Supplementary Figure 1

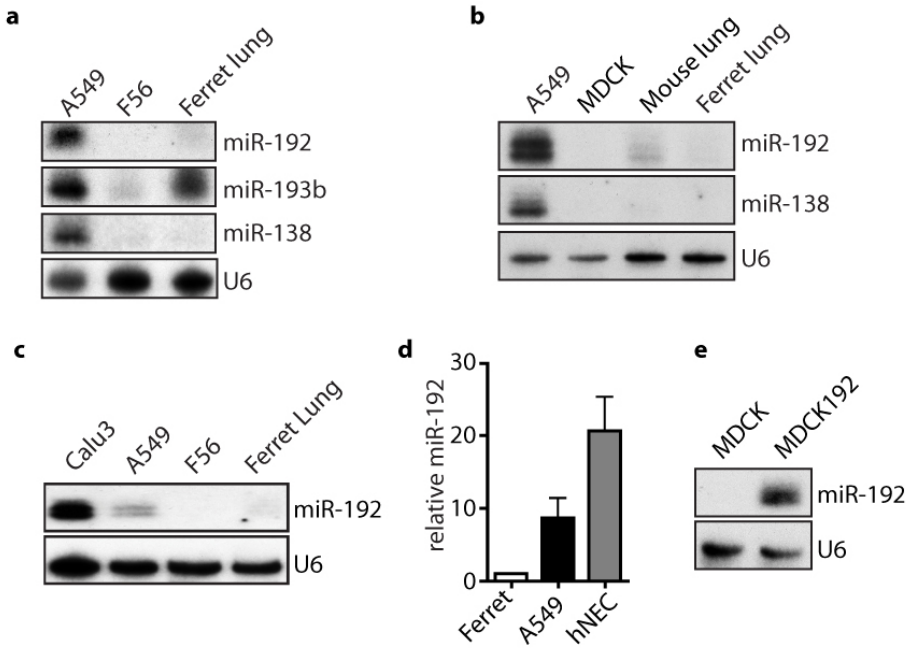

Figure S1: miR-192 expression confirmed by northern blot. **a,** RNA from A549 (human small airway epithelial cells), F56 (ferret fibroblasts and ferret whole lung were probed for miR-192, -193b, -138 and U6 small RNA (loading control) expression. **b,** RNA from A549, MDCK, whole mouse lung and ferret lung were probed for miR-192, -138 and U6 expression. **c,** RNA from Calu3 (human bronchial epithelial cells), A549, F56 and ferret lung probed for miR-192 and U6. **d,** RNA from MDCK and MDCK cells engineered to express miR-192 (MDCK192) probed for miR-192 and U6. **e,** Ferret lung, A549 and primary human nasal epithelial cells (hNEC) RNA were analyzed for mature miR-192 and miR-20a expression by qPCR. Y-axis represents miR-192 levels relative to miR-20a and normalized to the ferret lung. miR-20a was used for normalization as levels are similar between human A549 and ferret lung samples. Data are representative of 2-3 independent experiments.

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Supplementary Figure 2

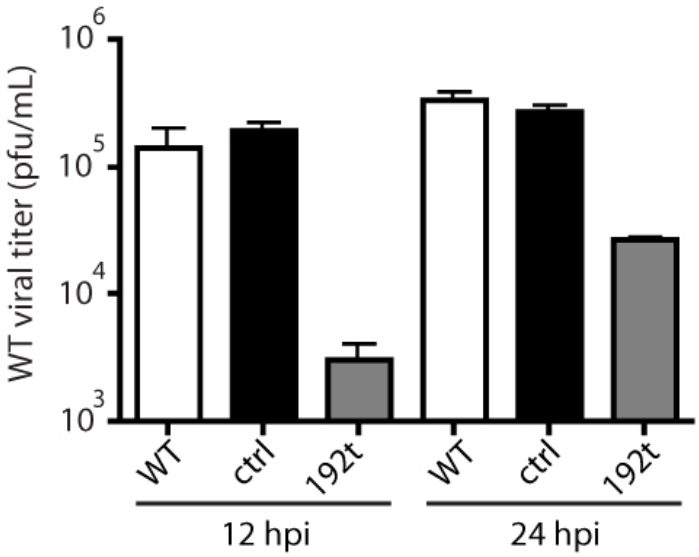

Figure S2: Targeted H5 HAlo virus is attenuated in A549 cells. A549 cells were infected at moi=0.01 with wild type (WT), control (ctrl) or miR-192 targeted (192t) H5 HAlo virus. Virus titers from supernatant were determined by plaque assay at 12 and 24 hours post infection (hpi). Error bars represent s.e.m. and are representative of two independent experiments.

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Supplementary Figure 3

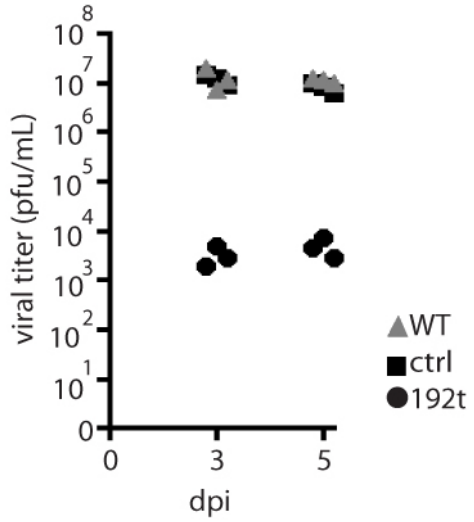

Figure S3: miR-192 targeted H5 HAlo virus is blunted *in vivo*. Mice were infected intranasally with 100pfu of WT, ctrl or 192t virus. Titers from whole lung homogenates were determined by plaque assay 3 and 5 days post infection (dpi). n=3 mice per group, representative of two independent experiments. Each dot represents an individual mouse.

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Supplementary Figure 4

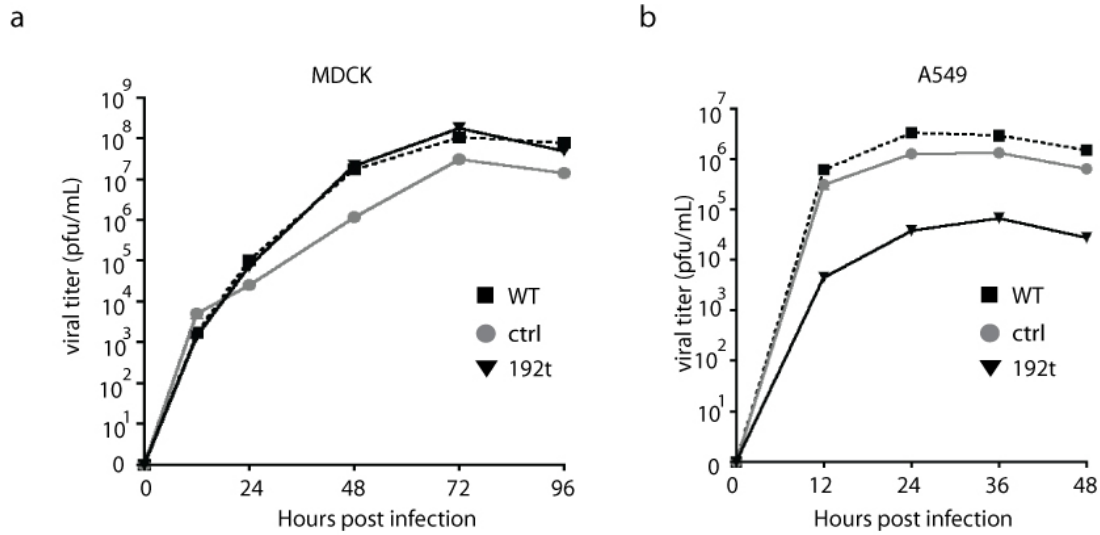

Figure S4: H3N2 Wyoming virus can be engineered to be sensitive to miR-192. MDCK cells **a,** and A549 cells **b,** were infected with wild type (wt), control (ctrl) or miR-192t (192t) virus and virus titers were determined at the indicated time points by plaque assay. Error bars represent s.e.m. with two-three samples per timepoint. Data are representative of three independent experiments.

Supplementary table 1: miRNA expression in A549, MDCK and ferret lung cells. Small RNA fractions from indicated cells were cloned and analyzed by deep sequencing. Annotated miRNA were divided by the total number of reads to yield the percent of miRNA in each cell-type or tissue. miRNA are ordered according to most abundant within A549 cells.

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