 | alue f whic |
| - | 0 | = P v8 ation |
| 1 77 | 229 | (LD) = /e loc |
| | 0.3525 | ntent; P (productiv |
| C606.U 864.U 0CC.U | 0.405 0.471 | ation co le main |
| 0000.0 | 0.405 | inform eflect th |
| 4 | 102 | hism bel re |
| ø | 102 | morp ny la |
| n | 43 | poly out a |
| 101-40E | | ity; PIC = and with |
| NI.66-76 | | terozygos g location;). |
| Indigenous | | sity: $H_0 =$ observed heterozygosity; PIC = polymorphism information content; P (LD) = P value for linkage disequilibrium between .) = no data; "sampling location; and without any label reflect the main productive location which reference as the China National sheric Resources (2011). |
| 17 | 247 | osity; H_0 (-) = no d |
| 2 | | l heterozyg pulations; of Animal C |
| liberan | All | $H_{\rm B} = \exp \left(\exp $ |

Diversity of DRA in goats

Genetics and Molecular Research 14 (2): 6925-6928 (2015)

Y.F. Huang et al.

al., 2014). Directional selection appears to have conserved these specific functional regions (antigens that are specific to infectious xenobiotics) in the DRA gene of ruminant animals. In comparison to the monomorphic allele in the North American mountain goat (*Oreamnos americanus*) (Shafer et al., 2012), a weak but valuable variant of exon 2 in DRA indicates great potential to improve goat varieties and promote animal husbandry development in the Chinese domestic goat.

Conflicts of interest

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

The authors alone are responsible for the content and writing of this article. Research supported by the Fundamental Research Funds for the Central Universities (#SWU114023), the National Natural Science Foundation of China (#31172195), and the 2013 Innovation Team Building Program in Chongqing Universities (#KJTD201334).

REFERENCES

- Ballingall KT, Rocchi MS, McKeever DJ and Wright F (2010). Trans-species polymorphism and selection in the MHC class II DRA genes of domestic sheep. *PLoS One* 5: e11402.
- China National Commission of Animal Genetic Resources (2011). Animal genetic resources in China: sheep and goats. Chinese Agricultural Press, Beijing.
- Park SDE (2001). Trypanotolerance in West African Cattle and the Population Genetic Effect of Selection. PhD Thesis, University of Dublin, Dublin.
- Rousset F (2008). Genepop'007: a complete reimplementation of the Genepop software for Windows and Linux. *Mol. Ecol. Resour.* 8: 103-106.
- Sena L, Schneider MPC, Brenig B, Honeycutt RL, et al. (2003). Polymorphisms in MHC-DRA and -DRB alleles of water buffalo (*Bubalus bubalis*) reveal different features from cattle DR alleles. *Anim. Genet.* 34: 1-10.
- Shafer AB, Fan CW, Côté SD and Coltman DW (2012). (Lack of) genetic diversity in immune genes predates glacial isolation in the North American mountain goat (*Oreamnos americanus*). J. Hered. 103: 371-379.
- Sun Y, Zheng H, Xi D, Zhang X, et al. (2014). Molecular characteristics of the MHC-DRA genes from yak (*Bos grunniens*) and Chinese yakow (*Bos grunniens* x *Bos taurus*). *Int. J. Immunogenet.* 41: 69-73.

Trowsdale J (1993). Genomic structure and function in the MHC. Trends Genet. 9: 117-122.

Zhou H, Hickford JG, Fang Q and Byun SO (2007). Identification of allelic variation at the bovine DRA locus by polymerase chain reaction-single strand conformational polymorphism. J. Dairy Sci. 90: 1943-1946.

Genetics and Molecular Research 14 (2): 6925-6928 (2015)