Genetic Variation in Genes for Host Resistance to Disease

Genomic variation is clearly a major factor in host resistance to pathogens in mammals including cattle and humans. Identification of specific DNA variants that predispose susceptibility/resistance will be fundamental to genetic selection of resistant breeding stock and more importantly, to understanding cellular and molecular mechanisms of host response which will lead to development of improved vaccines and treatment. These studies are important to advancing animal health within the livestock industry, to averting accidental or terrorist-initiated epidemics, and to developing models of human gene/pathogen interaction.

The cattle genome project has recently released a new assembly of the 7.5X whole genome bovine sequence. Within this sequence release is the revelation of an enormous number of single nucleotide polymorphisms (SNPs) derived from whole genome skims of cattle from seven different breeds. We propose to target candidate genes in an effort to identify SNPs in coding and regulatory elements with a high probability of contributing to genetic differences in host resistance to specific pathogens. Specific genes targeted include the Toll-like receptor (TLR) gene family and genes coding the two major families of antimicrobial peptides, the cathelicidins (CATHL) and defensins (DEFN). We propose to target specific chromosomal regions and candidate genes for genomic variation. These will include both European-derived taurus and Asian-derived indicus breeds. This will provide a tool to identify the ancestral derivation of blocks of DNA in individual animals or breeds, including recently derived breeds that take advantage of both taurus and indicus germplasm such as Brangus and Santa Gertrudis.

Process
- Resequencing candidate genes across a 10 breed panel to identify SNPs and other polymorphisms segregating in cattle populations.
- Utilizing the SNP database to identify SNPs in other genes with known immune function.

Outcomes
- Discovery and validation of a large number of SNPs in coding sequences of select candidate genes for host-resistance.
- Identification of haplotypes within and around select candidate genes for host-resistance.
- Development of a SNP-Chip which identifies genetic variants in approximately 200 genes most likely to influence innate and acquired immunity in cattle.
- Ultimate application of the work will be the identification of specific genetic variants that predispose individual cattle to resistance to Johnne’s disease, shipping fever and ticks as well as to diseases that might enter our borders accidentally or as acts of bioterrorism (such as foot and mouth disease and Rift Valley fever).