VETBIONET

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

Deliverable D21.1

Quantity of access provided over the duration of the project to BSL3 lab & animal facility

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

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

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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 - Animal Facility Access 1	Arnaud Bataille	CIRAD	France	Animal Facility	01.05.2020	30.06.2020	1
Study of virulence of Peste-des-Petits-Ruminants Virus in relation to variability of host response - Animal Facility Access 2	Arnaud Bataille	CIRAD	France	Animal Facility	02.05.2022	30.06.2022	1

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2. Final reports for each TNA provided

The present deliverable, D21.1 is linked to D23.1 “Quantity of access provided over the duration of the project to high-end molecular typing and immunological technologies”. All studies described in D21.1 and D23.1 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: 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 end of experiment on D14, when organs were also collected. Presence of virus was tested by RT-QPCR. PBMCs were isolated and used for flow cytometry, transcriptomic and proteomic analyses at selected dpi.

TNA2: 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. Organs and blood were collected for flow cytometry, transcriptomic, single cell sequencing, and histopathology.

Results (TNA 1 & 2)

We observed higher replication of the highly virulent strain MA08 in PBMCs in both in vitro and in vivo experiments. Also in both experiment, upregulation of genes and proteins associated with antiviral response was observed for all PPRV strains, especially the IFN-I response. However, upregulation was stronger for MA08, with also some immune pathways only up- or

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down-regulated in this group, such as the inflammatory response. It was also the only group where inhibition of lymphocyte proliferation and infection lead to a decrease in lymphocyte counts. Activation of the adaptive immune response was broadly similar across treatments. RNAseq results suggest that PPR infection was stronger in tonsils, the first target of viral infection, compared to other lymph nodes and white blood cells, with MA08 genetic material detected earlier than IC89. Analysis of genes associated with the innate immune response showed that patterns of upregulation of antiviral response and inflammatory response differ between organs. As seen in PBMCs, upregulation in IC89 was delayed in comparison to MA08, with no enrichment of the inflammatory response. In the case of the adaptive immune response, patterns of downregulations of gene, notably inhibition of cell division, differed between organs, with limited or no signal of downregulation for IC89 in tonsils and mesenteric lymph nodes.

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