**Supplementary figures and tables file**

# Defining cutaneous molecular pathobiology of arsenicals using phenylarsine oxide as a prototype

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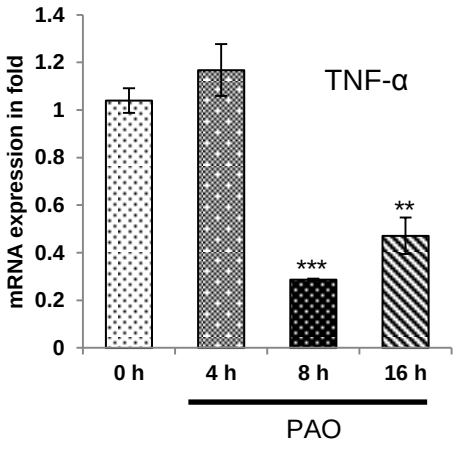
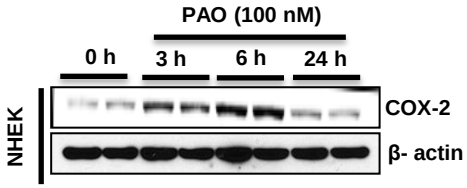
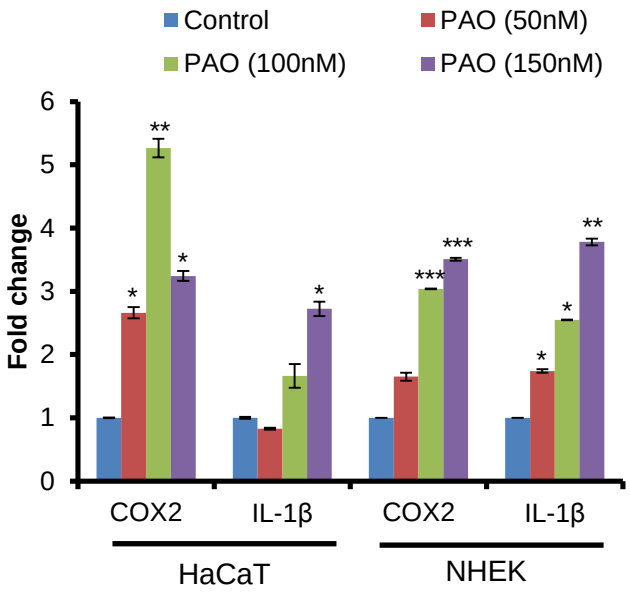


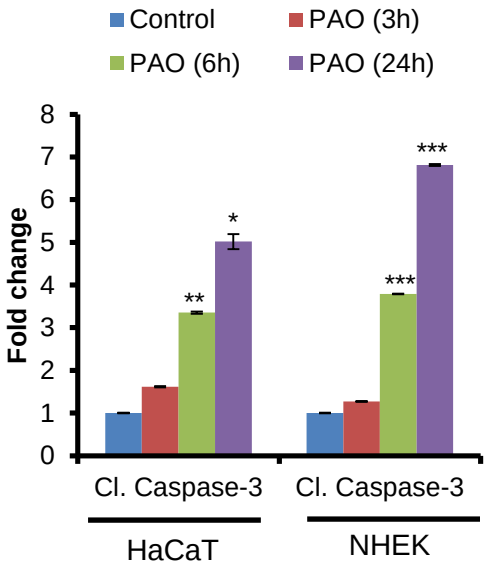

**Supplementary Fig. S1:** Real time PCR analysis of TNF-α in the skin of mouse either treated with vehicle or PAO (100 µg/mouse). Data are expressed as Mean ± SEM. **P<0.01 and ***P<0.001 indicate significant change when compared to control (0 h).



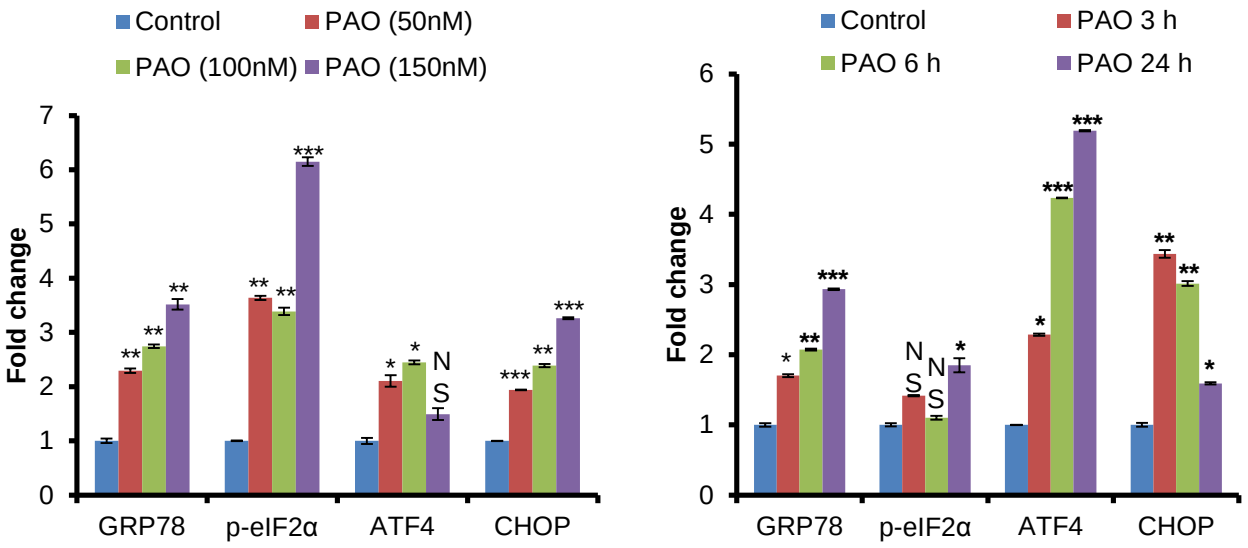

**Supplementary Fig. S2:** Time-dependent western blot analysis of COX-2 in the cell lysate of either PBS-treated or PAO-treated NHEK. β-actin was used as a loading control.



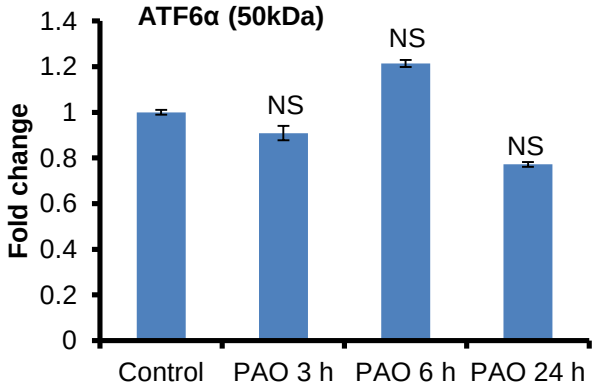

**Supplementary Fig. S3:** Dentiometric analysis of western blots for fig. 5C. β-actin was used as a loading control. *p<0.05, **P<0.01, ***P<0.001 when compared to their respective controls.



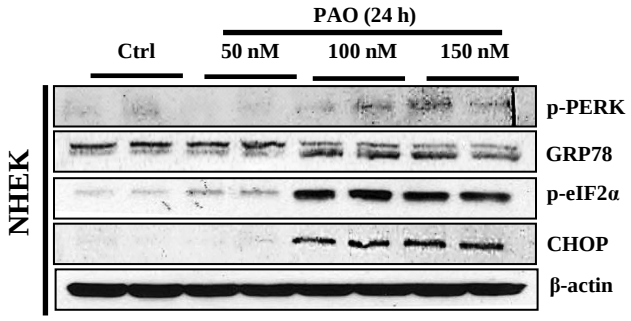

**Supplementary Fig. S4:** Dentiometric analysis of western blots for fig. 5E-II. β-actin was used as a loading control. *p<0.05, **P<0.01, ***P<0.001 when compared to their respective controls.



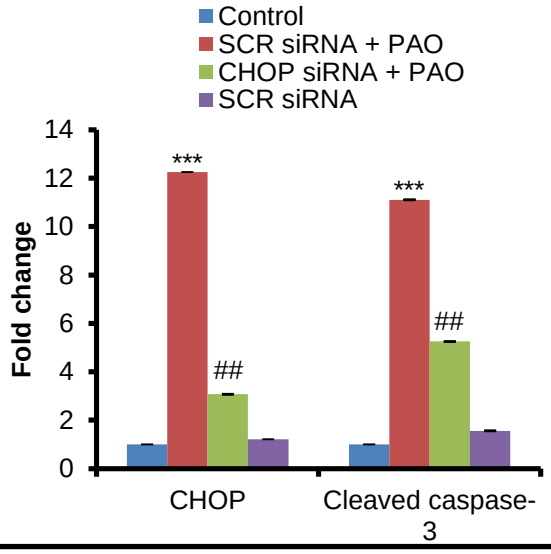

**Supplementary Fig. S5:** Dentiometric analysis of western blots for fig. 6A & 6B. β-actin was used as a loading control. *p<0.05, **P<0.01, ***P<0.001 when compared to their respective controls. NS- Non significant



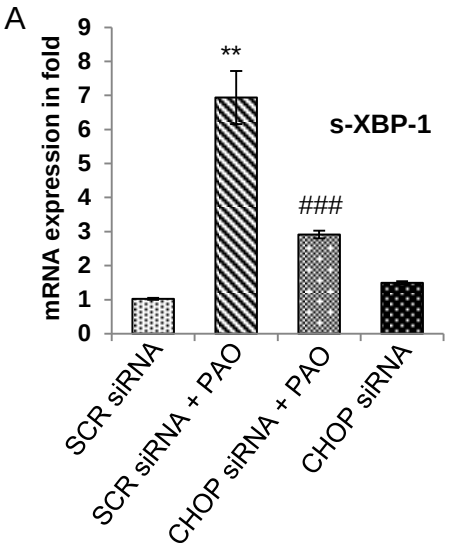

**Supplementary Fig. S6:** Dentiometric analysis of western blots for fig. 6F. β-actin was used as a loading control. NS- Non significant.

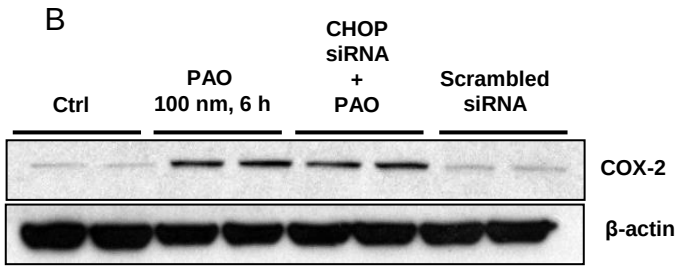



**Supplementary Fig. S7:** Dose-dependent western blot analysis of p-PERK, GRP78, p-eIF2α and CHOP in the cell lysate of either PBS-treated (control) or PAO-treated (50-150 nM, 24 h) NHEK. β-actin was used as a loading control.

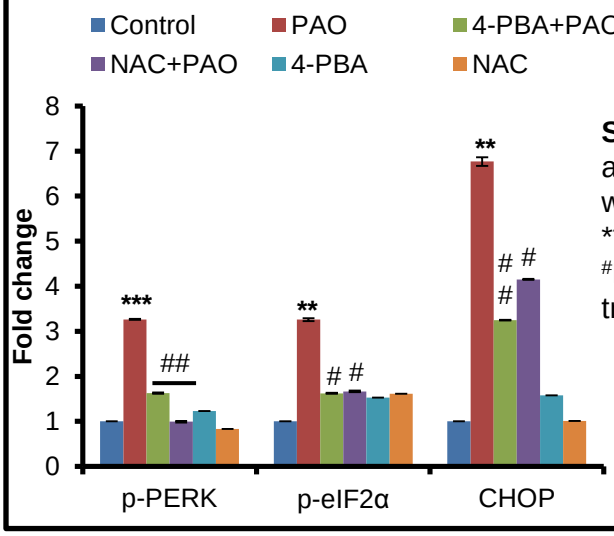



**Supplementary Fig. S8:** Dentiometric analysis of western blots for fig. 7C & 7D. β-actin was used as a loading control. ***P<0.001 when compared to control. ##P<0.01 when compared to SCR siRNA + PAO-treated group.

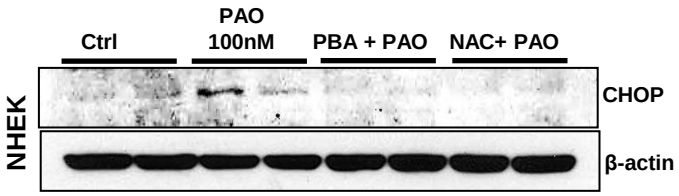


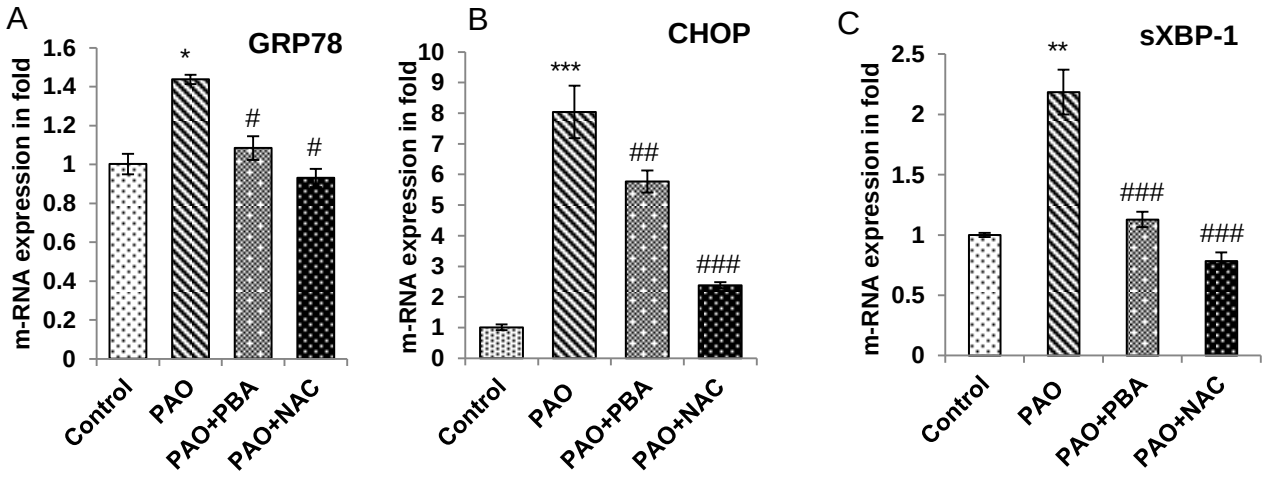

**Supplementary Fig. S9:** (A) Real time PCR analysis of sXBP-1 in CHOP knockdown HaCaT cells treated either with vehicle or PAO. (B) Western blot analysis of COX-2 in CHOP knockdown HaCaT cells treated either with vehicle or PAO. Scrambled siRNA was used as a negative control.

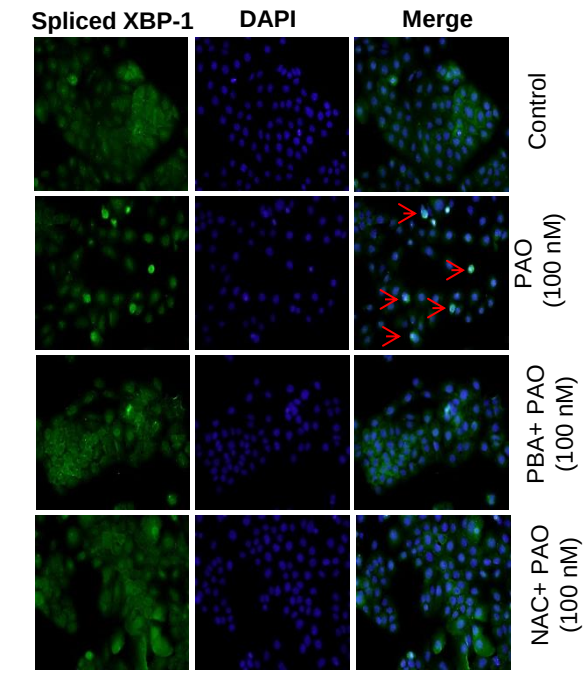



**Supplementary Fig. S10:** Dentiometric analysis of western blots for fig. 8D. β-actin was used as a loading control. **P<0.01, ***P<0.001 when compared to control. #P<0.05, ##P<0.01 when compared to PAO-treated group.

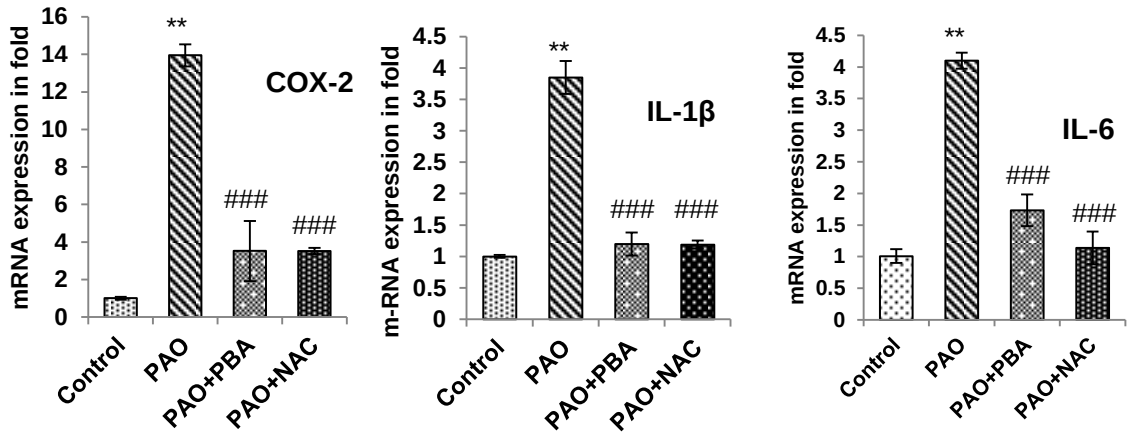



**Supplementary Fig. S11:** Western blot analysis of CHOP in NHEK cells treated with PAO in the presence or absence of 4-PBA or NAC.

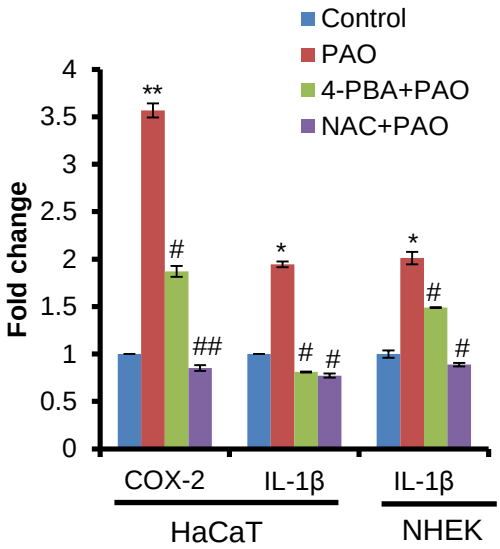


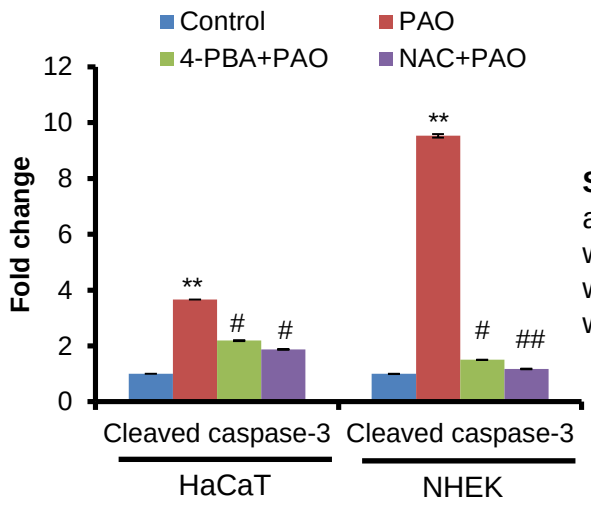

**Supplementary Fig. S12:** Real time PCR analysis of GRP78 (A), CHOP (B) and spliced (s) XBP-1 (C) in HaCaT cells treated with PAO in the presence or absence of 4-PBA or NAC. (D) Immunofluorescence staining of spliced (s) XBP-1 in HaCaT cells treated with PAO in the presence or absence of 4-PBA or NAC. Arrows indicate nuclear localization of sXBP-1. Data are expressed as Mean ± SEM. *P<0.05, **P<0.01 and ***P<0.001 when compared to control. #P<0.05, ##P<0.01 and ###P<0.001 when compared to PAO.




**Supplementary Fig. S13:** Real time PCR analysis of COX-2, IL-1β and IL-6 in HaCaT cells. **P<0.01 when compared to control. ###P<0.001 when compared to PAO.




**Supplementary Fig. S14:** Dentiometric analysis of western blots for fig. 8E. β-actin was used as a loading control. *P<0.05, **P<0.01 when compared to control. #P<0.05, ##P<0.01 when compared to PAO-treated group.




**Supplementary Fig. S15:** Dentiometric analysis of western blots for fig. 8F. β-actin was used as a loading control. **P<0.01 when compared to control. #P<0.05, ##P<0.01 when compared to PAO-treated group.

**Supplementary Table- S1:** PAO-induced skin changes in terms of clinical observation, erythema and edema.

| Draize Score | PAO-induced clinical observations |
|---|---|
| 0 | Unchanged from age matched control site |
| 1 | Mild edema, mild erythema, or other mild changes from age matched control mice (no necrosis) |
| 2 | Moderate edema, moderate erythema, or other moderate changes from age matched control mice (no necrosis) |
| 3 | Severe edema, Severe erythema, or other Severe changes from age matched control mice (no necrosis) |
| 4 | Focal necrosis: focal area of tissue is necrotic |
| 5 | Mild necrosis: 25-50% of tissue is necrotic |
| 6 | Moderate necrosis: 50-75% of tissue is necrotic |
| 7 | Severe necrosis: 75-100% of tissue is necrotic |

**Supplementary Table- S2:** List of primers used in this study.

| **Real Time Primers (mouse)** | **Sequences** |
|---|---|
| IL-1β | F 5`-AAAGCCTCGTGCTGTCGGACC-3` |
| | R 5`-CAGGGTGGGTGTGCCGTCTT-3` |
| IL-6 | F 5`-GGTGACAACCACGGCCTTCCC-3` |
| | R 5`-AAGCCTCCGACTTGTGAAGTGGT-3` |
| IFN-α | F 5-`CCCCTGACCCAGGAAGATGCC-3` |
| | R 5`-ACATTGGCAGAGGAAGACAGGGCTC-3` |
| TNF-α | F 5`-AGCCCACGTCGTAGCAAACCAC-3` |
| | R 5`-TCGGGGCAGCCTTGTCCCTT-3` |
| GAPDH | F 5'-CAATGTGTCCGTCGTGGATCT-3' |
| | R 5'-GTCCTCAGTGTAGCCCAAGATG-3' |
| **Real Time Primers (human)** | **Sequences** |
| Grp78 | F 5`-GCCTGTGGCTGGACTGCCTG-3` |
| | F-5`-ACGCCGACGCAGGAGTAGGT-3` |
| Chop | F-5`-GGTGGCAGCGACAGAGCCAA-3` |
| | F-5`-CAGCTGCCATCTCTGCAGTTGGA-3` |
| sXBP-1 | F-5`-GGTCTGCTGAGTCCGCAGCAGG-3` |
| | F-5`-GGGCTTGGTATATATGTGG-3` |
| GAPDH | F-5`-GGGGCTGGCATTGCCCTCAA-3` |
| | F-5`-GGCAGGGACTCCCCAGCAGT-3` |
| **TaqMan PCR Primers (human)** | **Cat. No. (ThermoFisher Scientific)** |
| COX-2 | Hs00153133-m1 |
| IL-6 | Hs00985639-m1 |
| IL-1β | Hs00174097_m1 |
| TGF-β | Hs00998133-m1 |
| GAPDH | Hs02758991-g1 |

**Supplementary Table- S3:** List of primary antibodies used in this study.
*IF- Immunofluorescence; **IHC- immunohistochemically

| Antibody | Company | Application | Dilution |
|---|---|---|---|
| IL-1β | Abcam | Western blot | 1000 |
| COX-2 | Cayman Chemicals | Western blot | 1000 |
| GRP78 | Cell signaling/Santa Cruz | Western Blot/*IF | 1000/200 |
| p-PERK | Cell signaling | Western Blot | 800 |
| CHOP | Cell signaling | Western Blot/**IHC | 1000/100 |
| ATF6α | Santa Cruz | Western Blot | 1000 |
| p-eIf2α | Cell signaling | Western Blot | 1000 |
| ATF4 | Abcam/Cell signaling | Western Blot/**IHC | 1000/100 |
| Cleaved caspase-3 | Cell signaling | Western Blot | 1000 |