SUPPLEMENTAL FIGURES

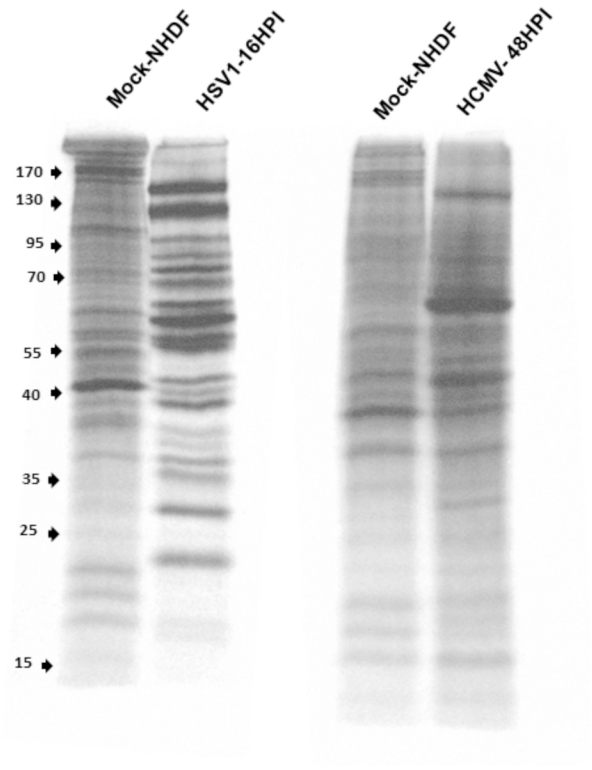
Figure S1. Differential response of ongoing cellular protein synthesis to HSV-1 vs. HCMV infection. Normal primary human fibroblasts (NHDFs) were mock-infected or infected with HSV1 or HCMV. At the indicated hours post-infection (HPI), cultures were metabolically labeled with ^{35}S amino acids for 1h. Total protein was harvested, fractionated by SDS-PAGE, and the fixed dried gel exposed to X-ray film. The migration of molecular weight standards (in Kd) is shown to the left. Note the strong impairment of ongoing host protein synthesis in HSV1-infected cells compared to HCMV-infected cells.

Figure S2. Validating RNA abundance for select gene targets. Total RNA was isolated from mock-infected (black bars) vs HCMV-infected (gray bars, MOI=3) cells at 48 hpi (left panel on each graph marked HCMV). Total RNA was also collected from NHDFs that express UL38 from a doxycyxline (Dox)-inducible promoter 72 h post-treatment without (black bars) or with (gray bars) dox (right panel on each graph marked UL38). For each of the indicated genes, RNA was analyzed by real-time qPCR and normalized to 18S rRNA levels. The values from the microarray experiment are included for comparison.

Figure S3. Additional host proteins induced upon UL38 expression in uninfected cells. Total protein was harvested from NHDFs that express UL38 from a doxycyxline (Dox)-inducible promoter 72 h post-treatment with or without dox . Triplicate samples were quantified by immunoblotting using the indicated

primary antibodies and a secondary antibody covalently linked to an infrared fluorophore. The membrane was scanned and the fold-change upon UL38-induction quantified using an Odyssey infrared imager. Each band was measured for raw intensity value and normalized to an actin loading control.

Figure S4. Target gene depletion selectively impacts HCMV replication, but not HSV-1 or Vaccina virus replication. A) NHDFs transfected with a control, non-silencing siRNA (*ctrl*) or individual siRNAs targeting PP1α (#5, #6) were infected with Vaccinia Virus (VacV) (MOI=0.1). After 24 hpi samples were harvested and analyzed by immunoblotting with the indicated antisera. B) NHDFs were mock-infected or infected (MOI=5) with HSV-1. At the indicated hours post-infection, total protein was collected and analyzed by immunoblotting with the indicated antisera. C) NHDFs transfected with a control, non-silencing siRNA (*ctrl*) or an siRNA targeting eIF6 were infected with HSV-1 (MOI=1). After 12 h cultures were metabolically pulse-labeled for 1 h with [^{35}S]Met-Cys. Total protein was harvested, fractionated by SDS-PAGE, and the labeled polypeptides visualized by autoradiography. The migration of molecular weight standards (in Kd) is shown to the left of the panel. D) As in C except after 13 h samples were harvested and analyzed by immunoblotting with the indicated antisera against HSV-1-encoded polypeptides (ICP0, VP16, Us11), eIF6, or actin.


Mock-NHDF
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Mock-NHDF
HCMV- 48HPI
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130
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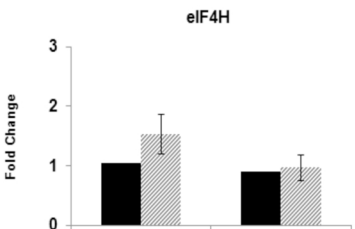
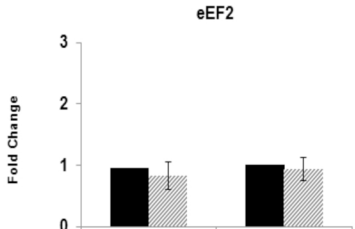
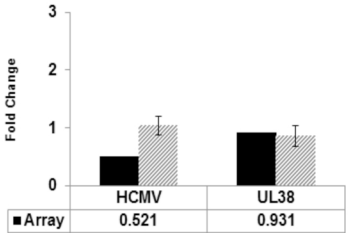
55
40
35
25
15



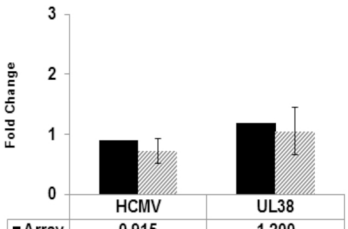
	HCMV	UL38
Array	1.046	0.904
qPCR	1.543	0.974



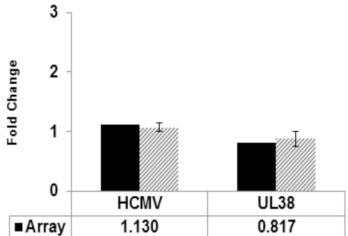
	HCMV	UL38
Array	0.962	1.009
qPCR	0.834	0.943



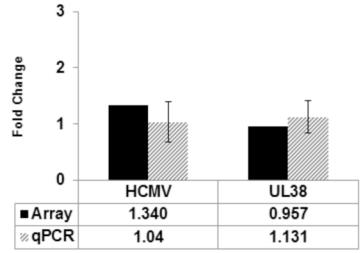
	HCMV	UL38
Array	0.521	0.931
qPCR	1.0432	0.8646



	HCMV	UL38
Array	0.915	1.200
qPCR	0.7345	1.06



	HCMV	UL38
Array	1.130	0.817
qPCR	1.076	0.884



	HCMV	UL38
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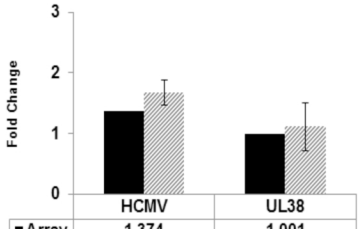
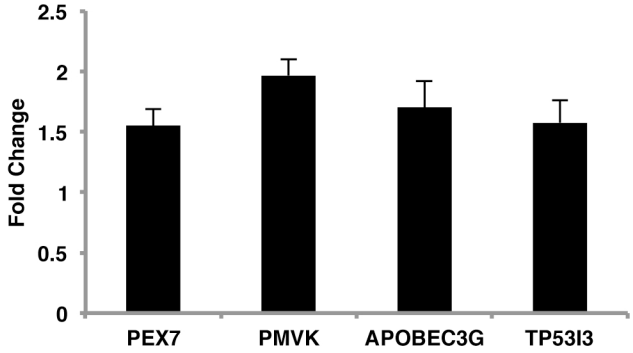
qPCR	1.04	1.131



	HCMV	UL38
Array	1.374	1.001
qPCR	1.675	1.116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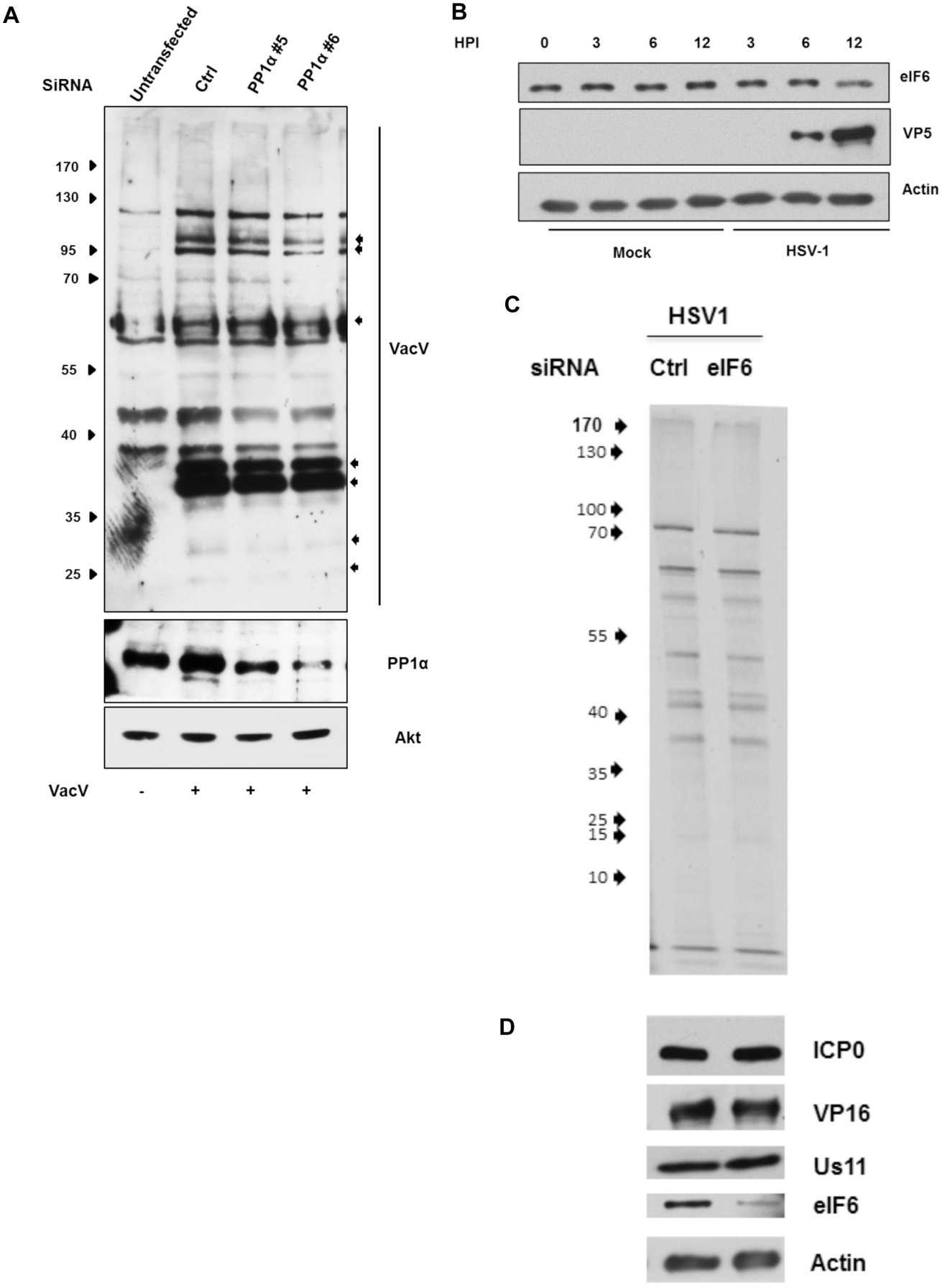
1.5
1
0.5
0
Fold Change
PEX7
PMVK
APOBEC3G
TP53I3


A
SiRNA
Untransfected
Ctrl
PP1α #5
PP1α #6
170
130
95
70
55
40
35
25
VacV
PP1α
Akt
VacV - + + +
B
HPI
0 3 6 12 3 6 12
eIF6
VP5
Actin
Mock
HSV-1
C
HSV1
siRNA
Ctrl eIF6
170
130
100
70
55
40
35
25
15
10
D
ICP0
VP16
Us11
eIF6
Actin