PROJECT FIGHT 2
Development of an Edible Bait Vaccine to Control Rabbit Haemorrhagic Disease Virus 2 (RHDV2) in Wild Rabbits


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Context of the study

RHDV2, a Calicivirus of the genus Lagovirus, causes rabbit haemorrhagic disease (RHD), an often-lethal systemic infection in the European rabbit (Oryctolagus cuniculus)1-2. Since its emergence in 2010 in France3, RHDV2 replaced the classical RHDV genogroups (G1-G6) that circulated previously1-4,5. Currently, RHDV2 is one main factor underlying the wild rabbits’ decline, which is a key component in the Mediterranean ecosystems of the Iberian Peninsula. RHDV2 affects adult and juvenile animals, hampering the recruitment of new individuals to wild populations compromising their dynamics, indirectly impacting on several endangered predator species6.

RHD cannot be eradicated due to the high environment resistance of the virus and easy spread by insects, rodents, birds of prey or anthropogenic actions. Also, disease control is difficult despite in the industry vaccination, good management practices and biosecurity measures are effective4.

Commercial RHDV2 vaccines currently available are inactivated, obtained from infected animal liver extracts and the route of administration is usually subcutaneous, requiring handling of the animals. Further than the risks associated with incomplete virus inactivation and the inadvertent release of infectious virus in the field, these vaccines are not suitable for wild rabbits, requiring capture for inoculation which causes great stress. The immunity induced by these vaccines is short and, hence, the protection transient. The previous commercial RHDV vaccines, most also inactivated, were shown to be ineffective in conferring cross-protection against RHDV22.

Main objectives

FIGHT-TWO (PTDC/CVT-CVT/29062/2017) strategic framework is the development and production of an edible and innocuous (pathogen- and genome-free) RHDV2 vaccine based in Virus-Like Particles (VLPs), to be distributed in the field as bait or in dry feed. This oral vaccine overcomes the need of capture and manipulation of the animals, feasible in wild populations, and will potentially protect a broad proportion of the rabbit populations, crucial to abrogate virus transmission leading to the control the infection.

VLP60 (major capsid protein) - VLPs are protein cages that mimic the overall structure of the native virions harbouring no genetic material7, although able to induce a protective immune response when administered parenterally8 or orally9. The oral immunogenicity of VP60 in rabbits has been described more than two decades ago10,11; however, this strategy was never implemented due to cost/benefit ratios. Currently, VLP-based vaccine technologies have the potential of producing higher concentration of VLPs in a much reduced time-frame. The VLP purification process required for rabbit immunization is expected to be simpler therefore less expensive6,12-15. The recombinant VP60-based VLPs RHDV2-vaccine, will be updated according to the virus evolution in an progressive modular system, as is the case of Influenza vaccines14 [Figure 1].

The National Institute of Agrarian and Veterinary Diseases (INIAV I.P.) that harbours the National Reference Laboratory for Animal Diseases, and the Instituto de Biologia Experimental e Tecnológica (IBET), a private institute with vast experience in animal and human vaccine production, coordinated the project. The direct partnership includes two Portuguese Veterinary Universities - Universidade de Évora (UE) and Faculdade de Medicina Veterinária de Lisboa (FMV). Other institutions are considered indirect partners of the consortium. The project aims to mobilize several other layers of society including the hunting sector [Figure 2].

Materials and Methods

The insect cells-baculovirus expression vector system (IC-BEVS) will be used to produce this novel vaccine.

Results and Conclusions

A nucleotide bank of RHDV2 vp60 sequences is being obtained to support the selection of a subset of representative strains to be included in the vaccine. The vp60 gene of those strains will be cloned and used to construct the recombinant baculoviruses.

FIGHT-TWO will allow to proceed with one of 12 measures specified in a National Action Plan for the Control of Rabbit Haemorrhagic Viral Disease in Rabbits (Dispatch 4757/17 of 31 May, Portuguese Ministry of Agriculture).

Project FIGHT-TWO supports other generalist management policies towards the recovery of wild rabbit populations and RHD control, the recovery of ecosystems where the rabbit is keystone and the reactivation of hunting activities in Portugal.

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References: