Porcine Reproductive and Respiratory Syndrome Virus infection Upregulates Negative Immune Regulators and T-cell Exhaustion Markers

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CELLULAR RESPONSE TO INFECTION

Porcine Reproductive and Respiratory Syndrome Virus Infection Upregulates Negative Immune Regulators and T-Cell Exhaustion Markers

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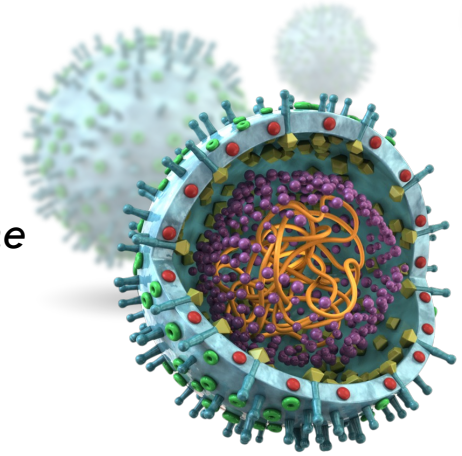
PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS (PRRSV)

- PRRSV is an enveloped, positive-sense, and single-stranded RNA virus.
- Belongs to the Order: *Nidovirales*; family: *Arteriviridae* and genus: *Portarterivirus*.
- It has a genome of approximately 15kb.



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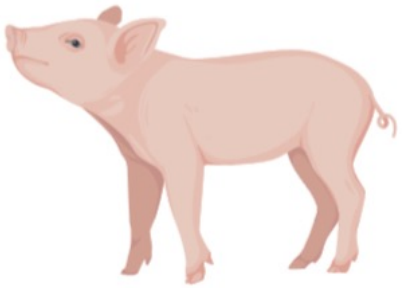
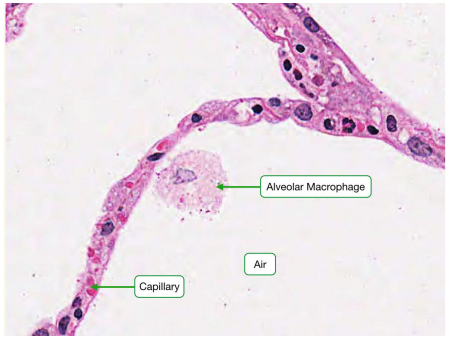
PRRSV HOST AND TISSUE TROPISM

- PRRSV is highly host and tissue restricted.
- The primary target cell of the virus is the pulmonary alveolar macrophage of the pig (PAM).

Host



Primary Target Cell



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APPROACH

- To study transcriptional changes in PAM in vivo infected with PRRSV.
- To evaluate differential effect of PRRSV infection on infected and bystander PAM transcriptome.
- To investigate potential mechanism behind PRRSV immune evasion.

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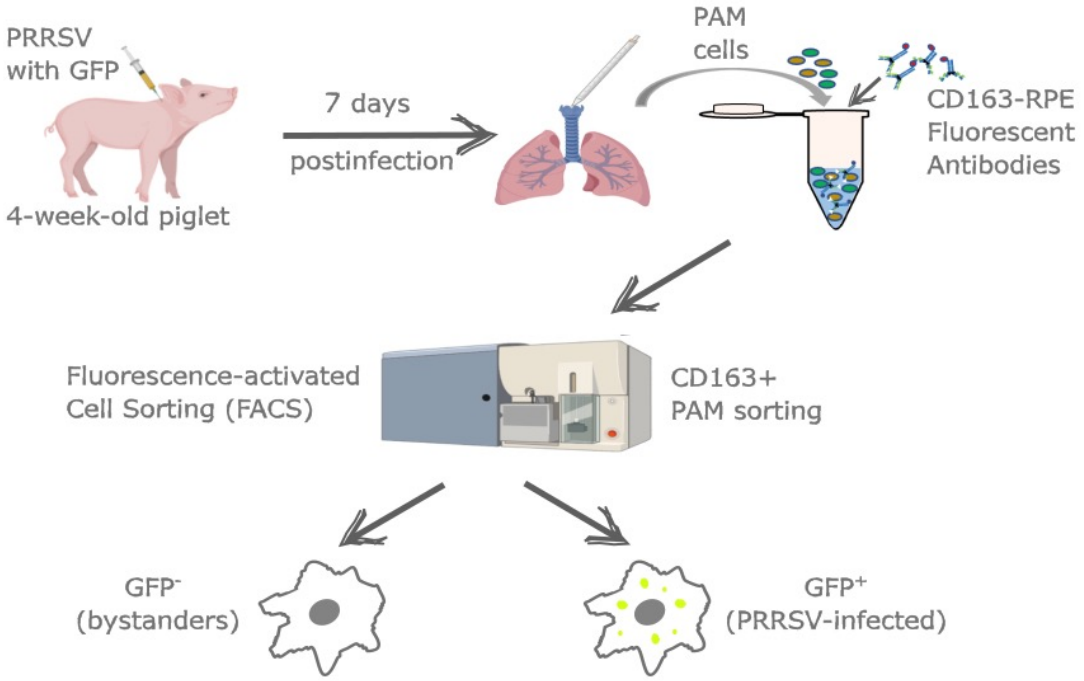
EXPERIMENTAL DESIGN



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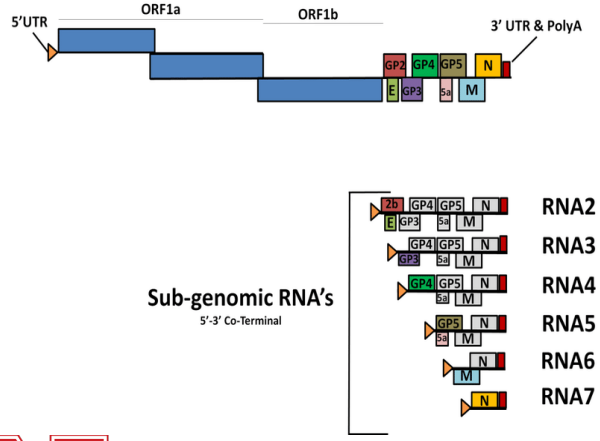
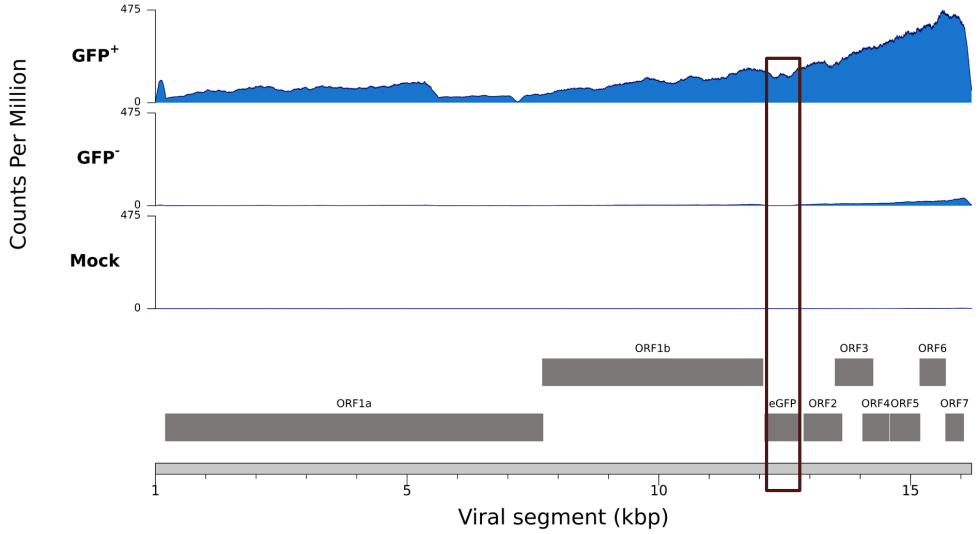
- Comparatively analyze the transcriptomic response of infected- and bystander- PAMs that were collected from pigs during an acute infection with PRRSV.

VIRAL READ COVERAGE

- PRRSV transcription





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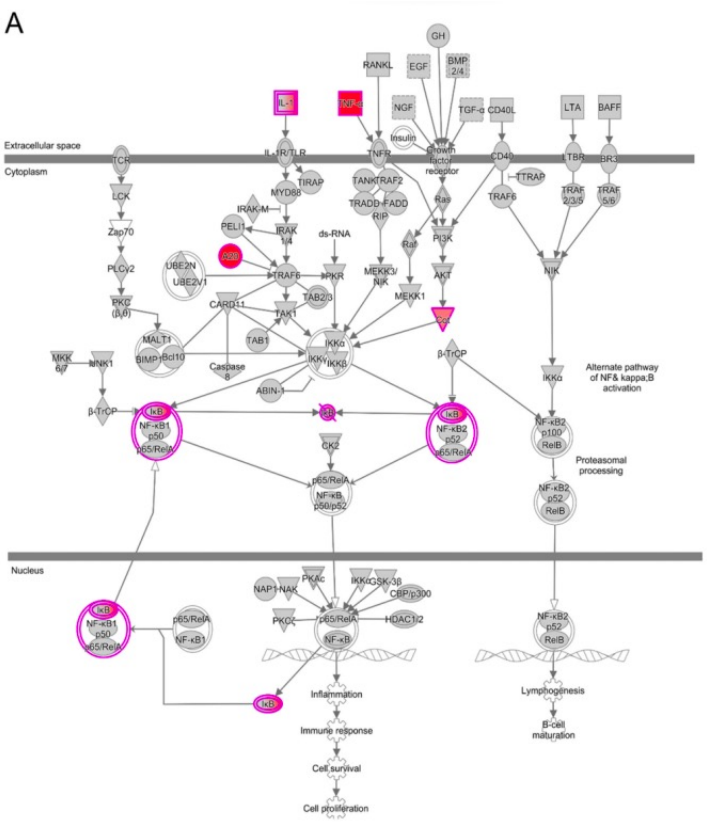
- PRRSV encodes subset of sub-genomic mRNAs for structural genes.
- Majority of viral reads from RNAseq are mapping to 3' end of the viral genome.

UPREGULATION OF NF-KB INHIBITORS (IKBS)



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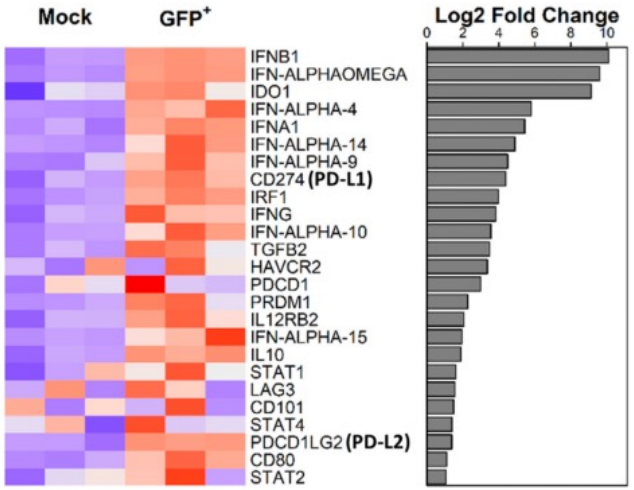
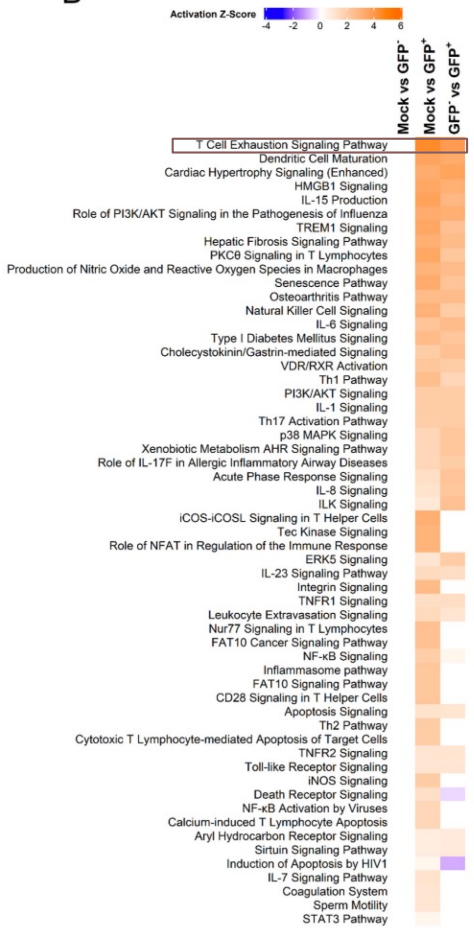
INCREASED EXPRESSION OF T-CELL EXHAUSTION MARKERS



B



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SUMMARY

- Significant overlapping of gene expression profile of GFP-(bystander) and GFP+ (Infected) cells.
- Activation of T-cell exhaustion and NF-κB signaling pathways in PRRSV infected PAM.
- Unique upregulation of NFκBIA, NFκBIZ, NFκBID, and TNFAIP3 in infected PAM and lung tissue.
- Upregulation of negative regulators might lead to sub-optimal adaptive immune response, which might help the virus establish persistent infection in the infected animals.
- Our findings provide further insight into PRRSV immunopathogenesis.

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