

Project: Large scale identification of MHC haplotypes in diverse cattle breeds (Ref PIR2)

Supervisor: Dorothea Harrison
Co-Supervisors: John Hammond, Graham Freimanis
Research Group: Immunogenetics

Project Summary:

The Major Histocompatibility Complex (MHC) is one of the most variable genomic regions within and between mammals (Kelley, Walter, and Trowsdale 2005). It contains many polymorphic genes that are responsible for initiating an immune response once an organism has been invaded by a pathogen. This is a fundamental immune recognition pathway in all vertebrates and as a consequence has been under intense diversifying selection pressure, which has at least in part been driven by rapid pathogen evolution and emergence. The cattle MHC is highly diverse, including large copy number variations of polymorphic MHC class I genes, but our knowledge of this diversity is mostly limited to the Holstein breed (Ellis and Hammond 2014). Characterising this immune variation and function in more breeds, including indigenous cattle to Africa, is key to understanding the genetic basis of differential disease resistance between individuals. This data will inform selective breeding programmes that could improve the health and well-being of livestock.

Details:

The objective of this project is to generate full length MHC gene sequences from a range of diverse cattle breeds using next generation sequencing (NGS) methods. A recently published study established a high-throughput protocol to determine MHC class I allele fragments from cDNA (Vasoya et al. 2016). This protocol will be adapted to use genomic DNA for haplotype identification. We will utilize gDNA already available in our lab, collected from breeds such as Holstein-Friesians, Highland, Chillingham and NZ Friesians to optimise the methodology. We will then use a range of gDNA sources to assess other breeds, including gDNA extracted from bulk milk and individual blood samples from different breeds of African cattle available through our current internal and external collaborators. The resulting data will greatly enhance our knowledge of MHC variation and form the basis for extensive comparative and evolutionary analysis that can be directed according to the student's interests.

Complete training will be provided within our lab as we have recently sequenced and assembled the first cattle MHC haplotype using a range of molecular and sequencing methods. The successful applicant will learn the process of a complete project pipeline from designing a large scale study, sample preparation for next generation sequencing and analysing the data. This will require understanding of genetics and molecular biology skills. The assembly of haplotypes will need higher computer skills and a basic understanding of statistics.

References for Suggested Reading:

- Ellis, Shirley A, and John A Hammond. 2014. "The Functional Significance of Cattle Major Histocompatibility Complex Class I Genetic Diversity." *Annual Review of Animal Biosciences* 2 (September 2013): 3.1–3.22.
- Kelley, James, Lutz Walter, and John Trowsdale. 2005. "Comparative Genomics of Major Histocompatibility Complexes." *Immunogenetics* 56 (10): 683–95. doi:10.1007/s00251-004-0717-7.
- Vasoya, Deepali, Andy Law, Kathryn Degnan, Paolo Motta, Mingyan Yu, Adrian Muwonge, Annie Cook, et al. 2016. "Rapid Identification of Bovine MHCI Haplotypes Using Next-Generation Sequencing." *Immunogenetics* 68 (10). Immunogenetics: 765–81. doi:10.1007/s00251-016-0945-7.