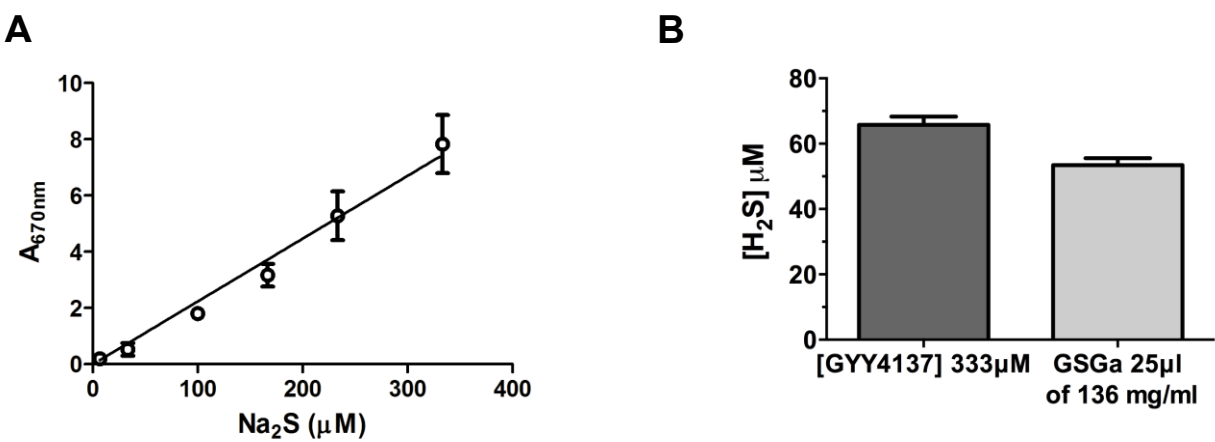
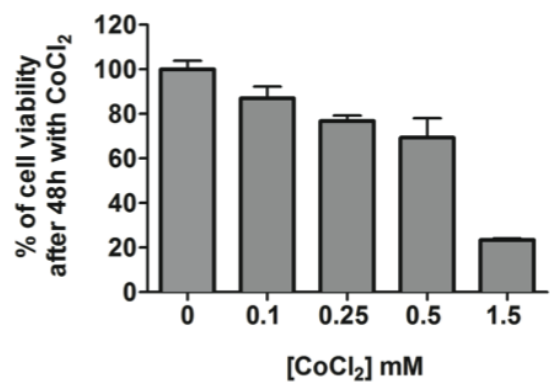


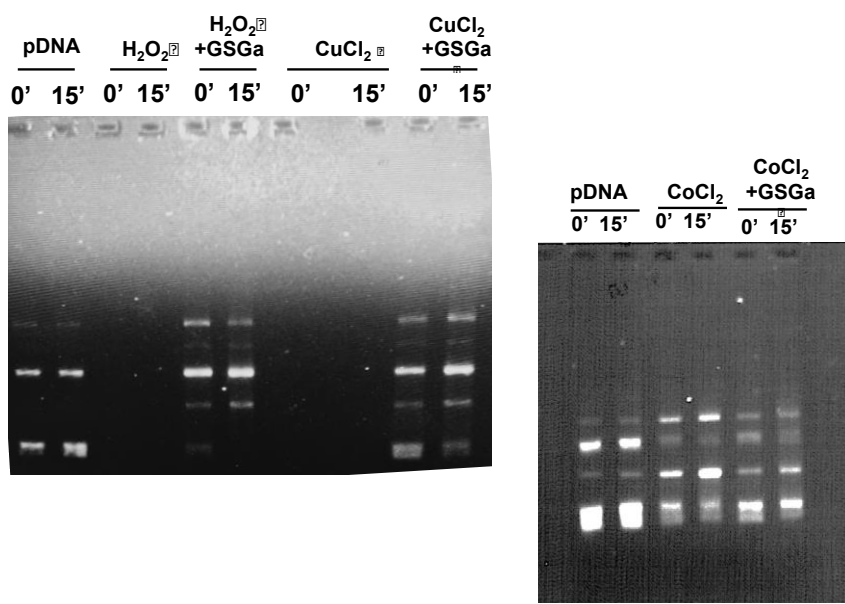
# Supplementary Materials



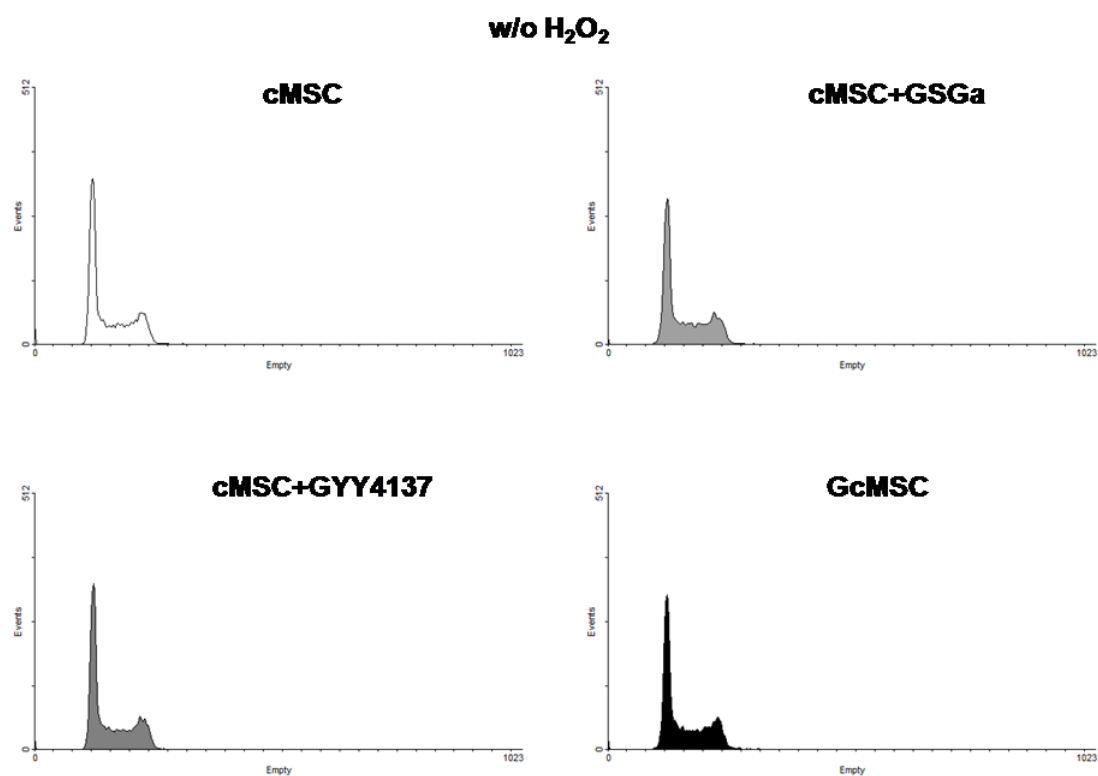
**Figure S1.** Calibration curve of H<sub>2</sub>S releasing. **A)** Calibration curve of H<sub>2</sub>S release by different concentrations of Na<sub>2</sub>S. **B)** Amount (μM) of H<sub>2</sub>S released by 333 μM GYY4137 and 25 μL of GSGa (136 mg/mL); measured by MB assay and spectrophotometric analysis.



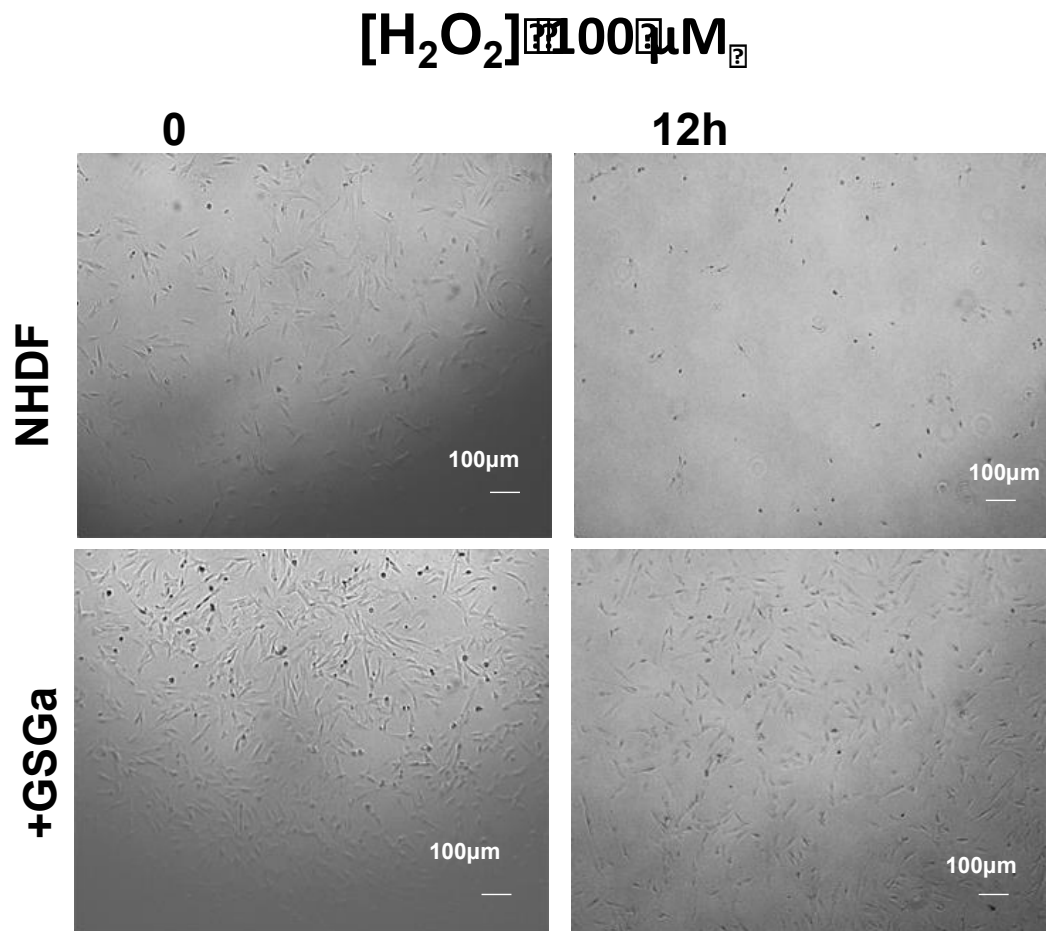
**Figure S2.** Cell viability of cMSC by MTT assay, after 48h of treatment with increased concentrations of CoCl<sub>2</sub>.



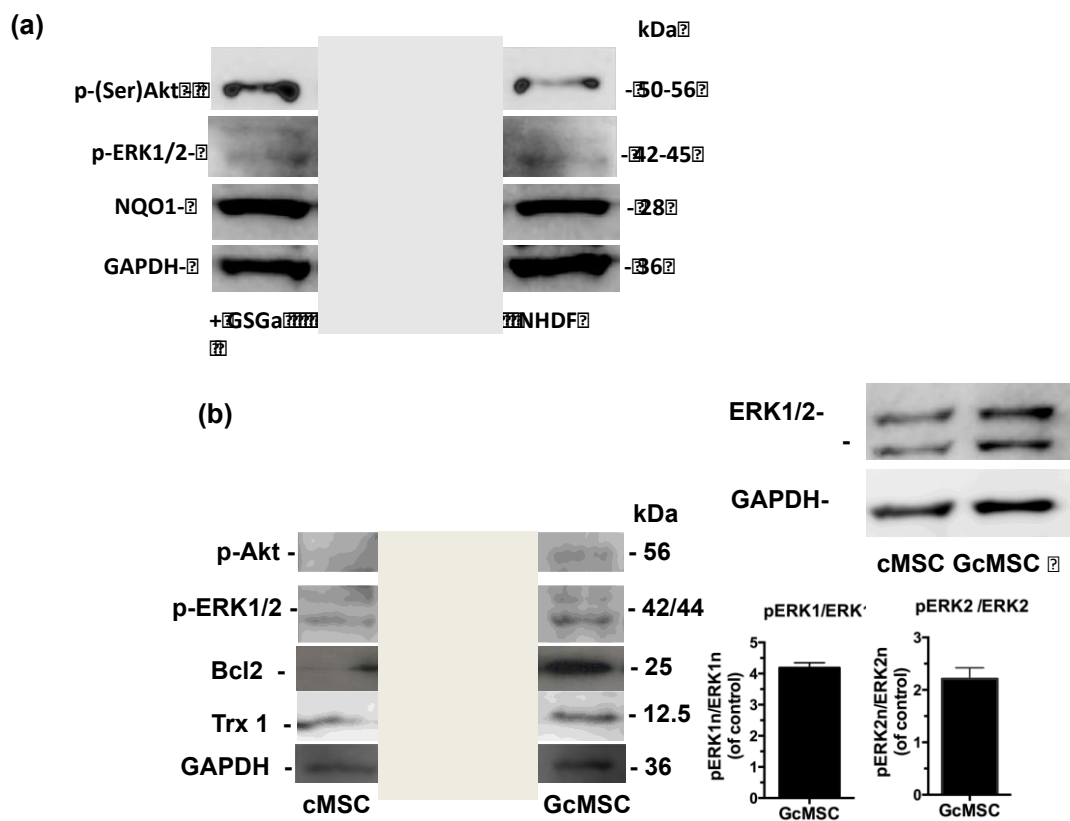
**Figure S3.** Integral images of the agarose gel elettrophoresis of pDNA incubated with H<sub>2</sub>O<sub>2</sub>, CuCl<sub>2</sub> or CoCl<sub>2</sub> in the presence and in the absence of GSGa corresponding to the Figure 2a,b.



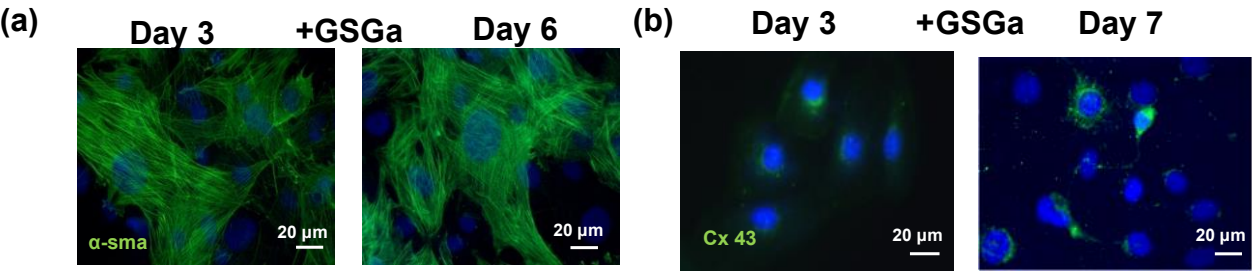
**Figure S4.** FACS cell cycle analysis of cMSC, cMSC growth in the presence of GSGa (680 µg/mL) (cMSC+GSGa) or of GYY4137 (80 mM) (cMSC+GY4137) and GcMSC cultured for 24 h in the absence of H<sub>2</sub>O<sub>2</sub>.



**Figure S5.** Magnification of the micrographs present in Figure 3a. Micrographs of NHDF after 0 and 12 h of treatment with H<sub>2</sub>O<sub>2</sub> (100 μM), with (+GSGa) or without (NHDF) the addition of 680 μg/mL GSGa.

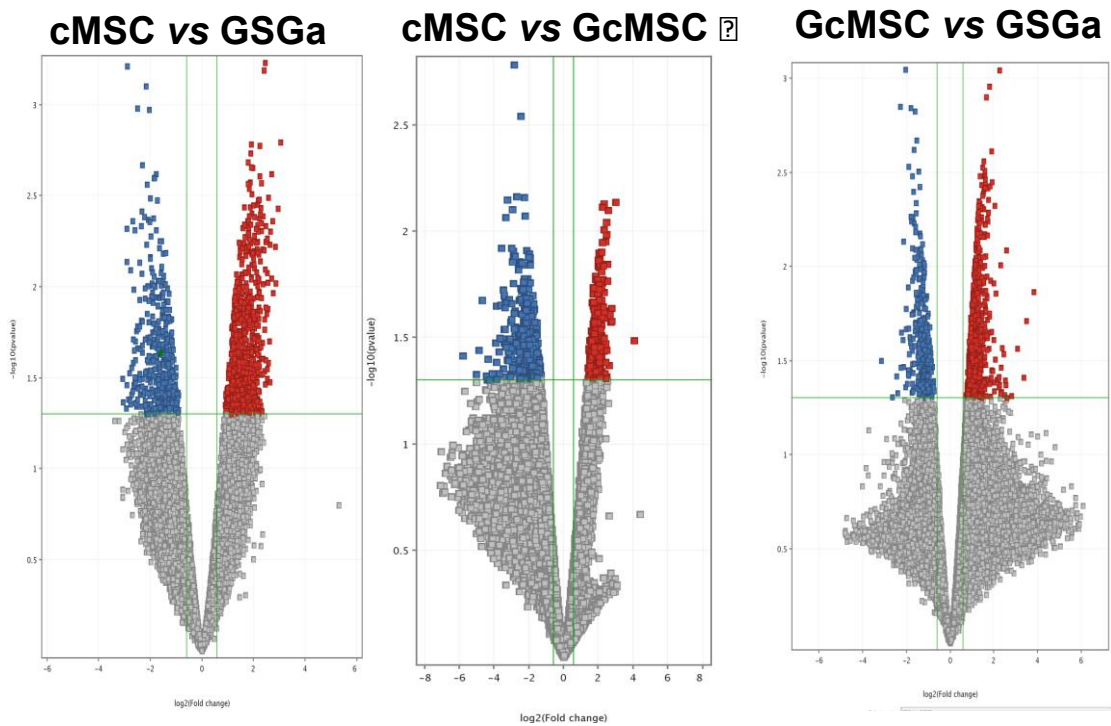


**Figure S6.** (a) Representative western blot analysis of the expression of p(Ser 473)Akt, p-ERK1/2, Bcl2, NQO1 in NHDF; (b) Representative western blot analysis of the expression of p(Ser 473)Akt, p-ERK1/2, Bcl2, Trx1 in cMSC and GcMSC.

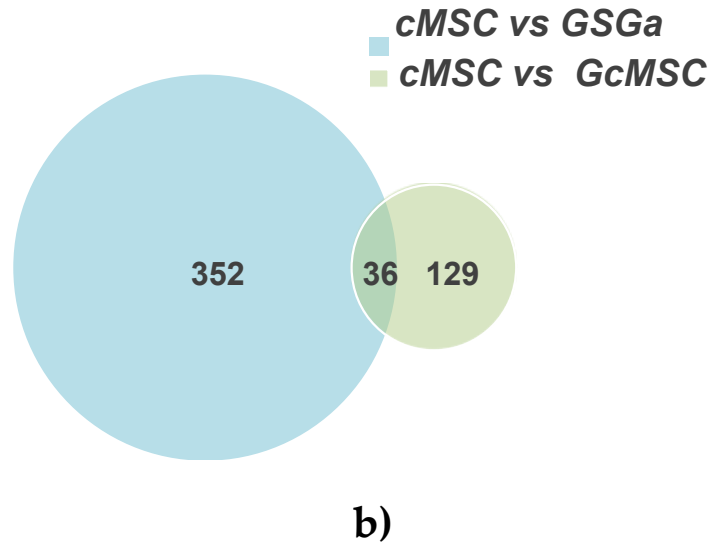


**Figure S7.** (a)  $\alpha$ -SMA expression at 3 and 6 days is shown in green and (b) Cx43 at 3 and 7 days is stained in green, the nuclei are stained with Hoechst 33342.

# Volcano Plots



a)



**Figure S8.** Microarray analysis. **a)** Volcano plots from microarray analysis. Volcano plots from transcriptional profiling analysis of cMSC following acute (GSGa) (3 days, left panel) or prolonged (right panel) (GcMSC) treatment with GSGa indicate variation of expression of analyzed genes. Blue and red dots indicate respectively significantly down-regulated and up-regulated genes.  $p$  value cut-off 0.05; fold change cut-off 1.5. **b)** Venn Diagram depicts overlap of differentially regulated genes after 3 days (GSGa) and 30 days (GcMSC) of treatment. The diagram has been generated by using InteractiVenn webtool (<http://www.interactivenn.net>) inputting the probe name lists from the gene array data.

**Table S1.** Analysis by David 6.8 of the genes that are changed in both the GSGa treatments.

| ID From   | To     | Species      | Gene Name                                                                        |
|-----------|--------|--------------|----------------------------------------------------------------------------------|
| 4208      | 781152 | Homo sapiens | myocyte enhancer factor 2C                                                       |
| 387036    | 812157 | Homo sapiens | glucuronidase, beta-like 1                                                       |
| 3115      | 783974 | Homo sapiens | major histocompatibility complex, class II, DP beta 1                            |
| 1572      | 780823 | Homo sapiens | cytochrome P450, family 2, subfamily F, polypeptide 1                            |
| 100170226 | 789502 | Homo sapiens | small ILF3/NF90-associated RNA C3                                                |
| 2906      | 786599 | Homo sapiens | glutamate receptor, ionotropic, N-methyl D-aspartate 2D                          |
| 187       | 805439 | Homo sapiens | apelin receptor                                                                  |
| 79843     | 794370 | Homo sapiens | family with sequence similarity 124B                                             |
| 387111    | 811718 | Homo sapiens | chromosome 6 open reading frame 181                                              |
| 133522    | 810592 | Homo sapiens | peroxisome proliferator-activated receptor gamma, coactivator 1 beta             |
| 115350    | 788996 | Homo sapiens | Fc receptor-like 1                                                               |
| 6521      | 791678 | Homo sapiens | solute carrier family 4, anion exchanger, member 1 (erythrocyte membrane protein |

|        |                                                                                         |              | band 3, Diego blood group)                                         |
|--------|-----------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------|
| 153443 | 811107                                                                                  | Homo sapiens | serum response factor binding protein 1                            |
| 3769   | 806972                                                                                  | Homo sapiens | potassium inwardly-rectifying channel, subfamily J, member 13      |
| 64320  | 772726                                                                                  | Homo sapiens | ring finger protein 25                                             |
| 57282  | 789195                                                                                  | Homo sapiens | solute carrier family 4, sodium bicarbonate transporter, member 10 |
| 89866  | 791541                                                                                  | Homo sapiens | SEC16 homolog B ( <i>S. cerevisiae</i> )                           |
| 83549  | 781739                                                                                  | Homo sapiens | uridine-cytidine kinase 1                                          |
| 23070  | 792478                                                                                  | Homo sapiens | FtsJ methyltransferase domain containing 2                         |
| 407006 | 772175                                                                                  | Homo sapiens | microRNA 221                                                       |
| 85004  | 776084                                                                                  | Homo sapiens | RAS-like, estrogen-regulated, growth inhibitor                     |
| 440131 | 792858                                                                                  | Homo sapiens | similar to bA90M5.1 (novel protein)                                |
| ID     | Gene Name                                                                               | Species      | COG_ONTOLOGY                                                       |
| 1572   | cytochrome P450, family 2, subfamily F, polypeptide 1                                   | Homo sapiens | Secondary metabolites biosynthesis, transport, and catabolism      |
| 4208   | myocyte enhancer factor 2C                                                              | Homo sapiens | Transcription                                                      |
| 83549  | uridine-cytidine kinase 1                                                               | Homo sapiens | Nucleotide transport and metabolism                                |
| ID     | Gene Name                                                                               | Species      | KEGG_PATHWAY                                                       |
| 187    | apelin receptor                                                                         | Homo sapiens | Neuroactive ligand-receptor interaction                            |
| 1572   | cytochrome P450 family 2, subfamily F, polypeptide 1                                    | Homo sapiens | Metabolism of xenobiotics by cytochrome P450, signaling pathway    |
| 2906   | glutamate receptor, ionotropic, N-methyl D-aspartate 2D major                           | Homo sapiens | Neuroactive ligand-receptor interaction                            |
| 3115   | histocompatibility complex, class II, DP beta 1 hsa04514:Cell adhesion molecules (CAMs) | Homo sapiens | Antigen processing and presentation                                |
| 4208   | myocyte                                                                                 | Homo         | MAPK signaling pathway                                             |

|      |                              |                 |                                       |
|------|------------------------------|-----------------|---------------------------------------|
|      | enhancer factor<br>2C        | sapiens         |                                       |
| 3549 | uridine-cytidine<br>kinase 1 | Homo<br>sapiens | Pyrimidine metabolism Drug metabolism |

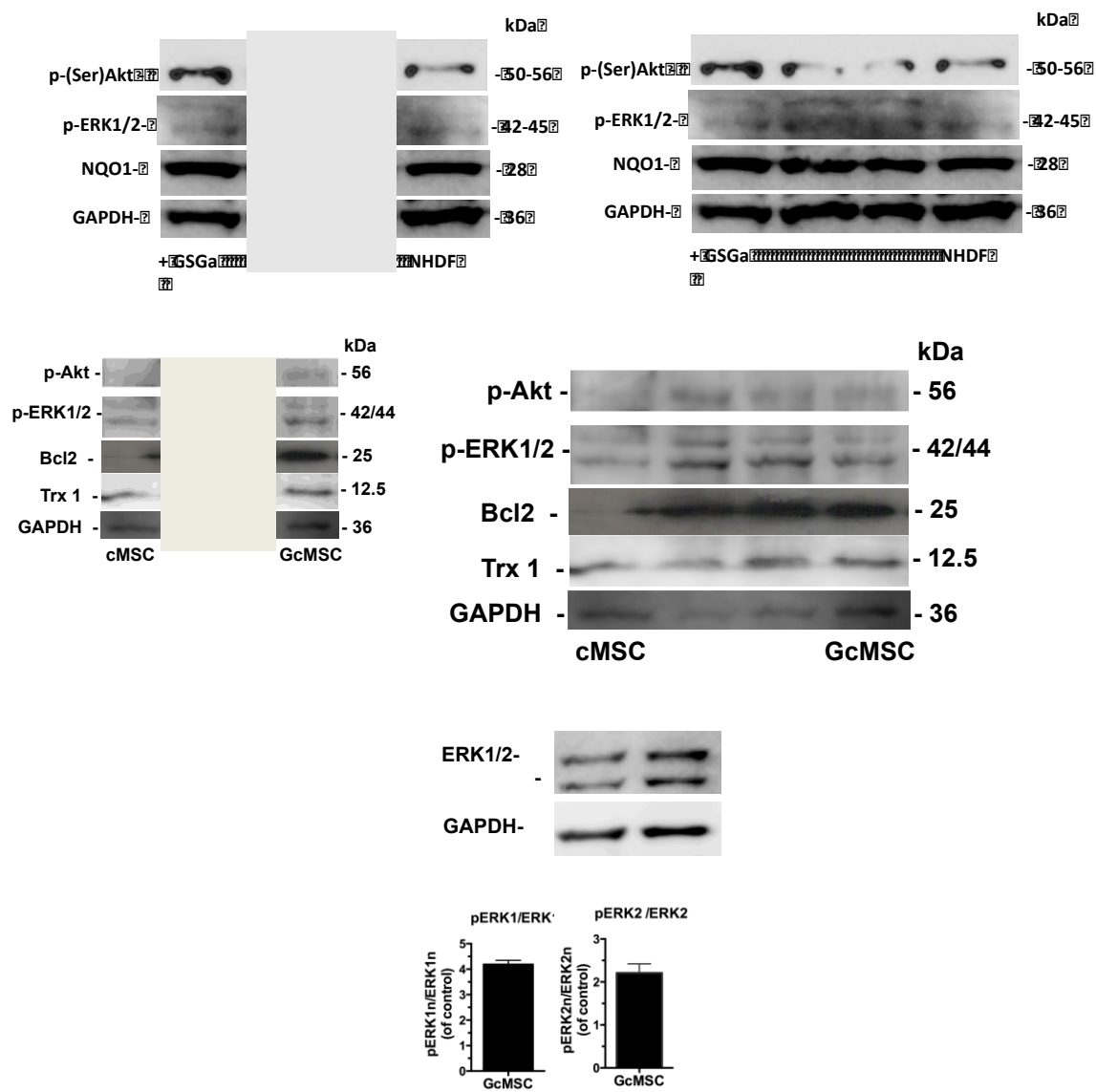
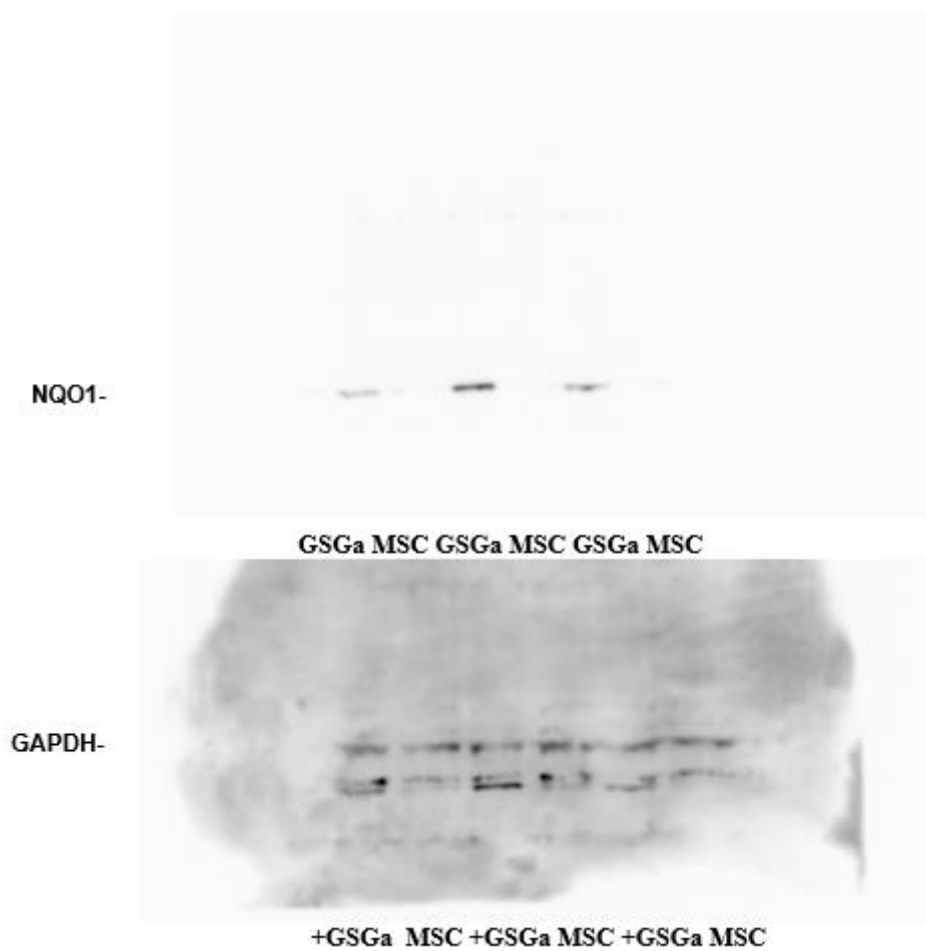


Figure S9. Original figures of the western blottings.



**Figure S10.** Original western blot of figure 4B that show the expression of NQO1 in MSC w/o treatment with GSGa.