APPLICATION OF MOLECULAR GENETIC TECHNOLOGIES FOR GENETIC IMPROVEMENT OF RUMINANTS

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Some applications of genomic technologies to ruminants

- Estimating genetic diversity
- Prioritising conservation
- Choosing among breeds globally
- Testing value of synthetic breeds
- Marker assisted selection
- Gene detection and biology (therapeutics/vaccines)
- Molecular EBV
- Restructure of ruminant breeding programs

Strategy presented at AAAP 2002

Dealt with here
Functional genomics to identify genes and networks influencing survival following Trypanosome challenge.
Trypanosomosis is a fatal disease of livestock. The livestock equivalent of sleeping sickness in humans is caused by the protozoa:

- **T. brucei rhodesiense**
- **T. gambiense**
- **T. congolense**
- **T. vivax**
Origins of N’Dama and Boran cattle
Mouse models of trypanotolerance.

Survival of F6 and parental strains

- F6
- AJ
- C57BL

Days Post Challenge

% Survival

0 10 20 30 40 50 60 70 80 90 100

1 21 41 61 81 101 121
Mouse model of trypanotolerance

C57 (resistant) vs A/J (susceptible)

Three major QTL regions involved

Experiment:

• Challenge strains with parasites

• Microarray assay of gene expression in liver at different time points

• Map differences in expression onto known pathways (e.g. Macrophage wiring)
Macrophage wiring: Day 3 vs 0, C57

A  Toll receptors and downstream signaling
B  Activation of phagocytosis

Wellcome Trust Trypanosome Consortium, 2006, unpublished
Macrophage wiring: Day 7 vs 0, C57

CSF-1 colony stimulating factor

Wellcome Trust Trypanosome Consortium, 2006, unpublished
Macrophage wiring: Day 9 vs 0, C57

D Stat 3 activation
E Lipid metabolism

Wellcome Trust Trypanosome Consortium, 2006, unpublished
Macrophage wiring: Day 9 vs 0, A/J

D Stat 3 activation + Stat 6......Th2 response
E Lipid metabolism
F Cholesterol metabolism
G mitochondria disrupted

Wellcome Trust Trypanosome Consortium, 2006, unpublished
QTL 1 congenic
Differentially expressed genes
resistant QTL vs susceptible QTL

Wellcome Trust Trypanosome Consortium, 2006, unpublished
QTL 1 congenic
Differentially expressed genes
resistant QTL vs susceptible QTL

Chromosome 1

Wellcome Trust Trypanosome Consortium, 2006, unpublished
High density snp arrays

- 500,000 snp assay for humans
- 30,000 snp array for cattle (soon)
- 20,000 snp array for sheep (2007)

Compared to 1990's markers

High speed (weeks vs years)

- 100-fold lower cost per marker
Beef CRC

10,000 snp assay for net-feed intake

Map significant markers to human homologues

Human chromosome A

Test statistic

(M. Goddard, pers comm)
Accuracy of predicting haplotype effects

(M. Goddard, pers comm)
Molecular EBV?

1. Undertake snp assay for variation across genome for all traits of economic importance
2. Find subset of markers that give high accuracy EBV for each trait
3. Produce a reduced snp assay for commercial use

Result: a single assay giving EBV for all traits.

Potential: could develop and validate assays in a few thousand animals and apply to the whole population. Sheep and cattle breeding structures would become same as pig and chicken breeding.
Information Nucleus of next Sheep CRC

Information nucleus
5,000 sheep bred by industry sires
Intensively recorded

SheepGenomics
Genome tools; functional biology; gene discovery

Breeders

Molecular EBV

QTL for validating
QTL for application

QTL for biology

Annual sampling of germplasm

SGA

2 to 4 years from discovery to application

Industry

New therapeutics, vaccines, interventions
Genetic research for a better future