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VETBIONET

Veterinary Biocontained facility Network for excellence in animal infectiology research and experimentation

Deliverable D23.1

Quantity of access provided over the duration of the project to high-end molecular typing and immunological technologies

Due date of deliverable: M72

Actual submission date: M72

Start date of the project: March 1st, 2017 **Duration:** 72 months

Organisation name of lead contractor: EDI-IVI

Revision: V1

Dissemination level	
Public	**X**
Confidential, only for members of the consortium (including Commission Services)	
Classified, as referred to in Commission Decision 2001/844/EC	

Table of contents

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement N°731014

1. TNA Provided

Name of the TNA project	Name of TNA user	Organisation of TNA user	Country of TNA user	Installation from the RI	Start date	End date	Number of units of access provided
Study of virulence of Peste-des-Petits-Ruminants Virus in relation to variability of host response - High Technology Lab Access 1	Arnaud Bataille	CIRAD	France	High Technology Lab	01.04.2019	31.05.2019	1
Study of virulence of Peste-des-Petits-Ruminants Virus in relation to variability of host response - High Technology Lab Access 2	Arnaud Bataille	CIRAD	France	High Technology Lab	01.04.2020	30.06.2020	2
Study of virulence of Peste-des-Petits-Ruminants Virus in relation to variability of host response - High Technology Lab Access 3	Arnaud Bataille	CIRAD	France	High Technology Lab	02.05.2022	30.06.2022	1

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2. Final reports of each TNA provided

The present deliverable, D23.1 is linked to D21.1 “Quantity of access provided over the duration of the project to BSL3 lab & animal facility”. All studies described in D23.1 and D21.1 are part of single TNA project with five different accesses provided to a user group (Arnaud Bataille, Vincent Lasserre, Philippe Totte and Roger Jr. Eloiflin) from CIRAD, France.

Project Summary

Peste des petits ruminants (PPR) is a highly pathogenic viral disease infecting small ruminants in Africa, Asia, and Middle-East. Host susceptibility varies widely among viral strains and host breeds. The factors determining this variability are unknown, making it hard to predict the impact of PPR emergence in different regions and on different host breeds, and therefore inform decision makers on the best control strategies. We postulate that host-pathogen interactions, and more specifically the modulation of host immune response, during infection of small ruminants by PPRV explain variation in pathogen virulence and host susceptibility. The aim of this study was to use reliable and reproducible experimental in vitro and in vivo challenge models for PPR and a multi-omics approach to:
1) Assess whether some host factors implicated in host immune response are differentially produced in relation to observed virulence of PPRV strains tested; 2) Assess whether viral genes/proteins are differentially expressed in relation to observed virulence of PPRV strains tested;
3) Determine whether specific viral genes mutations modify protein-protein interactions and may lead to change in PPRV virulence;
4) Determine if viral gene products modulate host immune response and if it varies among PPRV strains tested.

Experimental procedure

TNA1: Exploratory in vitro infection experiment on PBMCs from Saanen goats. Goat PBMCs were isolated from whole blood (n = 5 healthy adult Saanen goats) and proliferated before infection with MA08, IC89 or VN751. Viral replication and cell survival were followed from 24 to 120 hpi by flow cytometry. Differential gene and protein expressions were assessed by RNA sequencing (transcriptomics) and mass spectrometry (proteomics).

TNA2: In vivo challenge experiment to confirm patterns observed in the in vitro experiments. 24 goats were divided into 4 groups (mock-inoculated, vaccinated, IC89-infected and MA08-infected) of 6 animals. Clinical evaluation and sample collection (swabs, blood, serum) were performed daily until the end of experiment on D14, when organs were also collected. TNA2 was used for the wet lab analysis of the different endpoints of the in vivo challenge experiment. More precisely, presence of virus was tested by qPCR. PBMCs were isolated and used for flow cytometry, transcriptomic and proteomic analyses at selected dpi.

TNA3: In vivo challenge experiment to study immune gene expression in organs targeted by PPRV at early stage of infection. 18 goats were divided into 3 groups (mock-inoculated, IC89-infected and MA08-infected) of 6 animals. 3 animals in each group were euthanized at 3 dpi and 3 animals at 6 dpi. TNA2 was used for the wet lab analysis of the different endpoints of the in vivo challenge experiment: organs and blood were collected for flow cytometry, transcriptomic, single cell sequencing, and histopathology.

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Results TNA project

Overall, the results showed that the highly virulent PPR virus strain had better capacity to replicate in immune cells. Activation of the antiviral response was broadly similar with all virus strains, but more genes and proteins associated with the immune response were activated by the highly virulent strains. We compared expression of genes involved with the immune responses in different organs at the early stage of viral infection. Patterns of innate and adaptive immune gene expression differed between organs and between strains.

This project provided the first comparative study of the immune response of goats to infection by PPR virus strains of variable virulence. Our results confirm that it is key to study host-virus interaction in organs targeted at the early stage of infections and explore specific gene/ protein markers associated with the variability in infection outcome observed. This project has gathered a large amount of data allowing such exploration.

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