



**Supp. Fig. 2: Functional analyses of top candidate PB2 interactors.** **a**, Secondary screening of proteomic hits by siRNA treatment and reporter virus infection. After knockdown, 293T cells were infected with human (PB2-627K; MOI, 0.01) or avian-adapted (PB2-627E; MOI, 0.05) WSN NLuc virus for 24 h. Viral supernatants were titrated and normalized to a non-targeting control (NT). Control NXF1 (gray) and validated proteins highlighted (hnRNP UL1, cyan; MECR, yellow). Data are mean  $\pm$  SEM of  $n = 2-3$  biological replicates. **b**, Concordance of virus titer for PB2-627E vs PB2-627K virus infections in siRNA-treated cells (from **a**). Statistical analysis performed with a two-tailed Pearson correlation coefficient. **c**, Screening as in **a**, except A549 cells were infected with viruses as above for a single-cycle of infection (MOI, 0.1; 8 h) and virus gene expression in infected cells normalized as above. **d**, Concordance of gene expression (data from **c**, analyzed as in **b**).