**Institution:** University of Edinburgh and SRUC, Scotland's Rural College

**Unit of Assessment:** 6

**Title of case study:** Breeding a scrapie resistant international sheep flock

**1. Summary of the impact** (indicative maximum 100 words)

**Impact:** Economic, public policy and animal health and welfare: Selective breeding based upon identification of PRNP genotypes can eliminate animals that are susceptible to scrapie from the flock.

**Significance:** UK sheep meat exports are worth >£380million. Breeding for scrapie resistance protected the sheep industry from similar damage to that inflicted by BSE on cattle and the UK economy.

**Beneficiaries:** Farmers, animals, consumers

**Attribution:** Professor Hunter and Dr. Goldmann (Roslin Institute, now part of UoE) identified polymorphisms of the PrP (*PRNP)* gene linked to scrapie susceptibility and resistance in sheep.

**Reach:** International, programmes breeding for resistance to scrapie in sheep are now used in the UK, Europe and USA.

**2. Underpinning research** (indicative maximum 500 words)

Scrapie is a transmissible spongiform encephalopathy (TSE) of sheep and goats. It is a disease of considerable economic consequence to the small ruminant farming industry. Within the EU, scrapie is a notifiable disease named in Annex B group II; affected farms will face severe trading restrictions and may lose a significant number of animals. Scrapie is also a listed disease in the OIE Terrestrial Animal Health Code (2008) and as such affects wider international trade.

Following the bovine transmissible spongiform encephalopathy (BSE) epidemic, concerns arose that a zoonotic BSE epidemic in sheep or goats could be misdiagnosed for scrapie, this was indeed later shown to have happened in a UK goat in the 1990s. Consequently, at the EU level, scrapie control became a priority in both species.

Selection of sheep for scrapie resistance became a possibility after the pioneering work by Hunter (Group Leader, Roslin Institute and UoE, employed 1986-onwards) demonstrated strong association between prion protein (PrP) genotype (*PRNP*) and scrapie susceptibility (research from 1993 onwards). Considerable additional work with Goldmann (Group Leader, Roslin Institute and UoE employed 1989-onwards) extended the linkage information [3.1-3.3]. Epidemiological studies consolidated this association for natural scrapie outbreaks [3.4].

Hunter/Goldmann demonstrated that sheep with *PRNP* genotype VRQ/VRQ are highly susceptible to classical scrapie, whereas ARR/ARR animals are resistant [3.1-3.3].

Based on the success in the reduction of sheep scrapie following the implementation of the various sheep breeding strategies [3.5], EU and UK research effort in ruminant TSEs since 2006 has focused on goat scrapie genetics. This has led recently to the discovery of new resistant goat *PRNP* alleles (e.g. IRK), which are currently tested in collaboration with the goat industry for their potential in breeding programs on commercial farms. This EU (UK) goat scrapie genetics research has been coordinated by Goldmann [3.6].

**3. References to the research** (indicative maximum of six references)

3.1. Goldmann W, Hunter N, Smith G, Foster J and Hope J. (1994) PrP genotype and agent effects in scrapie: change in allelic interaction with different isolates of agent in sheep, a natural host of scrapie. Journal of General Virology, 75: 989-99. http://dx.doi.org/10.1099/0022-1317-75-5-989

3.2. Hunter N, Foster JD, Goldmann W, Stear M, Hope J and Bostock C. (1996) Natural scrapie in a closed flock of Cheviot sheep occurs only in specific PrP genotypes. Archives of Virology

141: 809-824. http://dx.doi.org/10.1007/BF01718157

3.3. Hunter N, Cairns D, Foster JD, Smith G, Goldmann W and Donnelly, K (1997) Is scrapie solely a genetic disease? Nature 386: 137. http://dx.doi.org/10.1038/386137a0

3.4. Woolhouse, MEJ; Stringer, SM; Matthews, L; Hunter, N; Anderson, RM (1998) Epidemiology and control of scrapie within a sheep flock. In: Proceedings of the Royal Society B-Biological Sciences, Vol. 265, No. 1402, p. 1205-1210. http://dx.doi.org/10.1098/rspb.1998.0421

3.5. Defra TSE Surveillance Statistics http://tinyurl.com/nwtfkmn

3.6. Goldmann, W.,Ryan K, Stewart P, Parnham D, Xecohtencatl R, Fernandez N, Saunders G, Windl O, Gonzalez L, Bossers A, Foster J (2011) Caprine prion gene polymorphisms are associated with decreased scrapie susceptibility in goat herds in the United Kingdom. Vet Res 42, 110. http://dx.doi.org/10.1186/1297-9716-42-110

**4. Details of the impact** (indicative maximum 750 words)

The research results were communicated to the sheep industry directly by visits to agricultural shows (e.g. Royal Show, Highland Show, over several years) with information on posters, or on stands and by giving talks to breeders' and veterinarians groups, for example at ADAS, Redesdale, Northumberland and at AVTRW meetings.

**Impact on Policy**

The findings led directly to the implementation of the National Scrapie Plan (NSP) [5.2], which ran in the UK from 2001 to 2009 and, following the European Commission Decision 2003/100/EC, to similar programmes throughout the EU. These strategies were implemented with the twin aims of controlling classical scrapie, and protecting the consumer from the exposure to BSE via sheep meat, should the national flock have become infected. The genotyping components of these programmes imposed breeding strategies upon entire sheep industries, such that breeding flocks were required to select against susceptible *PRNP* alleles (i.e. VRQ) in favour of resistant alleles (e.g. ARR) [5.2].

The National Scrapie Plan, funded by the UK government, provided free genotyping of 1.8 million sheep in 11,000 flocks in an effort to control all TSEs, including BSE, in sheep. As a result of EU policy, sheep breeders both within and outside the EU require (Directive 91/68/EEC) [5.3] genotyping and health certificates in order to trade their sheep (OIE Terrestrial Animal Health Code, 2008) [5.4]. Scrapie continues to be a notifiable disease in the EU, trade in affected animals or animals coming from a flock known to have the disease in the last two years is prohibited, and genotyping for resistance remains the best means for disease control.

Selection for TSE resistance by *PRNP* genotyping has reduced the reported incidence of scrapie in sheep as a result of profound impact on the genetic structure of the entire UK sheep industry: between 2002 and 2006 the frequency of the susceptible VRQ allele decreased in ram lambs by 60% and the frequency of the ARR allele rose by 37% and as a direct result, the reported prevalence of sheep with scrapie has also decreased from 0.22% in 2003 to 0.04% in 2008 [5.5]. Voluntary *PRNP* genotyping continues, through the industry-funded Scrapie Monitoring Scheme (since January 2009), which issues certificates of sheep genotype for trading purposes.

**Impact on the Economy**

UK sheep meat exports are worth >£380million (2011 figures) [5.5]. Breeding for resistance to scrapie and BSE, and the fact that it was being carried out, undoubtedly protected the sheep industry from similar damage to that inflicted by BSE on cattle and the UK economy. WHO estimates US$6 billion losses to the UK and in addition, EU paid out 4.7 billion euros in control measures for cattle BSE.

In June 2013, the USDA followed the example of UK and the EU and implemented a Scrapie Free Flock Certification Program [5.6].

**Impact on Animal Welfare**

Sheep welfare has been improved by selection against *PRNP* genotypes linked to susceptibility to scrapie and subsequent reduction in incidence of disease. There is under-reporting of scrapie but

nevertheless, Defra statistics [5.5] indicate over 200 scrapie sheep were reported to them in 2002, and three in 2011.

Our work that established the genetic basis of scrapie resistance has ensured continuous maintenance of the UK (and international) sheep flocks in the face of potential disease outbreaks [5.5]. The expertise developed has continued to attract translational research funding from Defra and UE sources focussed specifically on modes of transmission of the disease.

PRNP gene based selection for eradication of TSEs and for the creation of resistant populations is now an accepted approach for control of all TSEs in livestock [3.5]. The EU regulations which were based on Hunter's/Goldmann's research now impact worldwide and have led to many genetic surveys of sheep and goat populations to assess their potential for resistance breeding.

**5. Sources to corroborate the impact** (indicative maximum of 10 references)

5.1 Dawson, M, Moore, R.C., Bishop, S.C. (2008). Progress and limits of PrP gene selection policy. Veterinary Research 39, 25. http://dx.doi.org/10.1051/vetres:2007064

5.2 Defra ARCHIVE: BSE: Other TSEs - National Scrapie Plan for Great Britain http://tinyurl.com/ovrsjob

5.3 Council Directive 91/68/EEC of 28 January 1991 on animal health conditions governing intra-Community trade in ovine and caprine animals http://tinyurl.com/oahcnzs

5.4 The OIE Terrestrial Animal Health Code (Terrestrial Code) sets out standards for the improvement of terrestrial animal health and welfare and veterinary public health worldwide, including through standards for safe international trade in terrestrial animals (mammals, birds and bees) and their products: http://tinyurl.com/pa732qr

5.5 TSE statistics - Animal Health and Veterinary Laboratories Agency http://tinyurl.com/qexvthf

5.6 The USDA Scrapie information website: http://tinyurl.com/oudeuab

5.7 Many sheep breeders' web sites list scrapie resistance genotypes routinely as sought-after features for rams in sales documents. Below are some examples of sources of corroboration.

National Sheep Association (www.nationalsheep.org.uk)
Swaledale Sheep Association (http://www.swaledale-sheep.com)
Suffolk Sheep Association (http://suffolksheep.org)
Shetland Sheep Society (http://Shetland-sheep.org.uk)
Shetland sheep breeders in France (http://Shetlandsheepinfrance.com)
Shropshire Sheep Association (http://www.shropshire-sheep.co.uk)
Hampshire Down Sheep Breeders Association (http://hampshiredown.org.uk)