

	GSE49710 (N=498)	E-MTAB-8248 (N=223)	TARGET-NBL (N=144)	GSE137804 (N=16)
Age				
<18 months	305 (61.2%)	104 (46.6%)	27 (18.8%)	7 (43.8%)
>18 months	193 (38.8%)	119 (53.4%)	117 (81.3%)	9 (56.3%)
MYCN status				
Amplified	92 (18.5%)	46 (20.6%)	30 (20.8%)	3 (18.8%)
Not amplified	401 (80.5%)	176 (78.9%)	113 (78.5%)	13 (81.3%)
Unknown	5 (1.0%)	1 (0.4%)	1 (0.7%)	0 (0.0%)
INSS stage				
Stage 1	121 (24.3%)	29 (13.0%)	0 (0.0%)	3 (18.8%)
Stage 2	78 (15.7%)	39 (17.5%)	1 (0.7%)	0 (0.0%)
Stage 3	63 (12.7%)	36 (16.1%)	6 (4.2%)	4 (25.0%)
Stage 4	183 (36.7%)	89 (39.9%)	117 (81.3%)	8 (50.0%)
Stage 4S	53 (10.6%)	30 (13.5%)	20 (13.9%)	1 (6.3%)
Clinical risk				
High risk	176 (35.3%)	NA	NA	NA
Non high risk	322 (64.7%)	NA	NA	NA
Progression				
Yes	183 (36.7%)	NA	NA	NA
No	315 (63.3%)	NA	NA	NA
Chr.1p status				
Aberration	NA	67 (30.0%)	NA	NA
Normal	NA	137 (61.4%)	NA	NA
Unknown	NA	19 (8.5%)	NA	NA
MKI				
High	NA	NA	32 (22.2%)	NA
Intermediate	NA	NA	38 (26.4%)	NA
Low	NA	NA	45 (31.3%)	NA
Unknown	NA	NA	29 (20.1%)	NA
Histology				
Favorable	NA	NA	26 (18.1%)	7 (43.8%)
Unfavorable	NA	NA	108 (75.0%)	9 (56.3%)
Unknown	NA	NA	10 (6.9%)	0 (0.0%)
COG risk group				
High risk	NA	NA	118 (81.9%)	11 (68.8%)
Intermediate risk	NA	NA	12 (8.3%)	2 (12.5%)
Low risk	NA	NA	14 (9.7%)	3 (18.8%)
Distant metastasis				
Yes	NA	NA	NA	9 (56.3%)
No	NA	NA	NA	7 (43.8%)

Supplementary Table 1. Baseline clinical characteristics of the datasets used in this study

INSS: International neuroblastoma staging system; MKI: Mitosis karyorrhexis index; COG: Children's oncology group; NA: Not available.

Gene	Sequences (5'-3')
sh-FEN1#1	TTGCCGTCTTGTACCCTTAAG
sh-FEN1#2	GCAGTGACTACTGTGAGAGTA

Supplementary Table 2. The shRNA targeting sequences for human FEN1 gene

shRNA: short hairpin RNA.





Supplementary Figure 1. Heatmap of MRGs expression in NB patients of GSE49710

Heatmap illustrating the expression levels of 105 MRGs across 2 distinct NB patient clusters identified in the GSE49710 dataset. MRG: mitochondria-related gene; NB: neuroblastoma.













Supplementary Figure 2. Sankey diagrams reflecting the distribution of clinical characteristics across Clusters A and B of GSE49710

The Sankey diagrams displaying the distribution of patients between Cluster A and B by age (A), clinical risk categories (B), INSS stage (C), MYCN status (D), and progression status (E).





Supplementary Figure 3. Heatmap of MRGs expression in NB patients of E-MTAB-8248

Heatmap illustrating the expression levels of 105 MRGs across 2 distinct NB patient clusters identified in the E-MTAB-8248 dataset. MRG: mitochondria-related gene; NB: neuroblastoma.











Supplementary Figure 4. Sankey diagrams reflecting the distribution of clinical characteristics across Clusters A and B of E-MTAB-8248

The Sankey diagrams displaying the distribution of patients between Cluster A and B by age (A), chromosome 1p status (B), INSS stage (C), and MYCN status (D). Chr: chromosome.





Supplementary Figure 5. Kaplan-Meier survival curves for each of the 33 intersecting genes in the GSE49710 dataset

The collection of panels (A-AG) depicting Kaplan-Meier survival curves for patients stratified by the median expression levels of each of the 33 intersecting genes in the GSE49710 dataset. Each panel corresponds to one gene, with P values denoting the significance of difference in survival between the two groups.





Supplementary Figure 6. Kaplan-Meier survival curves for each of the 33 intersecting genes in the E-MTAB-8248 dataset

The collection of panels (A-AG) depicting Kaplan-Meier survival curves for patients stratified by the median expression levels of each of the 33 intersecting genes in the E-MTAB-824 dataset. Each panel corresponds to one gene, with P values denoting the significance of difference in survival between the two groups.





Supplementary Figure 7. Violin plots depicting the distribution of mtScores across clinical characteristics in the GSE49710 dataset

(A) Comparison of mtScores across different age groups. (B) Comparison of mtScores across different MYCN status groups. (C) Comparison of mtScores across different progression status groups. (D) Comparison of mtScores across different clinical risk groups. (E) Comparison of mtScores across different INSS stages groups. (F) Comparison of mtScores between INSS stage 4 and other INSS stages.







Supplementary Figure 8. Violin plots depicting the distribution of mtScores across clinical characteristics in the E-MTAB-8248 Dataset

(A) Comparison of mtScores across different age groups. (B) Comparison of mtScores across different chromosome 1p status groups. (C) Comparison of mtScores across different MYCN status groups. (D) Comparison of mtScores across different INSS stage groups. (E) Comparison of mtScores between INSS stage 4 and other INSS stages.













D

6

COG risk group

Low risk

High risk

Favorable

Unknown

Low Intermediate

High

MYCN status Amplified Not amplified

Unknown

Unknown

Stage 2 Stage 3

Stage 4 Stage 4S

mtRisk Low

0.041

High

< 18 months > 18 months

Unfavorable

Histology

MKI

Intermediate risk







Favorable

Unfavorable

Histology

0

-2





Α

Supplementary Figure 9. Correlation of mtScore with clinical and molecular features in TARGET-NBL

(A) Heatmap depicting the distribution of 10 genes expression used to calculate mtScore stratified by high and low mtRisk, and the distribution of clinical features (COG risk group, histology, MKI, MYCN status, INSS stage, and age) stratified by high and low mtRisk. (B-G) Violin plots illustrating the distribution of mtScores in relation to various clinical factors: age groups (B), MYCN status (C), COG risk groups (D), histology (E), INSS stages (F), MKI classification (G). (***P<0.001, ****P<0.0001)









Supplementary Figure 10. Single-cell transcriptome sequencing data analysis to explore FEN1's essential role

(A) Dot plot of cell markers used in single-cell data annotation. (B) Cell-cell communication weights network of FEN1-high tumor cells with the surrounding microenvironment. (C) Cell-cell communication weights network of FEN1-low tumor cells with the surrounding microenvironment. pDC: plasmacytoid dendritic cell.