

## **The impact of MHC diversity on cattle T cell responses**

Shirley Ellis

Institute for Animal Health, Compton, UK

Major histocompatibility complex (MHC) genes encode molecules that bind and present pathogen-derived peptide to T cells. T cell receptor (TCR) recognition of an MHC-peptide complex leads to a variety of responses (e.g. cytotoxicity, cytokine production) aimed at elimination of the pathogen. Polymorphism is a crucial feature of MHC genes, leading to a range of alleles with distinct peptide-binding properties, thus allowing a proportion of individuals in a population to survive in the face of rapidly evolving pathogens. We have identified and characterised the MHC class I genes present in commercial Holstein and Friesian dairy cattle. Diversity is relatively low, and some haplotypes are very common. One of these common haplotypes has only a single expressed MHC class I gene, in contrast to the more usual two or three. This haplotype is immunodominant i.e. in heterozygous animals the majority of CD8 T cell responses are restricted by this single expressed allele. We have generated a crystal structure of this allele bound to a defined CD8 epitope. Results suggest an unusual binding conformation likely to impact significantly on TCR recognition and repertoire. This result will aid understanding of the structural basis for T cell dependent immune responses in cattle, vital for improved vaccine design and other disease control strategies.