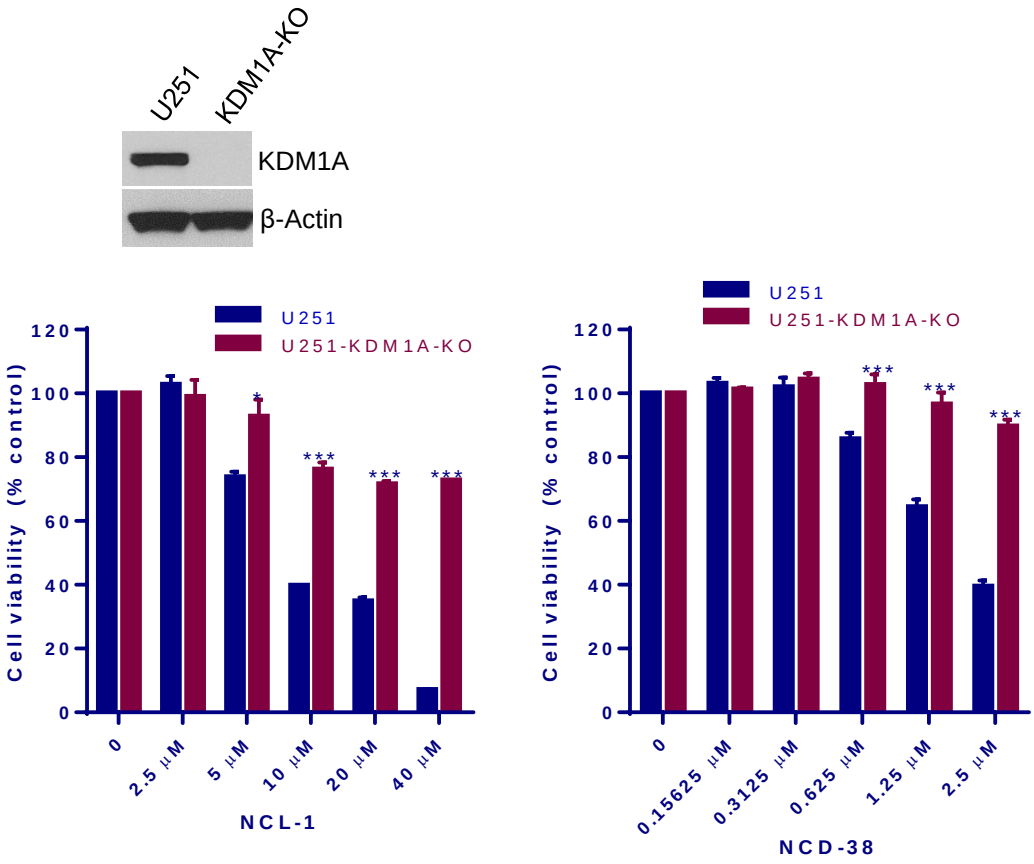


Supplementary Fig 1. KDM1A inhibitors showed minimal effect on KDM1A knockout cells. U251 cells were transfected with CRISPR/Cas9 plasmids targeting KDM1A (obtained from Horizon Discovery, St Louis, MO) and individual clones were screened for KDM1A gene deletion. KDM1A expression was determined using western blotting. U251 and U251-KDM1A-knockout cells were treated with KDM1A inhibitors NCL-1 and NCD-38 for 7days and the cell viability was determined by MTT assay. All experiments were representative of two independent experiments. Data are represented as mean ± SE. *$p < 0.05$, ***$p < 0.001$ based on the Student's t-test.

A

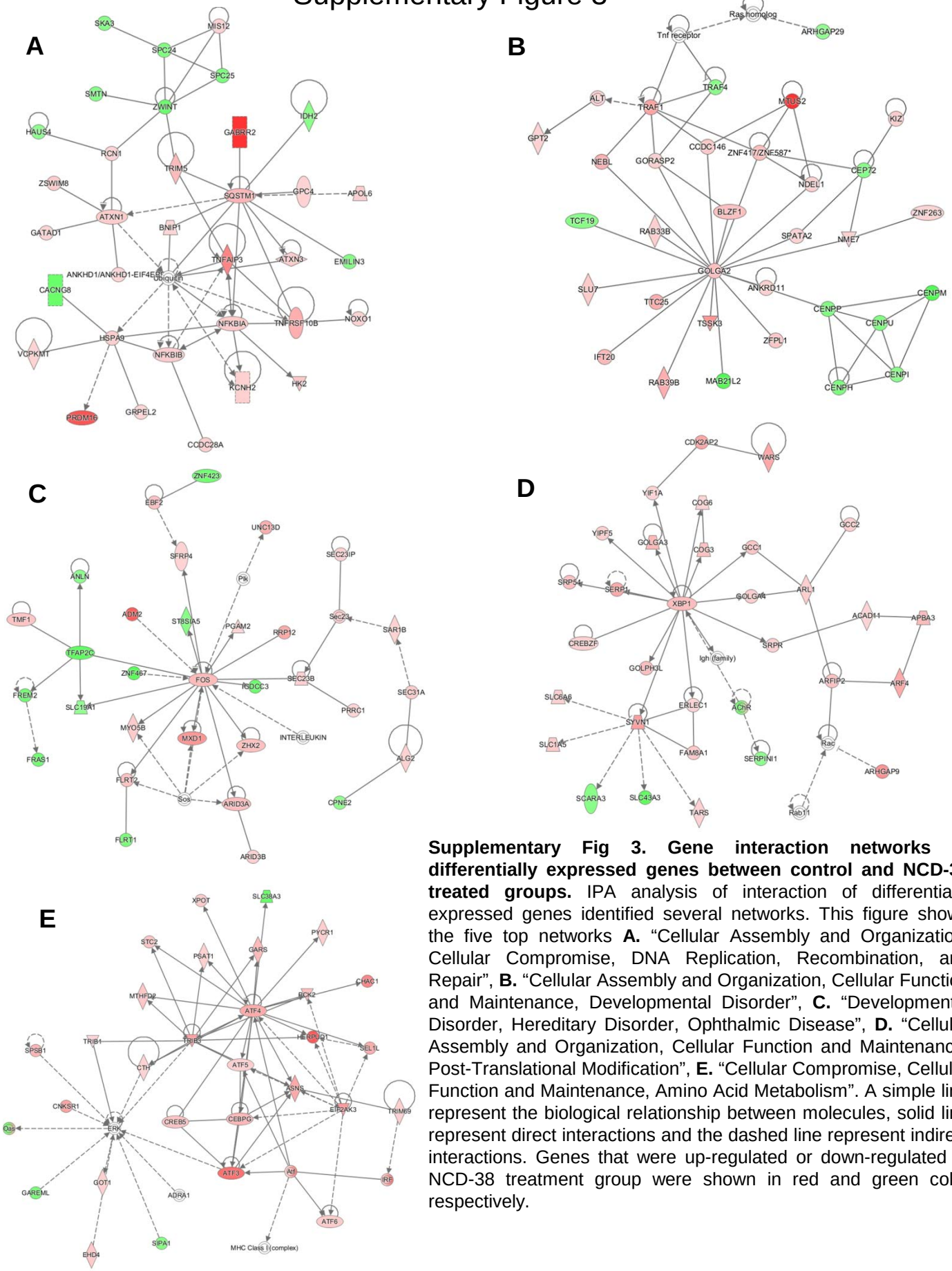
Associated Network Functions	Score
Cellular Assembly and Organization, Cellular Compromise, DNA Replication, Recombination, and Repair	45
Cellular Assembly and Organization, Cellular Function and Maintenance, Developmental Disorder	40
Developmental Disorder, Hereditary Disorder, Ophthalmic Disease	38
Cellular Assembly and Organization, Cellular Function and Maintenance, Post-Translational Modification	38
Cellular Compromise, Cellular Function and Maintenance, Amino Acid Metabolism	34

B

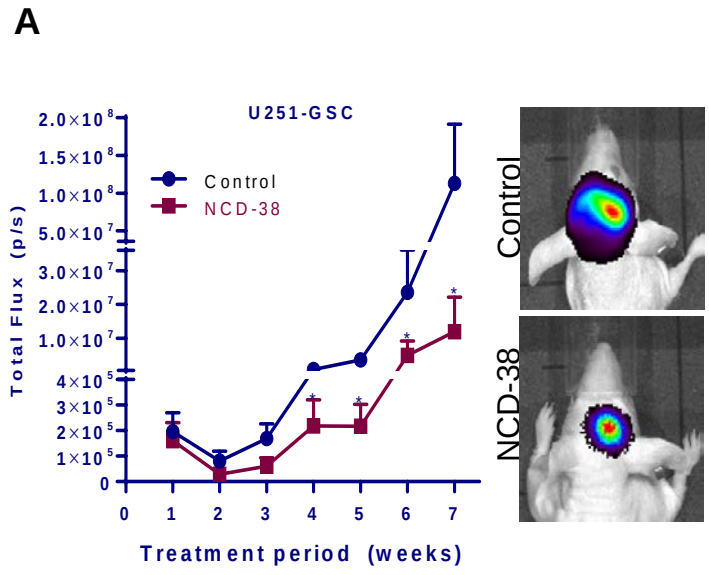
Top Molecular and Cellular Functions	p-value	#molecules
Cell Death and Survival	1.14E-03 - 1.95E-11	375
Cellular Compromise	7.34E-04 - 7.61E-09	35
Cellular Function and Maintenance	1.04E-03 - 7.61E-09	215
Cellular Growth and Proliferation	1.12E-03 - 3.30E-08	379
Cell Cycle	1.28E-03 - 5.46E-08	153

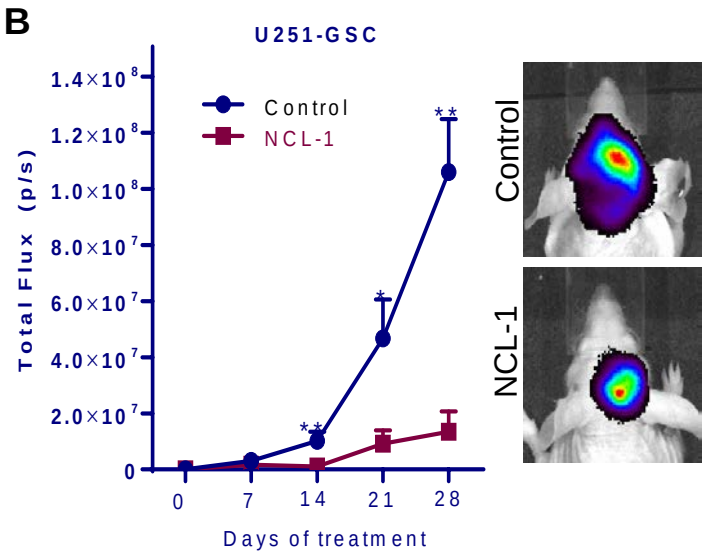
Supplementary Fig 2. Analysis of global transcriptome changes between control and NCD-38 treated groups. Differentially expressed genes were subjected to IPA analysis and the top five associated network functions (A) and the top five molecular and cellular functions (B) of differentially expressed genes are shown.

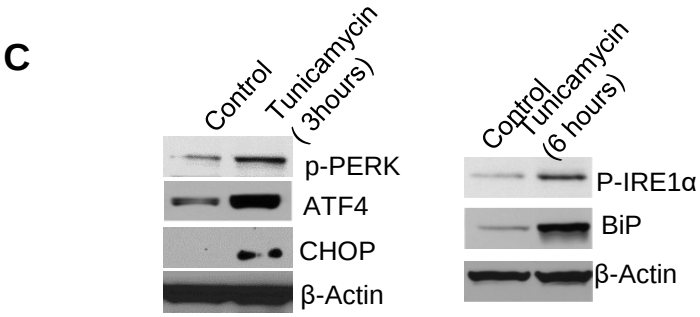
Supplementary Figure 3

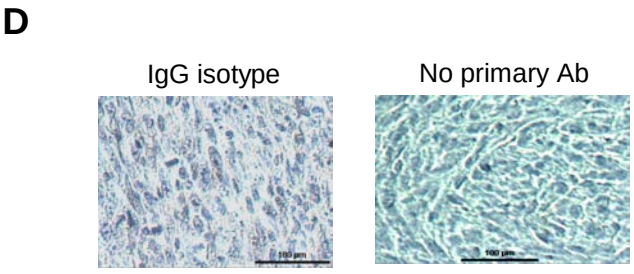


Supplementary Fig 3. Gene interaction networks of differentially expressed genes between control and NCD-38 treated groups. IPA analysis of interaction of differentially expressed genes identified several networks. This figure shows the five top networks **A.** "Cellular Assembly and Organization, Cellular Compromise, DNA Replication, Recombination, and Repair", **B.** "Cellular Assembly and Organization, Cellular Function and Maintenance, Developmental Disorder", **C.** "Developmental Disorder, Hereditary Disorder, Ophthalmic Disease", **D.** "Cellular Assembly and Organization, Cellular Function and Maintenance, Post-Translational Modification", **E.** "Cellular Compromise, Cellular Function and Maintenance, Amino Acid Metabolism". A simple line represent the biological relationship between molecules, solid line represent direct interactions and the dashed line represent indirect interactions. Genes that were up-regulated or down-regulated in NCD-38 treatment group were shown in red and green color respectively.

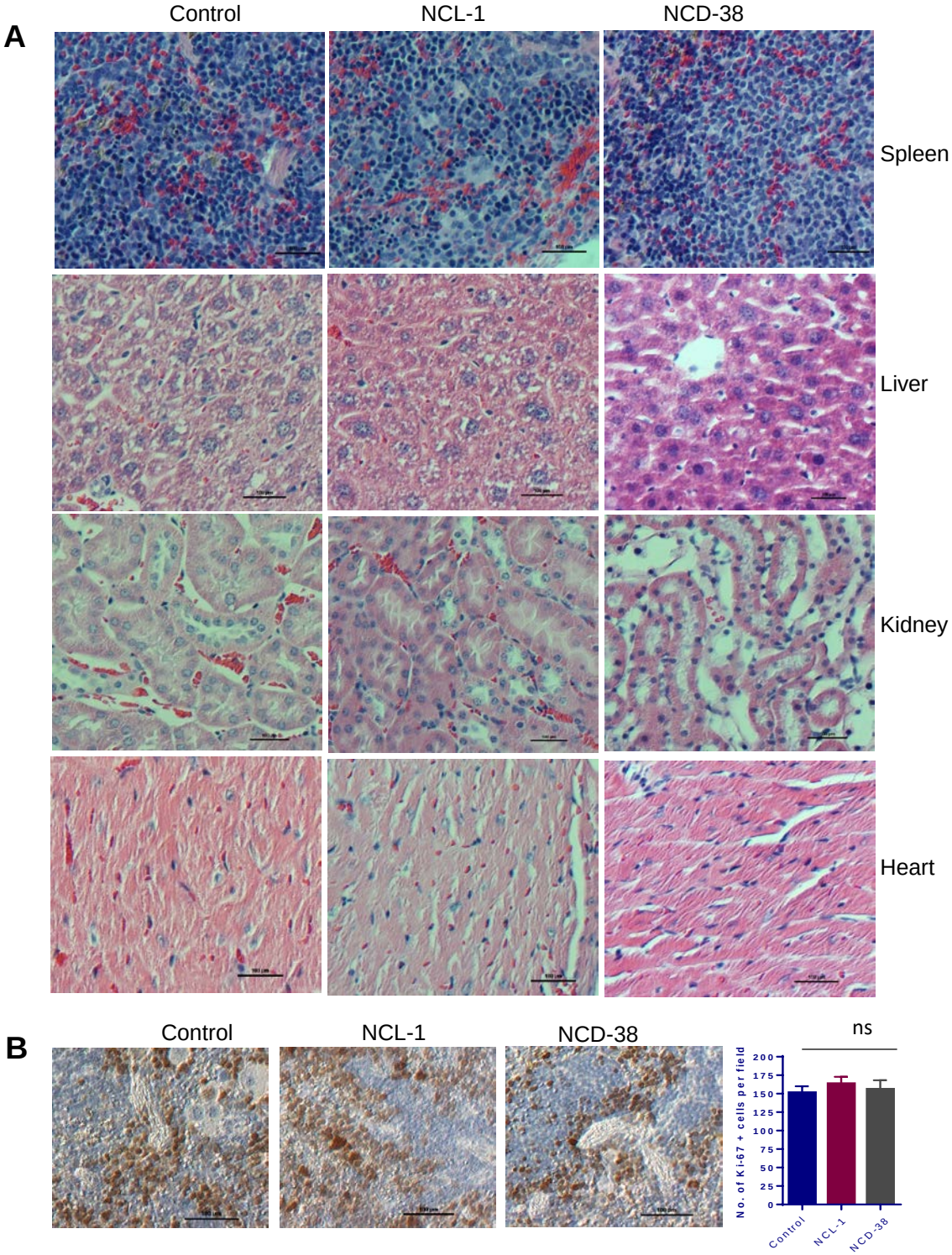




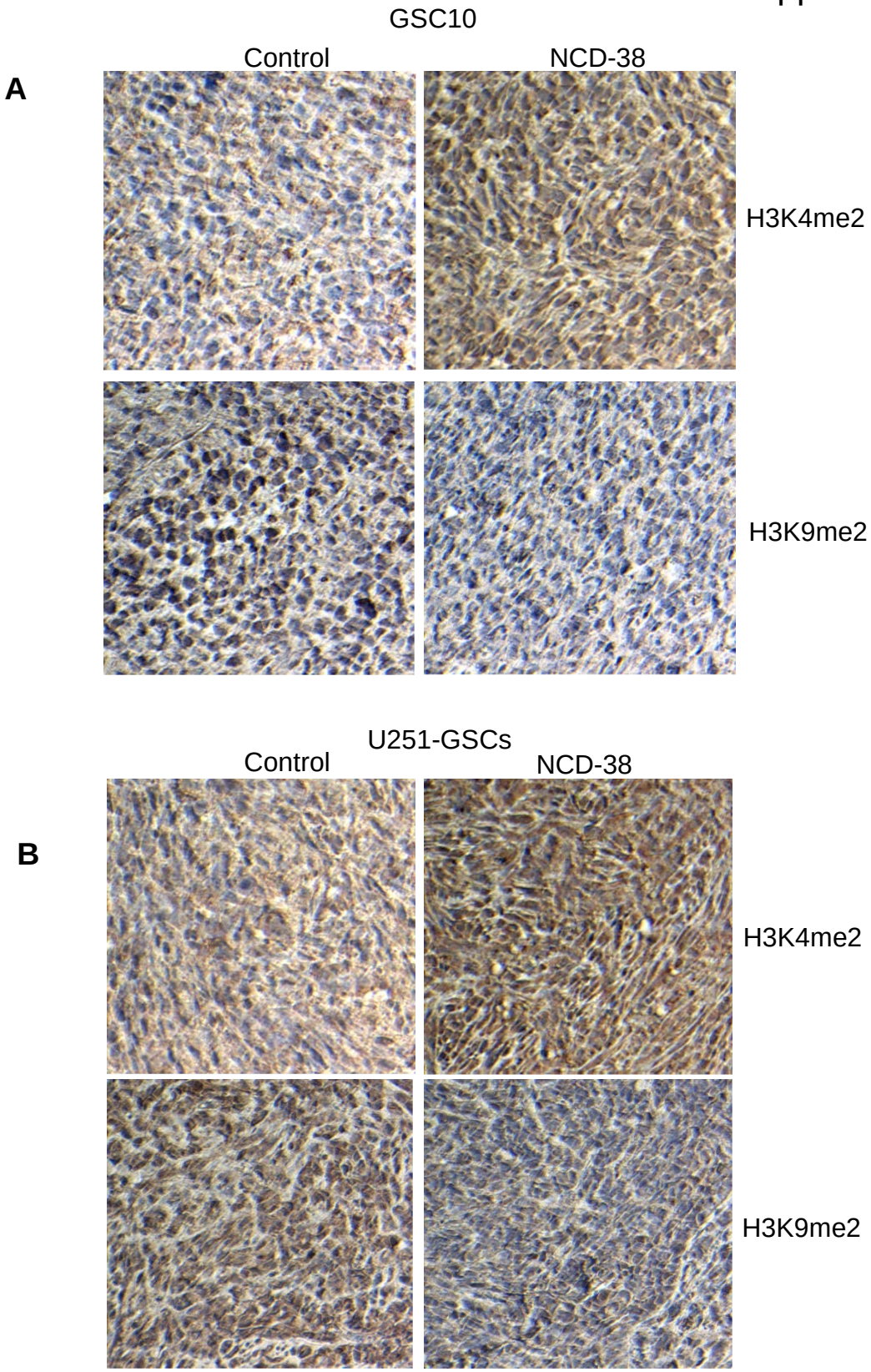




Supplementary Fig 4. KDM1A inhibitors reduced GSCs-mediated *in vivo* tumor progression. A, B, U251-GSCS stably expressing GFP-luciferase were implanted intracranially into the right cerebrum of nude mice. After the tumors established, mice were randomized to control or the treatment group and received either vehicle, NCD-38 (5 mg/kg body weight/day) or NCL-1 (10 mg/kg body weight/day). Tumor growth was monitored using Xenogen IVIS imaging every week (n = 7). Representative images of tumor bearing mice are shown. Data are represented as mean ± SE. *$p < 0.05$, **$p < 0.01$ based on the Student's t-test. C. U251-GSCs were treated with Tunicamycin (5 µg/ml) and the expression of p-PERK, ATF4, CHOP, p-IRE1α, and BiP were examined using western blotting. D. U251 GSCs tumor sections that are treated with KDM1A inhibitor were incubated with isotype IgG (rabbit) primary antibody followed by secondary antibody incubation (left panel) or primary antibody was omitted (right panel) and the immunoreactivity was visualized using DAB.



Supplementary Fig 5. KDM1A inhibitors NCL-1 and NCD-38 treatment did not cause toxicity in organs. A, The organs spleen, liver, kidney and heart were collected from both the control and KDM1A inhibitor-treated mice and fixed in formalin, subjected to H&E staining and analyzed histopathologically. B, Spleen sections were subjected to immunohistochemical staining for Ki67 as described in materials and methods. The number of Ki-67-positive cells from five different fields were counted and plotted as histogram. ns=non significant. Data are represented as mean ± SE. ns, not significant based on the Student's t-test.



Supplementary Fig 6. KDM1A inhibitor NCD-38 alters global histone methylation marks. Mouse brains collected from both the control and NCD-38-treated mice implanted with GSC10 (A) and U251-GSC (B) were fixed in formalin and subjected to immunohistochemical staining for H3K4me2 and H3K9me2 as described in materials and methods.