

Restriction of HSV-1 replication by Pistacia vera reveals a promising strategy for regulating virus-mediate chemokine response in THP-1 cells.

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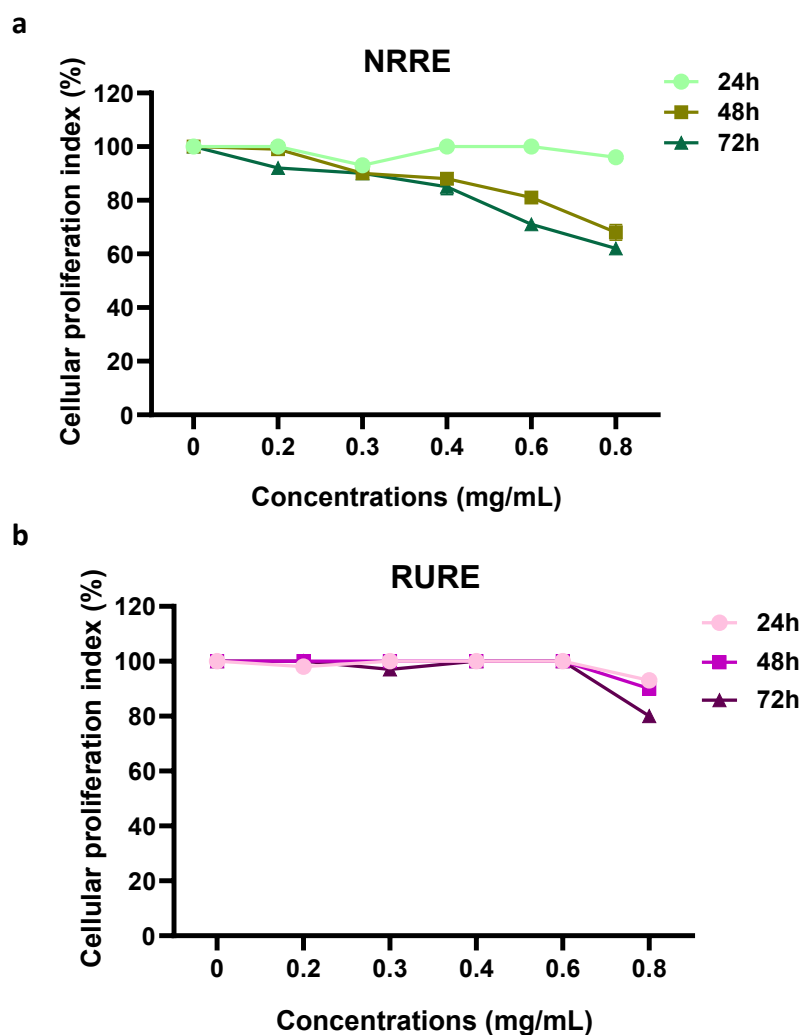


Figure S1. Cells viability of THP-1 cells treated with NRRE and/or RURE treatment. THP-1 cells were incubated with 0.8, 0.6, 0.4, 0.3 and 0.2 mg/mL of NRRE (panel **a**) and/or RURE (panel **b**) for 24h, 48h and 72h. Results represent the mean of three biological independent experiments $\pm$ SD.

Supplementary Table S1

Extract	24h	48 h	72 h
NRRE	>0,8	1,3	1,05
RURE	>0,8	>0,8	>0,8

Table S1. CC₅₀ values (mg/mL) of pistachio extracts at 24h, 48h and 72h (mg/mL).
CC₅₀: half maximal cytotoxic concentration.

Supplementary Table S2

Primers	Sequences
GAPDH-F GAPDH-R	5'-ACATCATCCCTGCCTCTAC-'3 5'-CTGCTTCACCACCTTCTTG-'3
CCL2-F CCL2-R	5'-ATC AAT GCC CCA GTC ACC TG-'3 5'-TCT CCT TGG CCA CAA TGG TC -'3
CCL4-F CCL4-R	5'-GCT TCC TCG CAA CTT TGT GG-'3 5'-TCA CTG GGA TCA GCA CAG AC-'3
CCL13-F CCL13-R	5'-AGC CAG ATG CAC TCA ACG TC-'3 5'-TCT CCT TGC CCA GTT TGG TT-'3
CXCL10-F CXCL10-R	5'-GCC ATT CTG ATT TGC TGC CT-'3 5'-ATG CTG ATG CAG GTA CAG CG-'3
CXCL11-F CXCL11-R	5'-ACT TGG GTA CAT TAT GGA GGC T-'3 5'-TGT CTT TGC ATA GGC CCT GG-'3
CXCL13-F CXCL13-R	5'-TCT GCT TCT CAT GCT GCT GG-'3 5'-ATT CCC ACG GGG CAA GAT TT-'3
CMKRL1-F CMKRL1-R	5'-CTG GGC AAT GGT CTG GTG AT-'3 5'-TGT CCC GGA AGA CGA GAG AT-'3
NFkB-F NFkB-R	5'-TAAAGCCCCCAATGCATCCAAC-'3 5'-CCAAATCCTTCCCAGACTCCAC-'3
ICP0-F ICP0-R	5'-TCTGCATCCCGTGCATGAAAAC-'3 5'-CTGATTGCCCGTCCAGATAAAG-'3
UL42-F UL42-R	5'-CTCCCTCCTGAGCGTGTTTC-'3 5'-CACAAAGCTCGTCAGTTCGC -'3
US11-F US11-R	5'-GGCTTCAGATGGCTTCGAG-'3 5'-GGGCGACCCAGATGTTTAC-'3
HSV-1-F HSV-1-R Probe	5'-CATCACCGACCCGGAGAGGGAC-'3 5'-GGGCCAGGCGCTTGTTGGTGTA-'3 5'-[FAM] CCG CCG AAC TGA GCA GAC ACC CGC GC [TAM] -'3

Table S2. Sequences of primers used for REAL TIME-PCR

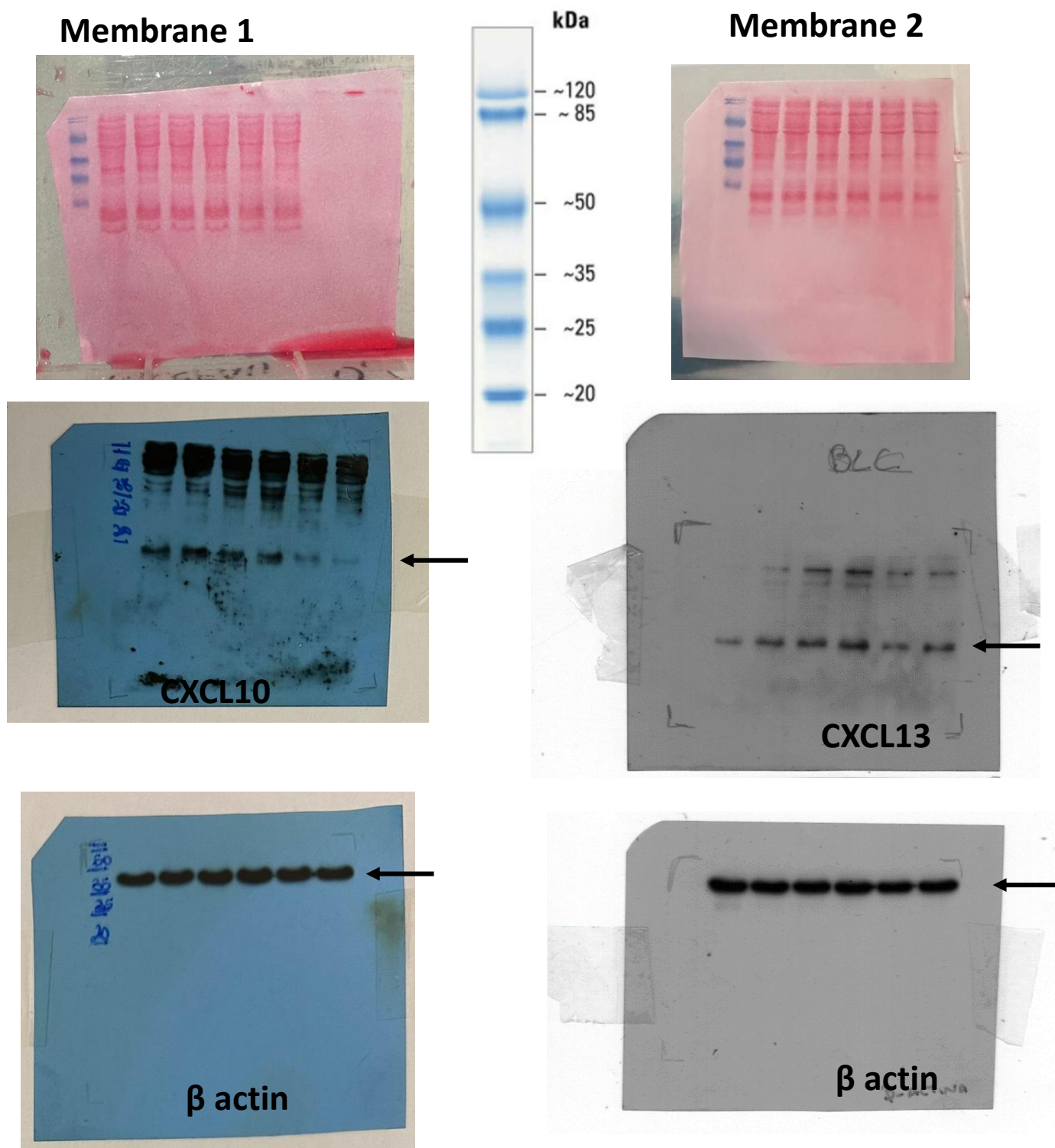
Table S3. Gene expression analysis of HSV-1-infected THP-1 cells untreated or treated with NRRE and RURE compared to untreated and uninfected cells using the Human Cytokines & Chemokines RT² Profiler PCR Array (PAHS-022Z, Qiagen).

Gene Symbol	HSV-1		NRRE		HSV-1+NRRE		RURE		HSV-1+RURE	
	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value
C5	0.46	0.003314	0.37	0.007553	0.27	0.000571	0.63	0.048797	0.56	0.007627
C5AR1	19.12	0.000004	2.22	0.000798	39.48	0.000095	4.08	0.000046	15.03	0.000005
ACKR2	0.16	0.000034	2.96	0.000078	1.65	0.037284	3.13	0.000014	3.14	0.000003
CCL1	2.90	0.005493	0.10	0.000029	0.69	0.006510	5.51	0.000451	7.64	0.000000
CCL11	0.96	0.984919	2.64	0.000050	2.75	0.000947	8.54	0.000004	10.40	0.000000
CCL13	534.94	0.009500	2.47	0.000013	2.65	0.008064	3.73	0.000001	8.84	0.000577
CCL14	0.51	0.011910	1.41	0.003347	0.91	0.292060	4.62	0.000001	1.97	0.009736
CCL15	1.05	0.645691	1.04	0.663813	1.60	0.008414	1.33	0.007855	3.06	0.000024
CCL16	17.74	0.012100	18.36	0.000470	17.35	0.000226	16.00	0.000006	28.92	0.000000
CCL17	1.02	0.734966	1.34	0.003046	1.84	0.005608	1.77	0.000138	2.92	0.000240
CCL18	2.49	0.000120	0.72	0.018301	1.01	0.909030	2.27	0.000039	3.92	0.011872
CCL19	0.94	0.522495	0.93	0.456109	1.21	0.105656	1.28	0.050670	2.36	0.016504
CCL2	508.90	0.000108	11.55	0.000710	21.09	0.000278	11.09	0.000050	17.69	0.000906
CCL20	1.07	0.165593	3.44	0.000821	9.86	0.000018	9.20	0.000624	16.04	0.000918
CCL21	0.89	0.488408	1.86	0.020794	1.99	0.008618	4.78	0.001978	4.17	0.002125
CCL22	0.41	0.003546	1.22	0.206400	0.96	0.676393	1.81	0.001030	1.78	0.017660
CCL23	0.39	0.002136	0.26	0.001103	0.17	0.000662	0.32	0.001586	0.43	0.008852
CCL24	9.93	0.000528	3.64	0.000428	4.54	0.000070	0.63	0.000681	6.77	0.000080
CCL25	0.57	0.075637	1.20	0.430296	2.08	0.007204	1.40	0.067267	0.27	0.007188
CCL26	3.80	0.004934	2.00	0.020127	3.39	0.000124	3.91	0.000012	2.94	0.000242
CCL27	0.91	0.769761	0.87	0.065421	1.09	0.349414	1.00	0.986969	1.44	0.007187
CCL28	0.34	0.020885	1.09	0.731001	0.10	0.385935	1.35	0.177243	1.58	0.042326
CCL3	70.86	0.000026	7.83	0.015018	15.94	0.001414	7.16	0.013546	21.49	0.002876
CCL4	721.90	0.000217	1.07	0.742393	7.53	0.001092	2.64	0.138380	11.81	0.000410
CCL5	2.87	0.074353	1.50	0.796666	3.35	0.036159	1.08	0.723047	3.51	0.026245
CCL7	7.51	0.086011	0.72	0.363872	3.76	0.668763	2.67	0.978393	7.67	0.077882
CCL8	6.82	0.000037	1.92	0.026485	3.18	0.000750	4.76	0.004839	4.13	0.000180
CCR1	5.09	0.151036	0.47	0.237391	0.54	0.251555	0.52	0.251446	1.75	0.645233
CCR10	0.78	0.204901	0.66	0.187687	2.12	0.555666	4.16	0.534328	4.66	0.372385
CCR2	0.89	0.516758	0.11	0.060735	0.08	0.055375	0.19	0.073648	0.23	0.081167
CCR3	1.64	0.177600	0.45	0.096634	0.54	0.136305	1.01	0.938066	1.93	0.064951
CCR4	16.64	0.000175	0.41	0.042900	0.88	0.499215	1.52	0.096329	0.35	0.032079
CCR5	0.77	0.357129	0.13	0.031356	0.07	0.026227	0.19	0.039327	0.19	0.038929
CCR6	3.44	0.002625	0.57	0.176980	2.48	0.016023	2.04	0.042401	7.37	0.000104
CCR7	12.47	0.000015	2.92	0.004930	2.10	0.003511	4.39	0.005957	4.15	0.002169
CCR8	1.59	0.001115	0.09	0.000107	3.06	0.000221	4.11	0.000070	7.61	0.001741
CCR9	0.43	0.156798	0.60	0.262738	1.87	0.153163	2.76	0.020387	2.29	0.056860
ACKR4	1.17	0.807303	1.49	0.375182	1.06	0.955632	1.73	0.115982	2.56	0.068978
CCRL2	11.91	0.000000	2.83	0.000014	1.92	0.000090	2.28	0.001389	3.06	0.000062
CKLF	0.50	0.024168	0.93	0.560440	0.98	0.815060	1.03	0.961594	1.28	0.190411
CMKLR1	178.77	0.000010	1.25	0.160114	0.79	0.104201	6.26	0.001409	6.53	0.000001
CMTM1	1.24	0.001435	1.31	0.000329	1.09	0.344859	1.63	0.007851	1.80	0.000067
CMTM2	0.76	0.001207	2.58	0.018215	4.35	0.000813	3.33	0.000284	1.80	0.000004

Gene Symbol	HSV-1		NRRE		HSV-1+NRRE		RURE		HSV-1+RURE	
	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value	Fold Change	p-value
CMTM3	1.09	0.362863	1.52	0.021440	1.08	0.473452	1.16	0.116844	1.48	0.031129
CMTM4	0.58	0.000327	1.18	0.025066	1.04	0.533340	1.39	0.015269	1.54	0.051471
CX3CL1	1.08	0.395677	0.58	0.007517	0.20	0.000423	3.76	0.000004	0.89	0.497411
CX3CR1	2.13	0.000160	2.68	0.000524	1.75	0.002612	0.11	0.543271	3.92	0.009006
CXCL1	3.95	0.000016	0.97	0.802167	0.65	0.008993	1.02	0.813540	0.81	0.268122
CXCL10	66813.25	0.003864	0.66	0.006629	11.17	0.000535	1.81	0.053265	26.80	0.001769
CXCL11	25121.12	0.000005	1.41	0.007003	24.38	0.000020	3.18	0.004499	63.76	0.000215
CXCL12	5.04	0.000051	0.34	0.000545	0.81	0.134626	0.39	0.000589	0.93	0.319286
CXCL13	194.31	0.000002	1.33	0.019956	4.96	0.000486	2.72	0.046895	8.77	0.000000
CXCL14	1.97	0.008232	0.92	0.790811	1.29	0.283498	1.75	0.018755	2.23	0.002796
CXCL16	5.17	0.000005	12.19	0.000115	17.90	0.000284	8.91	0.000017	19.95	0.000741
CXCL2	1.77	0.066810	0.64	0.207806	0.60	0.178365	0.57	0.202264	0.71	0.274590
CXCL3	12.42	0.000084	3.03	0.002093	26.60	0.000027	6.73	0.036664	18.87	0.000030
CXCL5	0.42	0.000603	0.66	0.008278	0.80	0.029949	1.00	0.966202	1.03	0.682236
CXCL6	1.45	0.075436	1.65	0.009406	1.23	0.170880	2.20	0.023099	30.89	0.113020
CXCL9	161.29	0.000266	3.23	0.001305	11.57	0.004454	5.11	0.000204	14.56	0.000196
CXCR1	0.91	0.623266	1.20	0.745586	2.07	0.114665	3.07	0.005336	3.35	0.083083
CXCR2	0.35	0.074091	0.40	0.088344	0.21	0.045582	0.59	0.184856	0.39	0.086098
CXCR3	0.78	0.120823	1.06	0.706780	1.14	0.353961	1.22	0.208393	2.28	0.000806
CXCR4	0.81	0.168454	0.25	0.003306	0.14	0.002009	0.29	0.004891	0.32	0.004690
CXCR5	0.91	0.417043	2.85	0.000917	1.29	0.080904	6.19	0.000021	4.93	0.000803
CXCR6	1.02	0.868389	0.54	0.006074	0.57	0.011693	0.87	0.203396	1.73	0.008084
ACKR3	1.25	0.121788	1.34	0.018201	0.54	0.001915	1.43	0.037732	1.96	0.005326
ACKR1	2.37	0.001249	4.07	0.000048	2.34	0.064026	2.49	0.015425	4.66	0.002174
FPR1	22.22	0.000000	11.23	0.000785	13.78	0.000041	16.92	0.000015	18.39	0.000152
GPR17	0.37	0.001329	1.17	0.166717	1.69	0.009747	0.90	0.537342	0.73	0.158149
HIF1A	0.99	0.866974	0.82	0.168728	0.88	0.341974	1.20	0.316943	2.01	0.028210
IL16	0.96	0.705008	3.40	0.000294	1.37	0.132840	2.81	0.001185	3.56	0.000724
IL1B	8.59	0.000003	11.99	0.000050	11.34	0.000000	9.27	0.000062	14.73	0.001562
IL4	5.35	0.000143	3.96	0.000100	16.98	0.000101	7.22	0.000002	16.23	0.000055
CXCL8	7.88	0.000039	0.81	0.316929	1.45	0.093433	0.61	0.163068	1.38	0.192072
PF4V1	2.00	0.004916	2.09	0.004113	5.88	0.003194	4.18	0.000514	3.91	0.000030
PPBP	2.88	0.000630	2.83	0.000811	1.50	0.280119	4.59	0.000266	8.65	0.000004
SLIT2	20.29	0.000482	7.92	0.000002	8.40	0.000091	5.07	0.000203	15.90	0.000865
TLR2	1.98	0.001934	0.98	0.889086	1.23	0.055766	1.56	0.013842	2.21	0.000149
TLR4	2.79	0.000755	1.97	0.004931	2.24	0.004025	1.49	0.047935	4.08	0.000057
TNF	9.37	0.000028	3.12	0.000366	2.32	0.093236	2.13	0.001196	4.23	0.002966
TYMP	25.62	0.000123	0.40	0.000126	1.52	0.005138	0.49	0.000301	3.03	0.000232
XCL1	4.03	0.004799	2.23	0.001378	4.22	0.000422	6.38	0.000357	6.62	0.040260
XCL2	1.28	0.036964	0.36	0.002089	3.38	0.001626	1.93	0.000540	5.78	0.000005
XCR1	2.34	0.000534	0.99	0.833199	3.15	0.000693	2.77	0.001036	2.65	0.000345

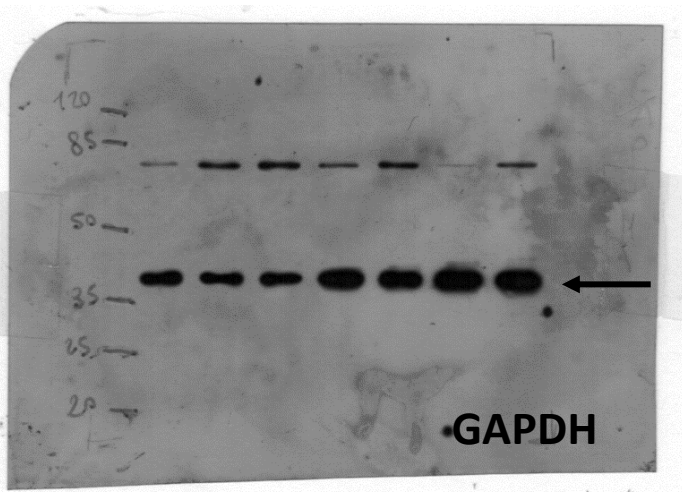
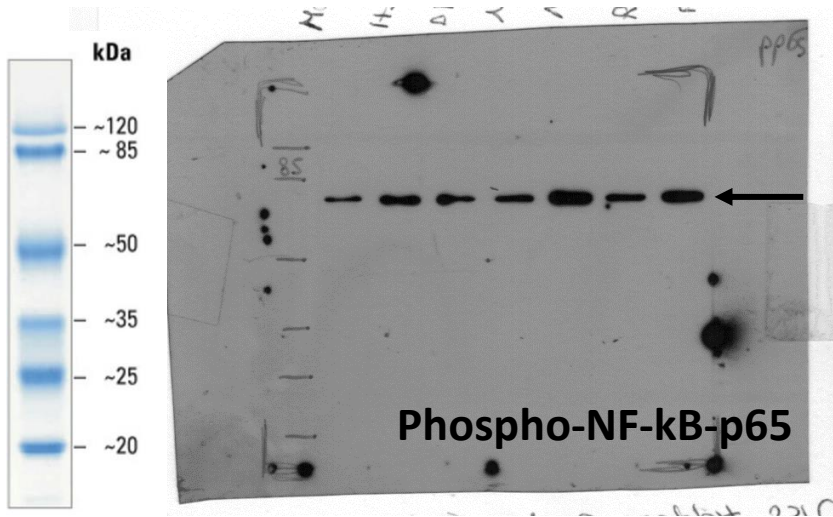
Gene expression levels highlighted in boldface were confirmed by real-time qPCR analysis.

Supplementary Figure 3b



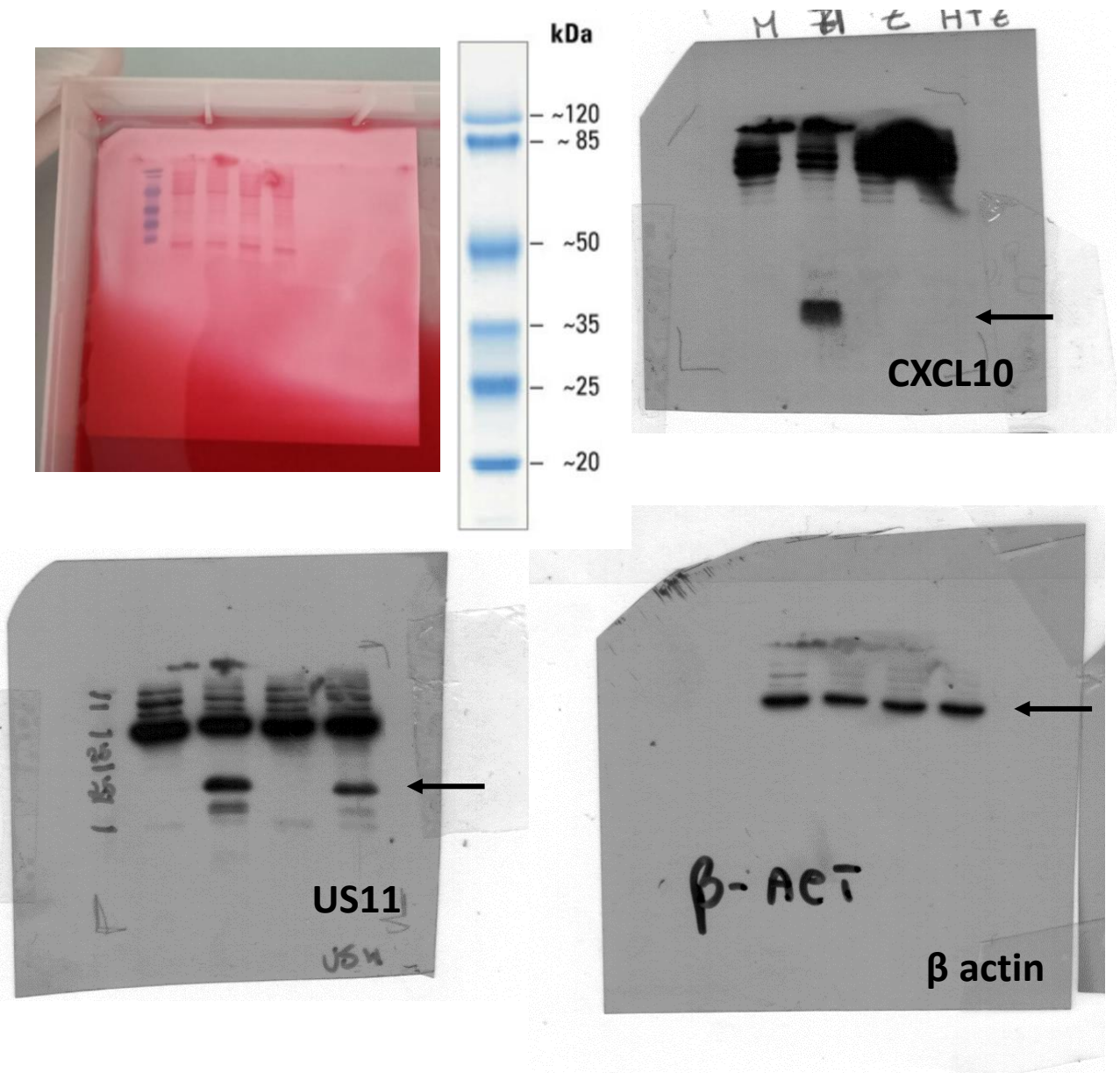
Supplementary Figure 3b. For membrane 1 and 2 it was used a 15% polyacrylamide gel. The membrane was blotted with CXCL10, CXCL13, US11 and β actin antibodies and detected using X-ray film. The original, uncropped blot and the Ponceau S-stained image are shown. Arrows indicate the specific bands. For these membranes, a Thermo Scientific Prestained Protein Molecular Weight Marker (Catalogue number 26612) was used.

Supplementary Figure 3d



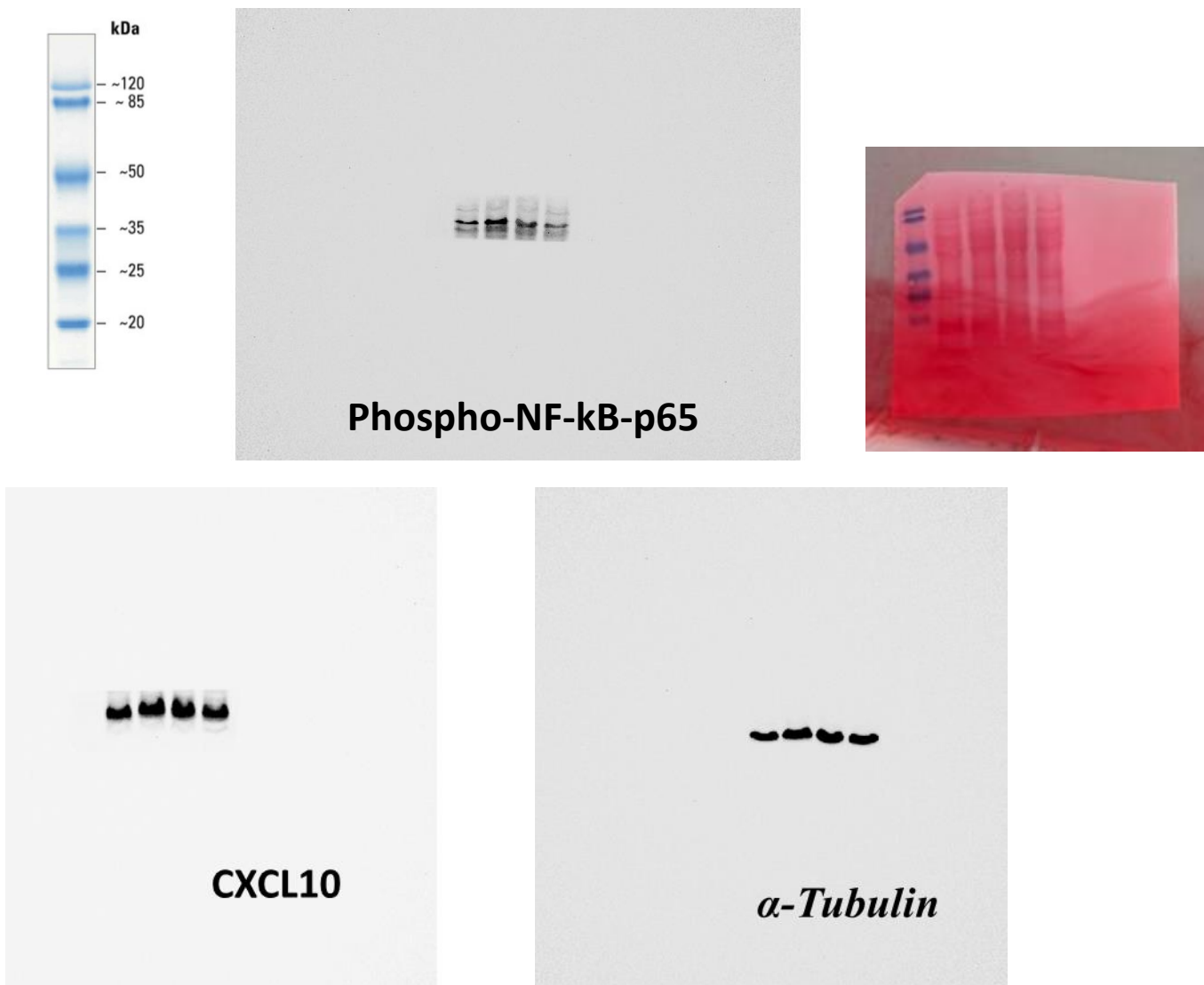
Supplementary Figure 3d. It used 10% polyacrylamide gel. The membrane was blotted with Phospho-NF-kB-p65 and GAPDH antibodies and detected using X-ray film. The original, uncropped blot and the Ponceau S-stained image are shown. Arrows indicate the specific bands. For this membrane, a Thermo Scientific Prestained Protein Molecular Weight Marker (Catalogue number 26612) was used.

Supplementary Figure 4b



Supplementary Figure 4b. It used 15% polyacrylamide gel. The membrane was blotted with CXCL10, US11 and β actin antibodies and detected using X-ray film. The original, uncropped blot and the Ponceau S-stained image are shown. Arrows indicate the specific bands. For this membrane, it was used the Thermo Scientific Prestained Protein molecular weight marker (Catalog number 26612).

Supplementary Figure 6c



Supplementary Figure 6c. A 15% polyacrylamide gel was used for both membranes 1 and 2. Membrane 1 was cut at approximately 35 kDa. The upper portion was incubated with anti-phospho-NF-κB p65 and anti-α-tubulin antibodies, while the lower portion was probed with an anti-CXCL10 antibody. Membrane 2 was also cut at ~35 kDa. The upper portion was incubated with anti-α-tubulin, and the lower portion was probed with an anti-US11 antibody. Signal detection was performed using the Bio-Rad ChemiDoc system, and quantification of the Western blot bands was carried out using Bio-Rad Image Lab 6 software. The original, uncropped blot and the Ponceau S-stained imageS are shown. Arrows indicate the specific bands.