University of Nottingham
UK | CHINA | MALAYSIA

Maedi Visna Breeding for Genetic Resilience

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The Problem

- Lentiviral disease of Sheep and Goats
- Respiratory disease, mastitis and “poor doers” most common clinical signs in sheep

- Long latent period before testing positive or showing signs of disease
- “Iceberg disease”

- No vaccine or treatment options
- Control limited to test and cull but current tests (serology) require repeated whole flock testing to be sure you have found them all
- National infection rate has increased despite SRUC and Axiom (voluntary) testing schemes

Year	Flock prevalence
1995-6	1.4%
2010	2.9%
2019-20	9.5%

Genetic Resistance, A Way Forward?

- TMEM154 is a major transmembrane protein gene

- Genome wide association screen (GWAS) has identified particular SNPs/alleles of TMEM154 are associated with decreased risk of MV

- K (at position 35 on exon 2 of TMEM154) encodes for the amino acid lysine.
- E at that position encodes for the amino acid glutamate.

- Sheep that are KK appear to be less susceptible to MV infection than those that are KE or EE
- (& there are also a number of “null” allelles of the gene that seem to give the same effect.)

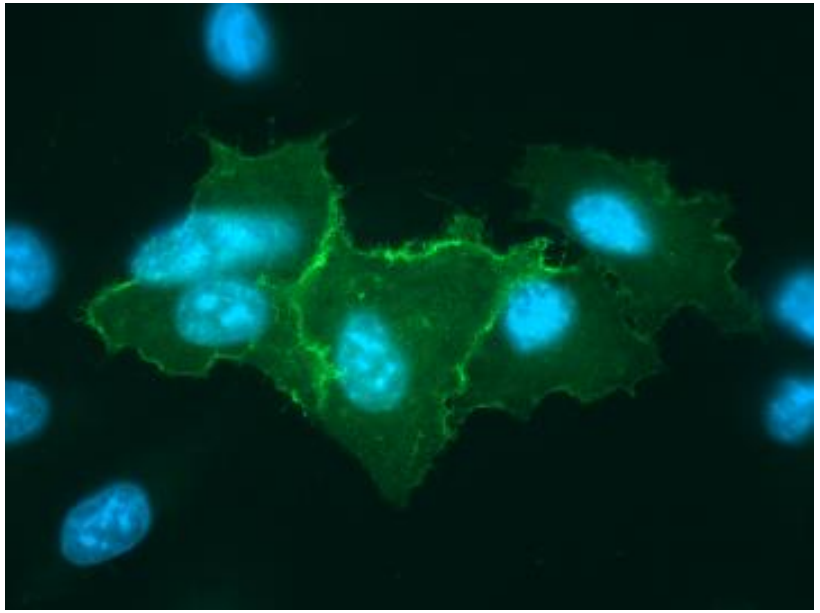
- KK sheep seem to be less likely to test positive for the virus and if they do test positive, they have a lower virus load

- Selection for this is an attractive proposition for reducing MV impact

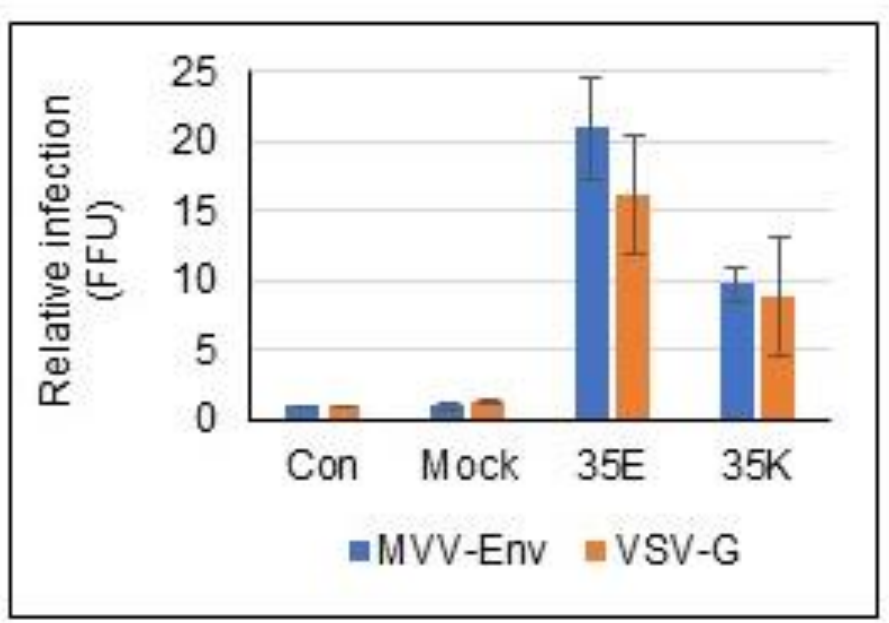
Current Project - Moredun

- 3 year UKRI/BBSRC funded project , £1.3 million Nottingham and Moredun with AHDB/SRUC support.

- Moredun arm (David Griffiths) : what is the function of the gene and how does in interact with the virus? Molecular biology work to determine this (transcriptomics, proteomics in sheep cells of different TMEM phenotypes)
- Preliminary work indicates that the protein is associated with cell membranes and interacts with virus entry. The K/K phenotype cells are harder to infect.



Immunofluorescence labelling of A549 cells expressing TMEM154-35E



TMEM154 E35 and K35 alleles increase transduction of 293T cells by MVV-reporter viruses.

Current Project – Nottingham

- For some UK breeds we have a good idea what the frequency of the resistant allele is:
- One part of this project is get SNP chip testing done (20 animals) for breeds that don't have any data
- SNP chip genotyping is <£30 a head
- 3 main providers in the UK: Neogen, Weatherby's (Ireland) and Innovis (Genomes NZ)
- Neogen chip has the relevant alleles on it, the Illumina chip used by the others doesn't but they are working on putting it on (us and USDA to provide known genotyped animals for validation)
- Project has sparked a LOT of interest from sheep breed societies
- Later part of the project will confirm cell culture results for TMEM 154 function in infected sheep flocks

Breed	% Resistant animals
Scottish Blackface	64
Texel	15
Easycare	30
Herdwick	58
Dorset Horn	90
Border Leicester	40
Soay	60
Welsh Mountain	15
Hardy Speckle	25
North Country Cheviot Hill	10
South Welsh Mountain	17
Brecon Hill Cheviot	13
Beulah	58

We Need Your Help !

- We can offer (free) genotyping for a small number of animals from breeds without existing data
- 20 individuals per breed (no more than 3 from an individual flock) females
- For Dorset, Suffolk, Lleyn, Romney Marsh, Roussin, South Co Cheviot, Charollais, Meatlinc and Exlana we can retrieve data from AHDB databases
- Flocks already participating in genotyping will be able to retrieve their data already.
- Breed societies wanting to do this themselves can approach Neogen Directly
- We also need your ideas about what would work best for testing and breeding guidelines as the end aim of the project is to write recommendations for this for the UK.

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