Relative fitness contribution of BoLA alleles in *T. parva* immune cattle: Interface with parasite genetic diversity

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**Introduction**

East Coast Fever is a tick-borne parasitic leukosis of cattle caused by *Theileria parva* and transmitted by *Rhipicephalus appendiculatus* ticks. ECF is endemic in eastern, central and southern Africa with substantial economic impact.

**Objectives**

Establish if allelic diversity at the extensively polymorphic and principal expressed MHC class II DRB3 locus plays a role in determining variation in protection against *T. parva* challenge with the polymorphic 67 KDa major sporozoite p67 antigen.

Identify and quantitate both known and novel BoLA class I allelic variants in cattle populations of different genetic compositions by simultaneous ultra deep amplicon pyrosequencing.

Establish the hierarchy of dominance in the capacity of individual MHC class I specificities as restricting elements for *T parva* specific CTLs and predict the binding specificities of the expressed BoLA class I alleles.

**Methods**

- RNA $\rightarrow$ MHC I PCR $\rightarrow$ 454 pyrosequencing
- Blood $\rightarrow$ DNA $\rightarrow$ Sequencing of p67 sporozoite neutralizing epitopes
- Sequencing of the extensively polymorphic and principal expressed MHC class II DRB3

**Results**

Characterization of the bovine MHC class I locus: variable haplotype composition, interlocus recombination and novel alleles.

Genes 1, 2 and 3 are equally polymorphic, under selection pressure and presumed to be functional. They can be used to predict a subset of peptides mediating cellular immunity, and providing broad allelic coverage.

Additional MHC I sequences detected that cannot be assigned to any of the 6 putative classical class I I genes.

p67/MHC class II DRB3 genotyping

p67 allele 1 (129 bp deletion in the central region), and allele 2 (no deletion) identified in addition to novel alleles that have not been previously detected in East African cattle and buffalo.

**Conclusion**

A truly global analysis of immune responses to *T. parva* by simultaneous genotyping the multiple co-amplifying MHC class I loci, high throughput computational epitope searches, assessing the allelic diversity at the extensively polymorphic and principal expressed MHC class II DRB3 locus and the sporozoite neutralizing p67 antigen will support the rational development of vaccines based on subunit components of the parasite.