

News on the Fight-2 Project

News nº 6



30th September 2019

Participation of the Fight-two Project in the 1st International Conference of the European College of Veterinary Microbiology (ECVM), Athens 26th & 27th September, 2019

The strategy and objectives of the **FIGHT-2** Project - development of an edible vaccine for the control of the type 2 viral hemorrhagic disease virus (RHDV2) in wild rabbits, funded by the Foundation for Science and Technology (FCT) (PTDC / CVT -CVT / 29062/2017-PT2020) - were presented by Elsa Leclerc Duarte, Assistant Professor in the Department of Veterinary Medicine at the University of Évora, at the 1st International Conference of the European College of Veterinary

Microbiology (ICECVM), which took place in Athens, Greece, on the 26th and 27th of September, 2019.



The **FIGHT-2** Project aims the development of an oral vaccine to control viral hemorrhagic disease, putting into practice one of the 12 measures of an Action Plan for the Control of Viral Hemorrhagic Disease in Wild Rabbits (Order 4757/17 of 31 May, MAFDR).

The panel was entitled “**FIGHT-2** strategic framework - Development of an edible vaccine for the control of the type 2 viral hemorrhagic disease virus (RHDV2) in the wild rabbit”.

Fight-Two Project - Development of an edible vaccine for the control of viral hemorrhagic disease (RHDV2) in wild rabbits

PTDC/CVT-CVT/29062/2017-PT2020 – Fundação para a Ciência e Tecnologia



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Participation of the Fight-two Project in the 1st International Conference of the European College of Veterinary Microbiology (ECVM), Athens 26th & 27th September, 2019

The 1st ICECVM was organized in collaboration with the Study Group for Veterinary Microbiology (ESGVM, Study Group for Veterinary Microbiology) of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID).



Maria José Saavedra, Associate Professor at UTAD and representative of Portugal at ESGVMESCMID (left) with Elsa Duarte, member of the Fight-Two team at the University of Évora (at the board, flanked by two students from the Veterinary Medicine course) at the University of Thessaloniki, Greece, at the 1st International Conference of the European College of Veterinary Microbiology, that took place in Athens, September 26-27, 2019

Essentially, it consisted of a forum dedicated to veterinary microbiology, organized in thematic sessions dedicated to i) Veterinary Bacteriology and Mycology, ii) Veterinary Virology, iii) Microbiological Diagnosis, MALDI-TOF, Genomics & Metagenomics, and iv) Anti-microbial Resistance, One Health and food microbiology.



Elsa Duarte and Eva Cunha (PhD student at CIISA-FMV) at the 1st International Conference of the European College of Veterinary Microbiology, Athens 26 to 27 September 2019.

Fight-Two Project - Development of an edible vaccine for the control of viral hemorrhagic disease (RHDV2) in wild rabbits

PTDC/CVT-CVT/29062/2017-PT2020 – Fundação para a Ciência e Tecnologia



PROJECT FIGHT 2

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

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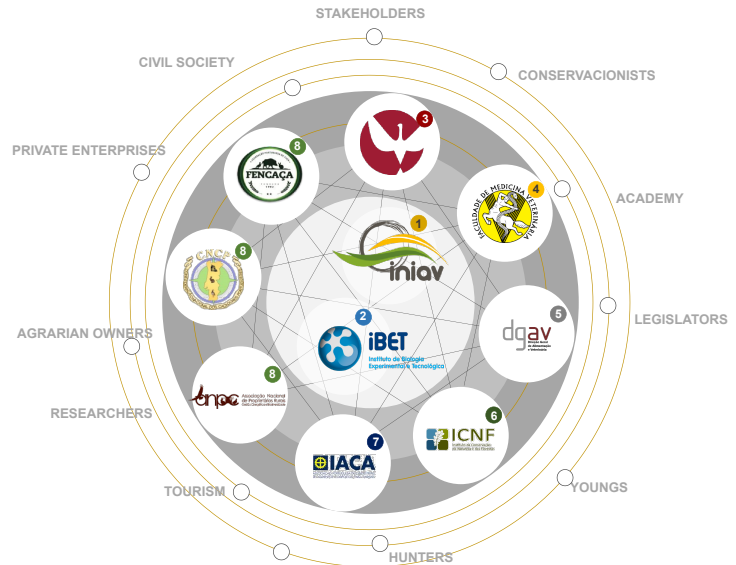
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Context of the study

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 France², RHDV2 replaced the classical RHDV genogroups (G1-G6) that circulated previously^{1,3,4}. Currently, RHDV2 is one main factor underlying the **wild rabbits' decline**, which is a key-stone species 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 species**⁵.

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 effective⁶.

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 RHDV⁶.



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, unfeasible 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.

VP60 (major capsid protein) -VLPs are protein cages that mimic the overall structure of the native virions harbouring **no genetic material**⁷, 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 ago⁹⁻¹³, 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 expensive**^{14,15}. The recombinant VP60 based-VLPs RHDV2-vaccine, will be **updated** according to the virus evolution in an progressive **modular system**, as it is the case of Influenza vaccines¹⁶ [Figure 1].

The **National Institute of Agrarian and Veterinarian 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].

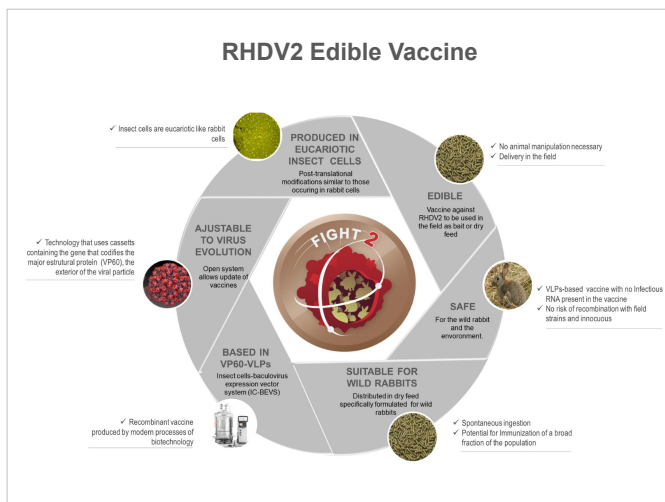


Figure 1. Characteristics of the VP60-VLPs based edible vaccine against RHDV2.



Figure 2. Project Fighth-two partnership.

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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