Current EU policy for control and eradication of scrapie (and BSE) in goats relies on the identification of positive herds and their complete destruction. Its application is debatable, because the agent is highly resistant and can survive on holdings for many. The massive stamping out has also a negative socio economical impact on the goat sector and public opinion.

Fortunately, after the successful TSE control programs in sheep by breeding for genetic resistance, also for goats a similar opportunity to control TSEs has recently become a promising solution. The proposed work in the GOAT-TSE-FREE project has now been largely completed and the produced data, necessary for a sound policy for TSE resistance breeding, are fulfilling the expectations.

The basis for genetic selection for TSE resistance is the variable (polymorphic) amino acid composition of the host prion protein (PrP) that during disease is transformed into a stable infectious and pathogenic isoform (PrP^{Sc}). IN GOATS, while the wild type amino acid sequence of mature PrP is similar to that of sheep, the ovine 171R resistant allele variant does not occur. Nevertheless, goat PrP is relatively polymorphic, and two loci (codons 222K, 146S and 146D) have been found that are associated with "resistance" against scrapie. The frequency of these alleles can be regionally low, and in most countries only the 222K allele is present, while in Cyprus, with a high scrapie incidence, only the 146 variants are occurring. However, in various sheep breeds it has been shown that breeding for resistance is feasible even starting with low frequencies. It is thus necessary also for goats to design a tailor made breeding strategy to enable an efficient allele dissemination.

The study has been working on three main issues: 1) Providing some necessary missing scientific data; 2) Involving goat production sectors in the participating countries to select 222K or 146S and 146D carriers and to start with breeding programs with resistance allele carriers; 3) Informing and encouraging policy makers and goat sector towards TSE resistance breeding.

The GOAT-TSE-FREE project produced a great amount of data, examining all the aspects that deserve attention before stating that the 222K PrP allele confer resistance to TSEs in goats: to which TSE agent(s) is the allele resistant; to which strains of scrapie is the allele resistant; the degree of the resistance given by the 222K allele in different conditions, i.e. tested in natural and experimental conditions, *in vivo* and *in vitro*.

All the obtained results yielded a convincing picture and all the performed activities gave consistent results, i.e. all pointing to the high resistance contributed by the 222K allele to classical scrapie and to cattle BSE in goats. No resistance is given against atypical scrapie while low resistance appeared against goat adapted BSE. This situation does not differ from what is known in sheep regarding the ARR allele. Recently, in one large experimental herd challenge study at Sardinia the scrapie resistant properties of the 222K allele was again confirmed.

The other two codons, 146S and 146D, when tested in *in vitro* conditions do show resistance. More data have to be awaited from studies being

performed with another EU funding using Cyprus derived goats. There might even be other polymorphisms with such property, however these generally can be considered rarely occurring.

In conclusion, from the scientific point of view, there is now an overwhelming body of evidence available that the 222K allele can be used to control classical scrapie in goats through genetic selection, as well as to bovine BSE, but not if BSE has been once passaged through goats.

The main added value given by the international collaboration was that 222K resistance could be consistently studied by the consortium using multiple approaches, in a collaborative and complementary way. In particular, the great value was the opportunity of a wide exchange of samples within the consortium, allowing that the 222K resistance could be completely characterized in relation to a big panel of TSE agents and strains. This was the crucial feature that allowed to definitely state the resistance against classical scrapie in goats given by the 222K allele, with no big gaps to be filled anymore after this project.

Moreover, the ample knowledge collected about the prevalence of 222K carrier goats with respect to geography and breed can now be of use either in future breeding plans or for further searches for 222K carrier goats serving the goal of resistance allele reservoir building.

All partners have finished their genotyping survey studies with a focus on searching resistant allele carriers. Depending on the regional situation, plans have been made for further continuation of the 222K carrier safeguarding and multiplications.

A major event was the invitation to our GOAT-TSE-FREE project by EFSA for a presentation to the TSE-network in October 2015. Then a broad set of aspects did convince both EU, DG-SANCO and OIE representatives that the moment is there for adaptations in the 999/2001 regulation to support breeding to TSE resistance in goats (as in place already for ARR-sheep).

The future of breeding TSE-resistant goats is uncertain. It will largely depend on whether the goat sector values this knowledge and will take the chance to eliminate scrapie (and BSE). A prompt adaptation of the EU regulations in favour for 222K breeding would be the necessary stimulus for the credibility of the such breeding activities.

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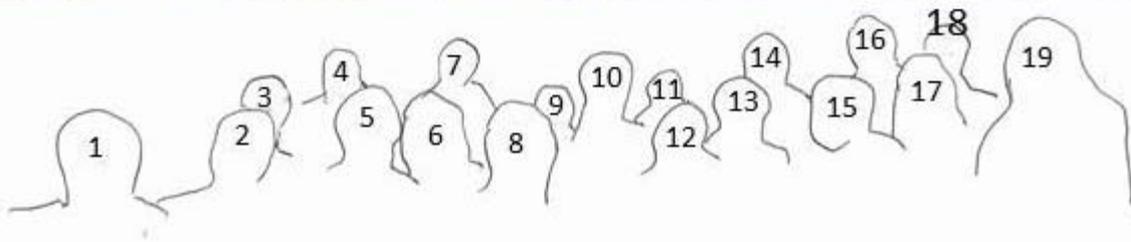
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