DISCONTOOLS

Small Ruminant Lentiviruses (SRLV)
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on SRLV. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details are available on the web site at http://www.discontools.eu/.

Disease profile

2. SRLV have a wide pathogenic variability, which is partially virus strain/genotype dependent and partially host dependent, causing progressive infiltration and proliferation of immune system cells. Lesions form in the lungs, lymph nodes, mammary gland, joints and central nervous system. The antibody response generated during infection is not protective. Host range includes sheep, goats, mouflon and some cervids.

Risk

3. Impact on production economics and animal welfare. In Norway eradication of CAEV in dairy goats has led to a 40% increase in milk production. Threat for rare breeds.

Diagnostics

4. The mainstay of SRLV control is the use of serological diagnostic techniques and several commercial ELISA kits are available internationally. Most serology tests have been validated against a consensus serological quasi-gold standard therefore only relative diagnostic sensitivity and specificity are reported, not true/absolute diagnostic Se/Sp. Large variation between reported Se/Sp of the available kits. This difference could suggest that updating serological tests by including antigen mixes is highly needed. Different commercial ELISAs lead in some cases to contradictory results, based on the context in which they were used and on the circulating genotypes, and some ELISA tests fail to detect animals with low antibody titres. Better knowledge of antigenicity / cross reactivity of viral proteins between different genotypes is needed. More scientific knowledge of antibodies against different viral proteins, and potential differences depending on homologous and heterologous infections Characterisation of immune responses after cross species transmission could be important to determine any differences which may be relevant to the choice of diagnostics. Immunoblotting could play a role as confirmatory test to declare the herd free of infection.

5. PCR will be useful in analysing animals which remain negative in serology to determine their true infection status. Some animals have delayed seroconversion, so PCR tests could be considered in control schemes and for lambs less than 1 year old. However, the technique is expensive for routine use and has low sensitivity due to the low amount of virus in diagnostic tissues.

Vaccines

6. Vaccination against lentiviruses is very difficult as experience with HIV has shown. For SRLV there is a need to establish a reliable method of vaccination (type, route, dose, boost, immunomodulators, etc) to show high levels of protection against homologous challenge in the first instance and heterologous challenge ultimately. There will be a need to overcome antigenic variation in target antigens and ideally determine the mechanism of immunity. It's not clear whether there are companies interested in developing the mRNA technology used for COVID, even for SRLV, knowing that the economic return is uncertain. We do not believe there is a great interest in the use of a vaccine, even if inexpensive, at present. Also, if used as part of an eradication programme a companion DIVA test would be needed.

Pharmaceuticals

7. A challenging gap to fill as the pathologies in SRLV would require complex biological and anti-inflammatory products which would not have a large market given the economics of sheep/goat production. Furthermore, such products would not be able to remove the virus from the host due to latency and would need to be administered continuously. A cost effective one-shot drug to eliminate SRLV infection or prevent it causing clinical problems would be challenging to develop, especially in a market where sheep/goat economics do not favour species-specific drugs.

Knowledge

8. In most countries there is no particular attention to SRLV infections. Up to now, there have been sporadic control plans mostly limited to goats and high value sheep. There is variable, limited data available on the effect on production. This is a significant gap as lack of this knowledge makes it difficult to persuade farmers to take control actions when the disease has a long incubation period and a considerable proportion of infected animals that remain asymptomatic. Increased knowledge needed on evaluation of production and economic losses in different production systems, breeds and geography.

9. Not much is known about the role of the innate response in preventing infection. In flocks we have studied about 5-10% animals remain persistently seronegative despite presumed exposure to circulating virus. It would be useful to know whether these animals are genuinely resistant.

10. We need to identify and understand the mechanisms involved in cell binding, entry and initiation of infection, genome replication, assembly and packaging, control of differential protein expression levels in target cells/organs, release and transmission of SRLV at the molecular, cellular and whole organism level. Identification of the receptor(s)/co-receptor(s) for SRLV, these have not yet been identified definitively.

11. Genetic heterogeneity amongst field strains remains to be fully characterized, which is important as this genetic variation in turn translates into virus strains and genetic sequences with different biological properties such as virulence. Which factors are responsible for a difference in disease outcome upon infection of sheep and goats with a specific strain?

12. The role of semen in transmission has not been fully studied, nor has the potential importance of biting flies. The former is important regarding advanced breeding technologies and the latter in relation to climate change and distributions of potential vectors. These should be looked at using molecular techniques.

Conclusions

13. Significant gaps still exist in our knowledge of the biology, immunology and epidemiology of SRLV, and, crucially, their effects on livestock production and welfare. These are inhibiting action being taken to effectively control the diseases they cause. Serological diagnosis is the best choice for SRLV detection in livestock. It has been widely applied in control programmes. However, serological methods may fail at detecting the whole infected population due to virus antigenic diversity or to delayed seroconversion. An update of existing serological methods to new variants is required. At present we still do not have good performance of either serology or PCR techniques. There is some promise from new multiplex serological techniques to improve sensitivity. It is unlikely that there will be significant progress on vaccines and therapeutics given the scientific challenges faced and the economics of the marketplace. However, developments in these areas should be monitored for potential application to SRLV.