

Supplementary material for *Talaromyces marneffe* suppresses macrophage inflammation by regulating host alternative splicing

Running title: *T. marneffe* regulates host AS

Wudi Wei^{1,2#}, Gang Wang^{1#}, Hong Zhang^{2#}, Xiuli Bao^{1#}, Sanqi An^{1,2}, Qiang Luo², Jinhao He², Lixiang Chen¹, Chuanyi Ning^{2,3*}, Jingzhen Lai^{2,4}, Zongxiang Yuan¹, Rongfeng Chen^{1,2}, Junjun Jiang^{1,2*}, Li Ye^{1,2*} and Hao Liang^{1,2,4*}

¹ Guangxi Key Laboratory of AIDS Prevention and Treatment, School of Public Health, Guangxi Medical University, Nanning 530021, Guangxi, China

² Guangxi-ASEAN Collaborative Innovation Center for Major Disease Prevention and Treatment, Life Sciences Institute, Guangxi Medical University, Nanning 530021, Guangxi, China

³ Nursing College, Guangxi Medical University, Nanning 530021, Guangxi, China

⁴ Guangxi Biobank, Life Sciences Institute, Guangxi Medical University, Nanning 530021, Guangxi, China

#Wudi Wei, Gang Wang, Hong Zhang and Xiuli Bao contributed equally to this paper.

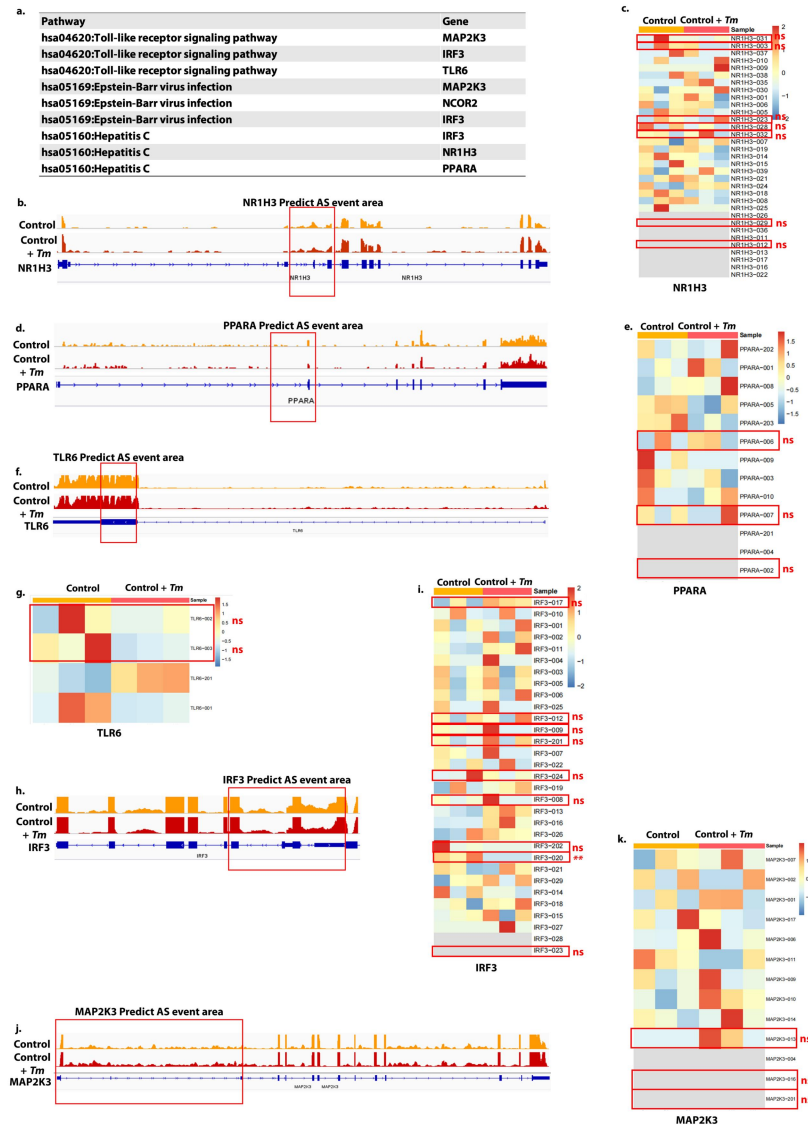
*Corresponding authors

Hao Liang, Email: lianghao@gxmu.edu.cn; Tel: 86-771-5323713; Fax: 86-771-5351624;

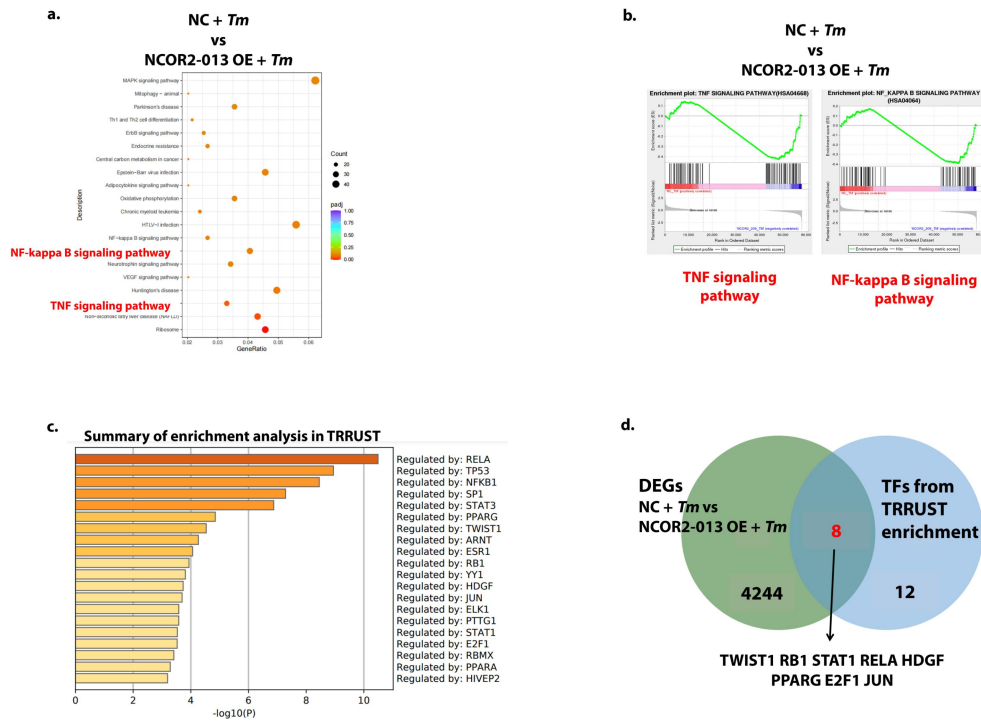
Li Ye, Email: yeli@gxmu.edu.cn; Tel: 86-771-5334215; Fax: 86-771-5351624

Junjun Jiang, Email: jiangjunjun@gxmu.edu.cn; Tel: 86-771-5334215; Fax: 86-771-5351624

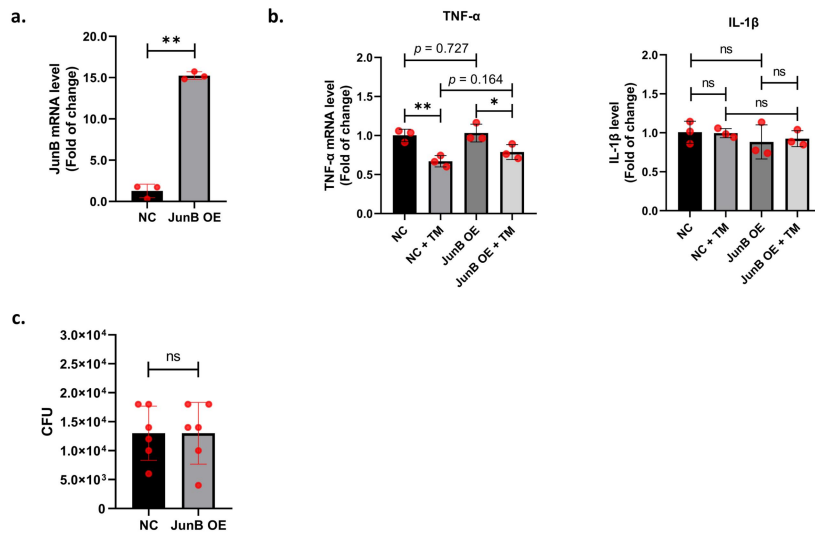
Keywords: *Talaromyces marneffe*, macrophages, NCOR2-013, TUT1, alternative splicing



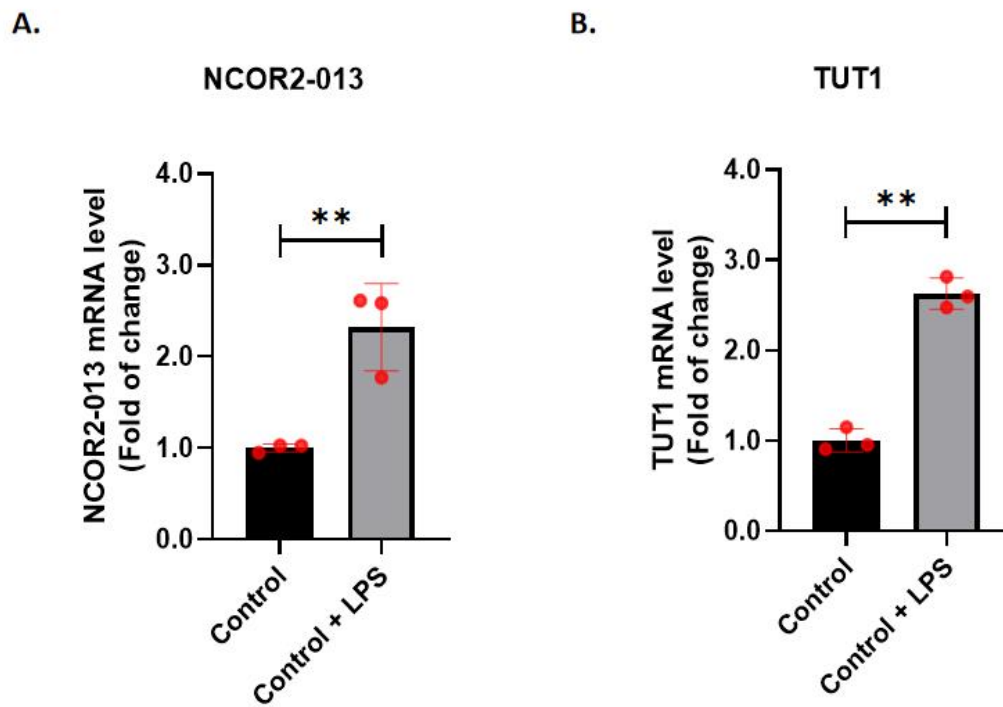
Supplementary Figure 1. The heatmaps and track plots of *NR1H3*, *PPARA*, *IRF3*, *MAP2K3* and *TLR6* transcripts. The human THP-1 macrophages were infected with *T. marneffei* conidia (MOI = 10) for 24 h. (a) Summary of the abundance of 3 KEGG pathways according to ES-type AS genes, with $FDR < 0.05$ and $|Lnclevel| > 0.5$ were exhibited. (b, d, f, h, j) Genome tracks plots show the reads from *NR1H3*, *PPARA*, *TLR6*, *IRF3*, *MAP2K3* genes and predicted AS areas by rMATS in *T. marneffei*-infected or uninfected macrophages at 24 h post infection. Gene coding regions and annotations are indicated in blue at the bottom. The exons and introns are represented by rectangles and straight lines, respectively. The red box represents the site of AS predicted. (c, e, g, k, i) The heatmap exhibits the expression levels of different transcripts of *NR1H3*, *PPARA*, *TLR6*, *IRF3*, *MAP2K3*. The red boxes represent the transcripts that are produced by predicted AS events and are known to exist. DESeq2 package was used to determine significance, denoted by * ($P_{adj} < 0.05$), ** ($P_{adj} < 0.01$), and ns (not significant). MOI, multiplicity of infection; *Tm*, *T. marneffei*.



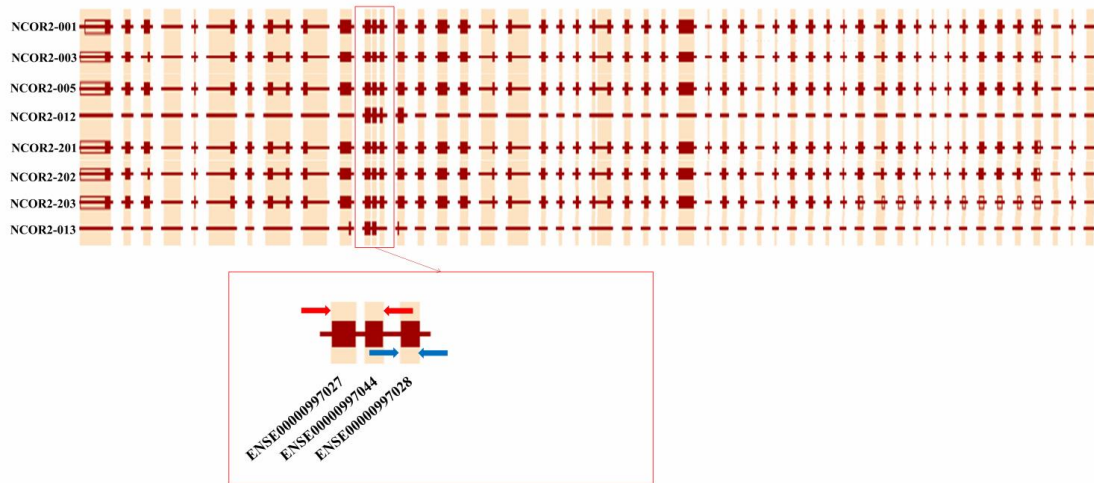
Supplementary Figure 2. Transcriptome profiles of *T. marneffei*-infected NCRO2-013 overexpressing THP-1 macrophages. The NCRO2-013 overexpressing THP-1 macrophages and control cells were infected with *T. marneffei* conidia at a MOI of 10 for 24 h. (a-b) KEGG pathway (a) and GSEA (b) enrichment analysis of DEGs (NCRO2-013 overexpressing THP-1 macrophages vs. control cells). (c)TRRUST analysis was performed to predict the set of transcription factors regulating DEGs. (d) The 20 transcription factors predicted by TRRUST analysis were intersected with DEGs, and 8 transcription factors were obtained, including TWIST1, RB1, STAT1, RELA, HDGF, PPARG, E2F1 and JUN, which may play a role in the regulation of *T. marneffei* infection by NCRO2-013. NC, negative control; NCOR2-013 OE, NCRO2-013 overexpression; TFs, transcription factors; *Tm*, *T. marneffei*.



Supplementary Figure 3. JunB overexpression effects on *T. marneffei* infection in THP-1 Macrophages. (a) JunB overexpression in THP-1 macrophages was confirmed by RT-qPCR (n = 3 biological replicates, data are presented as mean values \pm SD). (b, c) The JunB overexpressing THP-1 macrophages and control cells were infected with *T. marneffei* conidia (MOI = 10) for 24 h. The expression of *TNF- α* and *IL-1 β* was detected by RT-qPCR (b) (n = 3 biological replicates, data are presented as mean values \pm SD). *T. marneffei* CFUs were detected in JunB overexpressing THP-1 macrophages and control cells (c) (n = 6 biological replicates, data are presented as mean values \pm SD). Two-tailed Student's *t*-test was used to determine significance, denoted by * ($P < 0.05$), ** ($P < 0.01$), and ns (not significant). MOI, multiplicity of infection; NC, negative control; JunB OE, JunB overexpression; *Tm*, *T. marneffei*.



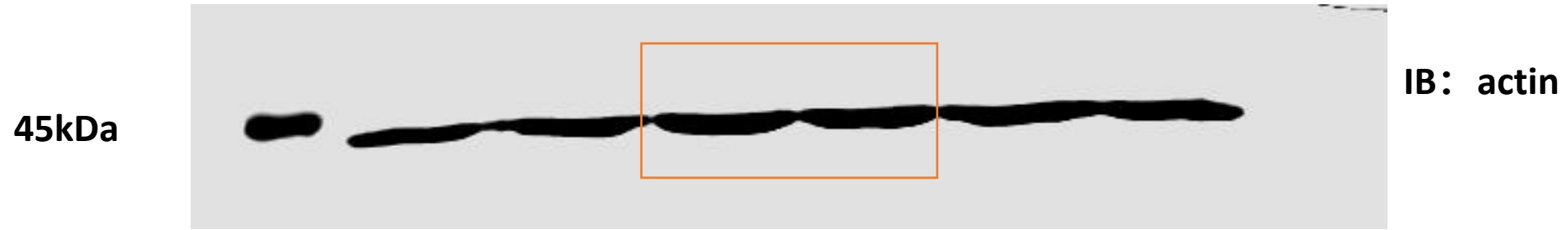
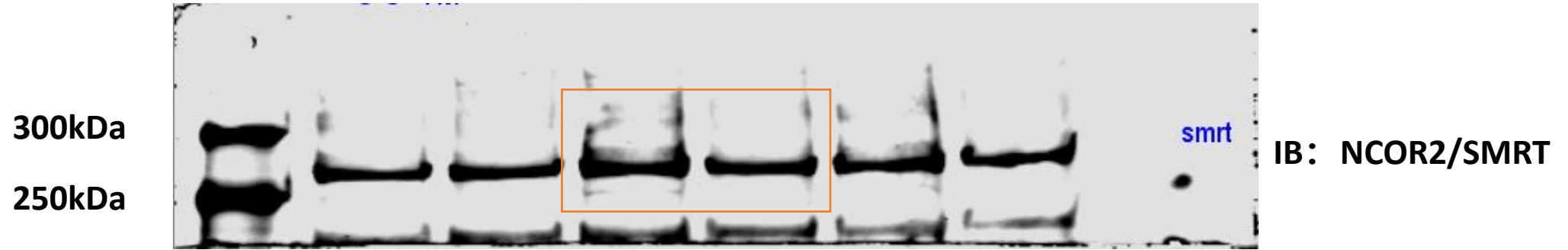
Supplementary Figure 4. THP-1 macrophages were stimulated with LPS (500 ng/mL) for 24 h. The expression of *NCOR2-013* (A) and *TUT1* (B) was detected by RT-qPCR. All data are shown as mean \pm SD from three biological replicates ($n = 3$). Two-tailed Student's *t*-test was used to determine significance, denoted by * ($P < 0.05$), ** ($P < 0.01$), and ns (not significant).



Supplementary Figure 5 . Primer design principles for calculating *NCOR2-013* expression levels. Exons 10 (ENSE00000997027) and 11 (ENSE00000997044) are all included among transcripts of *NCOR2*, which contain exon 12 (ENSE00000997028), while *NCOR2-013* transcript contains only exons 10 and 11, but not exon 12. Therefore, two pairs of primers were designed based on the combined sequence of exons 10 and 11 and the sequence of exon 12. The expression levels of these two pairs of primers were detected by qPCR. Finally, the expression level of exon 12 was subtracted from the expression level of exon 10/11 to indirectly calculate the expression level of *NCOR2-013* transcript.

Supplementary Figure 6
Unedited/uncropped western blot gels

Figure 2G



kDa

300

250

200

160

130

100

72

45

25

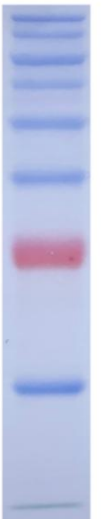


Figure 3C

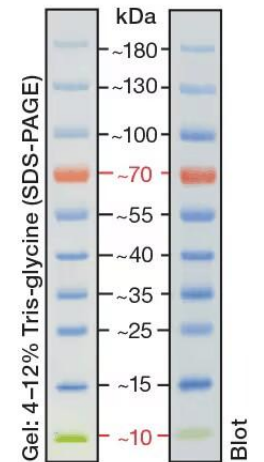
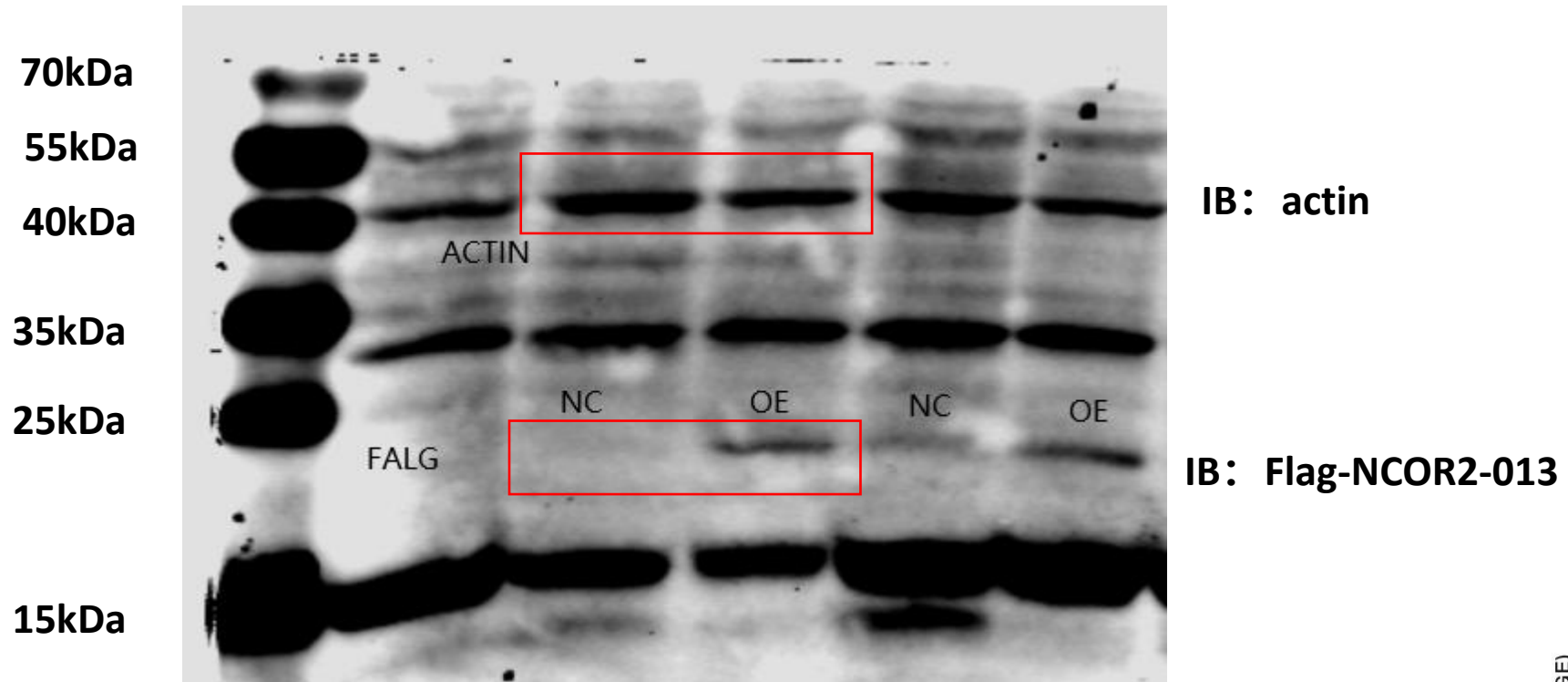
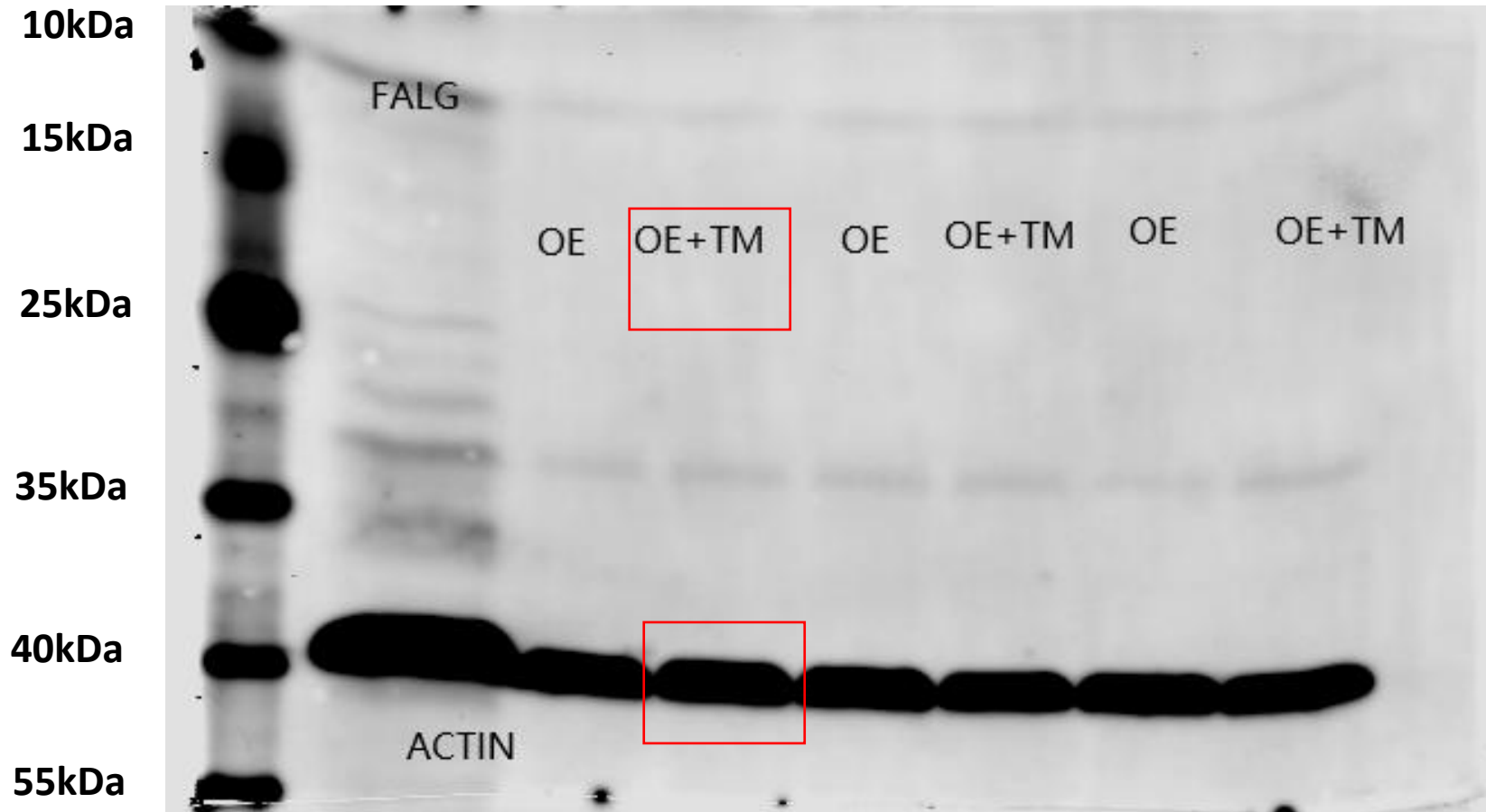


Figure 3E Cytoplasm



IB: Flag-NCOR2-013

IB: actin

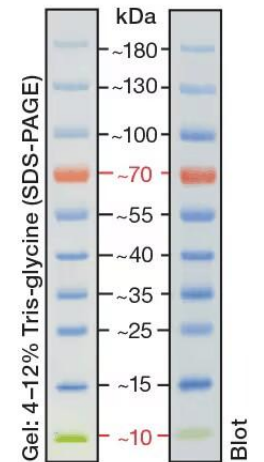
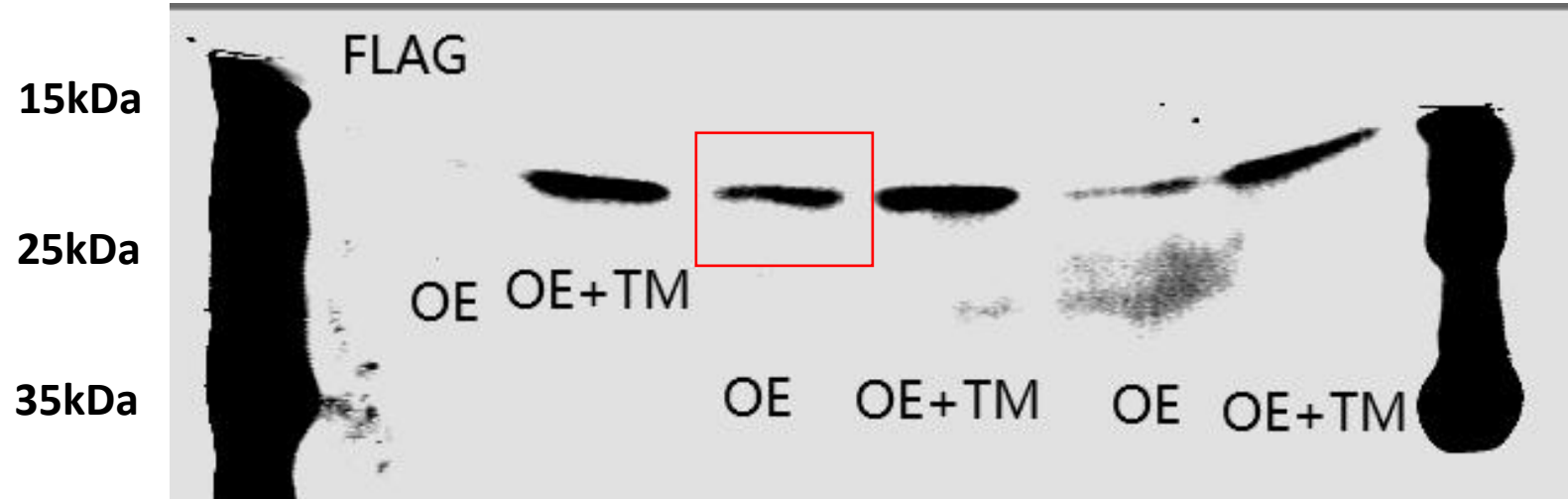
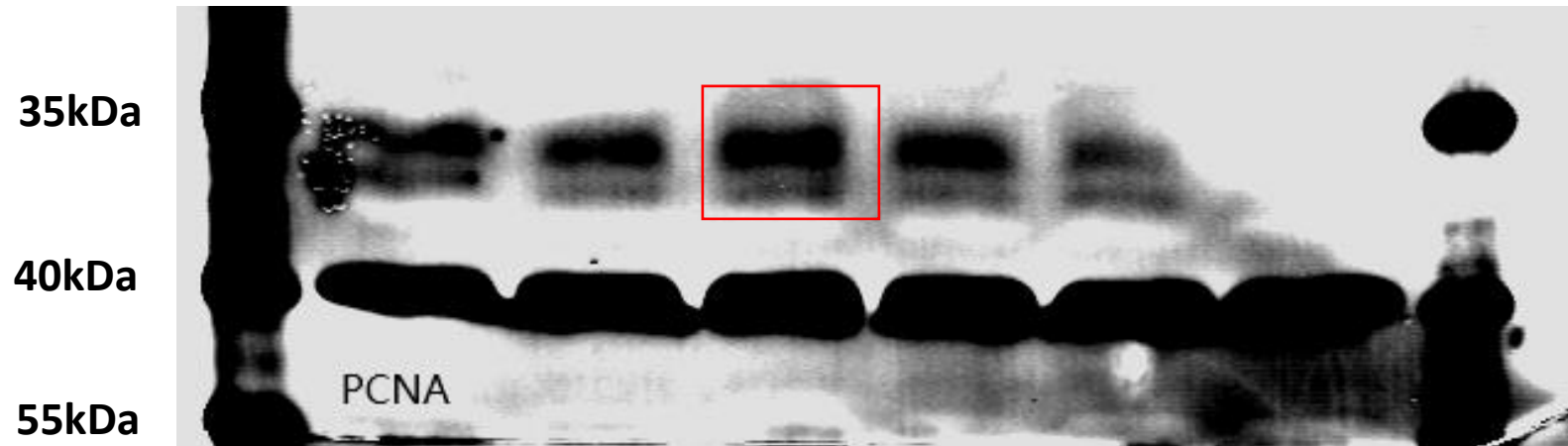


Figure 3E Nucleus



IB: Flag-NCOR2-013



IB: PCNA

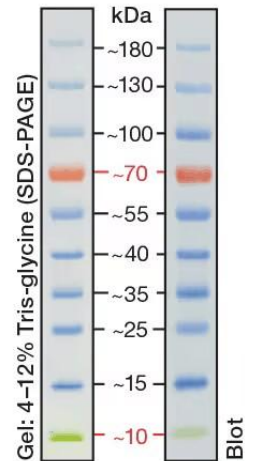


Figure 4B IP: Flag, IB: Flag-NCOR2-013, IB: JunB

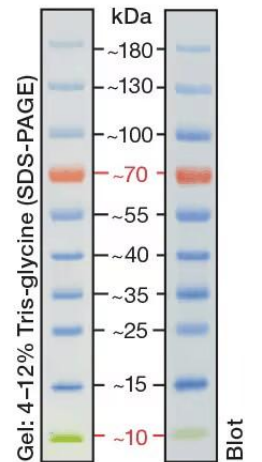
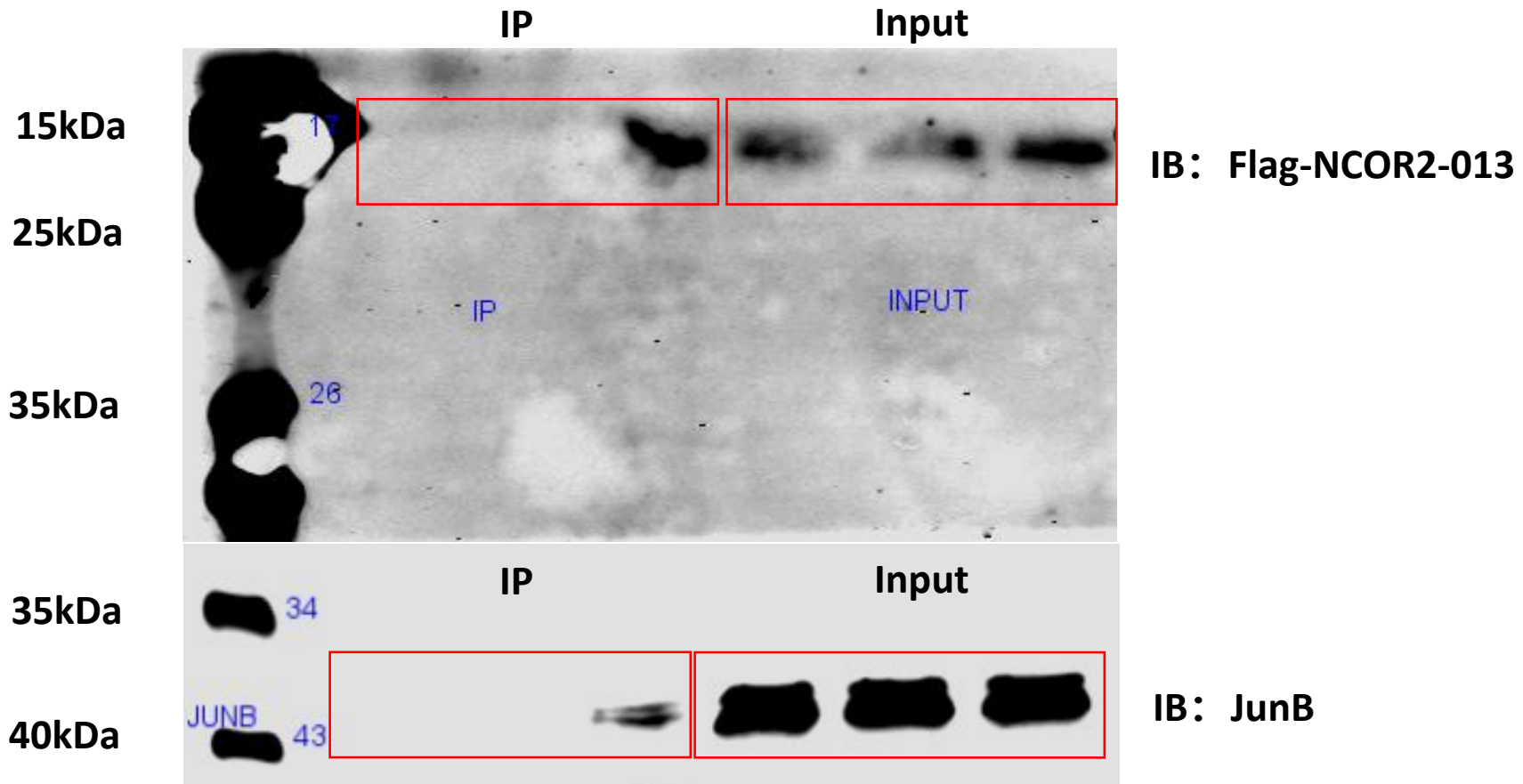


Figure 4B IP: Flag IB: TBL1XR1/TBLR1, IB: HDAC3

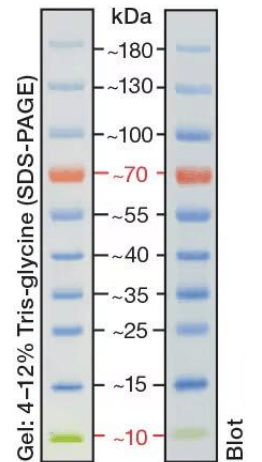
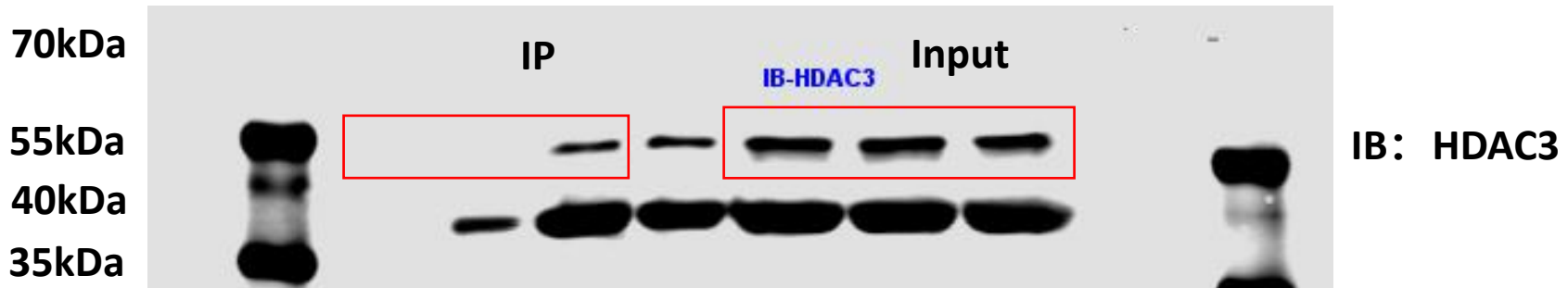
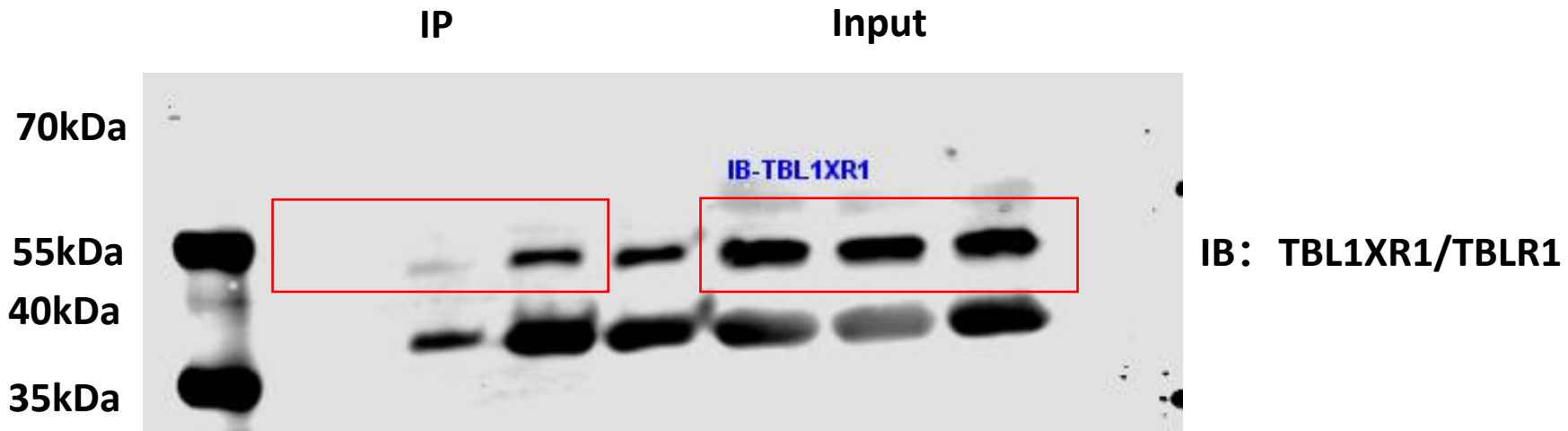


Figure 4B IP: Flag IB: NCOR2/SMRT

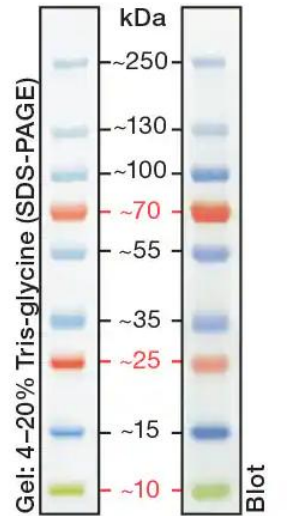
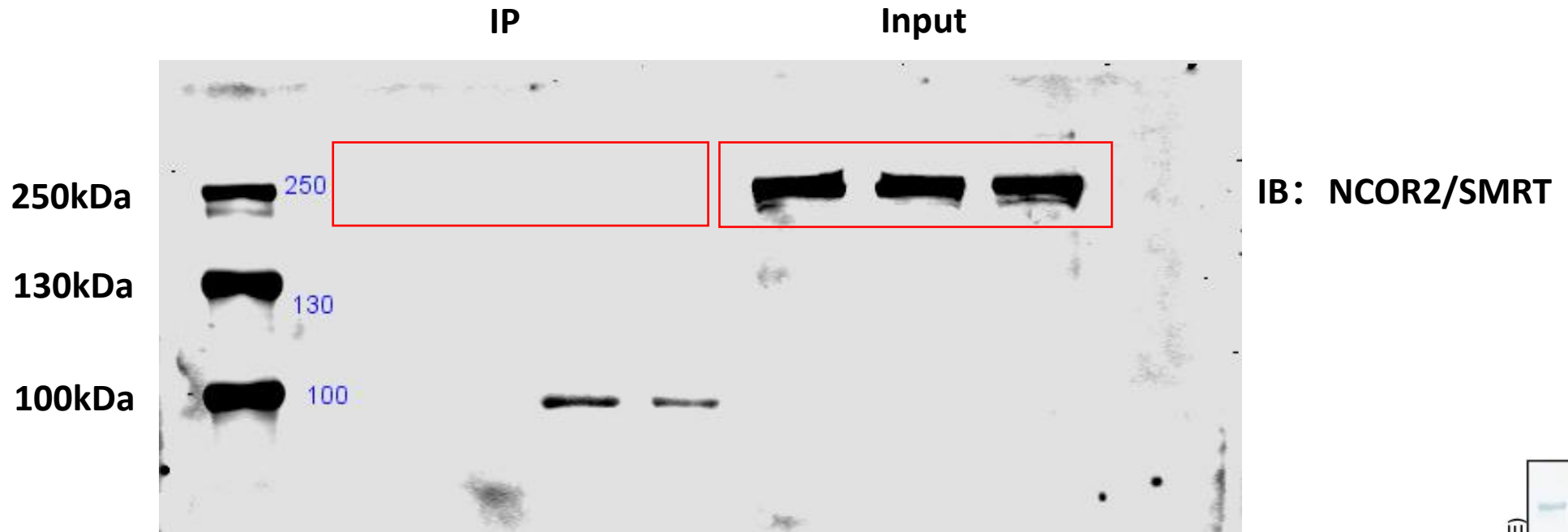


Figure 4C IP: JunB, IB: Flag-NCOR2-013, IB: JunB

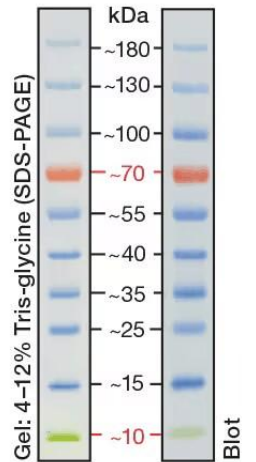
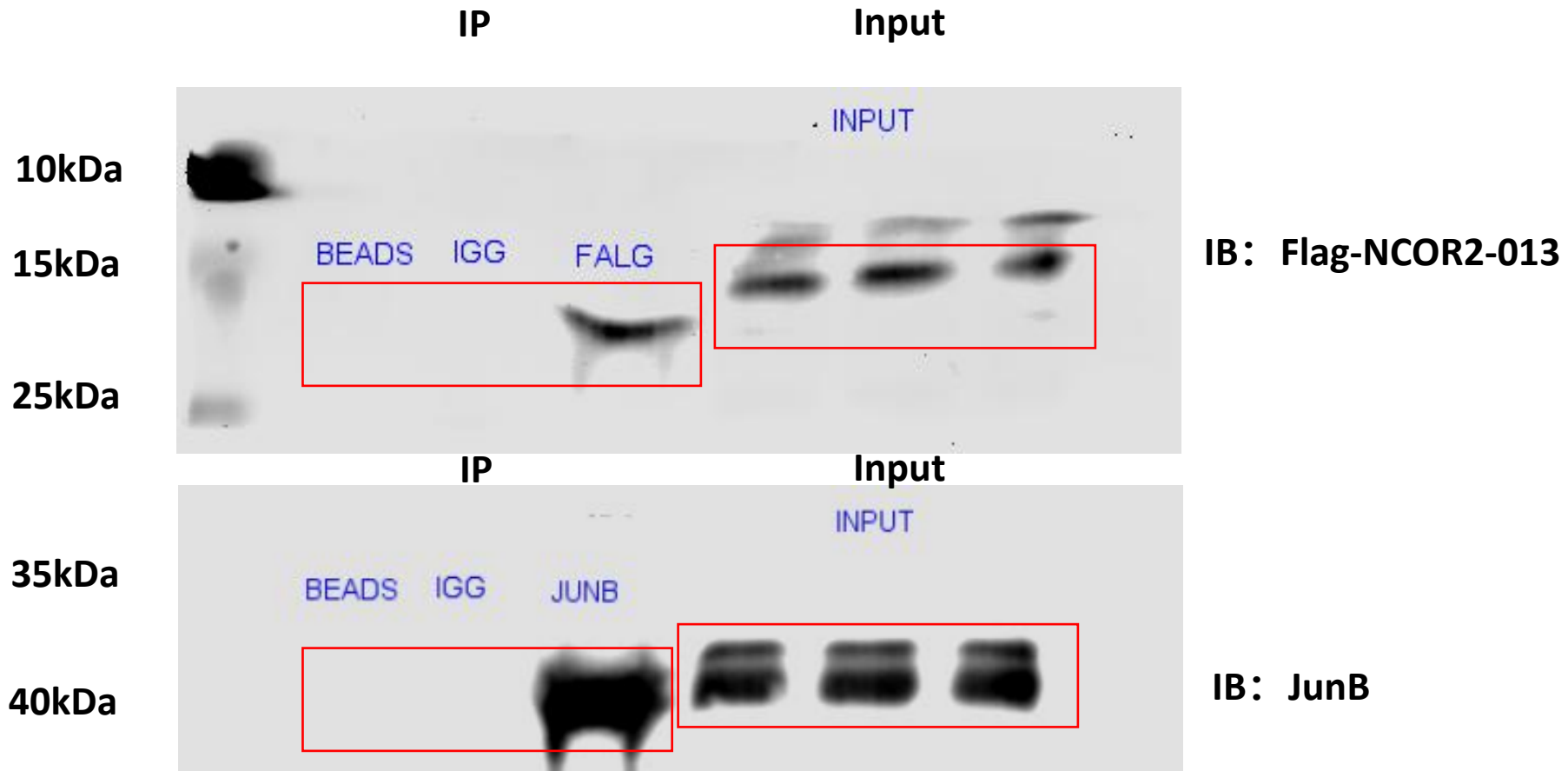


Figure 4C IP: JunB IB: TBL1XR1/TBLR1, IB: HDAC3

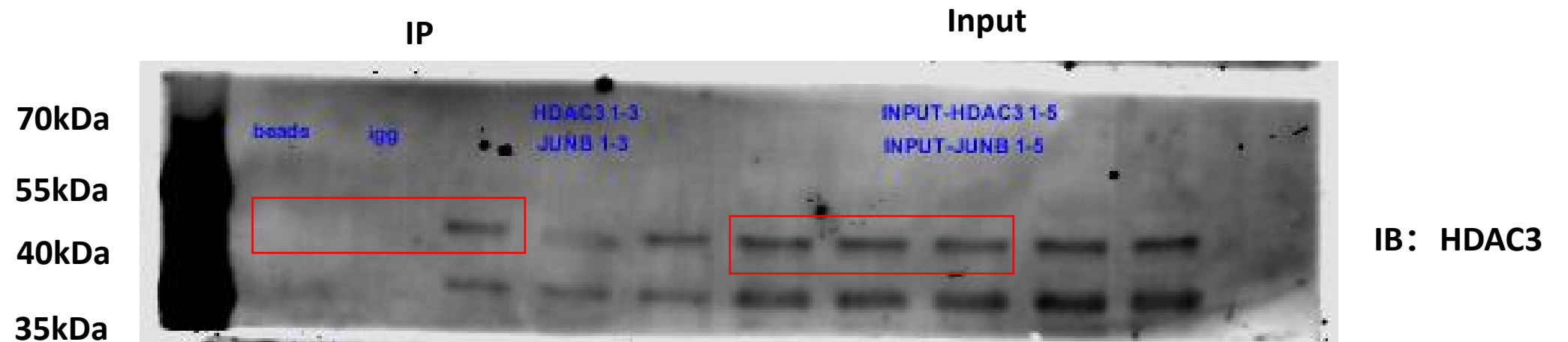
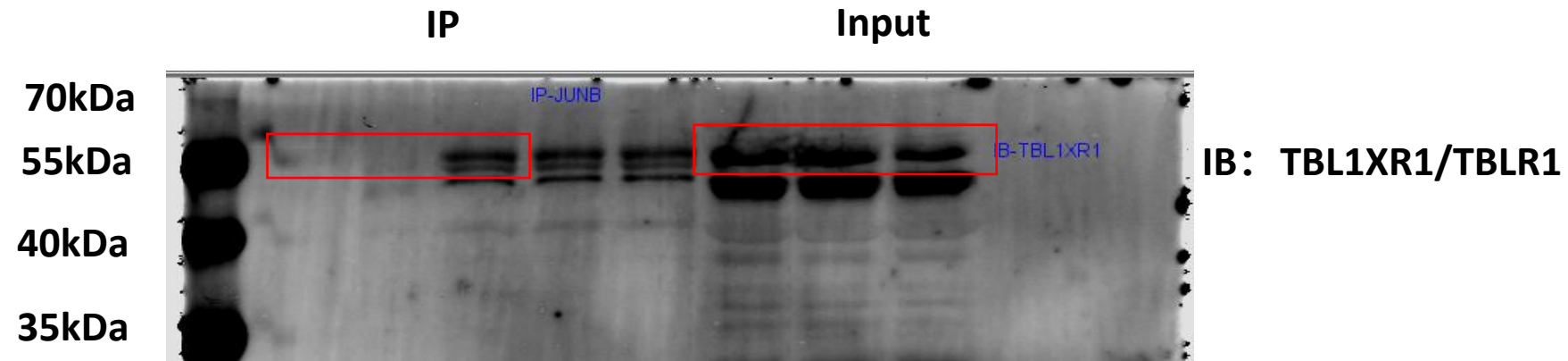


Figure 4C IP: Flag IB: NCOR2/SMRT

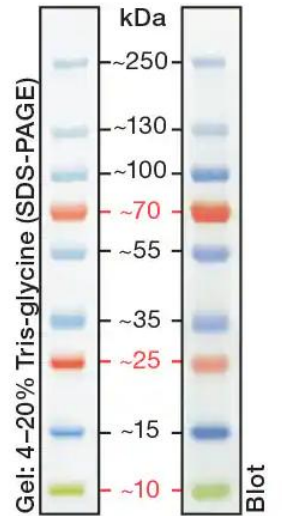
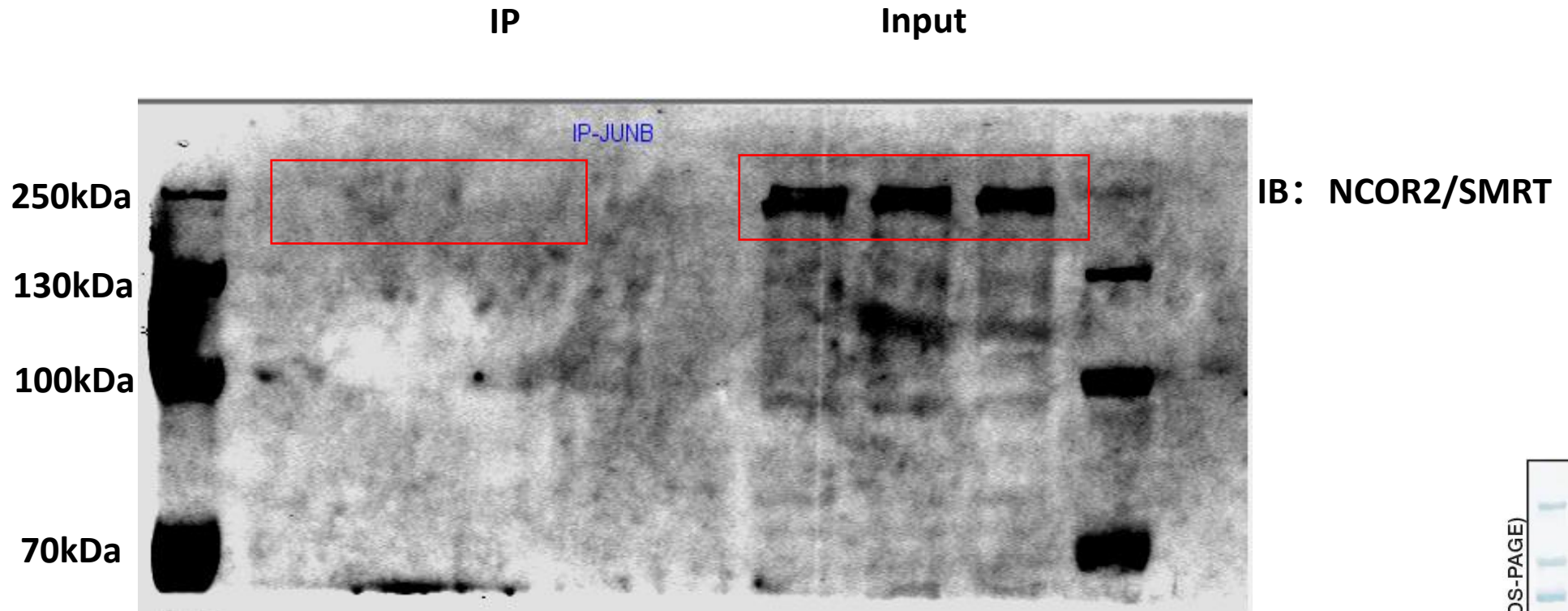


Figure 4D IP: TBL1XR1/TBLR1, IB: Flag-NCOR2-013, IB: TBL1XR1/TBLR1

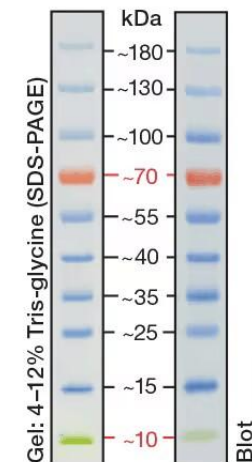
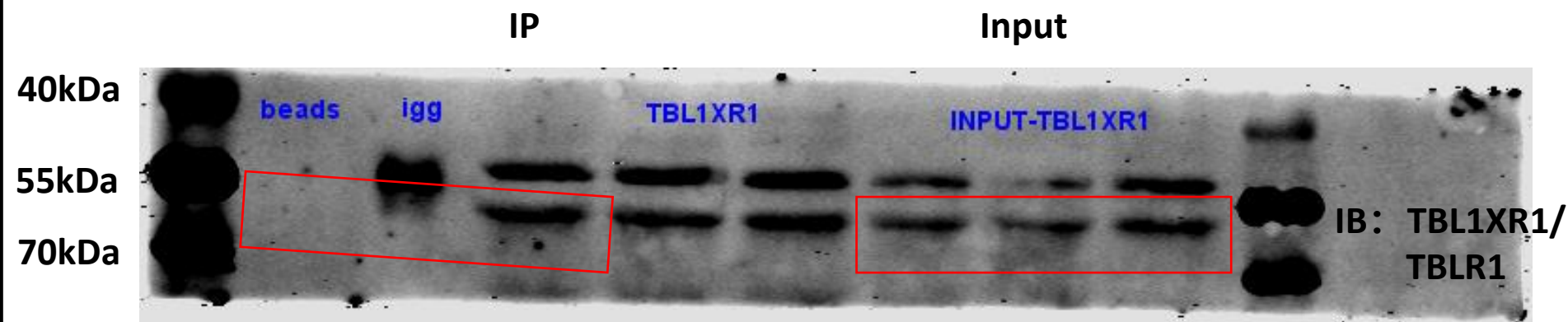
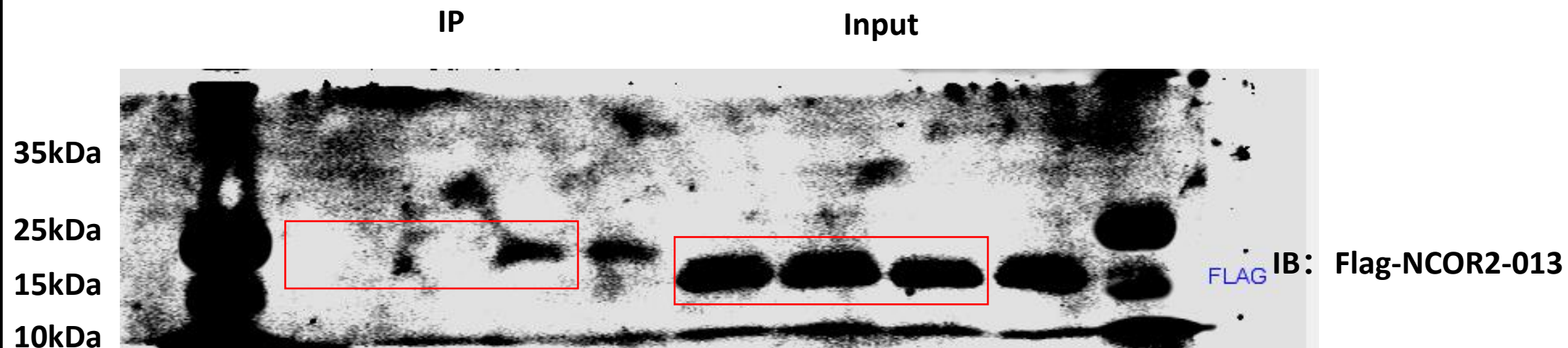


Figure 4D IP: TBL1XR1/TBLR1, IB: JunB, IB: HDAC3

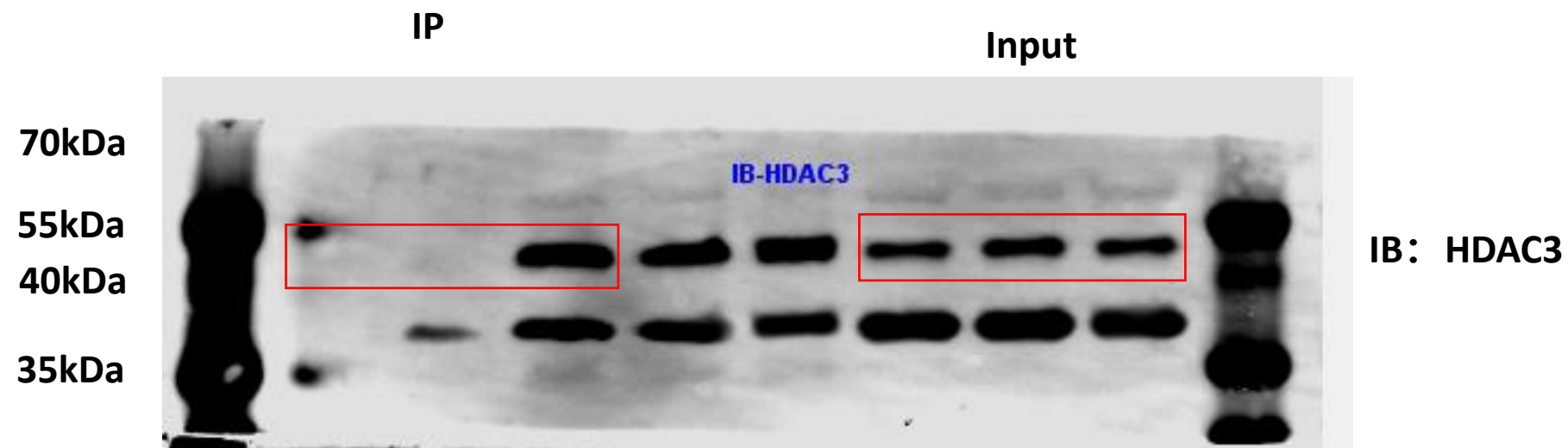
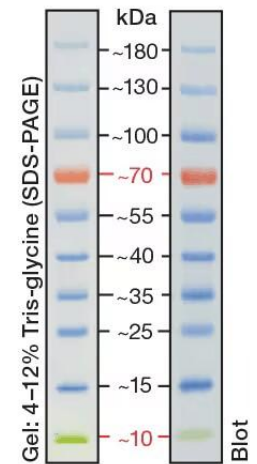
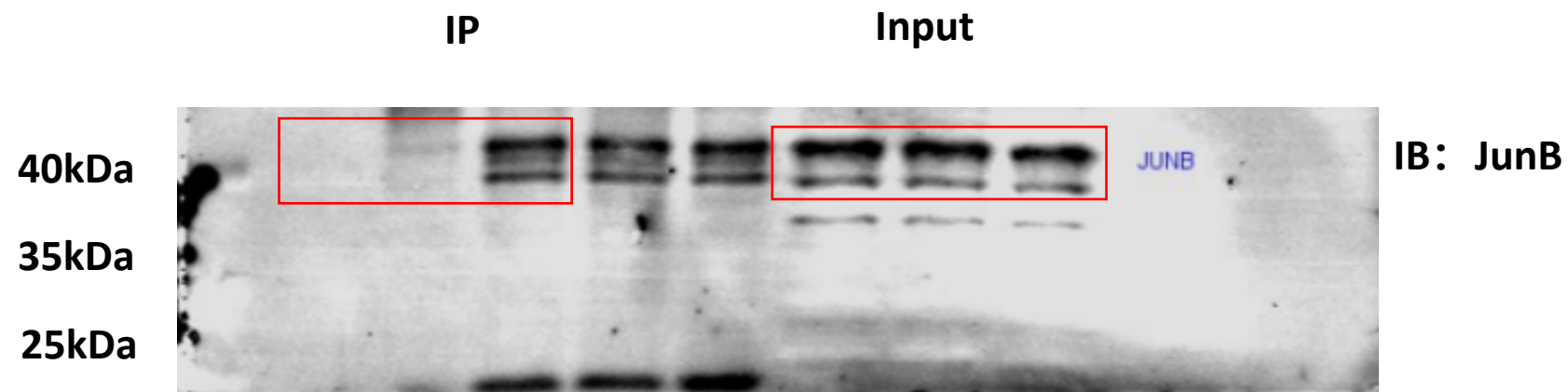


Figure 4D IP: TBL1XR1/TBLR1, IB: NCOR2/SMRT

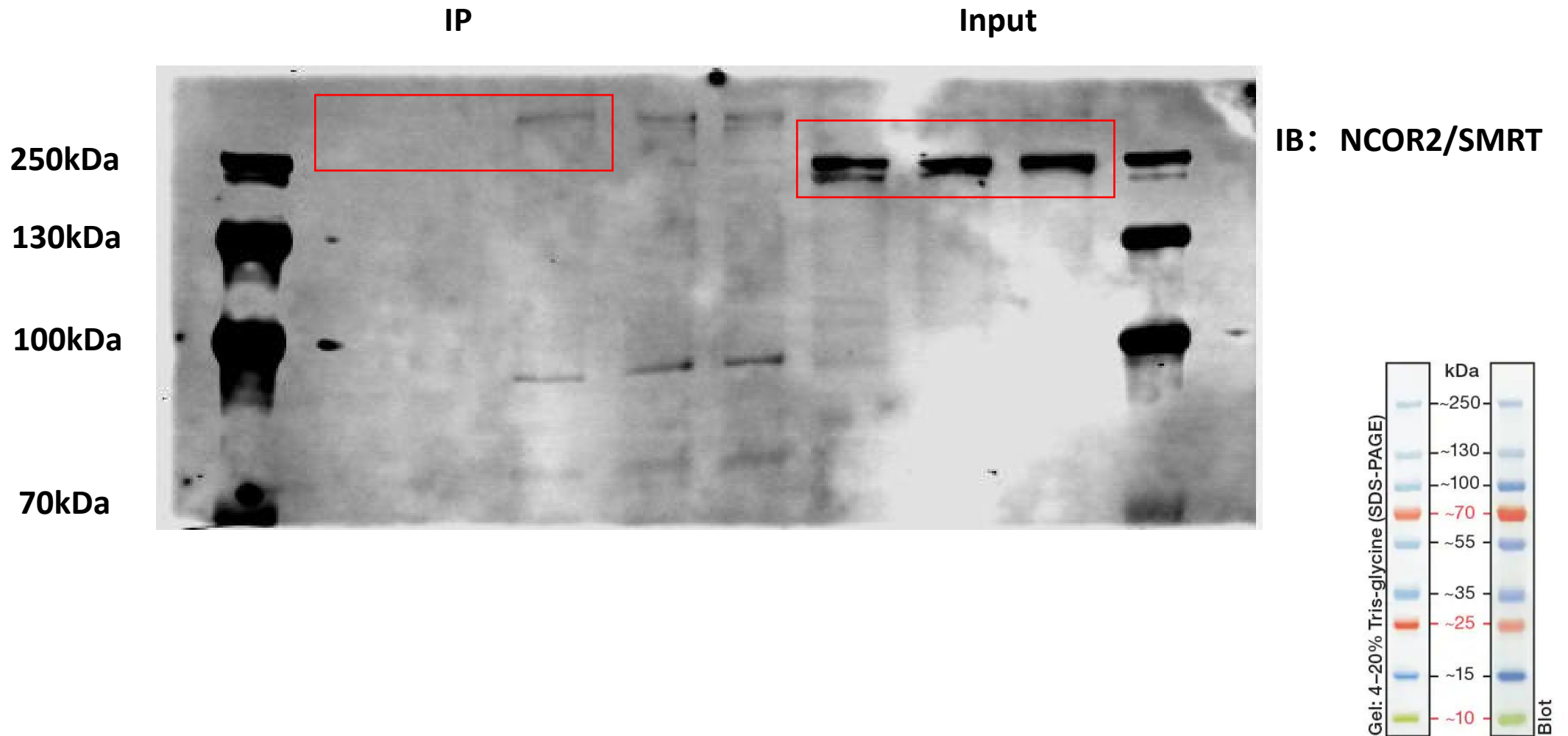


Figure 4E IP: HDAC3, IB: Flag-NCOR2-013, IB: HDAC3

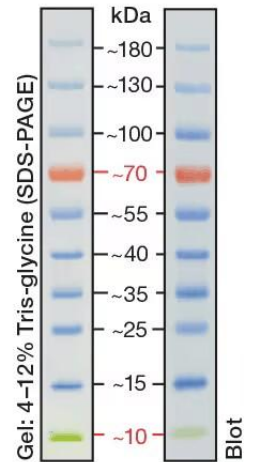
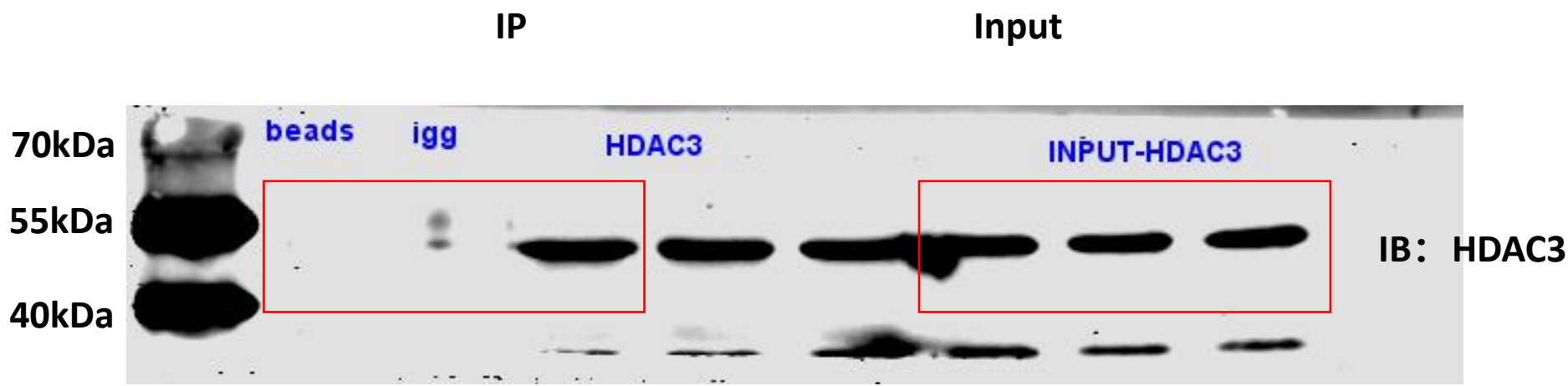
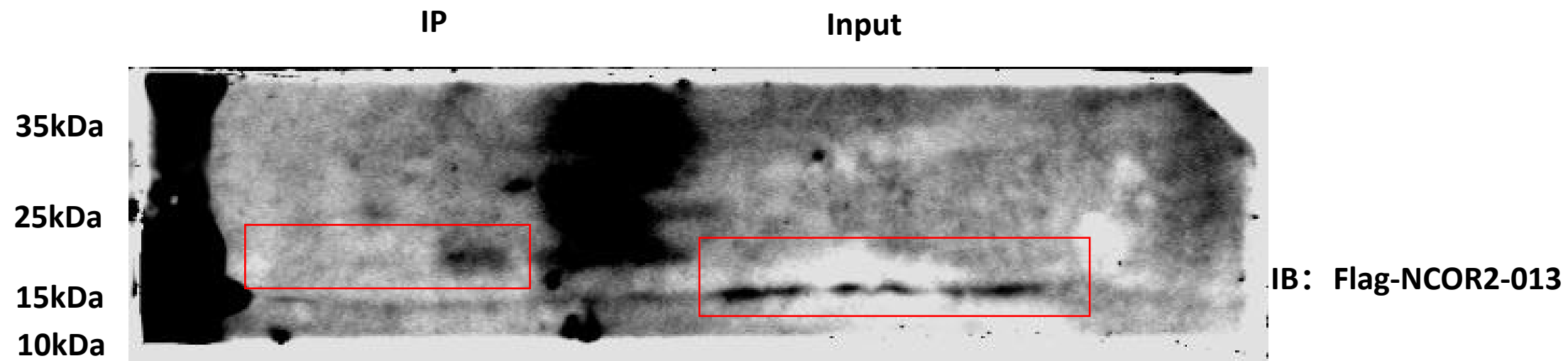


Figure 4E IP: HDAC3, IB: JunB, IB: TBL1XR1/TBLR1

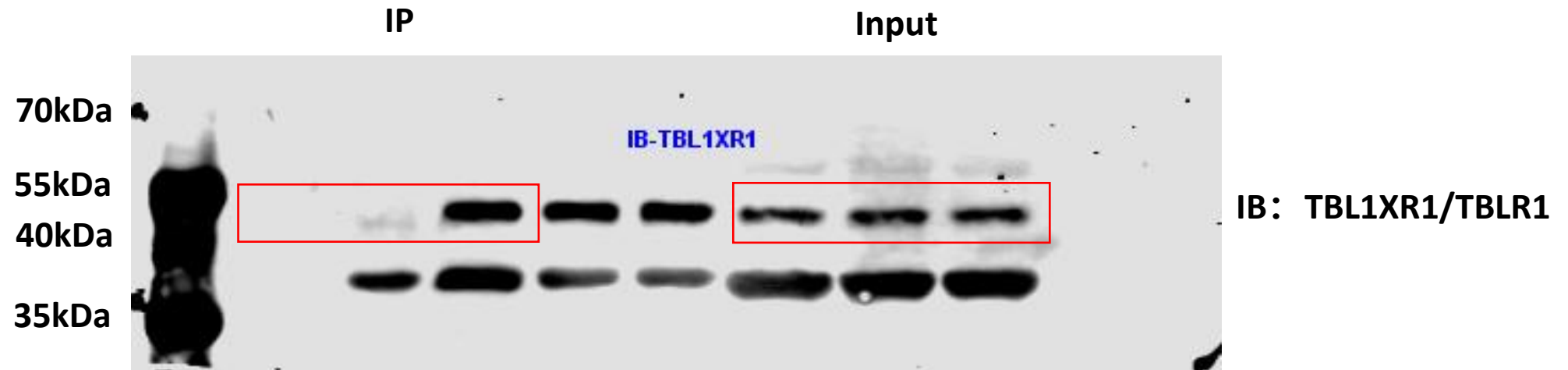
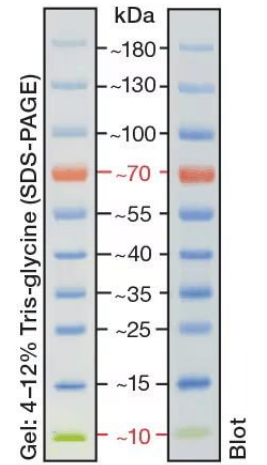
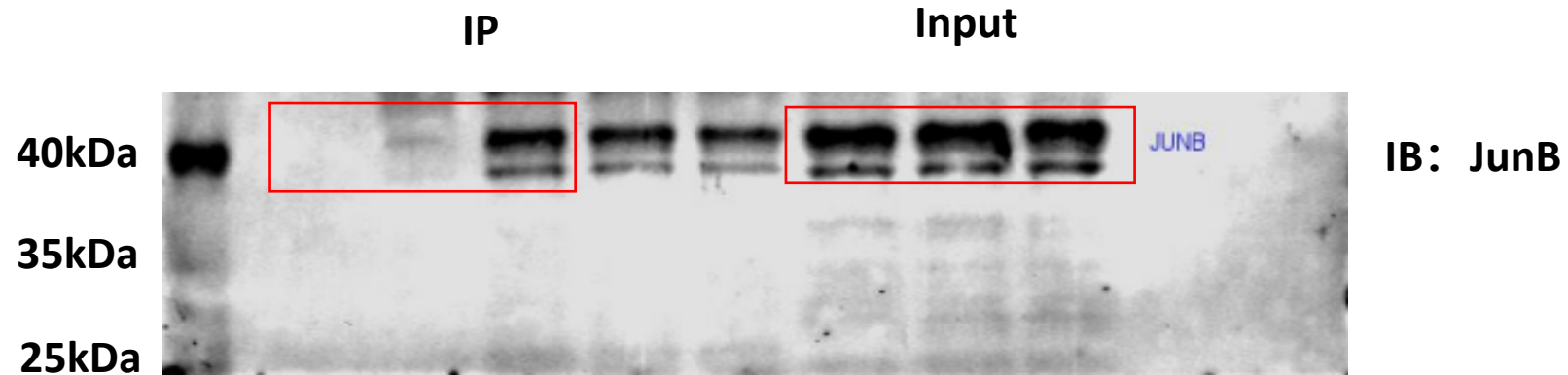


Figure 4E IP: HDAC3, IB: NCOR2/SMRT

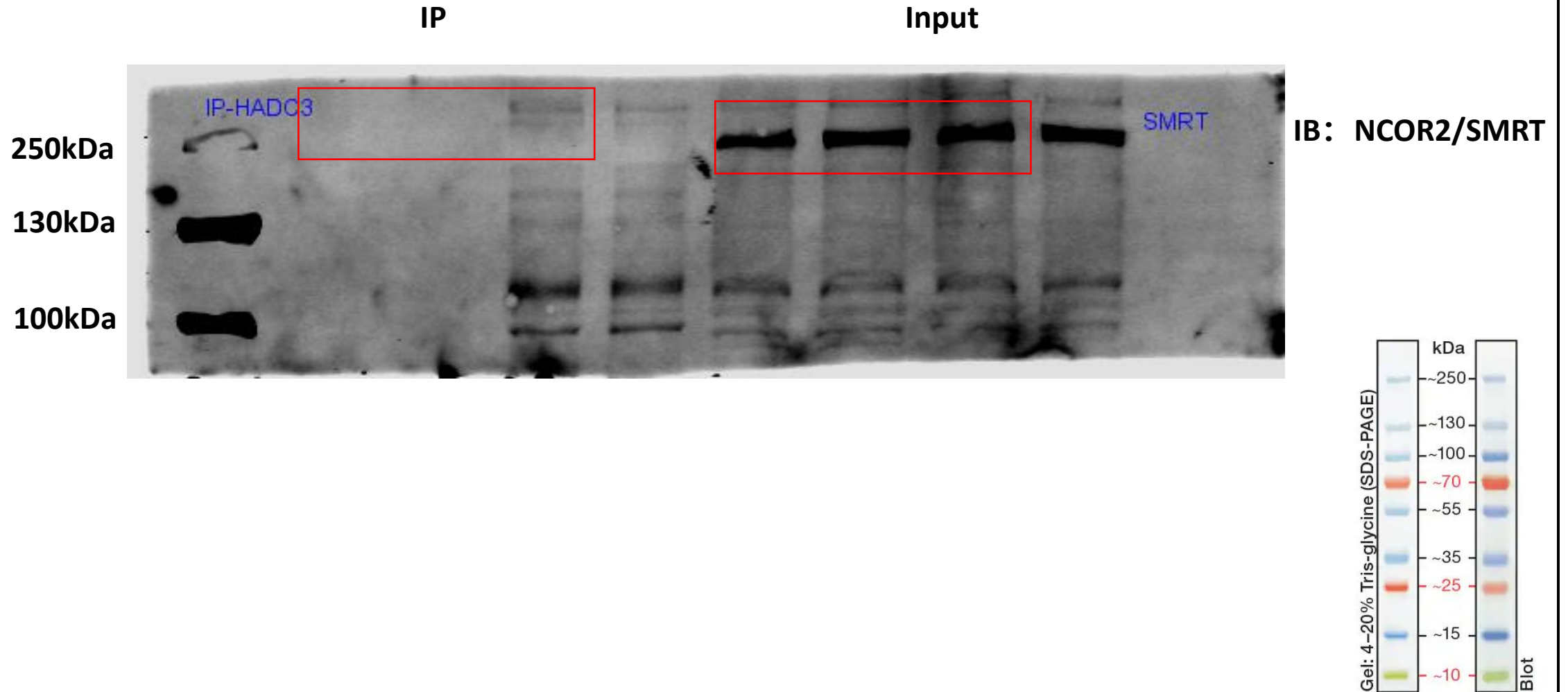


Figure 4F IP: Flag, IB: JunD, IB: Flag-NCOR2-013

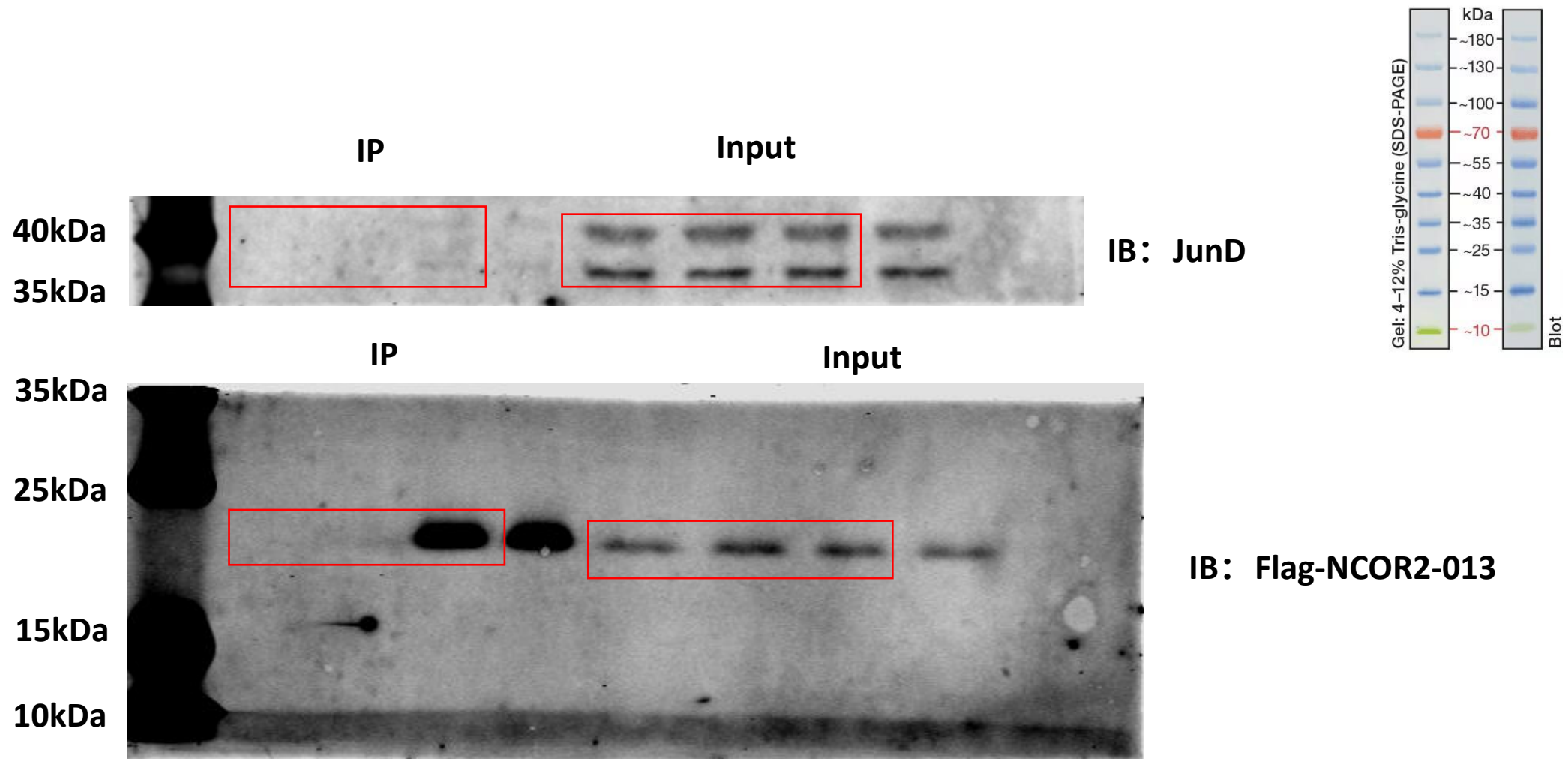


Figure 4G IP: Flag, IB: C-Jun, IB: Flag-NCOR2-013

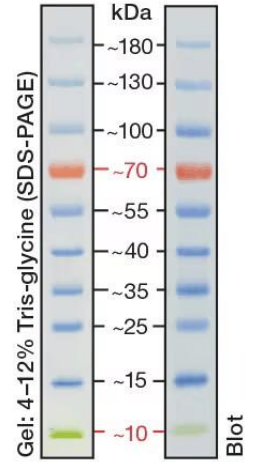
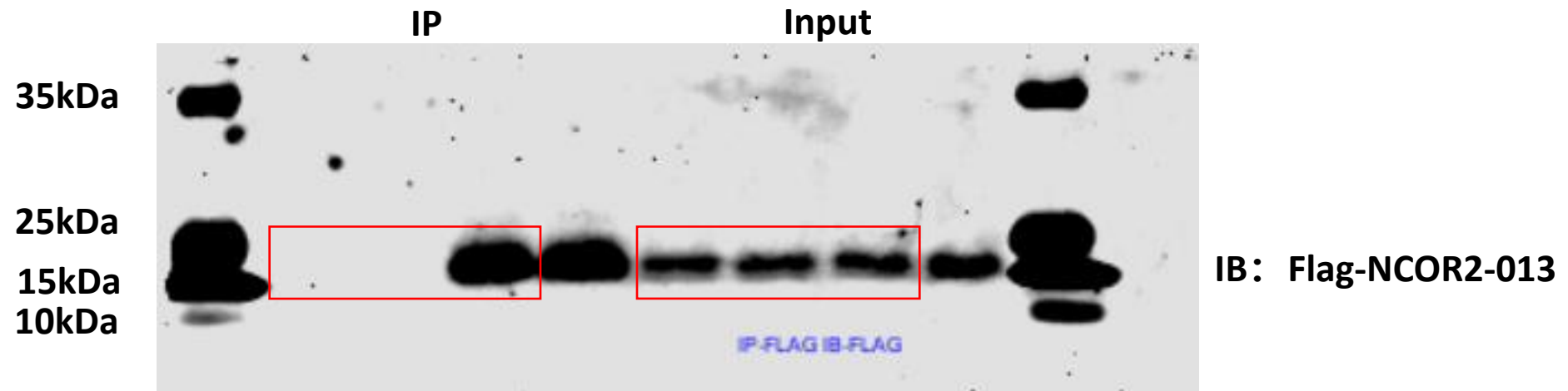
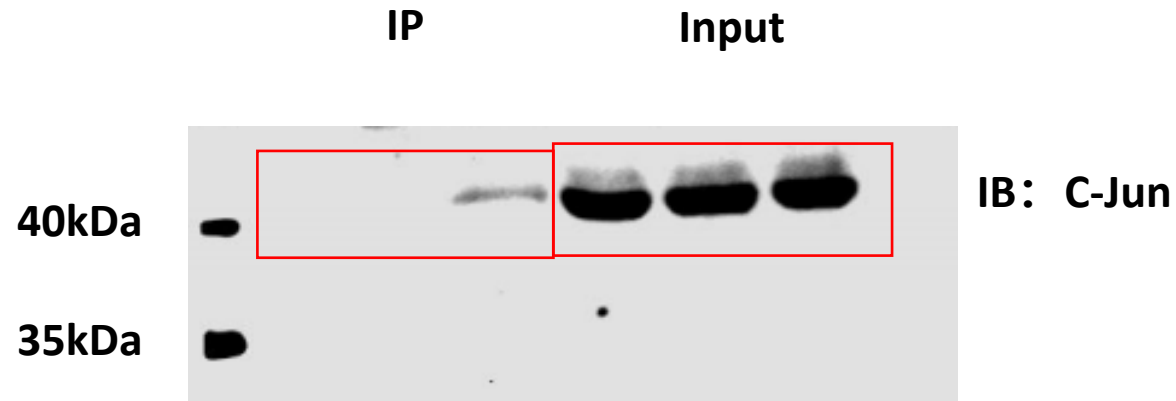
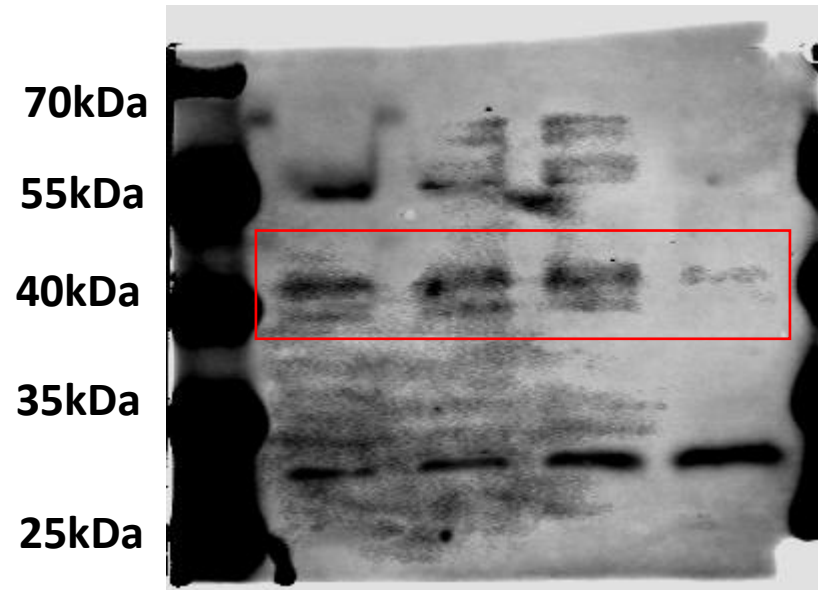
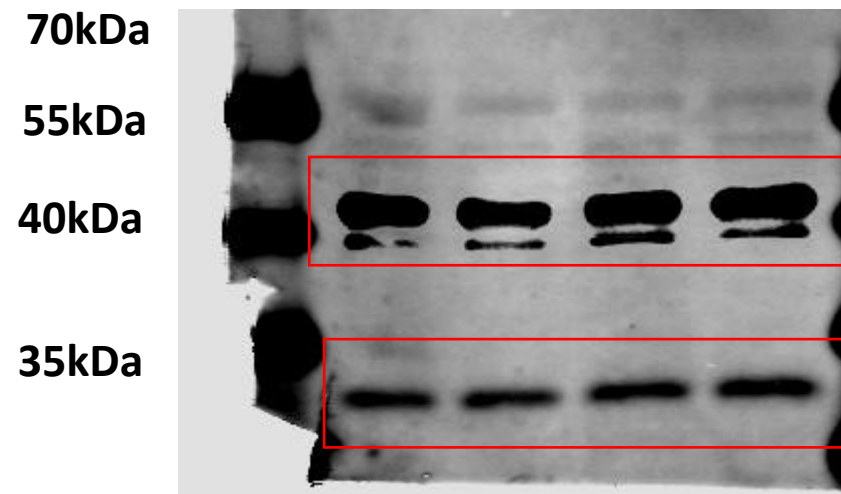
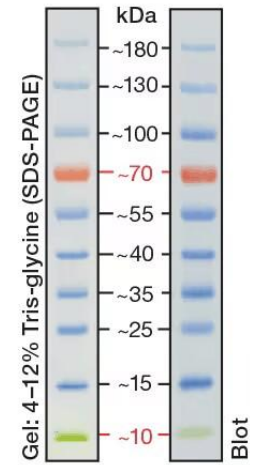


Figure 4H 24h



IB: p-JunB



IB: JunB

IB: GAPDH

Figure 4H 48h

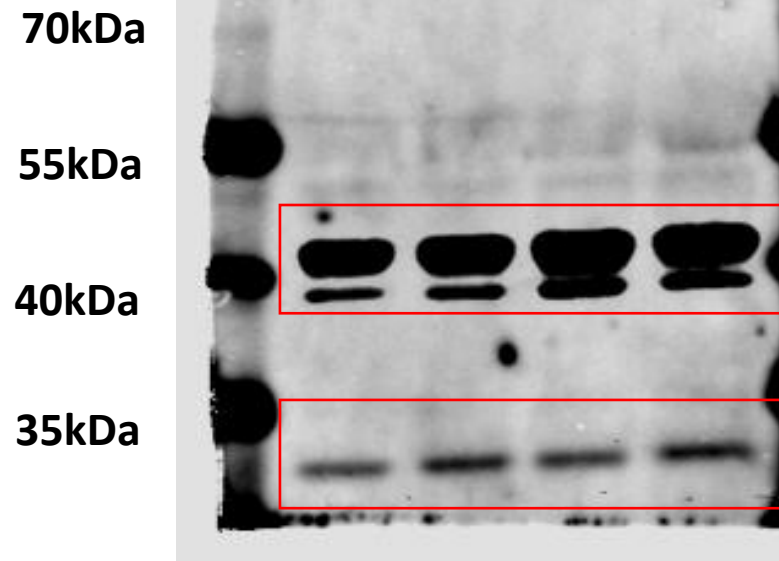
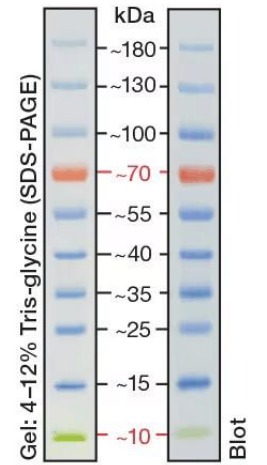
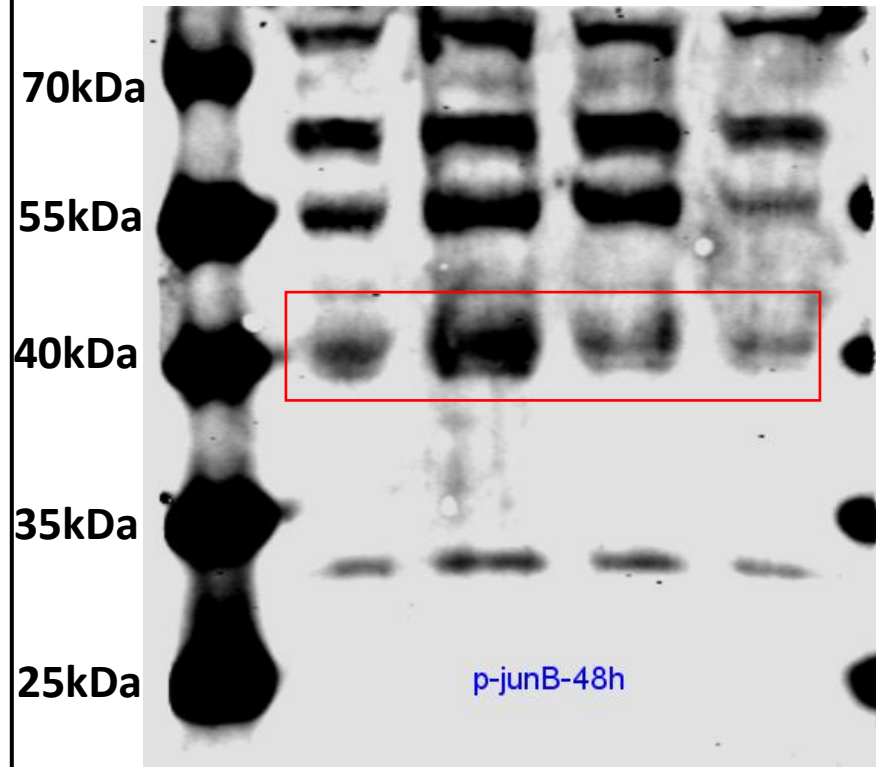


Figure 4I 24h

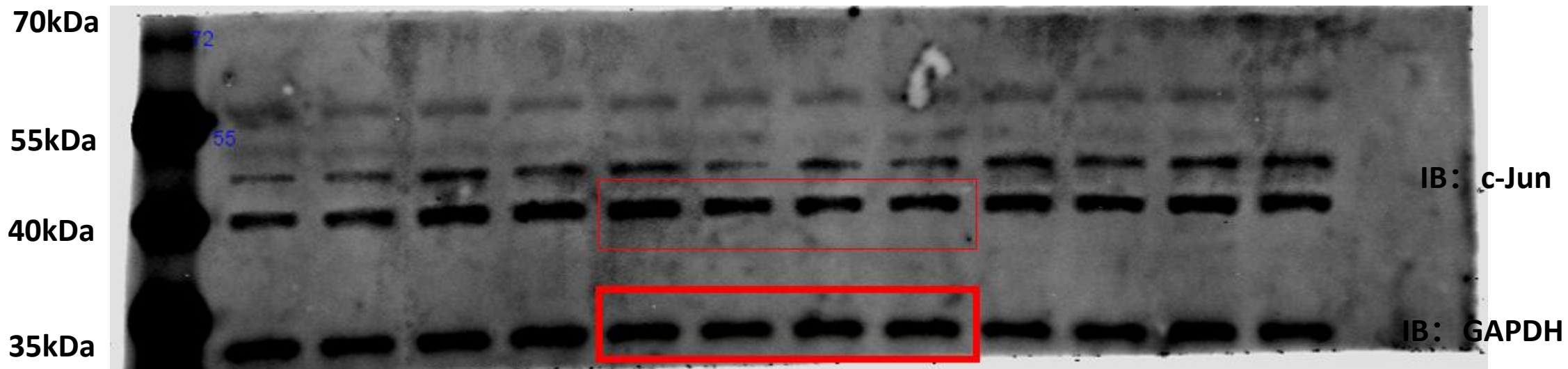
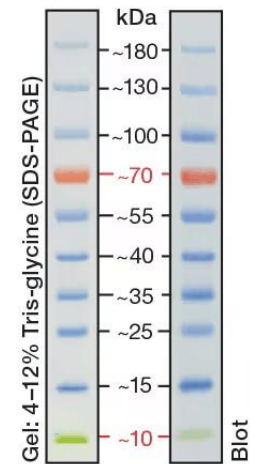
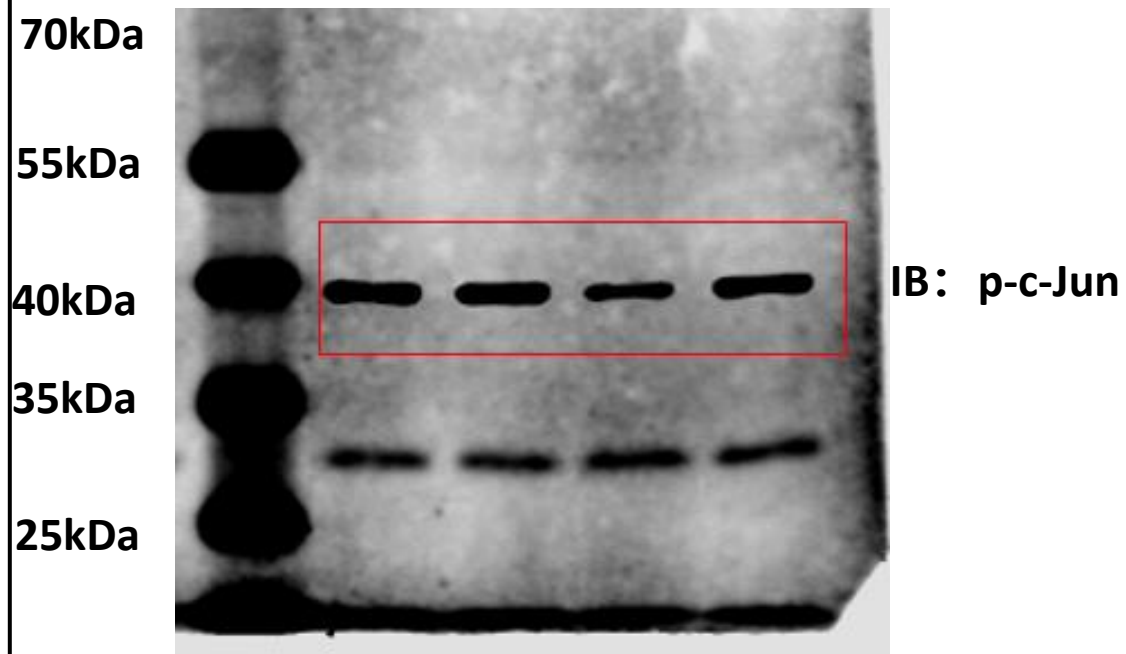
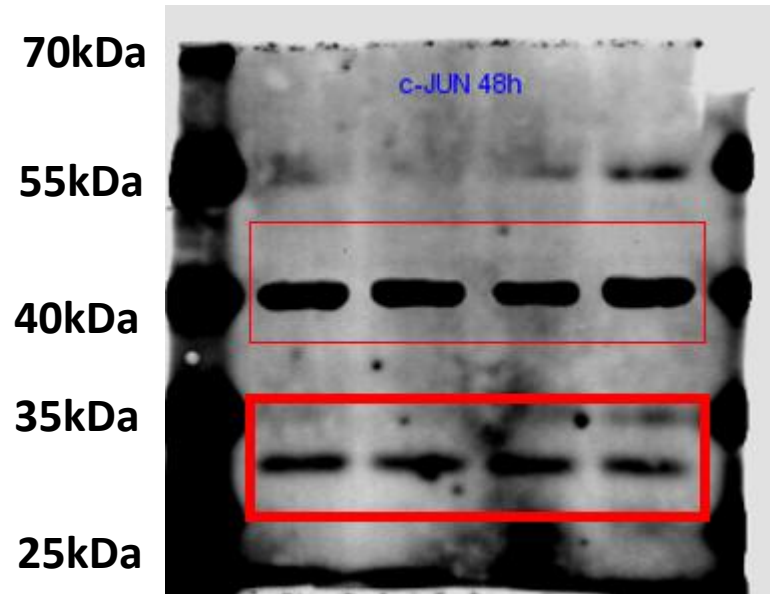
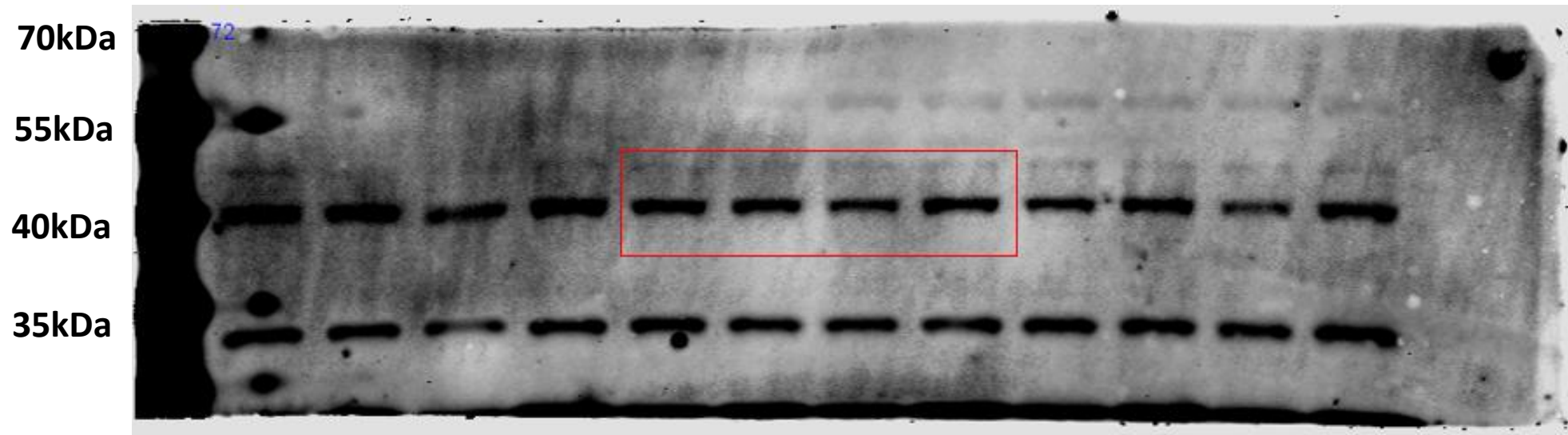
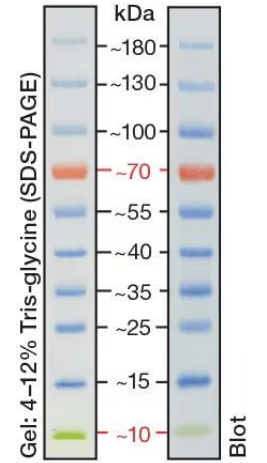


Figure 4I 48h



IB: c-Jun

IB: GAPDH



IB: p-c-Jun

Figure 6A

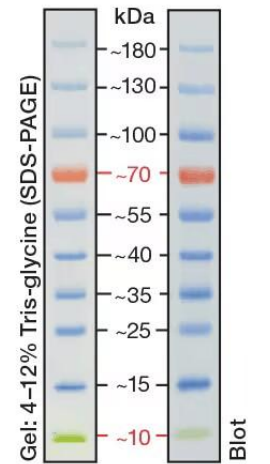
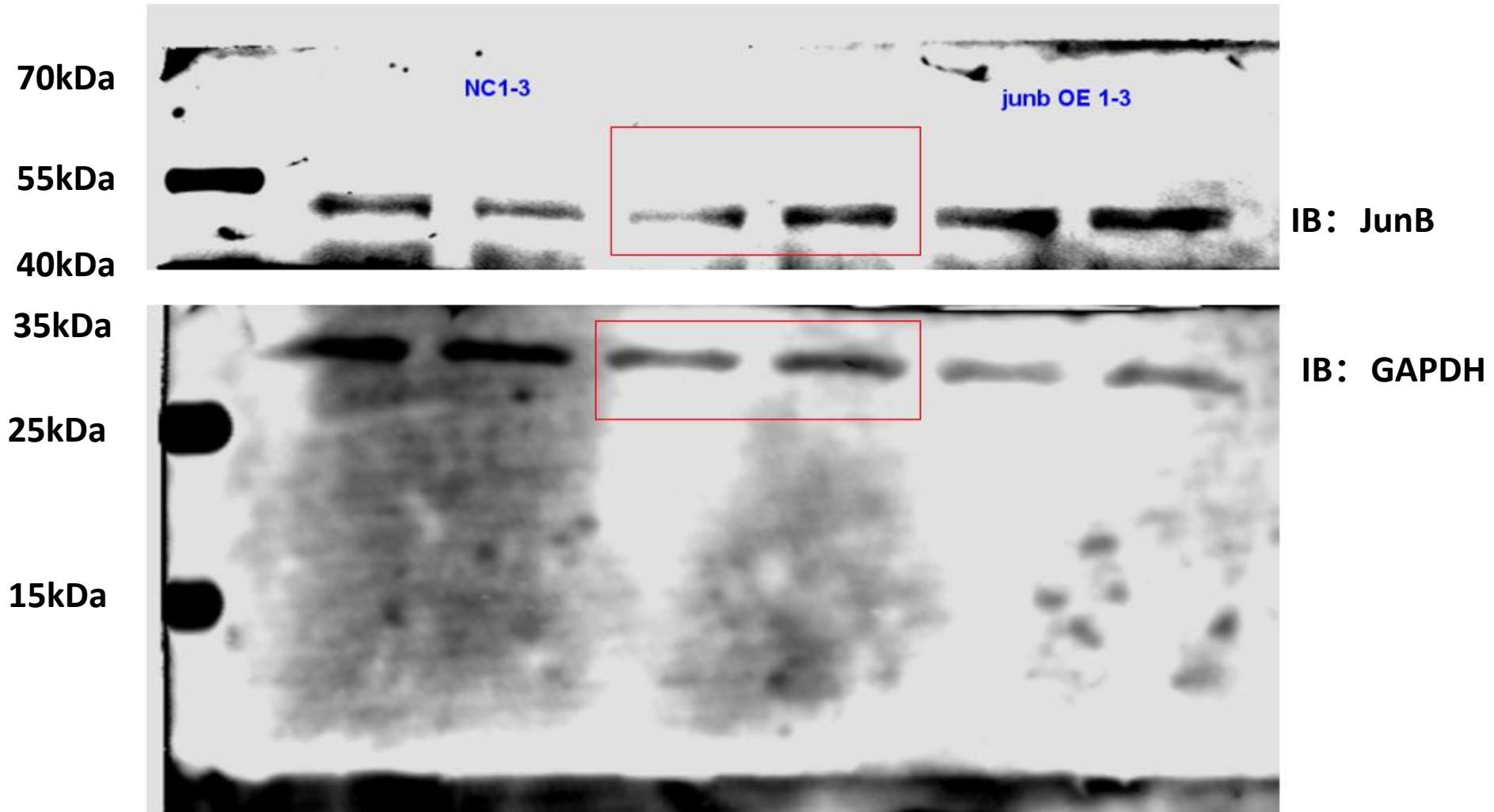


Figure 7C

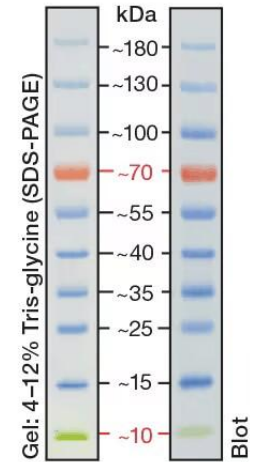
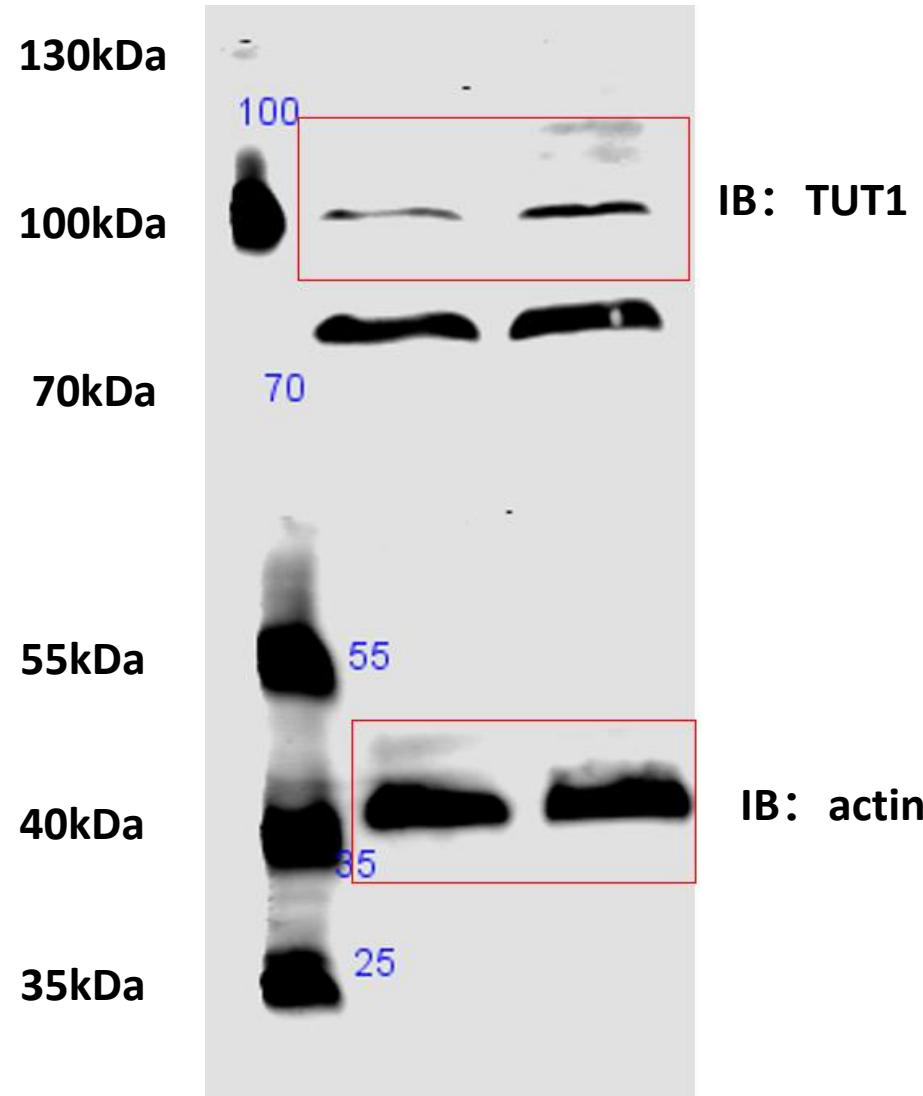


Figure 7F

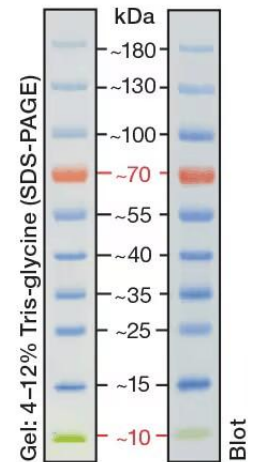
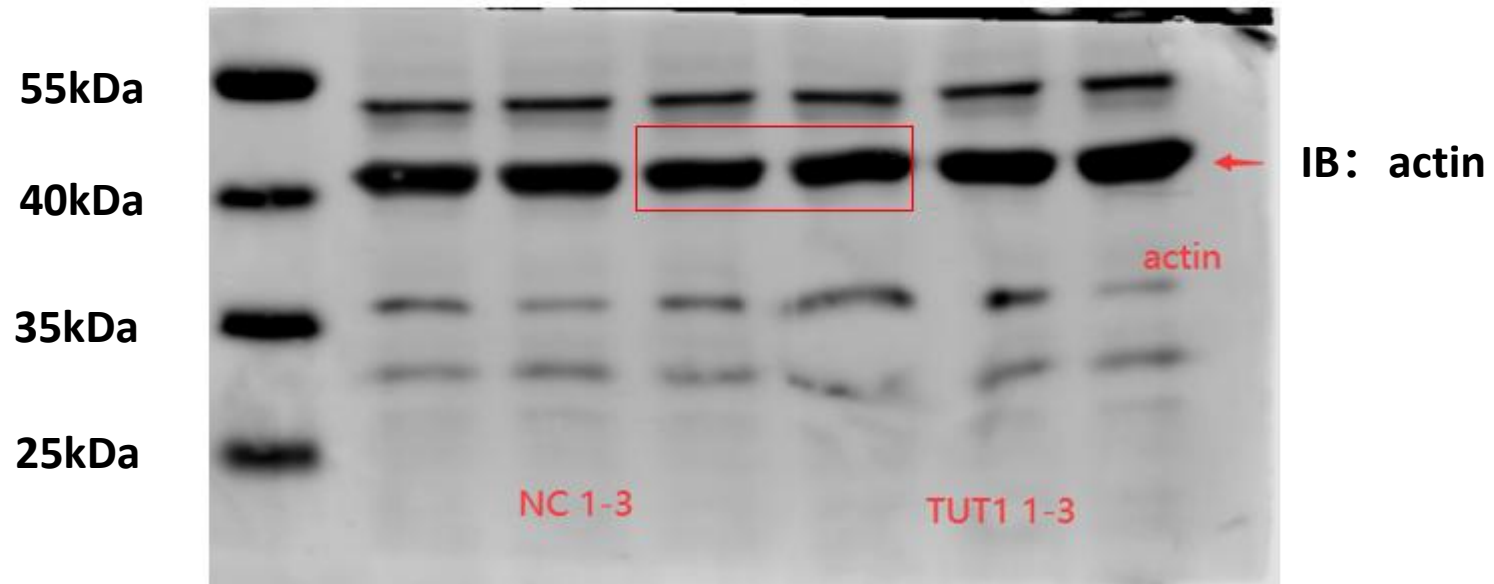
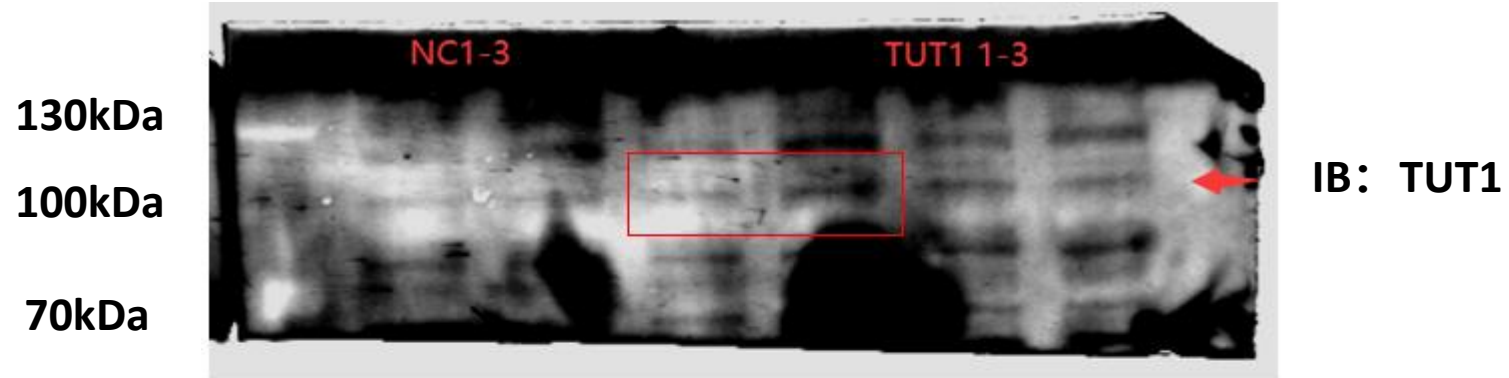
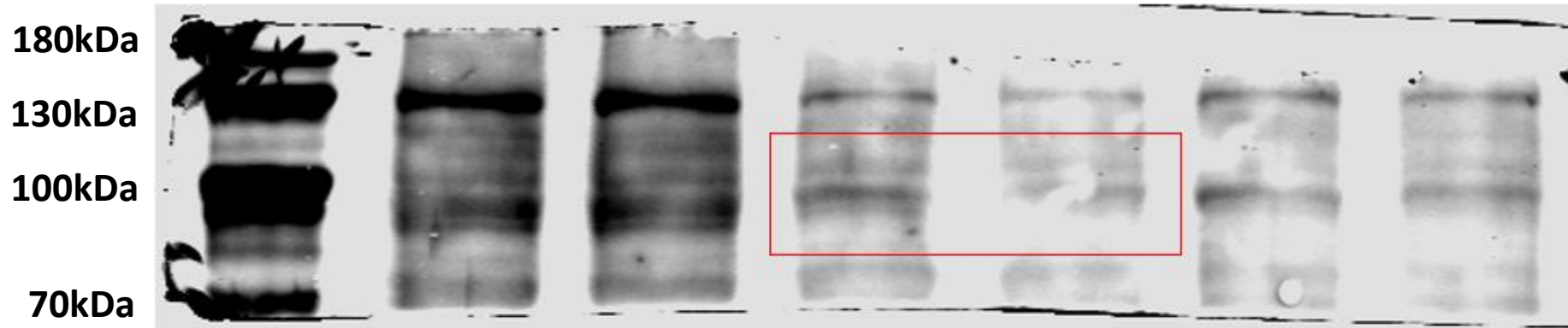
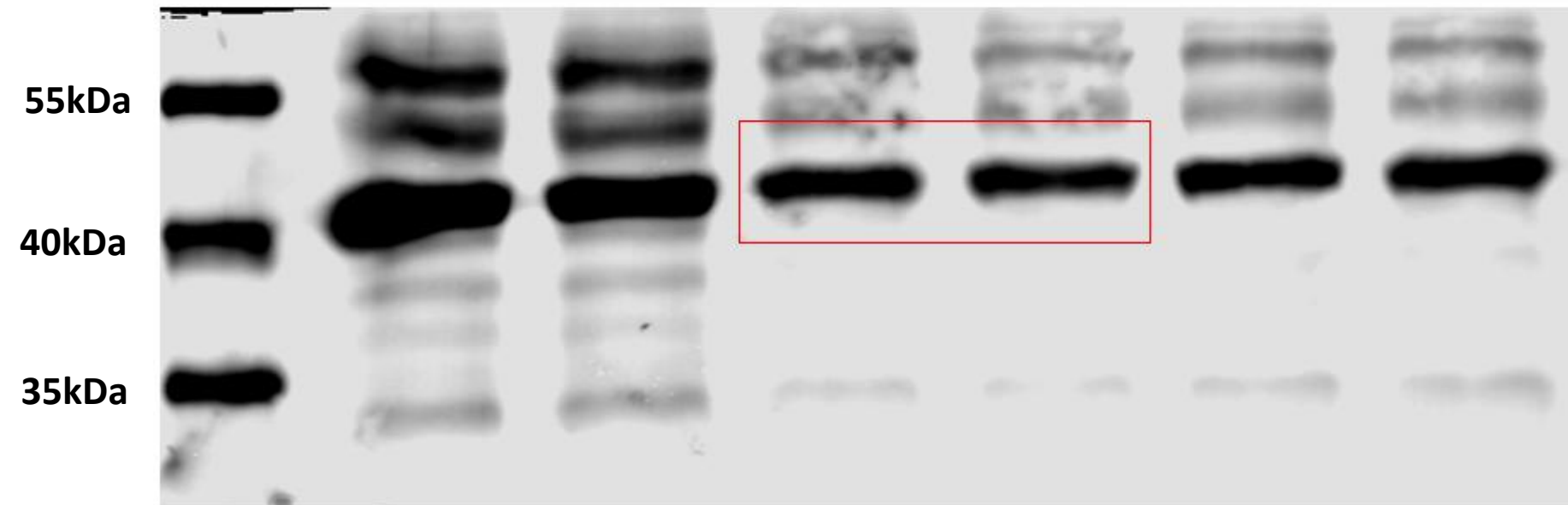


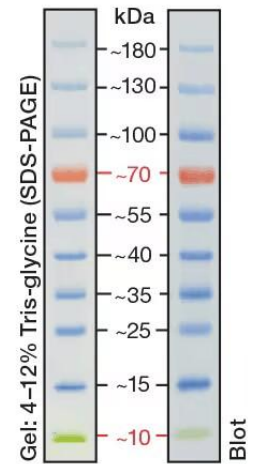
Figure 7G



IB: TUB1



IB: actin



Supplementary Table 1. The summary of the truncated transcripts generated by ES-type AS event predicted by rMATs

Gene	Predicted transcript(s) matched the currently known transcript(s)	Matched currently known transcript(s)	Matched transcript(s) NOT detected in uninfected cells	Matched transcript(s) differentially highly expressed in infected cells (<i>p</i> _{adj} <0.05)
<i>NR1H3</i>	Yes	<i>NR1H3-028, 029, 031, 003, 023, 012, 032</i>	<i>NR1H3-029, 012</i> , yes; others, no	No
<i>PPARA</i>	Yes	<i>PPARA-002, 006, 007</i>	<i>PPARA-002</i> , yes; others, no	No
<i>TLR6</i>	Yes	<i>TLR6-002, 003</i>	Yes	No
<i>IRF3</i>	Yes	<i>IRF3-017, 009, 008, 012, 201, 023, 024, 202, 020</i>	<i>IRF3-023</i> , yes; others, no	<i>IRF3-020</i> , yes; others, no
<i>MAP2K3</i>	Yes	<i>MAP2K3-201, 016, 013</i>	Yes	No
<i>NCOR2</i>	Yes	<i>NCOR2-013</i>	Yes	Yes

The strategy for the screening of particular truncated transcript. (1) The truncated transcripts generated by ES-type AS event predicted by rMATs should be matched the currently known transcripts. (2) The truncated transcript is differentially highly expressed in *T. marneffei*-infected macrophages. (3) The truncated transcript can not be detected in uninfected cells.

Due to the expression in uninfected cells or/and insignificant difference in transcript expression, *NR1H3*, *PPARA*, *TLR6*, *IRF3* and *MAP2K3* were excluded.

Supplementary Table 2. The differential expression analysis results of *NR1H3*, *PPARA*, *IRF3*, *MAP2K3* and *TLR6* transcripts in *T. marneffei*-infected THP-1 macrophages at 24 h post-infection.

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	<i>Tm1</i>	<i>Tm2</i>	<i>Tm3</i>	<i>pvalue</i>	<i>padj</i>
ENST0000 0440187	<i>NCOR2-0</i> <i>13</i>	0	0	0	17.755 60209	11.445 95335	26.842 60587	7.46E-0 6	0.0015 6278
ENST0000 0453428	<i>NCOR2-0</i> <i>12</i>	0	0	0	0	0	0	NA	NA
ENST0000 0420698	<i>NCOR2-0</i> <i>04</i>	0	0	0	5.0730 2917	3.5218 318	0	0.3066 841	NA
ENST0000 0356219	<i>NCOR2-2</i> <i>01</i>	541.10 04671	7563.0 25857	294.32 80142	10154. 51338	357.46 59277	9554.0 50361	NA	NA
ENST0000 0429285	<i>NCOR2-0</i> <i>01</i>	6080.0 9621	0	7615.9 77832	0	6804.1 79037	0	0.7864 2596	0.9999 8262
ENST0000 0397355	<i>NCOR2-2</i> <i>02</i>	978.14 31521	0	922.42 01491	0	23.772 36465	0	0.0529 0452	0.7865 0535
ENST0000 0405201	<i>NCOR2-0</i> <i>05</i>	567.11 49127	1.2313 6207	0	2227.0 59805	1686.0 76974	357.58 18568	0.2131 1123	0.9999 8262
ENST0000 0404621	<i>NCOR2-0</i> <i>02</i>	415.19 05507	522.09 75193	0.9618 5626	1051.8 08048	229.79 95249	1950.8 82248	0.2810 5049	0.9999 8262
ENST0000 0404121	<i>NCOR2-2</i> <i>03</i>	9.3652 0039	24.627 24147	5.7711 3753	9.3005 5347	4.4022 8975	4.7933 2248	0.2091 8319	0.9999 8262
ENST0000 0458234	<i>NCOR2-0</i> <i>03</i>	468.26 00196	1.2313 6207	542.48 69282	0	426.14 16478	0	0.6856 1495	0.9999 8262
ENST0000 0542927	<i>NCOR2-0</i> <i>24</i>	21.852 13425	18.470 43111	19.237 12511	14.373 58264	22.891 9067	16.297 29642	0.7193 9617	0.9999 8262
ENST0000 0443451	<i>NCOR2-0</i> <i>22</i>	347.55 29924	395.26 72257	382.81 87897	618.90 95585	415.57 61524	533.97 6124	0.0520 8474	0.7820 5829
ENST0000 0448008	<i>NCOR2-0</i> <i>19</i>	41.623 11286	38.172 22429	30.779 40018	34.665 69931	86.284 87909	35.470 58633	0.3690 7157	0.9999 8262
ENST0000 0418829	<i>NCOR2-0</i> <i>17</i>	2.0811 5564	0	15.389 70009	29.592 67015	9.6850 3745	9.5866 4495	0.3179 5707	0.9999 8262
ENST0000 0440337	<i>NCOR2-0</i> <i>15</i>	54.110 04671	64.030 82783	91.376 34428	100.61 50785	46.664 27135	40.263 90881	0.7723 0653	0.9999 8262
ENST0000 0461081	<i>NCOR2-0</i> <i>06</i>	118.62 58716	156.38 29834	75.024 78794	214.75 82348	61.632 05649	65.189 18569	0.9626 0225	0.9999 8262
ENST0000 0542565	<i>NCOR2-0</i> <i>08</i>	19.770 97861	75.113 0865	14.427 84383	149.65 43605	15.848 2431	126.54 37134	0.1921 929	0.9999 8262
ENST0000 0448614	<i>NCOR2-0</i> <i>09</i>	1.0405 7782	0	26.931 97516	0.8455 0486	6.1632 0565	1.9173 2899	0.3977 9333	0.9999 8262
ENST0000 0536195	<i>NCOR2-0</i> <i>20</i>	65.556 40275	39.403 58636	19.237 12511	27.056 15556	11.445 95335	54.643 87624	0.6154 9353	0.9999 8262
ENST0000 0413172	<i>NCOR2-0</i> <i>18</i>	11.446 35604	0	8.6567 063	43.966 25279	9.6850 3745	13.421 30294	0.1887 402	0.9999 8262

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	Tm1	Tm2	Tm3	pvalue	padj
ENST0000 0494460	<i>NCOR2-0</i> <i>07</i>	21.852 13425	12.313 62074	8.6567 063	16.910 09723	20.250 53285	5.7519 8697	0.9915 8308	0.9999 8262
ENST0000 0474079	<i>NCOR2-0</i> <i>14</i>	16.649 24514	2.4627 2415	9.6185 6256	9.3005 5347	5.2827 477	20.131 9544	0.7891 1548	0.9999 8262
ENST0000 0493859	<i>NCOR2-0</i> <i>10</i>	20.811 55643	2.4627 2415	5.7711 3753	11.837 06806	12.326 4113	29.718 59936	0.3753 9192	0.9999 8262
ENST0000 0473999	<i>NCOR2-0</i> <i>11</i>	41.623 11286	33.246 77599	63.482 51287	81.168 46669	54.588 3929	64.230 52119	0.2045 823	0.9999 8262
ENST0000 0464377	<i>NCOR2-0</i> <i>16</i>	12.486 93386	13.544 98281	10.580 41881	15.219 0875	9.6850 3745	43.139 90229	0.2491 9321	0.9999 8262
ENST0000 0495866	<i>NR1H3-02</i> <i>6</i>	0	0	0	0	0	0	NA	NA
ENST0000 0529540	<i>NR1H3-02</i> <i>9</i>	0	0	0	0	0	0	NA	NA
ENST0000 0395397	<i>NR1H3-03</i> <i>1</i>	0	307.84 05184	26.931 97516	25.365 14584	0	47.933 22477	0.3915 3591	0.9999 8262
ENST0000 0405576	<i>NR1H3-00</i> <i>3</i>	0	40.634 94843	22.122 69388	24.519 64098	0	0	0.6631 147	0.9999 8262
ENST0000 0531660	<i>NR1H3-03</i> <i>7</i>	0	0	19.237 12511	11.837 06806	0	0	0.8520 8738	0.9999 8262
ENST0000 0532630	<i>NR1H3-03</i> <i>6</i>	0	0	0	0	0	0	NA	NA
ENST0000 0407404	<i>NR1H3-00</i> <i>2</i>	0	0	0	0	0	0	NA	NA
ENST0000 0444396	<i>NR1H3-01</i> <i>0</i>	0	16.007 70696	0	0	0	24.925 27688	0.8642 3579	0.9999 8262
ENST0000 0457932	<i>NR1H3-01</i> <i>1</i>	0	0	0	0	0	0	NA	NA
ENST0000 0412937	<i>NR1H3-01</i> <i>2</i>	0	0	0	0	0	0	NA	NA
ENST0000 0449369	<i>NR1H3-01</i> <i>3</i>	0	0	0	0	0	0	NA	NA
ENST0000 0486991	<i>NR1H3-00</i> <i>9</i>	0	0	0	0	0	49.850 55376	0.1020 103	0.9345 5796
ENST0000 0437276	<i>NR1H3-01</i> <i>7</i>	0	0	0	0	0	0	NA	NA
ENST0000 0436029	<i>NR1H3-01</i> <i>6</i>	0	0	0	0	0	0	NA	NA
ENST0000 0476086	<i>NR1H3-03</i> <i>8</i>	0	0	26.931 97516	19.446 61181	0	11.503 97395	0.9487 0555	0.9999 8262
ENST0000 0530310	<i>NR1H3-03</i> <i>5</i>	0	0	0	6.7640 3889	9.6850 3745	0	0.1748 8353	0.9981 5157

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	Tm1	Tm2	Tm3	pvalue	padj
ENST00000441012	<i>NR1H3-03</i> <i>0</i>	218.52 13425	0	196.21 86761	188.54 75841	180.49 38797	407.43 24106	0.5918 476	0.9999 8262
ENST00000467728	<i>NR1H3-00</i> <i>1</i>	182.10 11187	124.36 75694	172.17 22698	239.27 78758	169.92 83843	71.899 83716	0.9893 9671	0.9999 8262
ENST00000405853	<i>NR1H3-00</i> <i>6</i>	39.541 95721	0	24.046 40639	27.901 66042	31.696 4862	0	0.9661 5561	0.9999 8262
ENST00000481020	<i>NR1H3-00</i> <i>5</i>	3.1217 3346	25.858 60355	17.313 4126	19.446 61181	6.1632 0565	8.6279 8046	0.6639 8459	0.9999 8262
ENST00000481889	<i>NR1H3-02</i> <i>3</i>	1.0405 7782	30.784 05184	13.465 98758	6.7640 3889	0.8804 5795	39.305 24431	0.9735 3898	0.9999 8262
ENST00000527464	<i>NR1H3-02</i> <i>8</i>	9.3652 0039	0	6.7329 9379	0.8455 0486	3.5218 318	0	0.3402 6224	0.9999 8262
ENST00000527949	<i>NR1H3-03</i> <i>2</i>	30.176 75682	32.015 41392	15.389 70009	27.901 66042	53.707 93495	15.338 63193	0.6326 7705	0.9999 8262
ENST00000436778	<i>NR1H3-00</i> <i>7</i>	7.2840 4475	7.3881 7244	1.9237 1251	8.4550 4861	5.2827 477	8.6279 8046	0.5715 5624	0.9999 8262
ENST00000420369	<i>NR1H3-01</i> <i>9</i>	78.043 3366	11.082 25866	72.139 21917	75.249 93266	54.588 3929	0	0.8529 354	0.9999 8262
ENST00000419652	<i>NR1H3-01</i> <i>4</i>	31.217 33464	44.329 03465	27.893 83141	27.901 66042	20.250 53285	15.338 63193	0.1252 3099	0.9644 7689
ENST00000461778	<i>NR1H3-01</i> <i>5</i>	2.0811 5564	0	4.8092 8128	1.6910 0972	0.8804 5795	0	0.4572 6338	NA
ENST00000525441	<i>NR1H3-03</i> <i>9</i>	13.527 51168	0	9.6185 6256	6.7640 3889	17.609 159	8.6279 8046	0.6916 3111	0.9999 8262
ENST00000473222	<i>NR1H3-02</i> <i>2</i>	0	0	0	0	0	0	NA	NA
ENST00000483882	<i>NR1H3-02</i> <i>1</i>	32.257 91246	61.568 10369	81.757 78173	74.404 4278	51.066 5611	29.718 59936	0.7683 0051	0.9999 8262
ENST00000462051	<i>NR1H3-02</i> <i>4</i>	24.973 86771	4.9254 4829	0.9618 5626	21.983 12639	16.728 70105	21.090 6189	0.4074 3449	0.9999 8262
ENST00000498548	<i>NR1H3-01</i> <i>8</i>	13.527 51168	16.007 70696	13.465 98758	9.3005 5347	10.565 4954	9.5866 4495	0.2610 7015	0.9999 8262
ENST00000487913	<i>NR1H3-00</i> <i>8</i>	15.608 66732	34.478 13806	38.474 25022	36.356 70904	21.130 9908	16.297 29642	0.6704 9247	0.9999 8262
ENST00000494018	<i>NR1H3-02</i> <i>5</i>	1.0405 7782	8.6195 3452	0.9618 5626	0.8455 0486	0.8804 5795	0.9586 645	0.2055 638	NA
ENST00000262735	<i>PPARA-2</i> <i>01</i>	0	0	0	0	0	0	NA	NA
ENST00000460086	<i>PPARA-0</i> <i>04</i>	0	0	0	0	0	0	NA	NA
ENST00000396000	<i>PPARA-2</i> <i>02</i>	75.962 18096	9.8508 9659	33.664 96895	7.6095 4375	16.728 70105	130.37 83714	0.7761 0553	0.9999 8262

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	Tm1	Tm2	Tm3	pvalue	padj
ENST0000 0407236	<i>PPARA-0</i> <i>01</i>	3.1217 3346	588.59 10712	229.88 36451	1713.8 38354	1075.0 39157	0	0.4485 5789	0.9999 8262
ENST0000 0402126	<i>PPARA-0</i> <i>08</i>	10.405 77821	27.089 96562	35.588 68146	36.356 70904	27.294 19645	86.279 80459	0.1756 1615	0.9990 6307
ENST0000 0493286	<i>PPARA-0</i> <i>05</i>	142.55 91615	169.92 79662	166.40 11322	74.404 4278	49.305 6452	162.01 42997	0.1895 055	0.9999 8262
ENST0000 0434345	<i>PPARA-2</i> <i>03</i>	112.38 24047	119.44 21212	202.95 16699	0 0	71.317 09394	0	0.2586 6364	0.9999 8262
ENST0000 0481567	<i>PPARA-0</i> <i>06</i>	4.1623 1129	12.313 62074	4.8092 8128	10.146 05834	10.565 4954	3.8346 5798	0.7789 5214	0.9999 8262
ENST0000 0415785	<i>PPARA-0</i> <i>09</i>	13.527 51168	0 0	5.7711 3753	0 0	0 0	0	0.1275 9294	0.9668 4162
ENST0000 0420804	<i>PPARA-0</i> <i>03</i>	10.405 77821	6.1568 1037	3.8474 2502	4.2275 2431	7.0436 636	0.9586 645	0.4594 1472	0.9999 8262
ENST0000 0440343	<i>PPARA-0</i> <i>02</i>	0 0	0 0	0 0	0 0	0 0	0	NA NA	NA NA
ENST0000 0496865	<i>PPARA-0</i> <i>10</i>	34.339 06811	22.164 51733	22.122 69388	19.446 61181	26.413 7385	32.594 59284	0.9840 7133	0.9999 8262
ENST0000 0484619	<i>PPARA-0</i> <i>07</i>	5.2028 8911	0 0	4.8092 8128	0 0	0 0	10.545 30945	0.9821 9648	0.9999 8262
ENST0000 0508254	<i>TLR6-002</i>	0 0	44.329 03465	17.313 4126	8.4550 48613	7.9241 21549	14.379 96743	0.5062 20585	0.9999 82619
ENST0000 0514655	<i>TLR6-003</i>	88.449 11482	50.485 84502	202.95 16699	5.9185 34029	19.370 0749	29.718 59936	0.0023 60778	0.1464 57759
ENST0000 0436693	<i>TLR6-201</i>	3953.1 55143	3221.2 43185	2689.3 50091	5714.7 67358	6466.0 83184	6560.1 41142	8.24E-0 5	0.0119 19942
ENST0000 0381950	<i>TLR6-001</i>	514.04 54438	4361.4 84465	3498.2 71202	294.23 56917	353.94 40959	699.82 50817	0.0033 98385	0.1865 89606
ENST0000 0483928	<i>MAP2K3-007</i>	0 0	25.780 3813	15.422 5221	12.707 00861	36.174 02188	11.538 19082	0.6982 21361	0.9999 47878
ENST0000 0496046	<i>MAP2K3-004</i>	0 0	0 0	0 0	0 0	0 0	0	NA NA	NA NA
ENST0000 0526076	<i>MAP2K3-016</i>	0 0	0 0	0 0	0 0	0 0	0	NA NA	NA NA
ENST0000 0361818	<i>MAP2K3-201</i>	0 0	0 0	0 0	0 0	0 0	0	NA NA	NA NA
ENST0000 0316920	<i>MAP2K3-013</i>	0 0	0 0	0 0	5.9299 37349	3.5291 72867	0	0.2649 85751	NA
ENST0000 0395491	<i>MAP2K3-002</i>	2733.4 6814	200.10 48644	3350.5 42927	88.949 06024	56.466 76587	3452.8 03602	0.6332 74201	0.9999 47878
ENST0000 0342679	<i>MAP2K3-001</i>	510.96 74486	3185.7 18547	345.07 89321	4043.3 70138	4075.3 12368	458.64 3085	0.3686 18072	0.9999 47878

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	Tm1	Tm2	Tm3	pvalue	padj
ENST0000 0583508	MAP2K3- 017	104.89 37242	14.731 64646	234.22 95545	73.700 64991	15.881 2779	0	0.2668 77176	0.9999 47878
ENST0000 0479129	MAP2K3- 006	1.0385 51725	0	41.448 02816	166.88 53797	0	24.999 41344	0.4120 20888	0.9999 47878
ENST0000 0529517	MAP2K3- 011	17.655 37932	11.048 73484	7.7112 61052	0	0	11.538 19082	0.3925 64918	0.9999 47878
ENST0000 0477540	MAP2K3- 009	140.20 44828	52.788 39981	84.823 87158	212.63 06107	63.525 1116	80.767 33573	0.6173 52873	0.9999 47878
ENST0000 0534743	MAP2K3- 010	24.925 24139	12.276 37205	26.025 50605	52.522 30223	39.703 19475	29.806 99295	0.0662 70357	0.8523 10358
ENST0000 0527123	MAP2K3- 014	22.848 13795	18.414 55807	11.566 89158	16.095 54423	37.938 60832	18.268 80213	0.4595 34279	0.9999 47878
ENST0000 0596822	IRF3-017	0	44.194 93938	0	65.229 31084	54.702 17943	48.075 79508	0.3723 83814	0.9999 47878
ENST0000 0598108	IRF3-028	0	0	0	0	0	0	NA	NA
ENST0000 0595034	IRF3-023	0	0	0	0	0	0	NA	NA
ENST0000 0593337	IRF3-027	0	0	0	0	10.587 5186	0	0.2893 32567	NA
ENST0000 0598808	IRF3-010	638.70 93107	2032.9 67211	374.96 00687	241.43 31635	2105.1 51615	294.22 38659	0.8576 26689	0.9999 47878
ENST0000 0377139	IRF3-001	341.68 35175	55.243 67422	252.54 37995	160.95 54423	96.169 96062	472.10 43076	0.8630 52384	0.9999 47878
ENST0000 0601291	IRF3-002	219.13 44139	94.528 06478	138.80 26989	462.53 51132	0	360.56 84631	0.6360 23397	0.9999 47878
ENST0000 0593922	IRF3-011	96.585 3104	14.731 64646	0	154.17 83711	127.93 25164	343.26 11768	0.1344 48832	0.9768 72822
ENST0000 0597198	IRF3-004	2.0771 0345	0	0	6.7770 71256	0	0	0.6625 73211	NA
ENST0000 0597636	IRF3-003	894.19 3035	310.59 22129	598.58 66392	881.86 63972	161.45 96587	798.05 81983	0.9711 15948	0.9999 47878
ENST0000 0599223	IRF3-005	244.05 96553	0	158.08 08516	279.55 41893	0	179.80 34736	0.9408 69351	0.9999 47878
ENST0000 0309877	IRF3-006	252.36 80691	29.463 29292	169.64 77432	219.40 76819	34.409 43545	418.25 94172	0.6175 24806	0.9999 47878
ENST0000 0596756	IRF3-025	10.385 51725	0	0	16.095 54423	0	0	0.8668 62799	0.9999 47878
ENST0000 0600022	IRF3-012	119.43 34483	0	149.40 56829	91.490 46196	0	219.22 56255	0.9341 58483	0.9999 47878
ENST0000 0599144	IRF3-009	147.47 43449	73.658 2323	31.808 95184	501.50 32729	0	0	0.7176 27621	0.9999 47878

transcript_ id	transcript _name	Contro I1	Contro I2	Contro I3	Tm1	Tm2	Tm3	pvalue	padj
ENST0000 0377135	<i>IRF3-201</i>	45.696 27589	0	17.350 33737	104.19 74706	0	72.113 69261	0.5261 32551	0.9999 47878
ENST0000 0600911	<i>IRF3-007</i>	76.852 82763	45.422 57658	0	165.19 11119	0	0	0.8986 83083	0.9999 47878
ENST0000 0593818	<i>IRF3-022</i>	13.501 17242	0	17.350 33737	0	28.233 38293	0	0.9660 59713	0.9999 47878
ENST0000 0601373	<i>IRF3-024</i>	25.963 79312	33.146 20453	254.47 16147	91.490 46196	23.821 91685	67.306 11311	0.4859 02207	0.9999 47878
ENST0000 0601809	<i>IRF3-019</i>	24.925 24139	46.650 21379	28.917 22895	33.885 35628	37.938 60832	44.229 73147	0.6092 86321	0.9999 47878
ENST0000 0596765	<i>IRF3-008</i>	16.616 8276	0	10.602 98395	74.547 78382	0	0	0.6473 12123	0.9999 47878
ENST0000 0594387	<i>IRF3-013</i>	127.74 18621	119.08 08089	113.74 11005	155.02 5505	175.57 63501	153.84 25442	0.0343 33565	0.6721 67551
ENST0000 0595240	<i>IRF3-016</i>	8.3084 13798	8.5934 60435	8.6751 68684	18.636 94595	26.468 7965	12.499 70672	0.0403 89643	0.7172 1687
ENST0000 0596788	<i>IRF3-026</i>	3.1156 55174	3.6829 11615	8.6751 68684	7.6242 05163	6.1760 52517	5.7690 95409	0.6777 00892	0.9999 47878
ENST0000 0442265	<i>IRF3-202</i>	41.542 06899	0	3.8556 30526	0	0	0	0.0570 26029	0.8125 91336
ENST0000 0600453	<i>IRF3-020</i>	39.464 96554	25.780 3813	54.942 735	0	0	0	1.04E-0 8	4.31E-0 6
ENST0000 0599680	<i>IRF3-021</i>	24.925 24139	19.642 19528	0.9639 07632	1.6942 67814	30.880 26258	19.230 31803	0.8939 60369	0.9999 47878
ENST0000 0597180	<i>IRF3-029</i>	6.2313 10349	14.731 64646	15.422 5221	20.331 21377	10.587 5186	20.191 83393	0.4377 51422	0.9999 47878
ENST0000 0597369	<i>IRF3-014</i>	207.71 0345	114.17 02601	181.21 46347	132.15 28895	132.34 39825	112.49 73605	0.2352 94529	0.9999 47878
ENST0000 0602190	<i>IRF3-018</i>	12.462 6207	17.186 92087	0.9639 07632	17.789 81205	15.881 2779	28.845 47705	0.3000 13039	0.9999 47878
ENST0000 0596644	<i>IRF3-015</i>	11.424 06897	14.731 64646	17.350 33737	30.496 82065	0.8822 93217	24.037 89754	0.7638 81833	0.9999 47878

Supplementary Table 3. RT-qPCR primers sequences for the study.

<i>TNF-α</i>	Forward	GAGGCCAAGCCCTGGTATG
	Reverse	CGGGCCGATTGATCTCAGC
<i>IL-1β</i>	Forward	ATGATGGCTTATTACAGTGGCAA
	Reverse	GTCGGAGATTCGTAGCTGGA
<i>TUT1</i>	Forward	TCACTTCCTATCGGATCGGC
	Reverse	CTGTACCGACAAAACACAAGC
<i>JunB</i>	Forward	ACGACTCATACACAGCTACGG
	Reverse	GCTCGGTTTCAGGAGTTTGTAGT

Supplementary Table 4. RT-qPCR primers sequences for *NCOR2-013*.

<i>NCOR2-013</i> -exon 10 to 11	Forward	TGCTCTGCTCTGTACCAGGTCTC
	Reverse	ACAAAACCAACCACCACGTCCTC
<i>NCOR2-013</i> -exon 12	Forward	AGGTAGGCAAGGCGGTCCATG
	Reverse	GCATCATCGACCTGTCCCAAGTG

Supplementary Table 5. ChIP-qPCR primers sequences for the study.

<i>TNF-α-1</i> (chr6: 31574664-31574737)	Forward	GTCCAGGGCTATGGAAGTCG
	Reverse	GGTCCTGGAGGCTCTTTCAC
<i>TNF-α-2</i> (chr6: 31575099-31575278)	Forward	CAACCCCGTTTTCTCTCCCTCAAG
	Reverse	GGCCACTGACTGATTTGTGTGTAGG
<i>TNF-α-3</i> (chr6: 31575339-31575412)	Forward	GGGAGTGTGAGGGGTATCCT
	Reverse	CTGCACCTTCTGTCTCGGTT
<i>IL-1β-1</i> (chr2: 112836446-112836756)	Forward	CTGGAGCAGAGGCTTTGACA
	Reverse	AACCTCTTCGAGGCACAAGG
<i>IL-1β-2</i> (chr2: 112837433-112837605)	Forward	CAGGTGCTGTTACCCTAGCC
	Reverse	ACTTTGCTGGTGTCTCGGTT
<i>IL-1β-3</i> (chr2: 112838165-112838491)	Forward	GTTTGCTGCTTGAATGGGTGAATGG
	Reverse	AGGAGGGCTCAGTGTTAGGAATGG