Peste des petit ruminants viruses (PPRV) can escape RNA interference *in vitro*

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INTRODUCTION

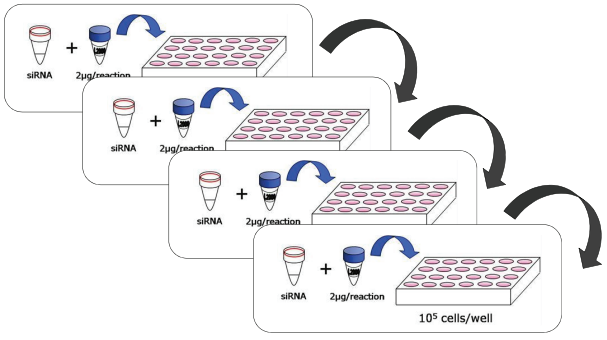
Peste des petits ruminants (PPR) is a highly contagious and infectious disease of domestic and wild small ruminants. It is caused by an enveloped non-segmented negative single-stranded RNA virus (PPRV). The virus is classified in the genus *Morbillivirus* within the family *Paramyxoviridae*. The disease is widely spread in Africa, the Middle-East and South-West Asia. In spite of the existence of efficient vaccines against this disease, no effective or specific treatments exist for infected animals. The development of a curative tool could consequently be interesting to help in the control of the disease. A promising approach is the possibility to block the expression of virus genes by RNA interference (RNAi). RNAi is a mechanism of post-transcriptional gene silencing triggered by double-stranded RNA in a sequence-specific manner. However, a major problem of all antiviral therapies is the emergence of resistant variants. Many RNA viruses escape RNAi-mediated suppression by counteracting the RNAi machinery through mutations of the targeted region. CIRAD recently identified three synthetic interfering RNA (siNPPRV1, siNPPRV6 and siNPPRV7) able to prevent *in vitro* at least 90% of PPRV replication. The three siRNAs target conserved areas of the essential gene encoding the viral nucleoprotein.

OBJECTIF

In this study, we investigated the ability of PPRV to escape the inhibition conferred by three previously identified siRNAs after several consecutive transfections *in vitro*.

MATERIAL & METHODS

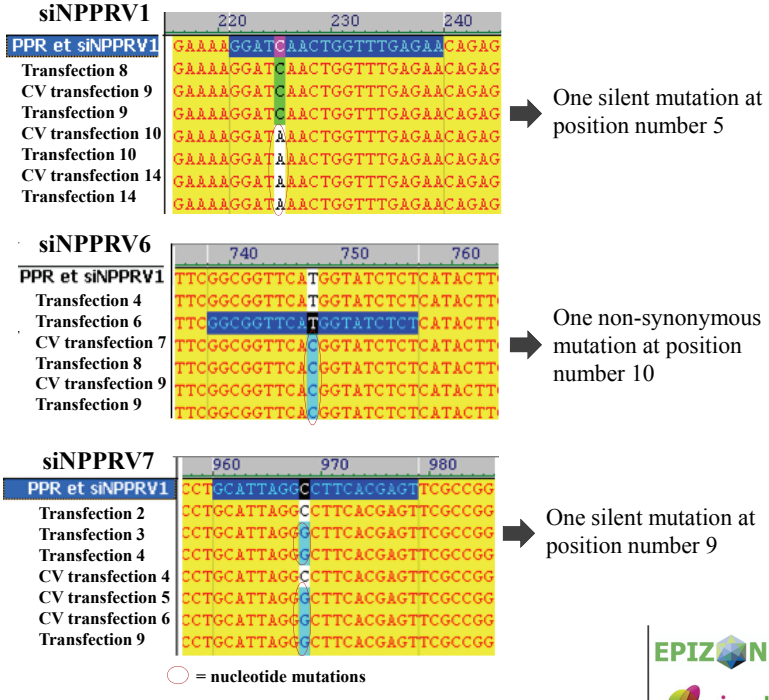
Consecutives transfections



Observation of the CPE ⟷ **Sequencing**

RESULTS

For the three siRNAs, we could recover new virus populations with single nucleotide mutations that were able to escape from siRNA inhibition. Interestingly, only for the siNPPRV6, the mutation generated an original Thr→Met amino acid substitution never observed before in any morbillivirus ever sequenced at that position.



PERSPECTIVES

The role of the detected mutations in escaping RNA interference will be soon confirmed by using a reporter gene system based on the luciferase gene placed under the original or mutated target sequences. The perspectives of this study are also to quantify by QPCR the dynamics of mutant development versus wild-type virus population after each passage. In parallel, the combination of two or three different siRNA will be tested and the capacity of the virus to resist to a multi-target treatment will be assessed.

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