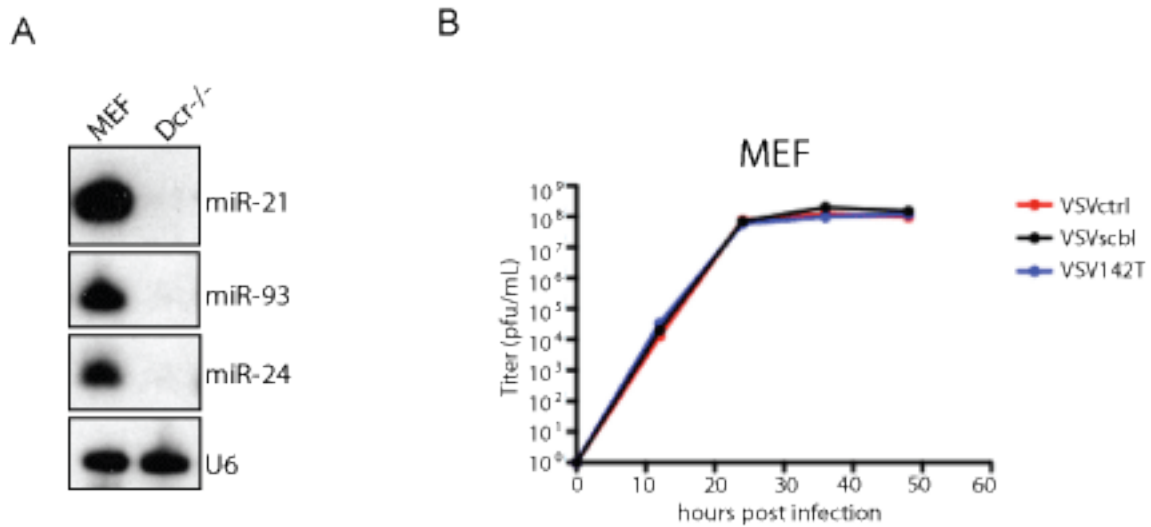


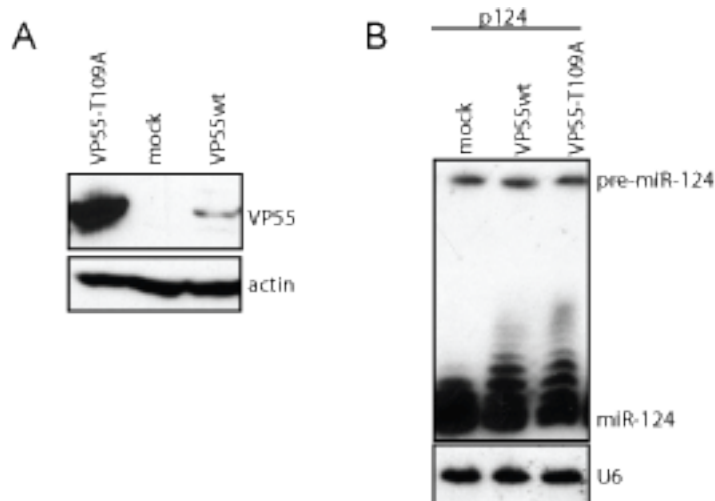
## Supplemental Information



**Figure. S1. VSV142T is specifically targeted by miR-142.**

(related to Figure 2)

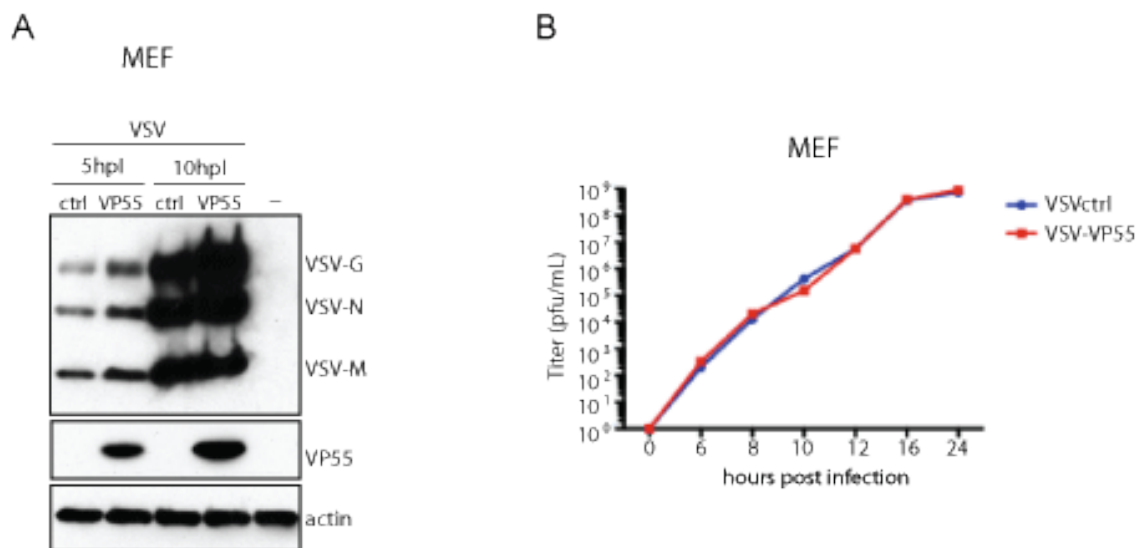
**(A)** Uninfected wildtype fibroblasts (MEF) and dicer-deficient cells (Dcr<sup>-/-</sup>) were analyzed by Northern blot for presence of cellular miRNAs (miR-21, miR-93, miR-24) and U6. **(B)** Multicycle growth curve of VSVctrl, VSV142T and VSVscbl on MEF. Supernatants were analyzed at the indicated time points by plaque assay.



**Figure. S2. Site-directed mutagenesis mediated evolution of VP55.**

(related to Figure 3)

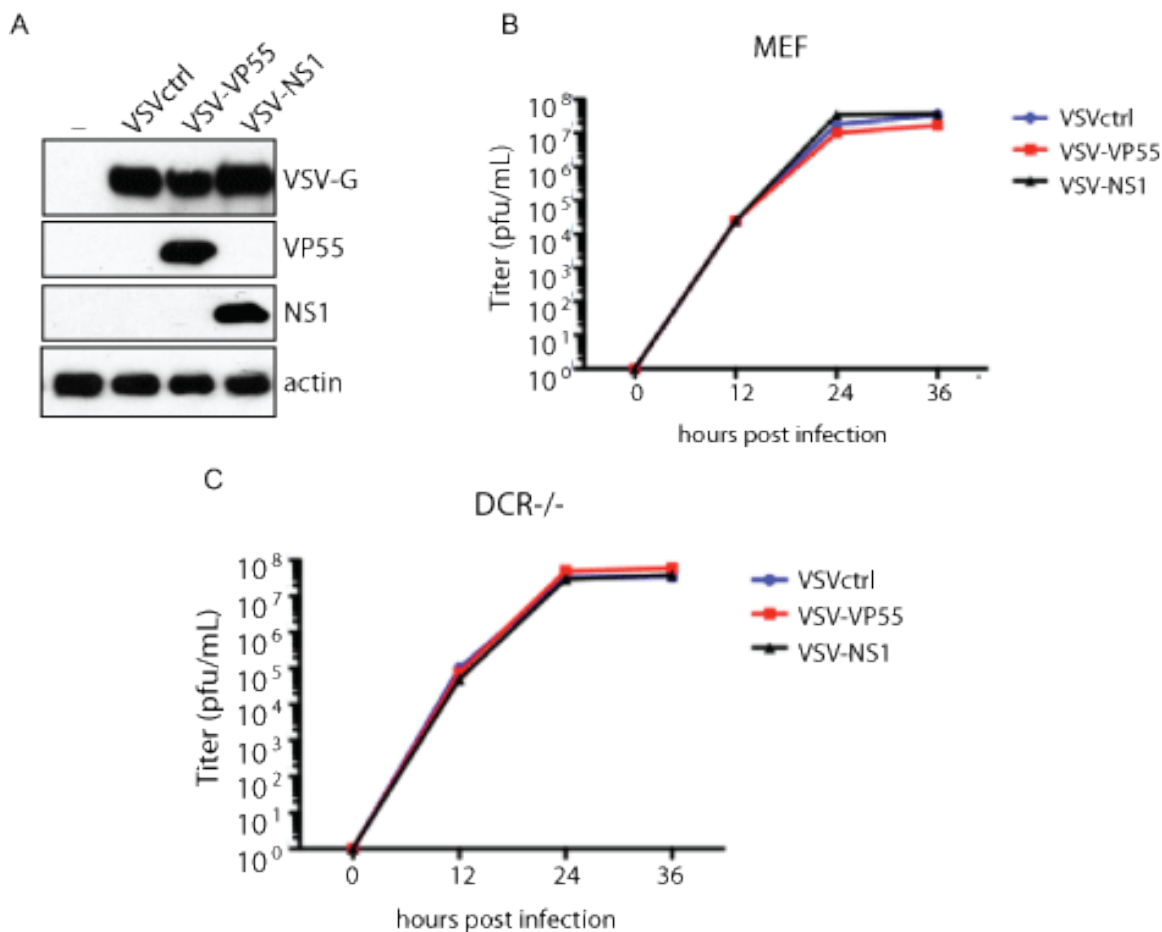
**(A)** Western blot analysis of BHK transfected with VP55-T109A or VP55wt for VP55 expression. **(B)** Analysis of BHK co-transfected with a plasmid encoding for miR-124 (p124) and plasmids encoding for VP55wt or VP55-T109A. Northern blot was probed for miR-124 and U6.



**Figure. S3. Small RNAs do not impact VSV replication.**

(related to Figure 4)

**(A)** and **(B)** Growth curve of VSVctrl and VSV-VP55 (MOI of 1) on murine wildtype fibroblasts (MEF). **(A)** Cells were analyzed at 5 and 10hrs post infection for expression of VSV proteins and VP55. **(B)** Supernatants were analyzed at 6, 8, 10, 12, 16 and 24 hrs post infection by plaque assay.



**Figure S4. Interferon response does not impact VSV replication *in vitro*.**

(related to Figure 6)

**(A)** Analysis of murine fibroblasts infected with VSVctrl, VSV-VP55 or VSV-NS1 (MOI of 1 for 10 hrs). Western blot was probed for VSV-G, VP55, NS1 and actin expression. **(B)** and **(C)** Multicycle growth curve of VSVctrl, VSV-VP55 and VSV-NS1 (MOI of 0.01) on **(B)** wildtype murine fibroblasts (MEF) and **(C)** murine dicer-deficient cells (Dcr<sup>-/-</sup>). Supernatants were analyzed at the indicated time points by plaque assay.

**Table S1. Small virus-specific RNA profiling (18-25 nt fraction) of Vesicular stomatitis virus (VSV)-, Sindbis virus (SV)-, Borna disease virus (BDV)- and Influenza A virus (IAV)-infected cells** (related to Figure 1).

**Table S2. mRNA sequencing of bone-marrow-derived macrophages mock-infected or infected with VSVctrl or VSV-VP55** (related to Figure 5).

**Table S3. Small virus-specific RNA profiling (18-25 nt fraction) of VSVctrl or VSV-VP55-infected mouse lungs** (related to Figure 6).