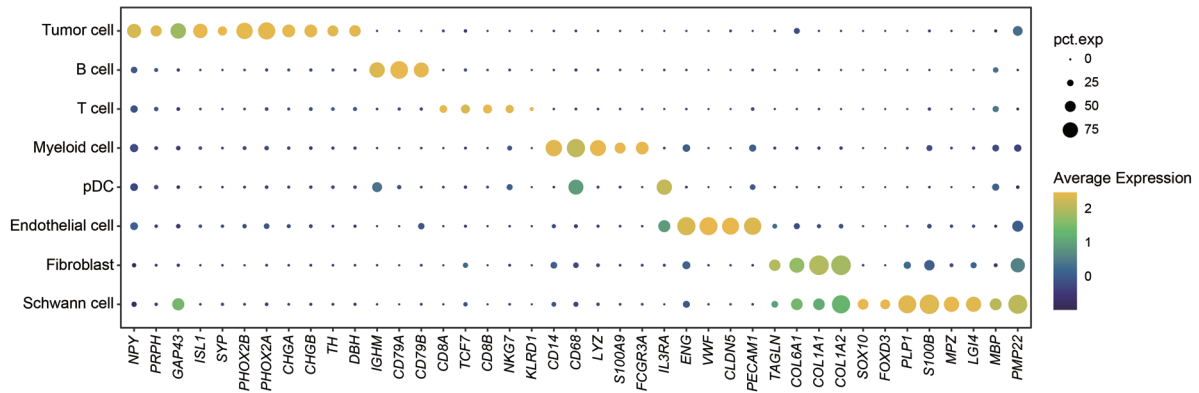


A.



B.

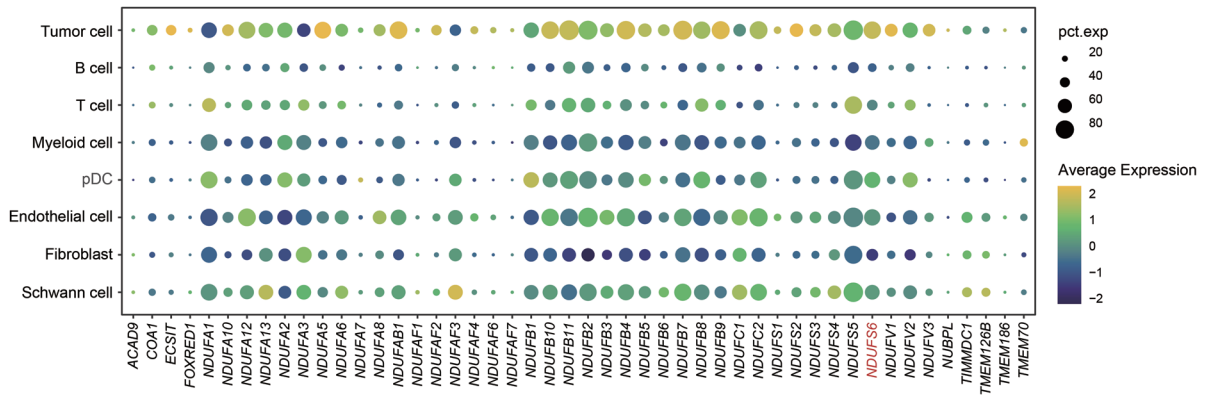
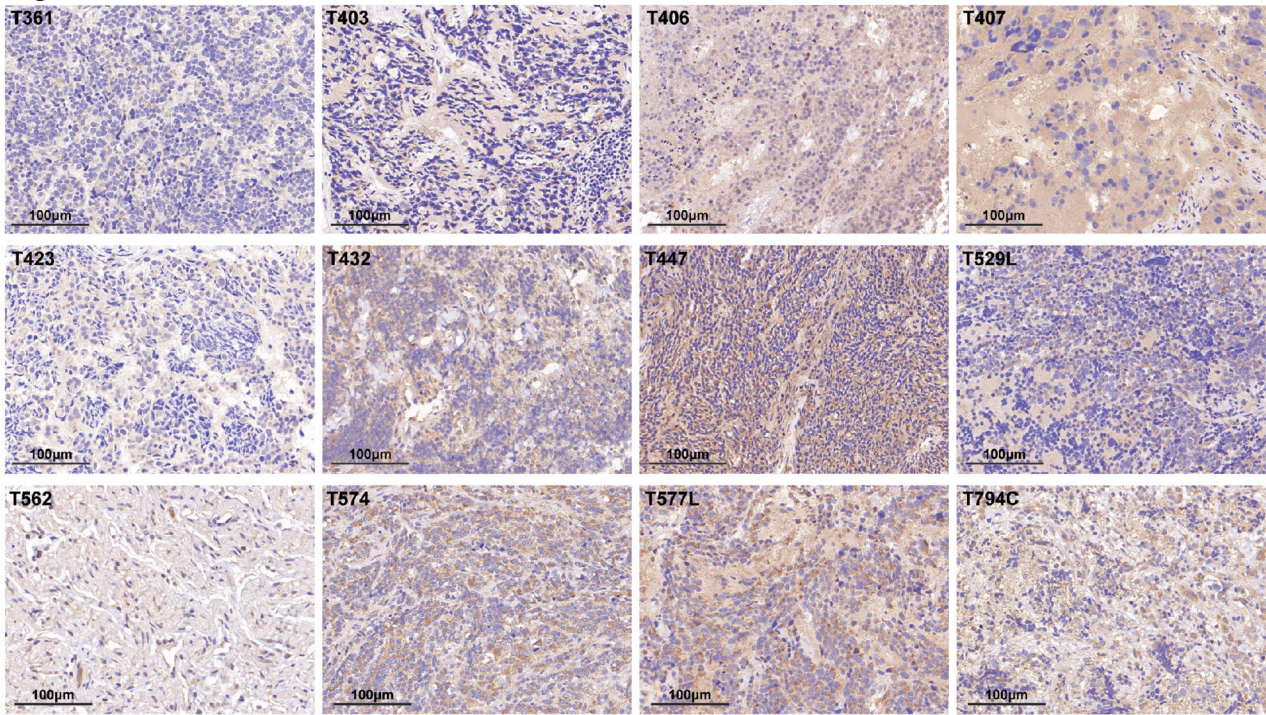


Figure S1 The expression of selected genes in the scRNA dataset GSE137804. (A) Dot plot showing the expression of canonical marker genes across different cell types. (B) Dot plot showing the expression of genes associated with CI complex across different cell types in NB.

High-risk



Intermediate-risk

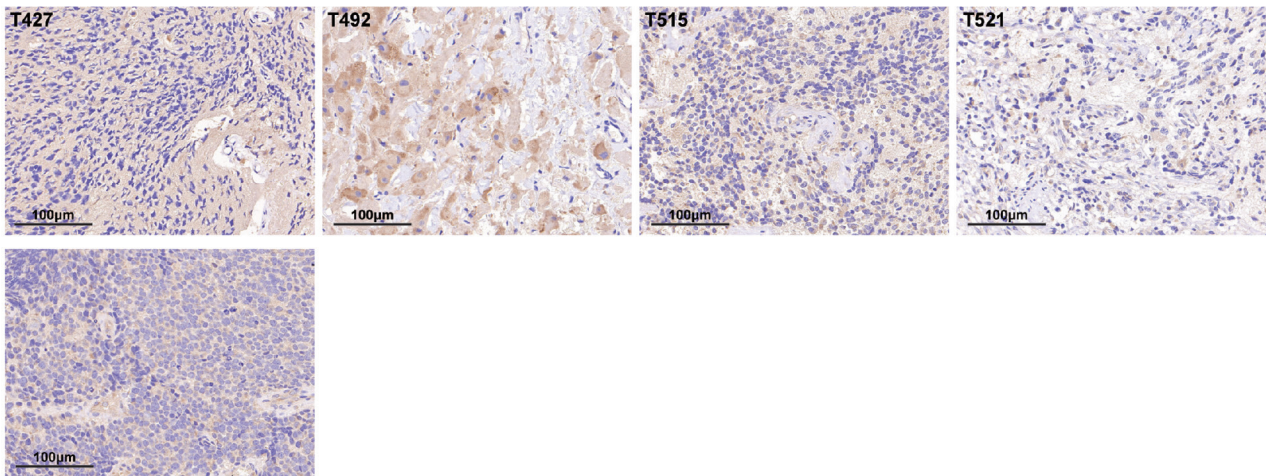


Figure S2 Immunohistochemistry staining of NDUFS6 in high-risk and intermediate-risk NB tissues.

Low-risk

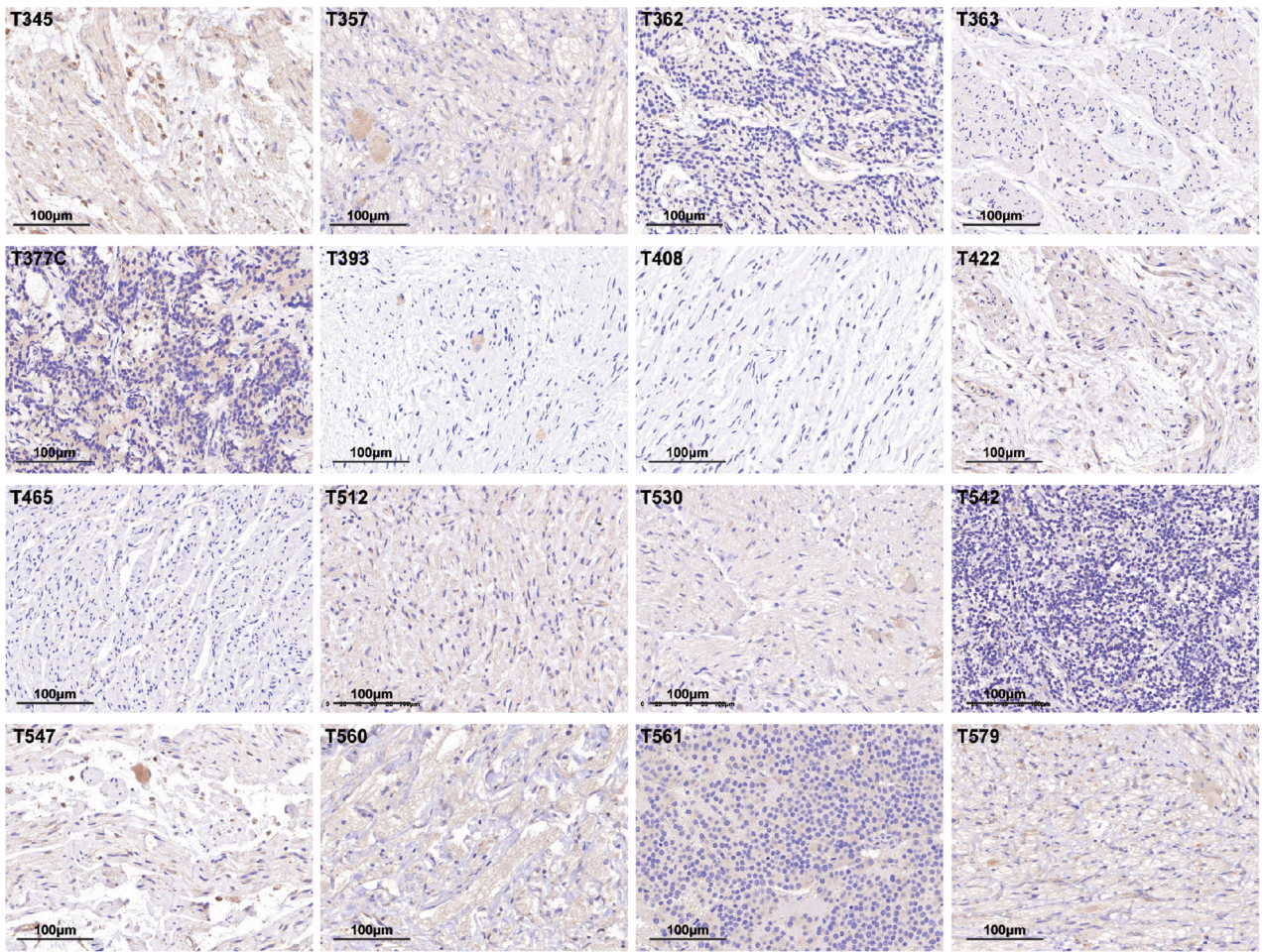


Figure S3 Immunohistochemistry staining of NDUFS6 in low-risk NB tissues.

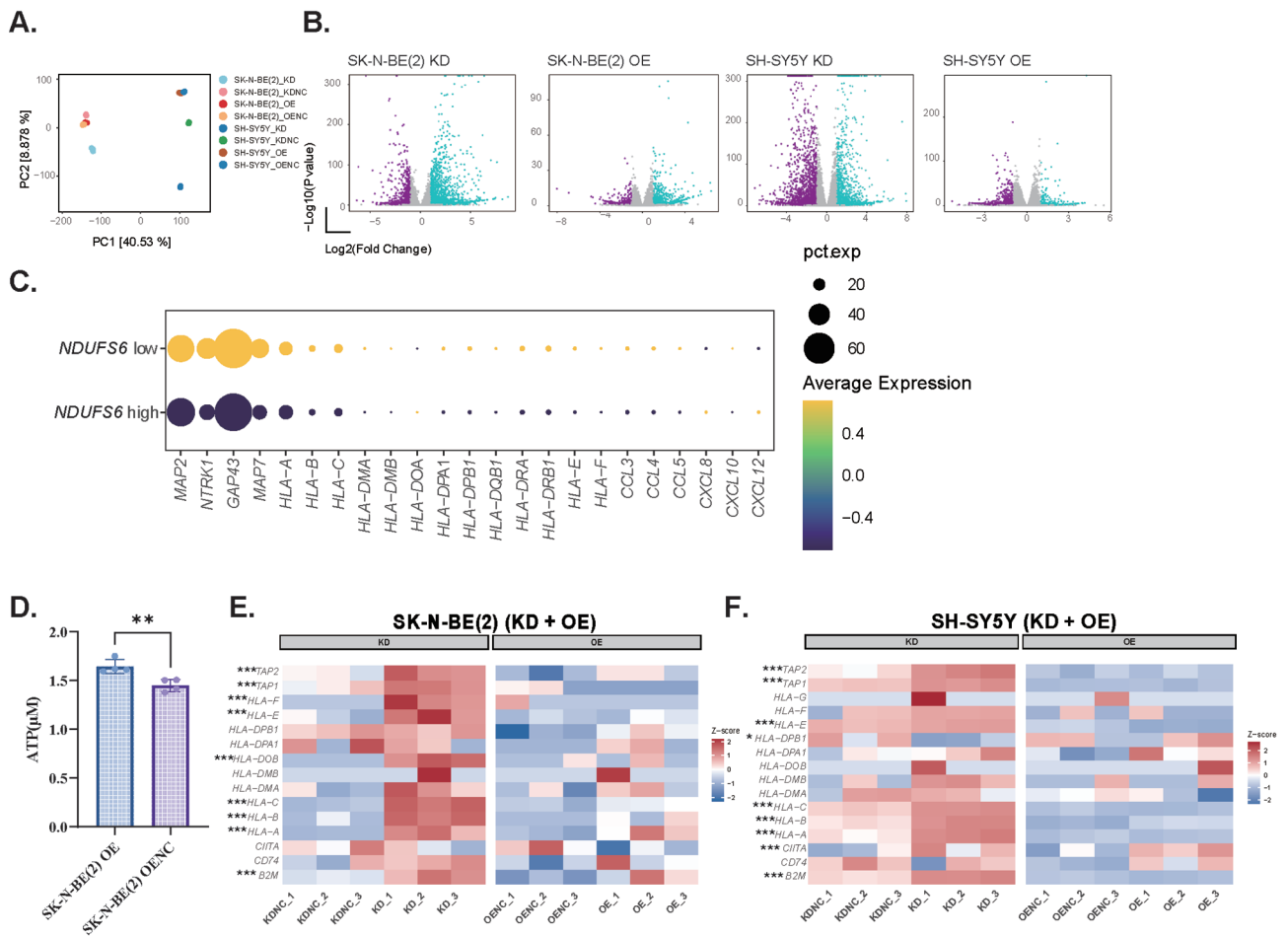


Figure S4 Transcriptomic analysis following NDUFS6 overexpression or knockdown, and ATP production assays. (A) PCA plot showing the distribution of samples across different experimental groups. (B) Volcano plot displaying significantly upregulated and downregulated genes after NDUFS6 OE and KD. (C) Dot plot showing the expression of neuron differentiation, MHC and chemokine genes in NDUFS6-high versus NDUFS6-low tumor cells from the scRNA-seq dataset GSE137804. (D) NDUFS6 overexpression enhanced intracellular ATP production. (E) NDUFS6 knockdown upregulated MHC molecule expression in NB cell line SK-N-BE(2). (F) NDUFS6 knockdown upregulated MHC molecule expression in NB cell line SH-SY5Y. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$. KD, knockdown; KDNC, knockdown negative control; OE, overexpression; OENC, overexpression negative control.

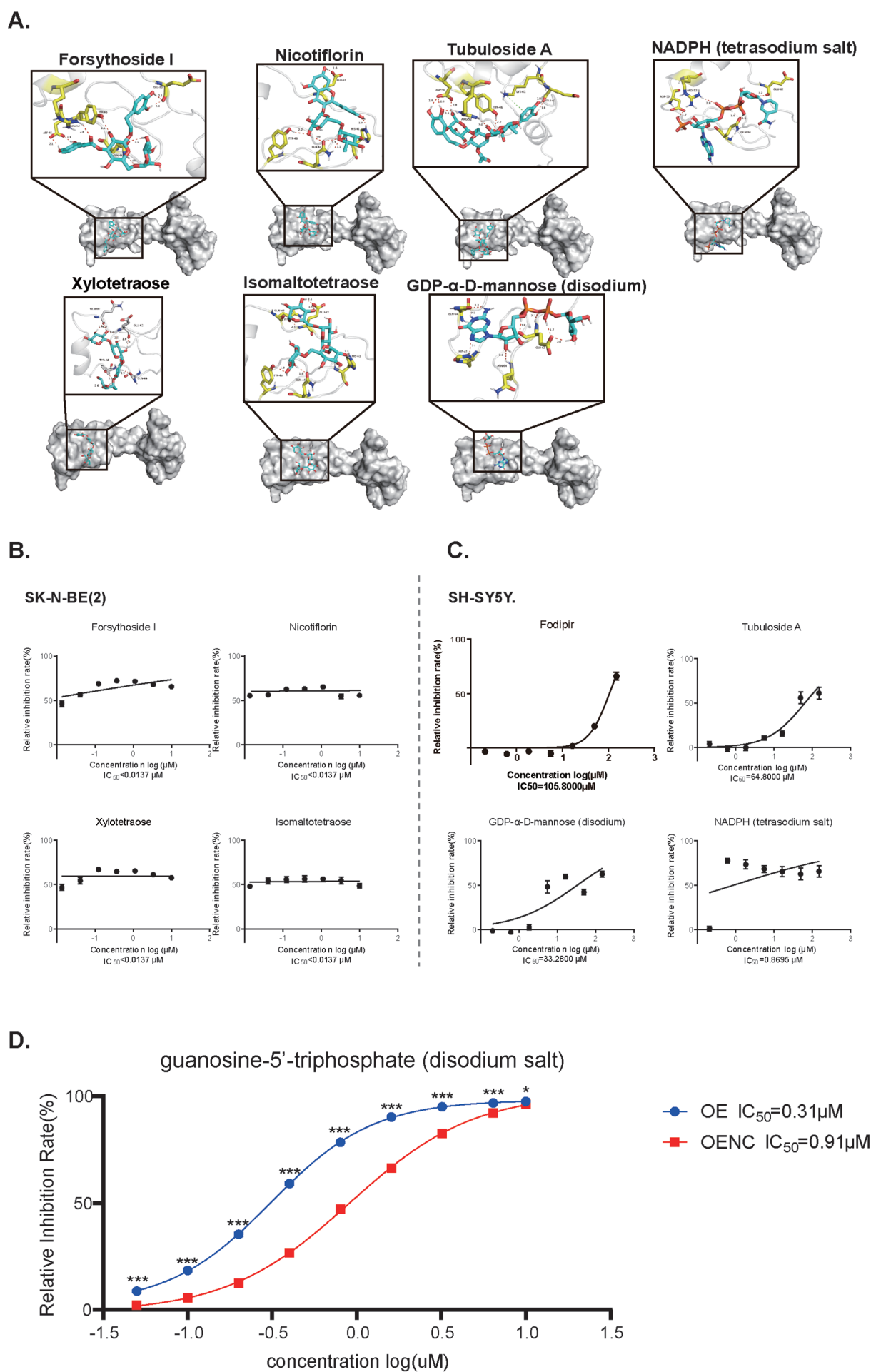


Figure S5 Identification of NDUF6-targeting compounds and functional validation of NDUF6 in neuroblastoma cells. (A) Representative docking diagrams illustrating the binding of selected small-molecule compounds with the NDUF6 protein. (B) Dose-response inhibition curves of candidate compounds targeting NDUF6 in SK-N-BE(2) cells. (C) Dose-response inhibition curves of candidate compounds targeting NDUF6 in SH-SY5Y cells. (D) NDUF6 overexpression increased cellular sensitivity to guanosine-5'-triphosphate. * $P<0.05$; ** $P<0.01$; *** $P<0.001$. OE, overexpression; OENC, overexpression negative control.

Table S1 Clinical characteristics of NB samples used for immunohistochemical staining of NDUFS6

| Sample ID | Gender | Age | Pathological Subtype | MYCN Status | INSS Stage | Risk Group | Metastasis | Sample Site |
|-----------|--------|--------|----------------------|---------------|------------|-------------------|-------------------------|------------------|
| T361 | Female | 3y6m | NB | Non-amplified | 4 | High Risk | Skull, rib | Primary Tumor |
| T372M | Male | 20m15d | NB | Unknown | 4 | High Risk | Greater omentum, liver | Metastatic Tumor |
| T403 | Female | 6y | NB | Non-amplified | 4 | High Risk | Bone | Primary Tumor |
| T406 | Female | 3y | NB | Non-amplified | 4 | High Risk | Bone | Primary Tumor |
| T407 | Female | 2y3m | NB | Unknown | 4 | High Risk | Bone, lymph node | Metastatic Tumor |
| T423 | Female | 9y1m | NB | Non-amplified | 4 | High Risk | Lung | Primary Tumor |
| T432 | Female | 2y10m | NB | Amplified | 4 | High Risk | Bone, lymph node | Primary Tumor |
| T447 | Male | 3y2m | NB | Non-amplified | 4 | High Risk | Bone | Primary Tumor |
| T529L | Male | 2y11m | NB | Non-amplified | 4 | High Risk | Bone | Metastatic Tumor |
| T562 | Male | 4y9m | GN | Non-amplified | 4 | High Risk | Bone | Primary Tumor |
| T574 | Male | 12y10m | GNB | Unknown | 4 | High Risk | Bone, lymph node | Metastatic Tumor |
| T577L | Female | 5y9m | NB | Non-amplified | 4 | High Risk | Bone | Metastatic Tumor |
| T794C | Female | 5y3d | NB | Amplified | 4 | High Risk | Liver, bone, lymph node | Metastatic Tumor |
| T427 | Female | 14m10d | NB | Unknown | 3 | Intermediate Risk | None | Primary Tumor |
| T492 | Female | 8y8m | NB | Non-amplified | 3 | Intermediate Risk | None | Primary Tumor |
| T515 | Female | 12m13d | NB | Non-amplified | 2 | Intermediate Risk | None | Primary Tumor |
| T521 | Male | 23m13d | NB | Non-amplified | 2 | Intermediate Risk | None | Primary Tumor |
| T782 | Female | 5m2d | NB | Non-amplified | 3 | Intermediate Risk | Lymph node | Metastatic Tumor |
| T345 | Female | 7y5m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T357 | Male | 2y6m | GNB | Unknown | 1 | Low Risk | None | Primary Tumor |
| T362 | Male | 7m10d | NB | Non-amplified | 2 | Low Risk | None | Primary Tumor |
| T363 | Female | 3y10m | GNB | Non-amplified | 2 | Low Risk | None | Primary Tumor |
| T377C | Female | 20d | NB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T393 | Female | 3y1m | GNB | Non-amplified | 2 | Low Risk | None | Primary Tumor |
| T408 | Male | 5y10m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T422 | Female | 7y8m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T465 | Female | 2y10m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T512 | Male | 4y11m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T530 | Male | 3y10m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T542 | Female | 4m22d | NB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T547 | Female | 7y11m | GN | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T560 | Male | 2y5m | GNB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T561 | Female | 18m9d | NB | Non-amplified | 1 | Low Risk | None | Primary Tumor |
| T579 | Female | 9y2m | GN | Non-amplified | 1 | Low Risk | None | Primary Tumor |