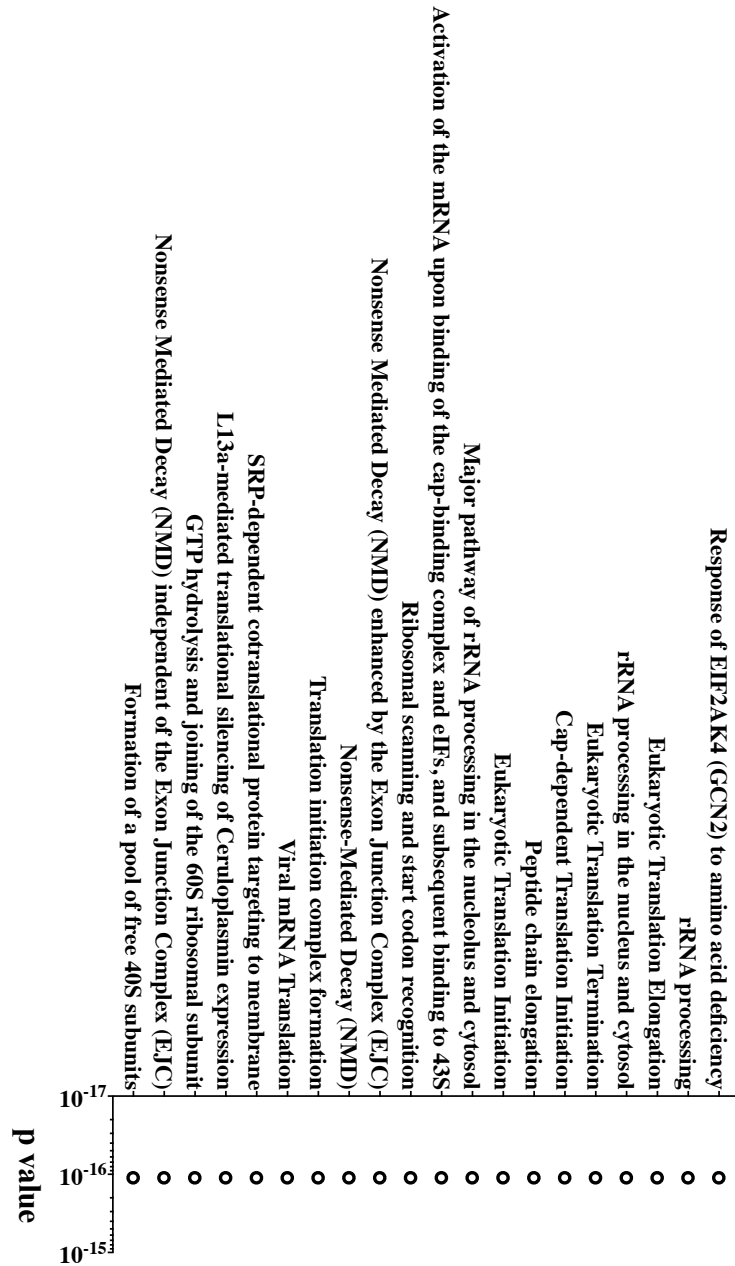


Reactome pathways (top 20)

**b**

NDFIP2 interactome
(*Mentha* database)

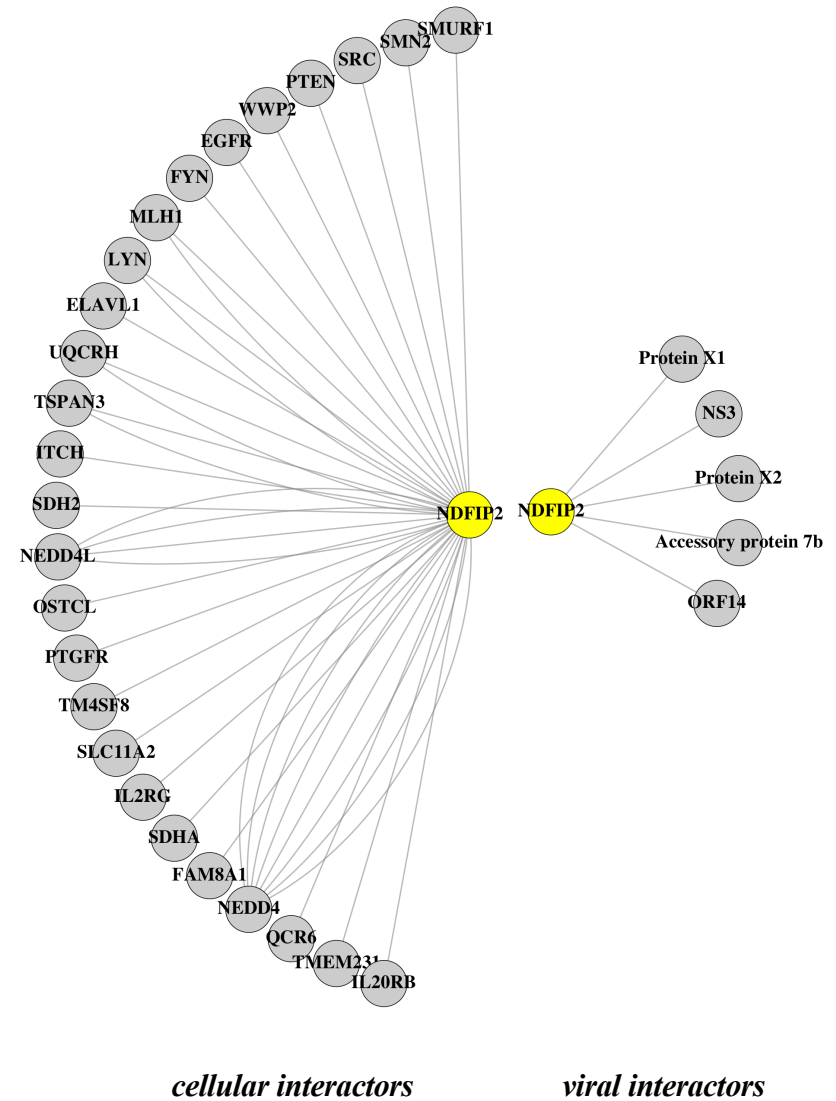
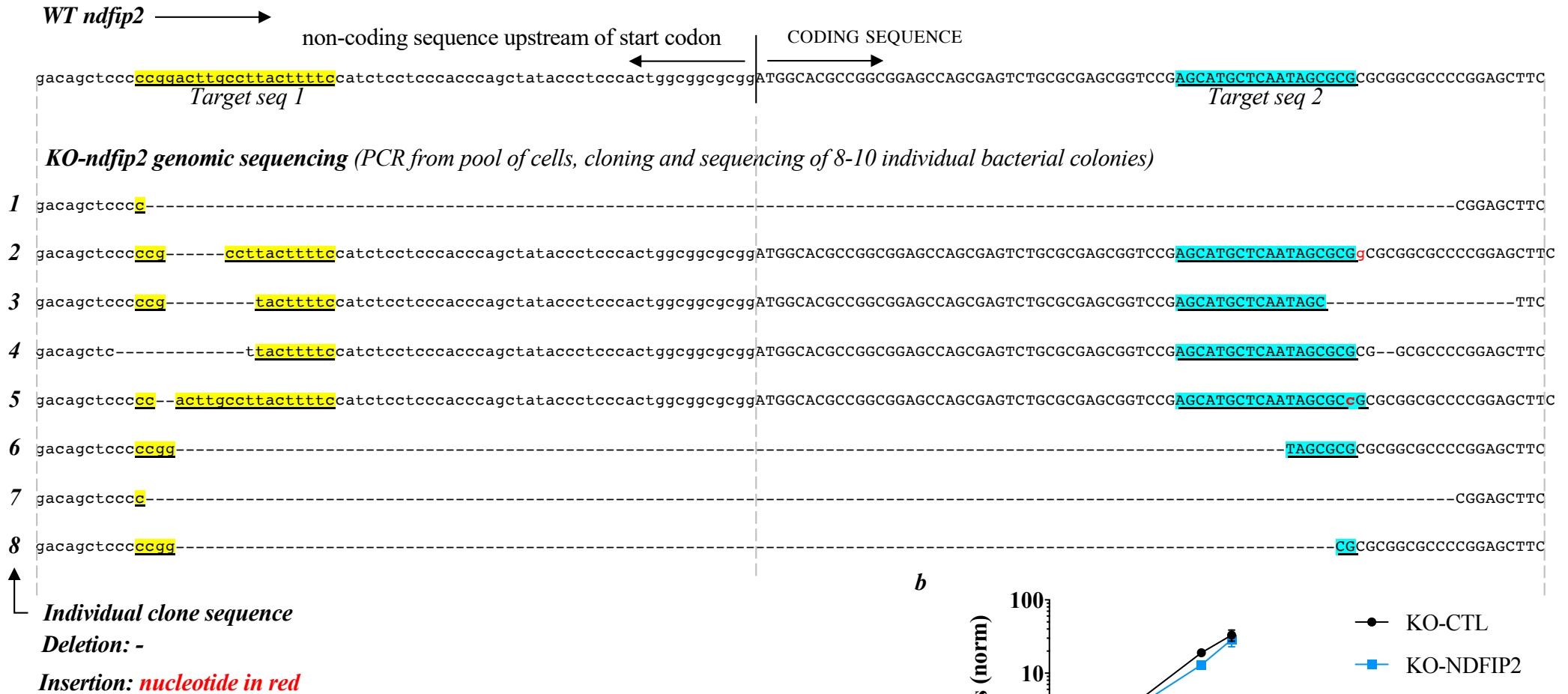


Figure S1. Reactome pathways analysis of proteins enriched in IFITM3-exosomal fractions. **a)** The graph represents the top 20 Ingenuity pathways identified among proteins differentially incorporated in IFITM3- over control-exosomal fractions. **b)** Analysis of the interactome of NDFIP2 (Mentha database).

a



b

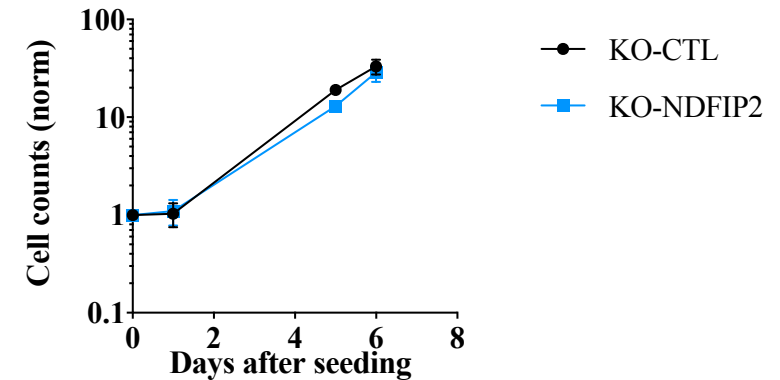


Figure S2. Characterization of A549 epithelial lung cells knocked out for NDFIP2. Pools of control or *ndfip2* A549 genetic KO cells were generated upon lentiviral-mediated gene transduction of CRISPR/Cas9 and selection. a) Genomic DNA was extracted and the region spanning the CRISPR target sequences was PCR-amplified, cloned and individual colonies sequenced. The sequences obtained after amplification from CRISPR control cells were *wild-type* and are thus not shown here for simplicity. b) Cells were seeded and counted at the indicated time points to estimate the cell doubling time. No effects of *ndfip2* deletion were observed under these experimental conditions (n=3).

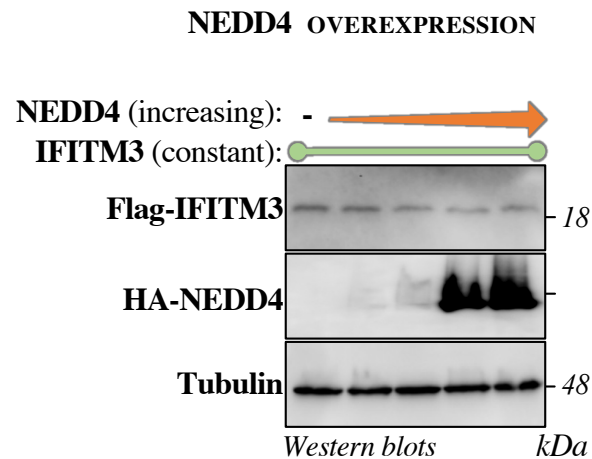
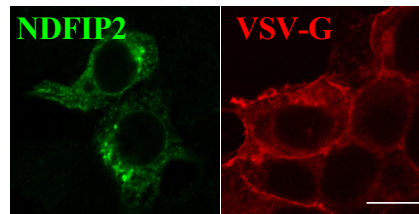


Figure S3. NEDD4 overexpression does not lead to modifications of the steady-state levels of IFITM3 in HEK293T cells. HEK293T cells were transfected with a constant amount of DNA coding Flag-IFITM3 together with increasing doses of DNA coding HA-NEDD4 (0.1 μ G of IFITM3 and from 0.05 to 0.4 μ G of HA-NEDD4 coding plasmid, in 24-well plates), prior to WB analysis twenty-four hours post transfection, in the same experimental conditions of the experiment presented in Fig. 2b. The WB panels present typical results obtained (n>3).

Transfection of single proteins



Co-transfection of NDFIP2+VSV-G

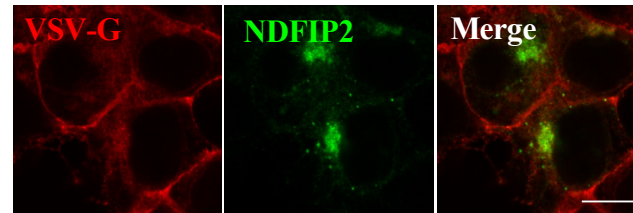


Figure S4. Lack of specific relocalization of VSV-G upon co-expression of NDFIP2. HEK293T cells transfected with DNAs coding NDFIP2 alone or together with the protein G of the Vesicular Stomatitis Virus (VSV-G) used here as control protein unrelated to IFITM3. The pictures present typical results obtained.