

## SUPPORTING INFORMATION

**File S1. Results obtained for all pair wise combinations of screens.** Lists of shared genes, overlap significance analysis and p-values.

**Figure S1. Statistical analysis of EHF targeting.** **A.** EHF direct targeting compared to random simulation. 925 genes were randomly drawn from the genome 1,000 times, and the 1,000 numbers of EHF directly targeted by influenza proteins were plotted. The observed value of 17 directly targeted EHF is indicated by the vertical arrow with its significance. **B.** EHF indirect targeting compared to random simulation. 925 genes were randomly drawn from the genome 1,000 times, and the 1,000 numbers of EHF indirectly targeted by influenza proteins were plotted. The observed value of 204 indirectly targeted EHF is indicated by the vertical arrow with its significance.

**Table S1. Details on influenza screens.** For each screen, the cell line, the time point analysed, the virus, if necessary the preselection filter, the MOI, the siRNA library, the siRNA concentration, the format, the read-out, the detection and the threshold used to perform the experiments are given.

**Table S2. List of the 925 influenza EHF.** For each screen, the lists of proviral and antiviral genes referenced on NCBI Entrez Gene are given. The final list of 925 EHF is given in the last sheet.

**Table S3. Tissue expression data for the 925 influenza EHF.** For each influenza EHF, gene expression in lung or trachea is indicated when known.

**Table S4. Gene Ontology enrichment analysis performed on the 925 influenza EHF.** For each GO term, its identifier (column 1), its ontology (column 2), its definition (column 3), the number of genes associated in the sample (column 4), the total number of genes associated (column 5), the list of UniProtKB/Swiss-Prot Id of associated genes from the sample (column 6), the log-odds ratio (column 7) and finally the adjusted p-value (column 8) are given.

**Table S5. List of the 69 influenza EHF identified in at least 2 screens.** For each EHF, its presence (1) or absence (0) is indicated for each screen together with the total number of influenza screens in which it was identified.

**Table S6. Gene Ontology enrichment analysis performed on the 69 influenza EHF identified in at least two screens.** For each GO term, its identifier (column 1), its ontology (column 2), its definition (column 3), the number of genes associated in the sample (column 4), the total number of genes associated (column 5), the list of UniProtKB/Swiss-Prot Id of associated genes from the sample (column 6), the log-odds ratio (column 7) and finally the adjusted p-value (column 8) are given.

**Table S7. Gene Ontology enriched terms shared by at least two screens.** For each GO term, its description (column 1), its identifier (column 2) and its presence (1) or absence (0) in each screen is given.

**Table S8. Influenza-human protein-protein interaction list.** For each interaction, the name of the influenza protein, the Ensembl Gene ID of the human protein and the name of the human protein are given.

**Table S9. Drug-Influenza virus target network data. (drugs)** Each drug is described with its DrugBank ID (column 1), 1<sup>st</sup> letter of ATC code (column 2), FDA status (column 3) and name (column 4). **(associations)** Influenza EHF and their drugs are listed.

**Table S10. Interactomics characteristics of the 100 drugged EHF.** For each drugged EHF (name in column 1), interactomic characteristics are given: whether the EHF is directly targeted by an influenza virus protein (column 2), whether the EHF is indirectly targeted by an influenza virus protein (column 3) and whether the EHF is connected to at least an EHF in the human interactome (column 4). In yellow, 33 preferential targets.