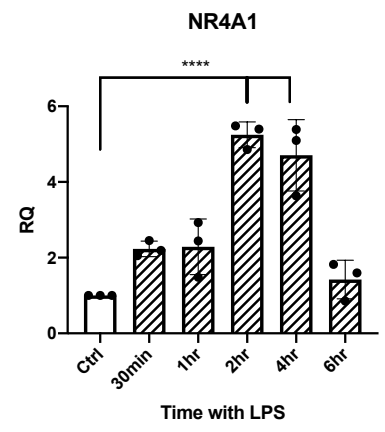
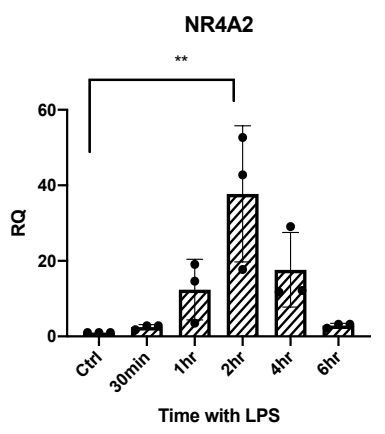


**Figure. S1**

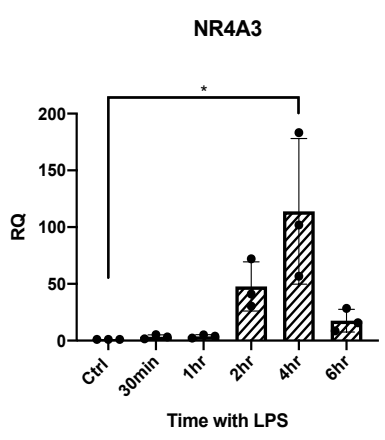
**A.**



**B.**



**C.**



**D.**

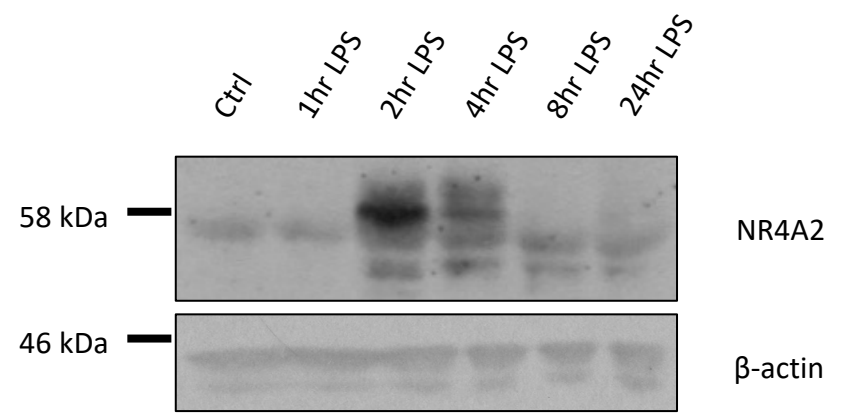
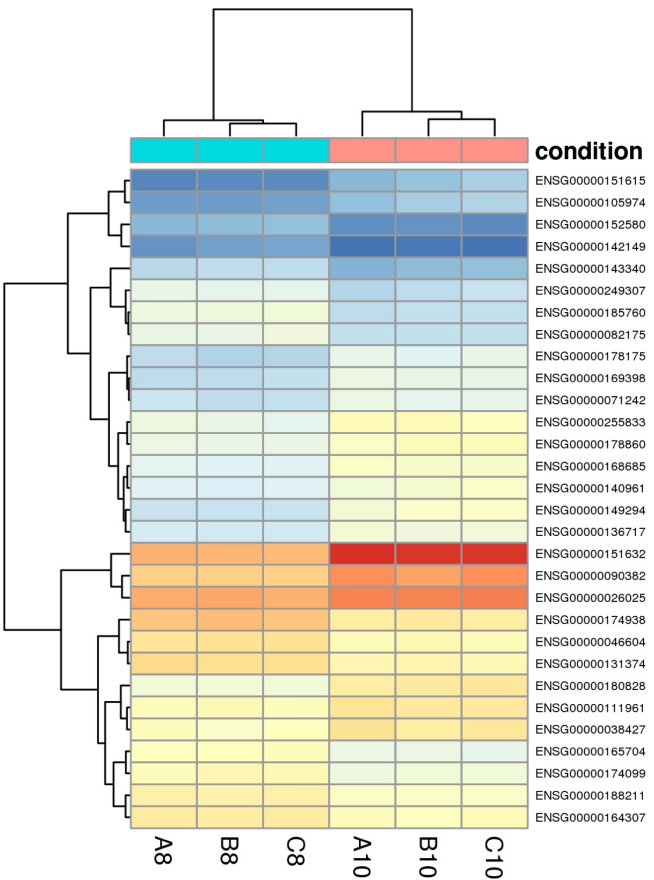


Figure. S2

A.

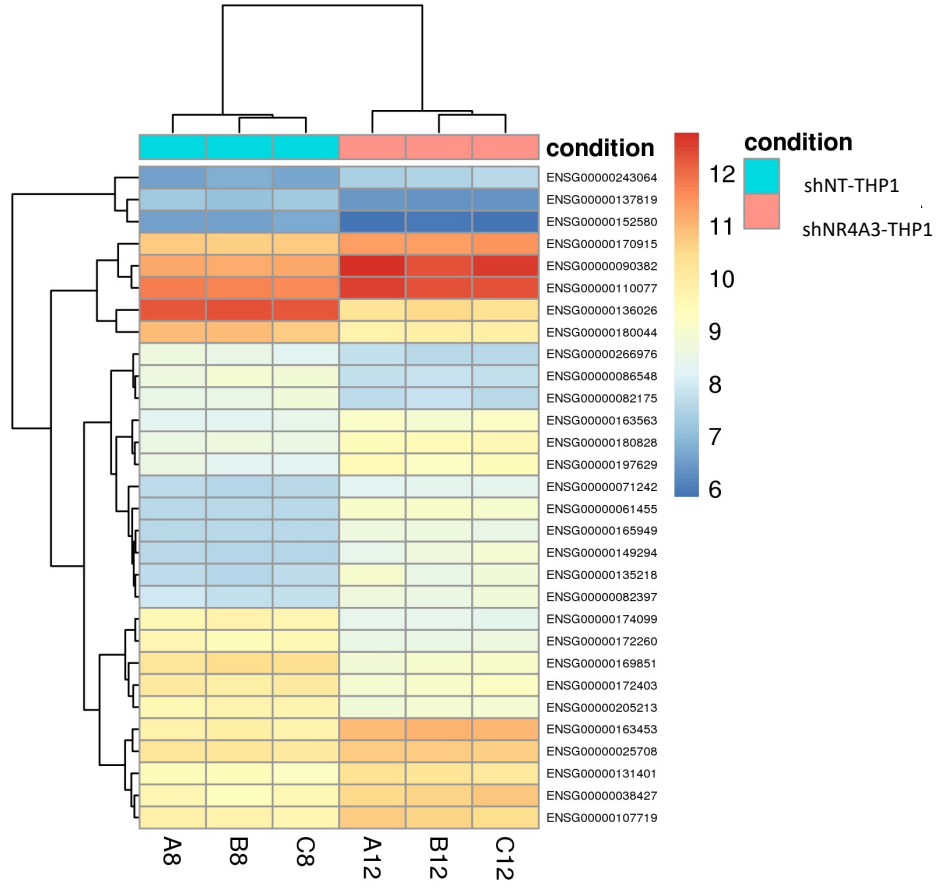
shNR4A2



shNT-THP1 shNR4A2-THP1

B.

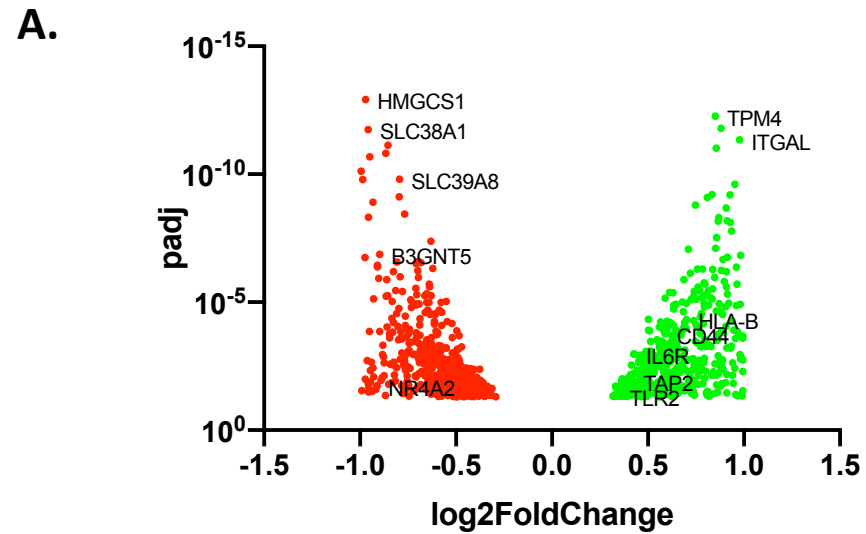
shNR4A3



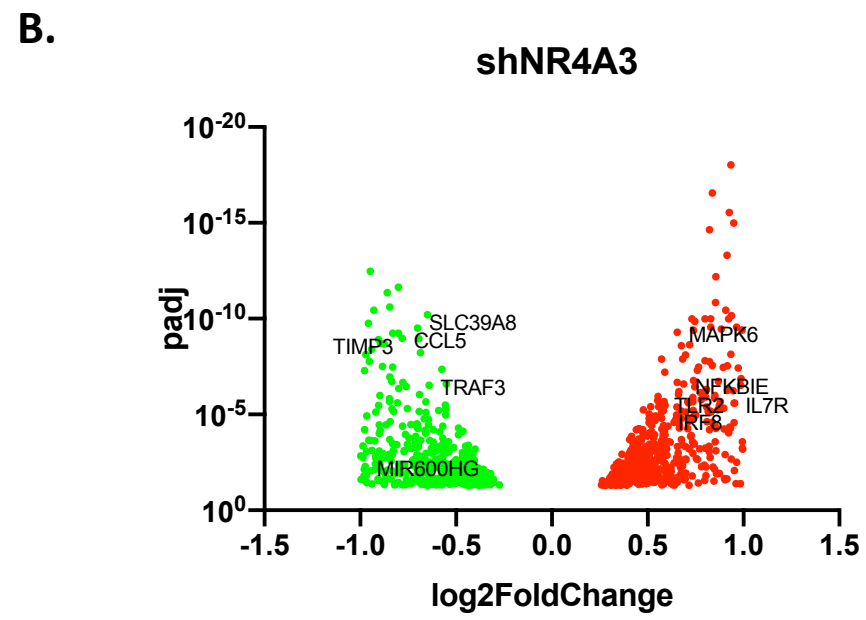
shNT-THP1 shNR4A3-THP1

Figure. S3

shNR4A2



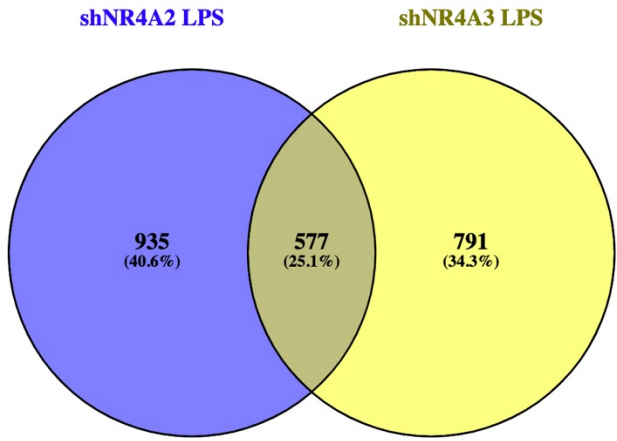
shNR4A3



**Figure. S4**

**A.**

- 4. shNR4A2 only regulated genes in the presence of LPS (935)
- 5. shNR4A3 only regulated genes in the presence of LPS (791)
- 6. shNR4A2 & shNR4A3 regulated genes in presence of LPS (577)

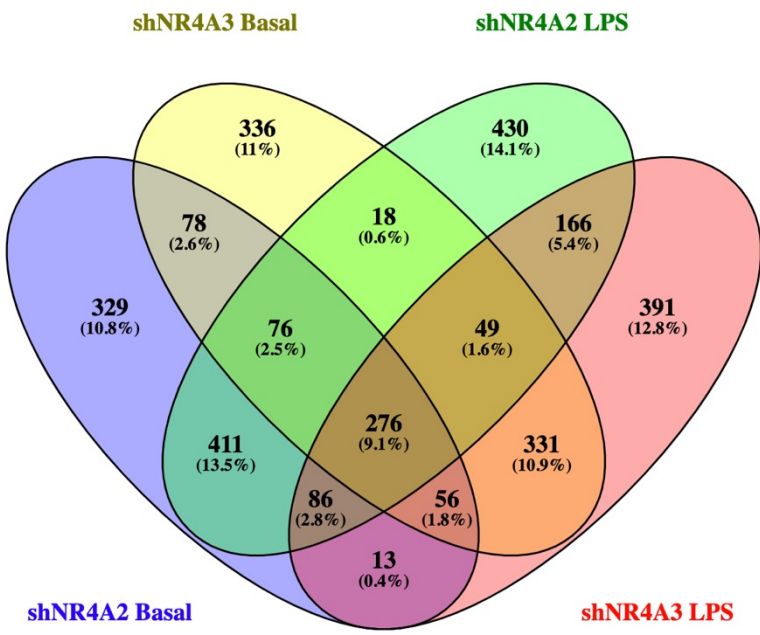


**B.**

	Cluster 4	Cluster 6	Cluster 5
<b>GO Term</b>	(i) Antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway, TAP-independent (GO:0002486) (ii) Antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway (GO:0002484) (iii) Antigen processing and presentation of endogenous peptide antigen via MHC class Ib (GO:0002476)	(i) T cell activation via T cell receptor contact with antigen bound to MHC molecule on antigen presenting cell (GO:0002291) (ii) Regulation of guanyl-nucleotide exchange factor activity (GO:1905097) (iii) Regulation of chemokine-mediated signaling pathway (GO:0070099)	(i) Positive regulation of monocyte aggregation (GO:1900625) (ii) p38MAPK cascade (GO:0038066) (iii) Cellular response to interferon-alpha (GO:0035457)
<b>Genes</b>	(i) <i>HLA-C, HLA-E, HLA-B, HLA-F, HLA-A, HLA-G, HLA-H</i> (ii) <i>HLA-C, HLA-E, HLA-B, HLA-F, HLA-A, HLA-G, HLA-H</i> (iii) <i>HLA-E, HLA-F, HLA-G, HLA-H, TAP2</i>	(i) <i>ITGAL, FGL2, ICAM1</i> (ii) <i>GPSM1, MET, CCPG1, PBXIP1</i> (iii) <i>EDN1, ROBO1, PADI2, SH2B3</i>	(i) <i>NR4A3, HAS2, AL133330</i> (ii) <i>ZFP36, ZFP36L1, LGALS9</i> (iii) <i>IFIT2, OAS1, IFIT3, AXL, GAS6PHYSIP</i>

**Figure. S5**

7. Genes that appear to be equally regulated by shNR4A2 and shNR4A3 in both the basal and stimulated state (276)

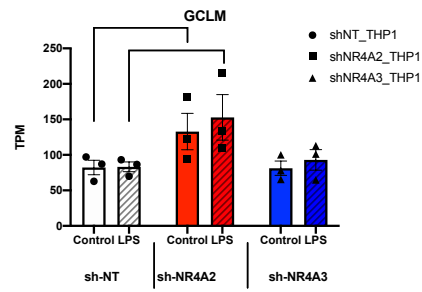


GO Term	<ul style="list-style-type: none"> <li>(i) Negative regulation of chemokine-mediated signaling pathway (GO:0070100)</li> <li>(ii) Amyloid-beta clearance (GO:0097242)</li> <li>(iii) Endothelial cell migration (GO:0043542)</li> <li>(iv) I-kappaB kinase/NF-kappaB signaling (GO:0007249)</li> </ul>
Genes	<ul style="list-style-type: none"> <li>(i) <i>ROBO1, PADI2, SH2B3</i></li> <li>(ii) <i>ITGB2, CD36, ABCA7, IGF1R</i></li> <li>(iii) <i>ITGB2, NRP1, DPP4, GPX1, LPXN, NRP1, ROBO1</i></li> <li>(iv) <i>TLR7, NLRC3, TIFAB, BCL3, TNIP2, IRAK1BP1</i></li> </ul>

## Fibroblast activation genes GO:0072537

Figure. S6

A.

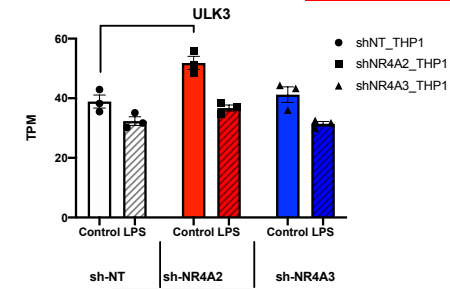


Padj

Padj

shNT Control vs shNR4A2 Control: <b>0.0044</b>	shNT Control vs shNR4A3 Control: 0.94
shNT + LPS vs shNR4A2 + LPS: <b>0.0016</b>	shNT + LPS vs shNR4A3 + LPS: 0.58

B.

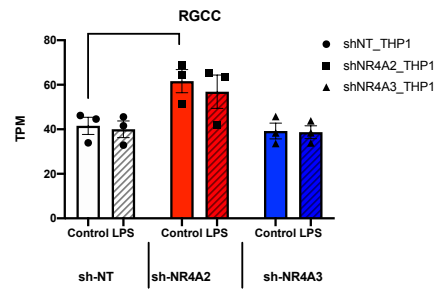


Padj

Padj

shNT Control vs shNR4A2 Control: <b>0.040</b>	shNT Control vs shNR4A3 Control: 0.71
shNT + LPS vs shNR4A2 + LPS: 0.27	shNT + LPS vs shNR4A3 + LPS: 0.96

C.

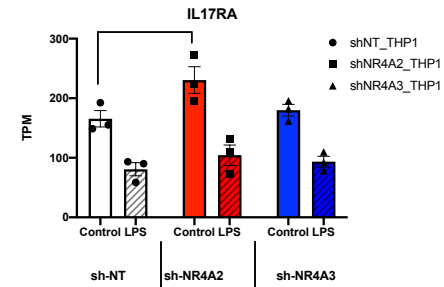


Padj

Padj

shNT Control vs shNR4A2 Control: <b>0.031</b>	shNT Control vs shNR4A3 Control: 0.95
shNT + LPS vs shNR4A2 + LPS: 0.052	shNT + LPS vs shNR4A3 + LPS: 0.98

D.



Padj

Padj

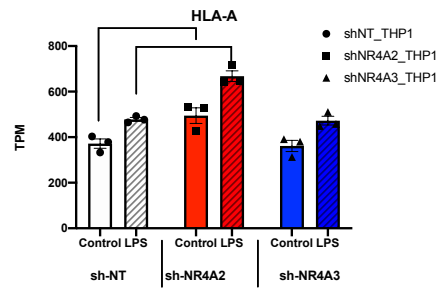
shNT Control vs shNR4A2 Control: <b>0.018</b>	shNT Control vs shNR4A3 Control: 0.49
shNT + LPS vs shNR4A2 + LPS: 0.20	shNT + LPS vs shNR4A3 + LPS: 0.36

## Antigen processing and presentation of exogenous

Peptide antigen via MHC class I,  
TAP independent GO:0002480

Figure. S7

A.



Padj

Padj

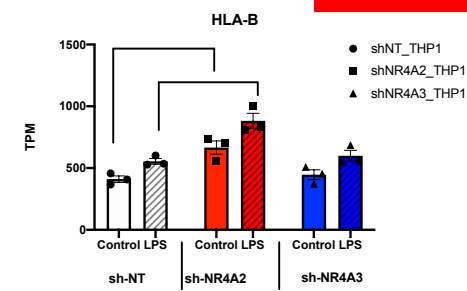
shNT Control vs shNR4A2 Control: **0.035**

shNT Control vs shNR4A3 Control: 0.99

shNT + LPS vs shNR4A2 + LPS: **0.00016**

shNT + LPS vs shNR4A3 + LPS: 0.87

B.



Padj

Padj

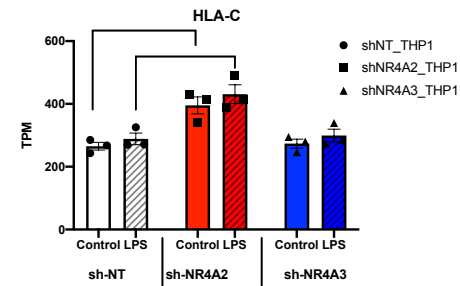
shNT Control vs shNR4A2 Control: **4.80 E-05**

shNT Control vs shNR4A3 Control: 0.57

shNT + LPS vs shNR4A2 + LPS: **9.93E-06**

shNT + LPS vs shNR4A3 + LPS: 0.50

C.



Padj

Padj

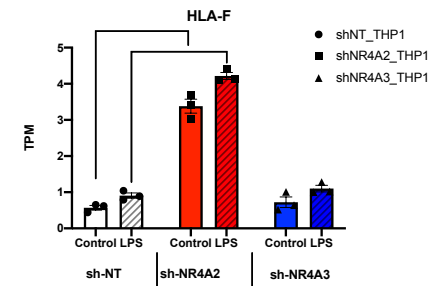
shNT Control vs shNR4A2 Control: **0.00061**

shNT Control vs shNR4A3 Control: 0.77

shNT + LPS vs shNR4A2 + LPS: **0.00046**

shNT + LPS vs shNR4A3 + LPS: 0.71

D.



Padj

Padj

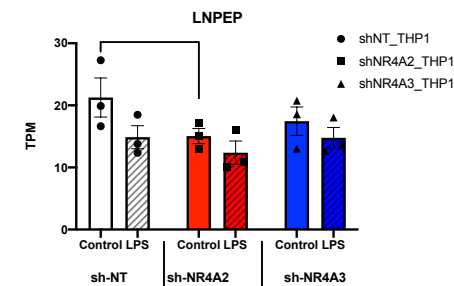
shNT Control vs shNR4A2 Control: **7.60E-11**

shNT Control vs shNR4A3 Control: 0.78

shNT + LPS vs shNR4A2 + LPS: **7.47 E-13**

shNT + LPS vs shNR4A3 + LPS: 0.71

E.



Padj

Padj

shNT Control vs shNR4A2 Control: **0.029**

shNT Control vs shNR4A3 Control: 0.47

shNT + LPS vs shNR4A2 + LPS: 0.55

shNT + LPS vs shNR4A3 + LPS: 0.91

# Antigen processing and presentation of endogenous peptide antigen GO:0002483

shNR4A2 selective – Cluster 1

**Figure. S8**

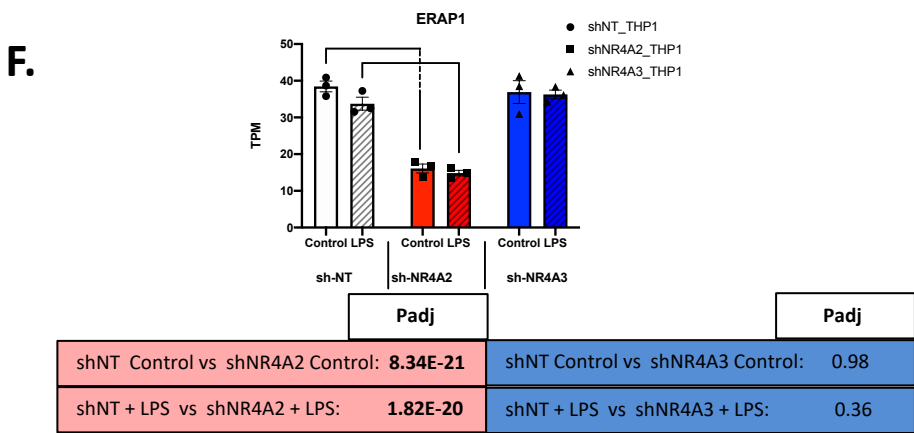
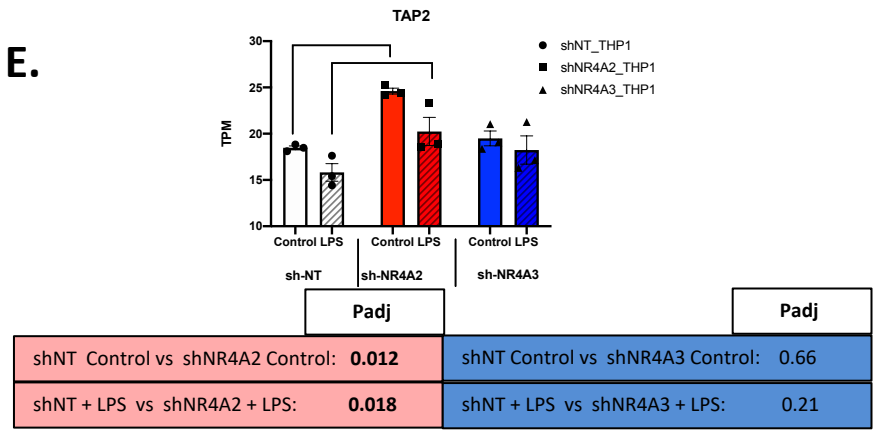
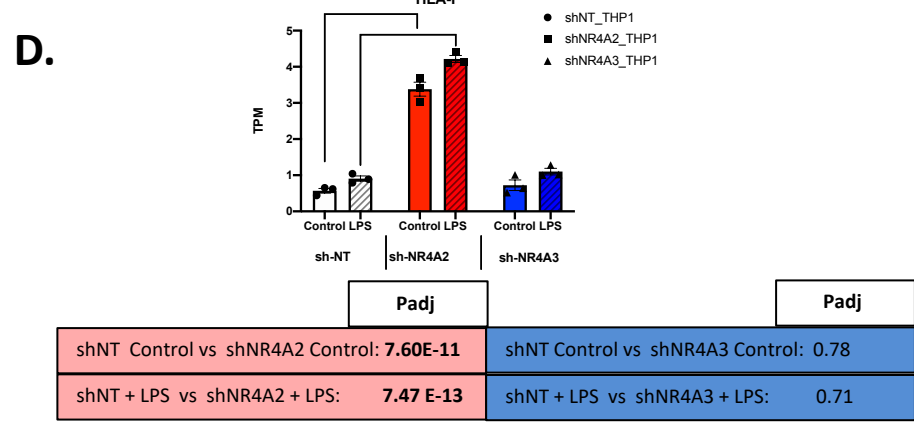
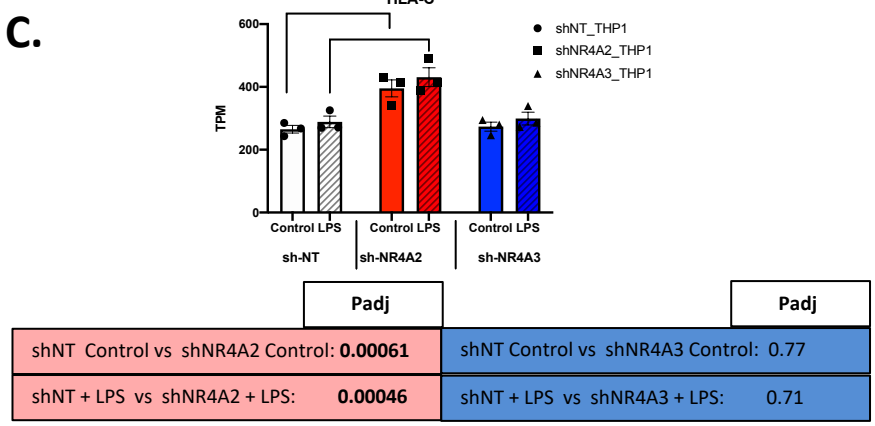
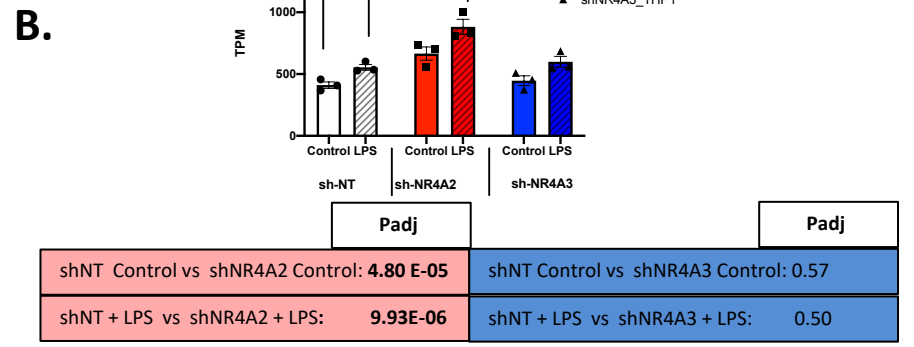
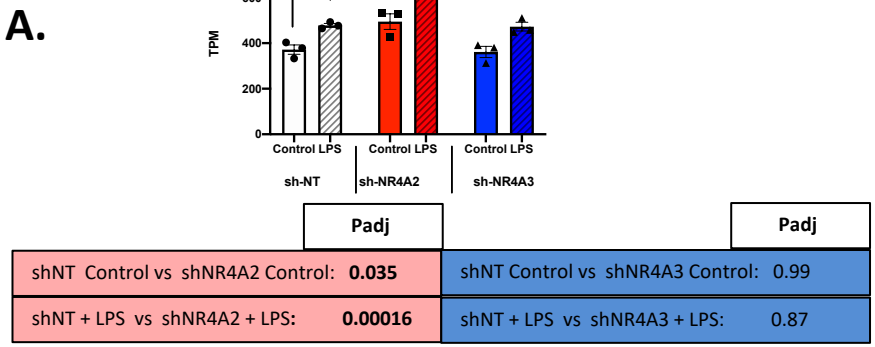


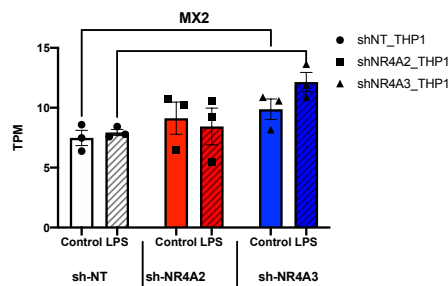


Figure. S9

Response to interferon alpha GO:035455

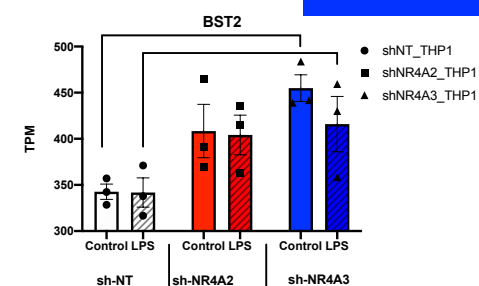
shNR4A3 selective – Cluster 2

A.



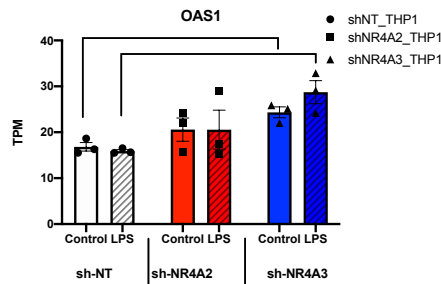
Padj	Padj
shNT Control vs shNR4A2 Control: 0.39	shNT Control vs shNR4A3 Control: <b>0.024</b>
shNT + LPS vs shNR4A2 + LPS: 0.77	shNT + LPS vs shNR4A3 + LPS: <b>8.87E-06</b>

B.



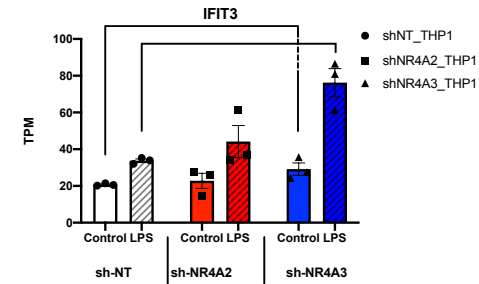
Padj	Padj
shNT Control vs shNR4A2 Control: 0.25	shNT Control vs shNR4A3 Control: <b>0.00019</b>
shNT + LPS vs shNR4A2 + LPS: 0.095	shNT + LPS vs shNR4A3 + LPS: <b>0.045</b>

C.



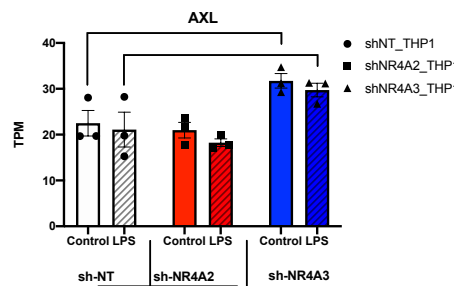
Padj	Padj
shNT Control vs shNR4A2 Control: 0.31	shNT Control vs shNR4A3 Control: <b>0.00011</b>
shNT + LPS vs shNR4A2 + LPS: 0.24	shNT + LPS vs shNR4A3 + LPS: <b>1.64E-07</b>

D.



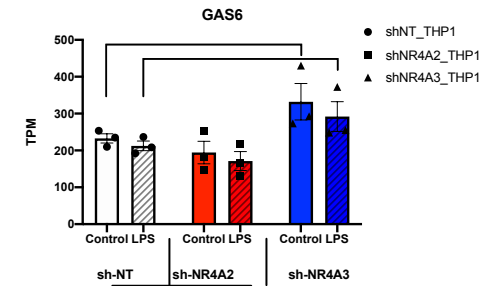
Padj	Padj
shNT Control vs shNR4A2 Control: 0.80	shNT Control vs shNR4A3 Control: <b>0.0083</b>
shNT + LPS vs shNR4A2 + LPS: 0.20	shNT + LPS vs shNR4A3 + LPS: <b>6.84E-12</b>

E.



Padj	Padj
shNT Control vs shNR4A2 Control: 0.829	shNT Control vs shNR4A3 Control: <b>0.0076</b>
shNT + LPS vs shNR4A2 + LPS: 0.747	shNT + LPS vs shNR4A3 + LPS: <b>0.039</b>

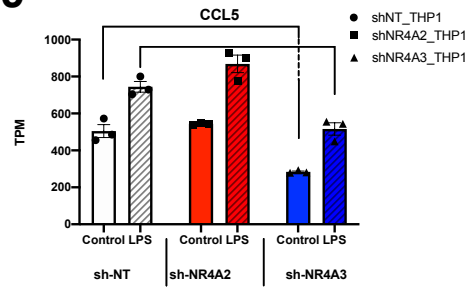
F.



Padj	Padj
shNT Control vs shNR4A2 Control: 0.439	shNT Control vs shNR4A3 Control: <b>0.0068</b>
shNT + LPS vs shNR4A2 + LPS: 0.494	shNT + LPS vs shNR4A3 + LPS: <b>0.026</b>

Figure. S10

A.

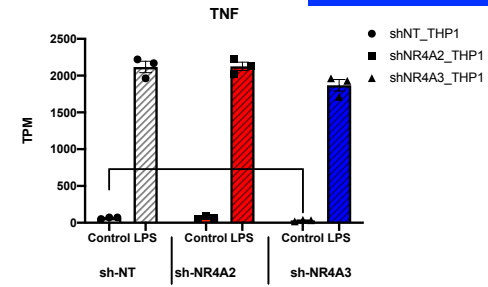


Padj

Padj

shNT Control vs shNR4A2 Control: 0.72	shNT Control vs shNR4A3 Control: <b>1.06E-09</b>
shNT + LPS vs shNR4A2 + LPS: 0.20	shNT + LPS vs shNR4A3 + LPS: <b>0.0101</b>

B.

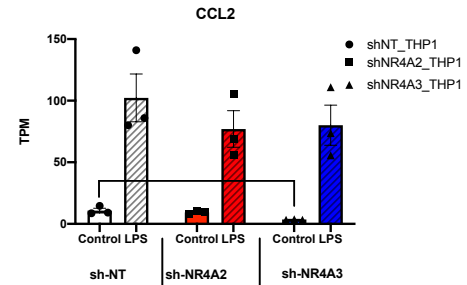


Padj

Padj

shNT Control vs shNR4A2 Control: 0.78	shNT Control vs shNR4A3 Control: <b>3.45E-05</b>
shNT + LPS vs shNR4A2 + LPS: 0.81	shNT + LPS vs shNR4A3 + LPS: 0.65

C.

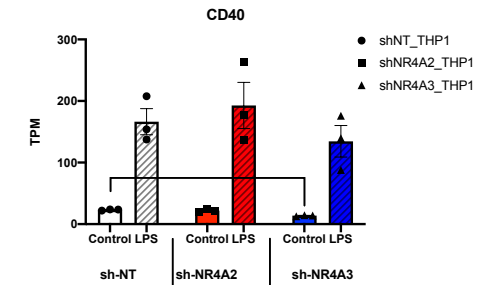


Padj

Padj

shNT Control vs shNR4A2 Control: 0.67	shNT Control vs shNR4A3 Control: <b>4.07E-06</b>
shNT + LPS vs shNR4A2 + LPS: 0.51	shNT + LPS vs shNR4A3 + LPS: 0.79

D.

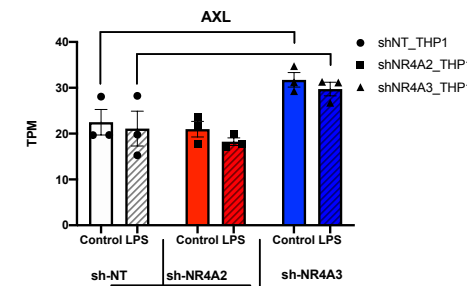


Padj

Padj

shNT Control vs shNR4A2 Control: 0.87	shNT Control vs shNR4A3 Control: <b>0.00014</b>
shNT + LPS vs shNR4A2 + LPS: 0.58	shNT + LPS vs shNR4A3 + LPS: 0.79

E.

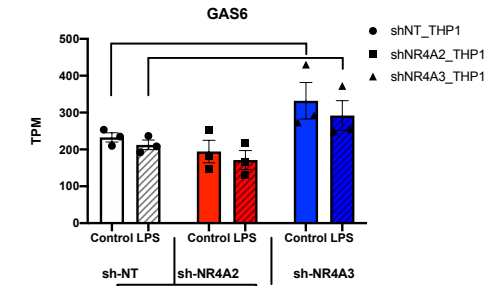


Padj

Padj

shNT Control vs shNR4A2 Control: 0.83	shNT Control vs shNR4A3 Control: <b>0.0076</b>
shNT + LPS vs shNR4A2 + LPS: 0.75	shNT + LPS vs shNR4A3 + LPS: <b>0.039</b>

F.



Padj

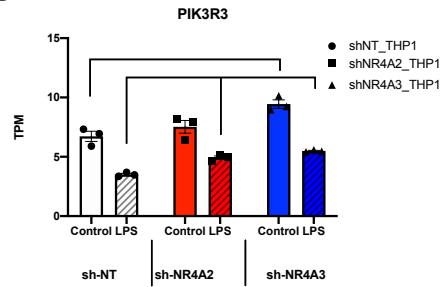
Padj

shNT Control vs shNR4A2 Control: 0.44	shNT Control vs shNR4A3 Control: <b>0.0068</b>
shNT + LPS vs shNR4A2 + LPS: 0.49	shNT + LPS vs shNR4A3 + LPS: <b>0.026</b>

# Protein Kinase B Signaling GO:0043491

## Figure. S10

### G.



Padj

Padj

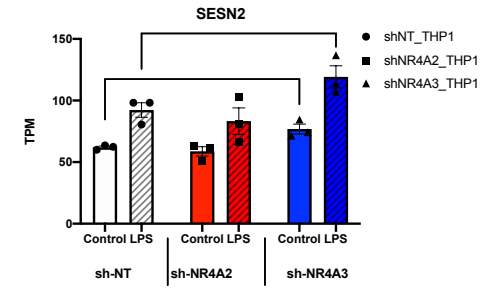
shNT Control vs shNR4A2 Control: 0.65

shNT Control vs shNR4A3 Control: **0.0035**

shNT + LPS vs shNR4A2 + LPS: **0.018**

shNT + LPS vs shNR4A3 + LPS: **0.00068**

### H.



Padj

Padj

shNT Control vs shNR4A2 Control: 0.85

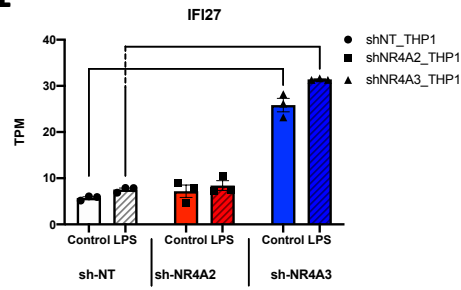
shNT Control vs shNR4A3 Control: **0.018**

shNT + LPS vs shNR4A2 + LPS: 0.86

shNT + LPS vs shNR4A3 + LPS: **0.025**

Figure. S11

A.

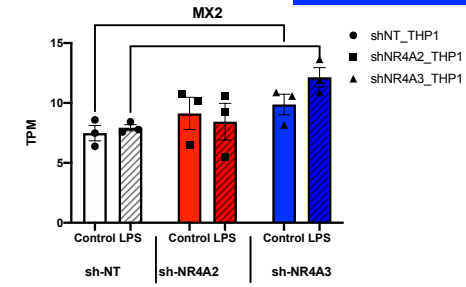


Padj

Padj

shNT Control vs shNR4A2 Control: 0.48	shNT Control vs shNR4A3 Control: <b>1.47E-45</b>
shNT + LPS vs shNR4A2 + LPS: 0.63	shNT + LPS vs shNR4A3 + LPS: <b>2.2E-48</b>

B.

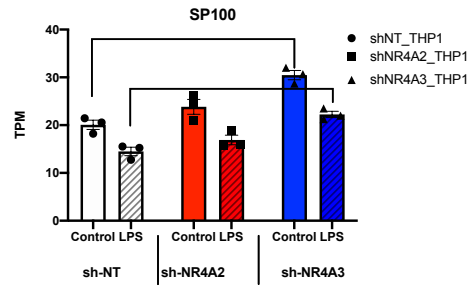


Padj

Padj

shNT Control vs shNR4A2 Control: 0.39	shNT Control vs shNR4A3 Control: <b>0.024</b>
shNT + LPS vs shNR4A2 + LPS: 0.77	shNT + LPS vs shNR4A3 + LPS: <b>8.87E-06</b>

C.

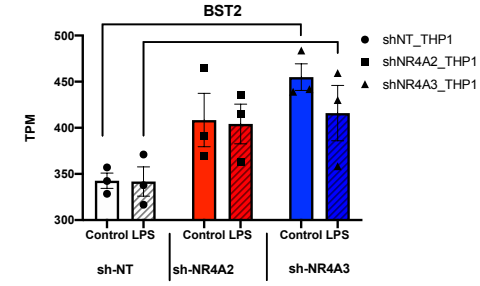


Padj

Padj

shNT Control vs shNR4A2 Control: 0.24	shNT Control vs shNR4A3 Control: <b>2.08E-07</b>
shNT + LPS vs shNR4A2 + LPS: 0.13	shNT + LPS vs shNR4A3 + LPS: <b>5.35E-08</b>

D.

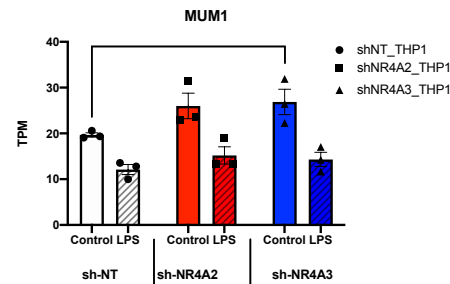


Padj

Padj

shNT Control vs shNR4A2 Control: 0.25	shNT Control vs shNR4A3 Control: <b>0.00019</b>
shNT + LPS vs shNR4A2 + LPS: 0.095	shNT + LPS vs shNR4A3 + LPS: <b>0.045</b>

E.

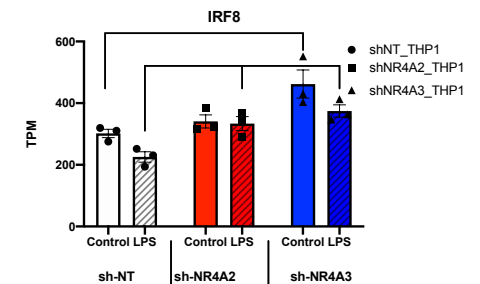


Padj

Padj

shNT Control vs shNR4A2 Control: 0.067	shNT Control vs shNR4A3 Control: <b>0.0021</b>
shNT + LPS vs shNR4A2 + LPS: 0.12	shNT + LPS vs shNR4A3 + LPS: 0.24

F.



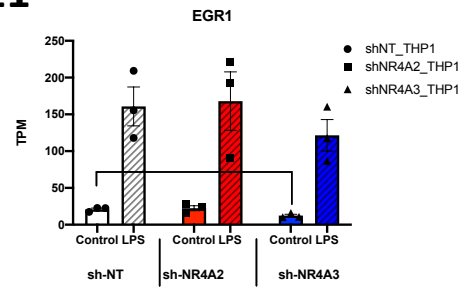
Padj

Padj

shNT Control vs shNR4A2 Control: 0.51	shNT Control vs shNR4A3 Control: <b>4.08E-06</b>
shNT + LPS vs shNR4A2 + LPS: <b>1.31E-5</b>	shNT + LPS vs shNR4A3 + LPS: <b>2.81E-11</b>

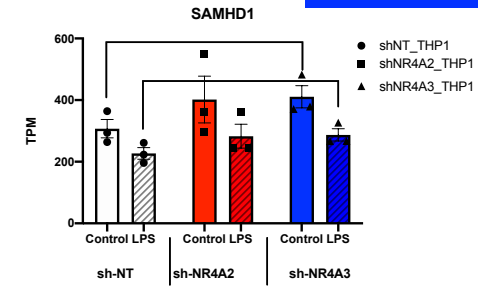
Figure. S11

G.



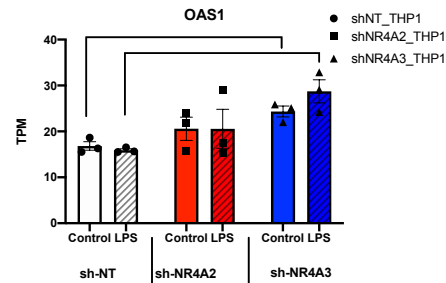
Padj		Padj	
shNT Control vs shNR4A2 Control:	0.85	shNT Control vs shNR4A3 Control:	<b>0.0030</b>
shNT + LPS vs shNR4A2 + LPS:	0.92	shNT + LPS vs shNR4A3 + LPS:	0.35

H.



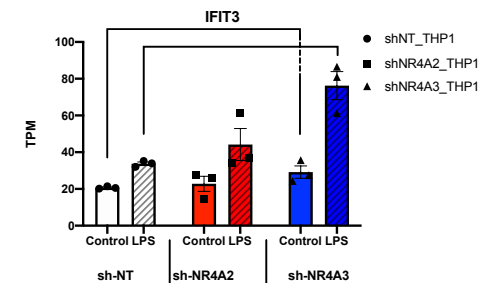
Padj		Padj	
shNT Control vs shNR4A2 Control:	0.20	shNT Control vs shNR4A3 Control:	<b>0.012</b>
shNT + LPS vs shNR4A2 + LPS:	0.20	shNT + LPS vs shNR4A3 + LPS:	<b>0.048</b>

I.



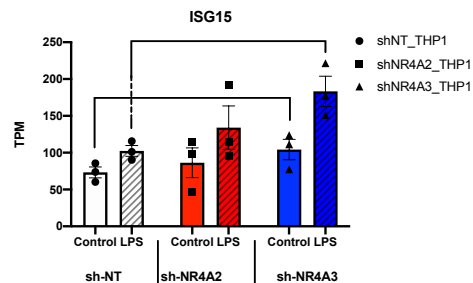
Padj		Padj	
shNT Control vs shNR4A2 Control:	0.31	shNT Control vs shNR4A3 Control:	<b>0.00011</b>
shNT + LPS vs shNR4A2 + LPS:	0.24	shNT + LPS vs shNR4A3 + LPS:	<b>1.64E-07</b>

J.



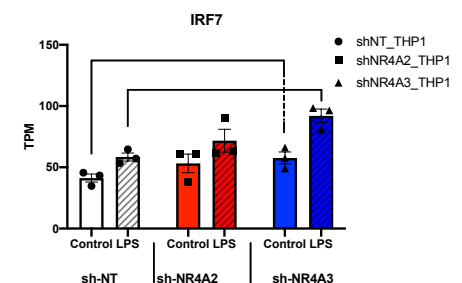
Padj		Padj	
shNT Control vs shNR4A2 Control:	0.80	shNT Control vs shNR4A3 Control:	<b>0.0083</b>
shNT + LPS vs shNR4A2 + LPS:	0.20	shNT + LPS vs shNR4A3 + LPS:	<b>6.84E-12</b>

K.



Padj		Padj	
shNT Control vs shNR4A2 Control:	0.82	shNT Control vs shNR4A3 Control:	<b>0.016</b>
shNT + LPS vs shNR4A2 + LPS:	0.25	shNT + LPS vs shNR4A3 + LPS:	<b>7.41E-06</b>

L.

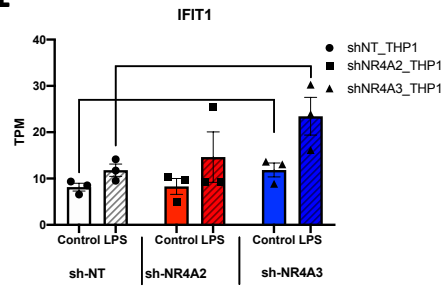


Padj		Padj	
shNT Control vs shNR4A2 Control:	0.23	shNT Control vs shNR4A3 Control:	<b>0.0042</b>
shNT + LPS vs shNR4A2 + LPS:	0.24	shNT + LPS vs shNR4A3 + LPS:	<b>3.4E-05</b>

## Type 1 interferon signaling pathway GO:0060337

Figure. S11

M.



Padj

Padj

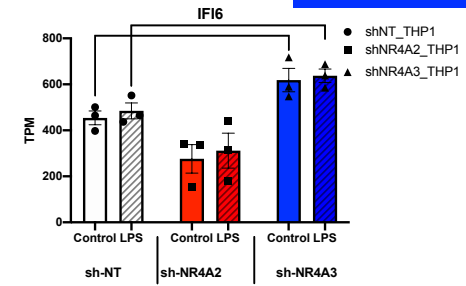
shNT Control vs shNR4A2 Control: 0.97

shNT Control vs shNR4A3 Control: **0.025**

shNT + LPS vs shNR4A2 + LPS: 0.77

shNT + LPS vs shNR4A3 + LPS: **0.00011**

N.



Padj

Padj

shNT Control vs shNR4A2 Control: 0.26

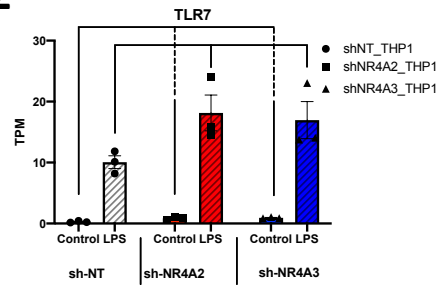
shNT Control vs shNR4A3 Control: **0.0086**

shNT + LPS vs shNR4A2 + LPS: 0.12

shNT + LPS vs shNR4A3 + LPS: **0.013**

Figure. S12

A.

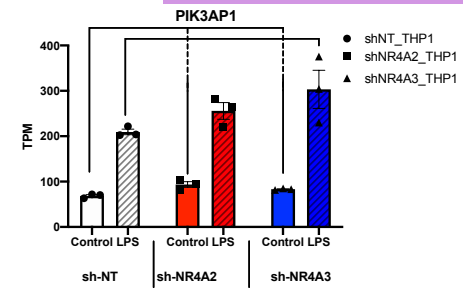


Padj

Padj

shNT Control vs shNR4A2 Control: <b>0.042</b>	shNT Control vs shNR4A3 Control: <b>0.013</b>
shNT + LPS vs shNR4A2 + LPS: <b>0.0011</b>	shNT + LPS vs shNR4A3 + LPS: <b>0.0034</b>

B.

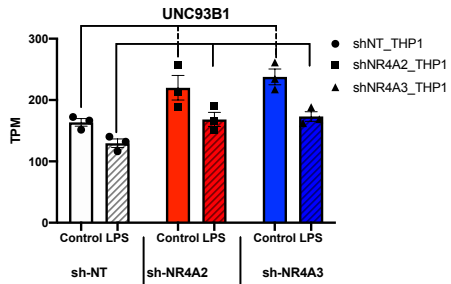


Padj

Padj

shNT Control vs shNR4A2 Control: <b>0.0047</b>	shNT Control vs shNR4A3 Control: <b>0.011</b>
shNT + LPS vs shNR4A2 + LPS: 0.12	shNT + LPS vs shNR4A3 + LPS: <b>0.0094</b>

C.

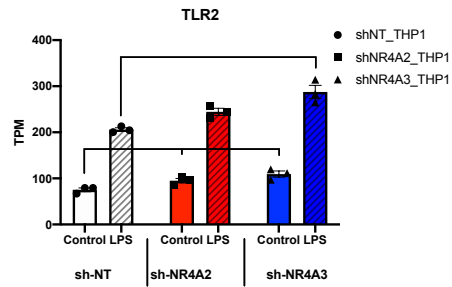


Padj

Padj

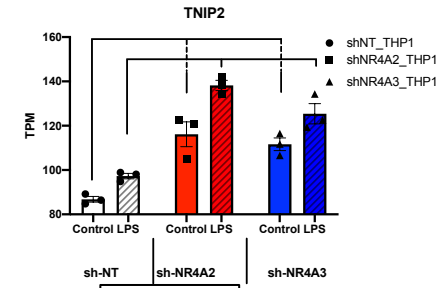
shNT Control vs shNR4A2 Control: <b>0.035</b>	shNT Control vs shNR4A3 Control: <b>6.20E-06</b>
shNT + LPS vs shNR4A2 + LPS: <b>0.0041</b>	shNT + LPS vs shNR4A3 + LPS: <b>0.00012</b>

A.



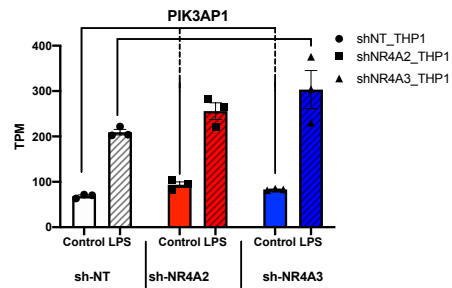
Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>0.046</b>	shNT Control vs shNR4A3 Control:	<b>3.33E-06</b>
shNT + LPS vs shNR4A2 + LPS:	0.079	shNT + LPS vs shNR4A3 + LPS:	<b>8.74E-05</b>

B.



Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>0.0123</b>	shNT Control vs shNR4A3 Control:	<b>0.0029</b>
shNT + LPS vs shNR4A2 + LPS:	<b>5.63E-05</b>	shNT + LPS vs shNR4A3 + LPS:	<b>0.0020</b>

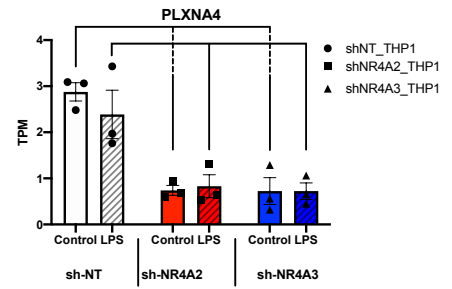
C.



Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>0.0047</b>	shNT Control vs shNR4A3 Control:	<b>0.011</b>
shNT + LPS vs shNR4A2 + LPS:	0.12	shNT + LPS vs shNR4A3 + LPS:	<b>0.0094</b>

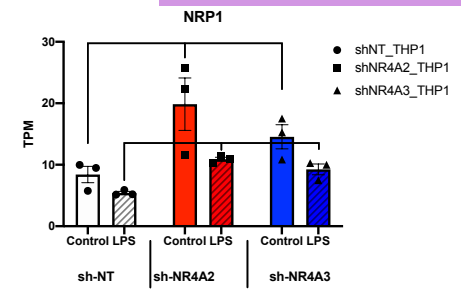


A.



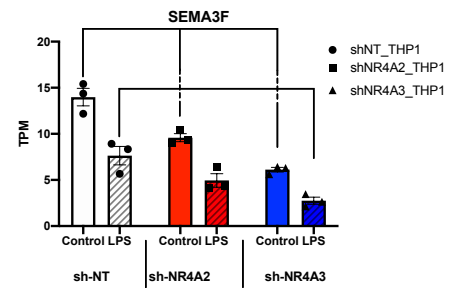
Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>1.39E-16</b>	shNT Control vs shNR4A3 Control:	<b>0.0054</b>
shNT + LPS vs shNR4A2 + LPS:	<b>0.00015</b>	shNT + LPS vs shNR4A3 + LPS:	<b>6.77E-07</b>

B.



Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>0.022</b>	shNT Control vs shNR4A3 Control:	<b>0.00027</b>
shNT + LPS vs shNR4A2 + LPS:	<b>2.4E-12</b>	shNT + LPS vs shNR4A3 + LPS:	<b>2.99E-05</b>

C.



Padj		Padj	
shNT Control vs shNR4A2 Control:	<b>0.014</b>	shNT Control vs shNR4A3 Control:	<b>8.87E-10</b>
shNT + LPS vs shNR4A2 + LPS:	0.081	shNT + LPS vs shNR4A3 + LPS:	<b>6.74E-08</b>