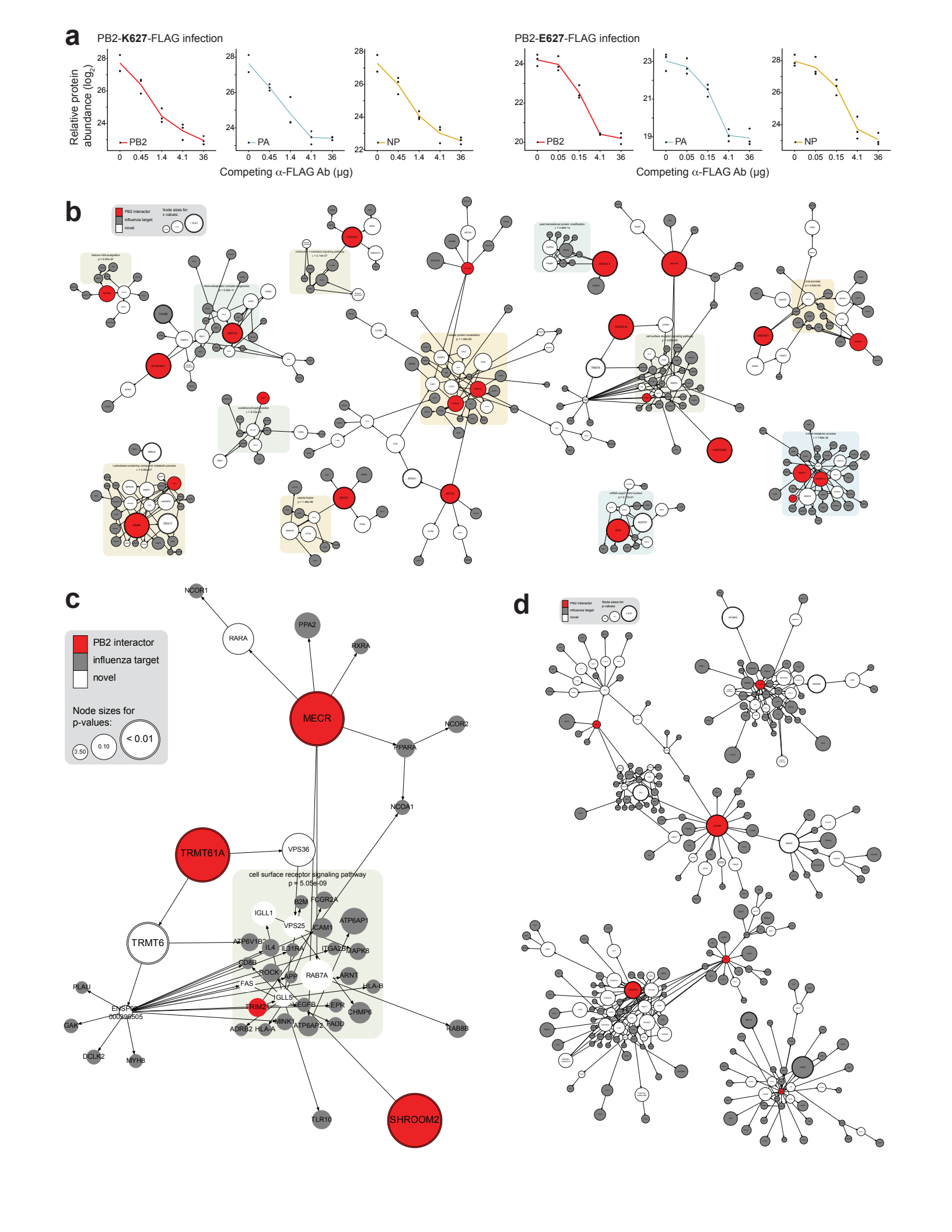
a
PB2-K627-FLAG infection
PB2-E627-FLAG infection
Relative protein abundance (log2)
PB2
PA
NP
Competing α-FLAG Ab (μg)
b
PB2 interactor
influenza target
novel
Node sizes for p-values:
c
PB2 interactor
influenza target
novel
Node sizes for p-values:
0.50
0.10
< 0.01
NCOR1
RARA
PPA2
RXRA
MECR
NCOR2
PPARA
NCOA1
TRMT61A
VPS36
TRMT6
cell surface receptor signaling pathway
p = 5.05e-09
B2M
FCGR2A
IGLL1
VPS25
ICAM1
ATP6AP1
ATP6V1B2
IL4
IL31RA
ITGA2B
MAPK8
CD8B
ROCK1
APP
RAB7A
ARNT
FAS
IGLL5
HLA-B
PLAU
TRIM25
VEGFB
EPR
CHMP6
ENSP00000505
GAK
ADRB2
HLA-A
MINK1
ATP6AP2
FADD
RAB8B
DCLK2
MYH8
TLR10
SHROOM2
d
PB2 interactor
influenza target
novel
Node sizes for p-values:

(***Previous page***) **Supp. Fig. 1: Validation of ICC-MS and network analysis. a**, Relative protein abundance of PB2 (red), PA (cyan), and NP (yellow) in PB2 ICC-MS samples shows decreasing capture with increasing competition antibody. Data shown are in biological triplicate. **b**, Fully annotated and zoomable version of the diagram in **Fig 1d**. Minimum-cost flow simulations connect top PB2 interactors identified by ICC-MS (red) to influenza host factors (gray) through novel host proteins (white). Modules comprising different PB2 interactors with enriched GO terms and *P* values indicated. Node sizes indicate empirical *P* values based on the control flow simulation. **c**, Enlarged view of MECR-containing module. **d**, Validation shows that flow simulation networks of protein-protein interactions reflect biochemical pathways that regulate viral replication. Flow simulation captured PKR interactions with RNA binding proteins DHX30, IGF2BP2, and TARBP, and linked RIG-I with TRIM14 through MAVS, and also IFIT3, LGP2, and USP15. Additionally, export pathways were faithfully reconstructed with NXF1 connecting with NXT2 and CRM1 connecting with NXF3. Our networks linked EXOSC3 to the exosome components EXOSC4, EXOSC5, and EXOSC8 and with the NEXT accessory complex (RBM7), both of which are important for influenza transcription (Rialdi et al., 2017).