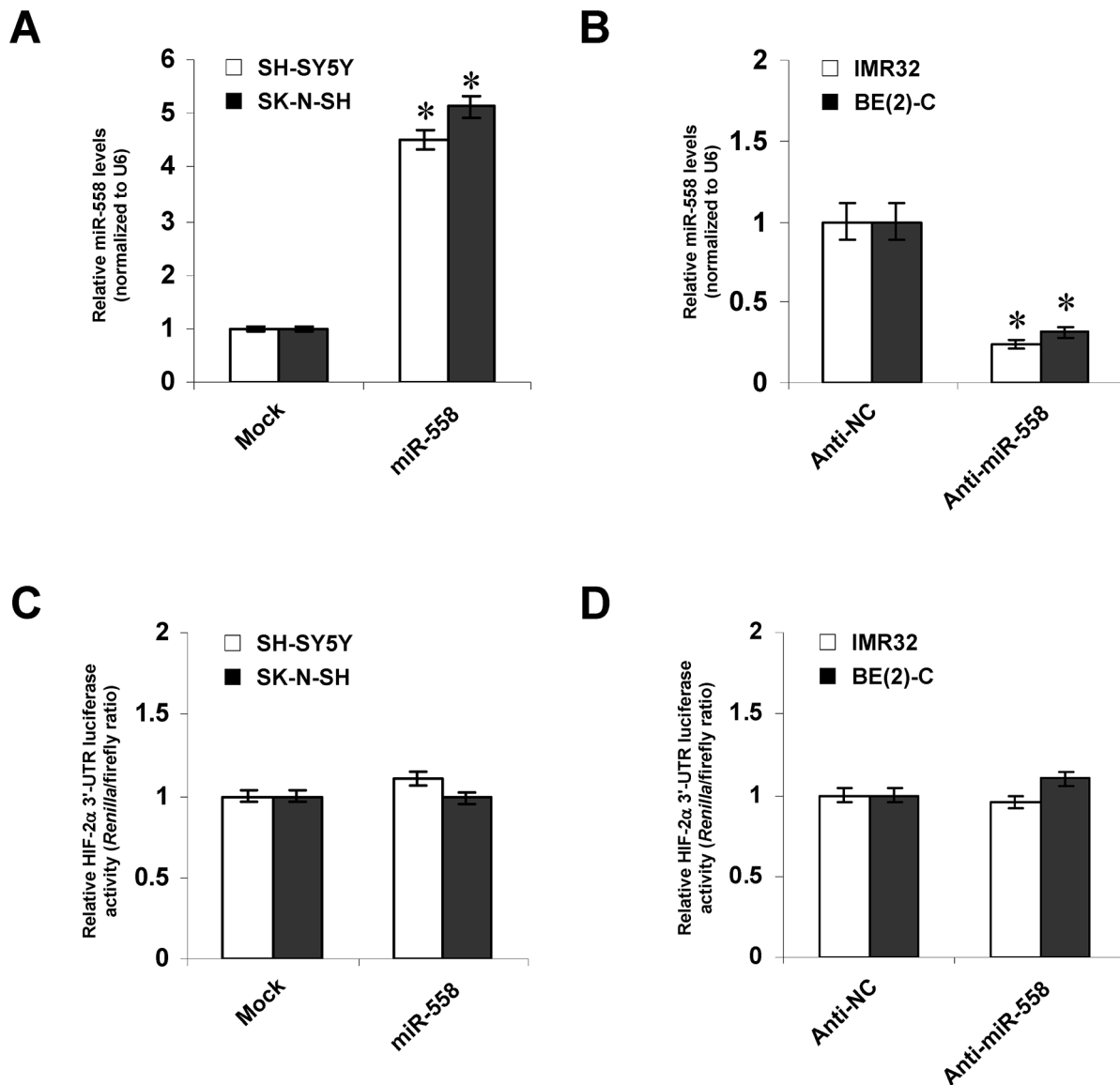
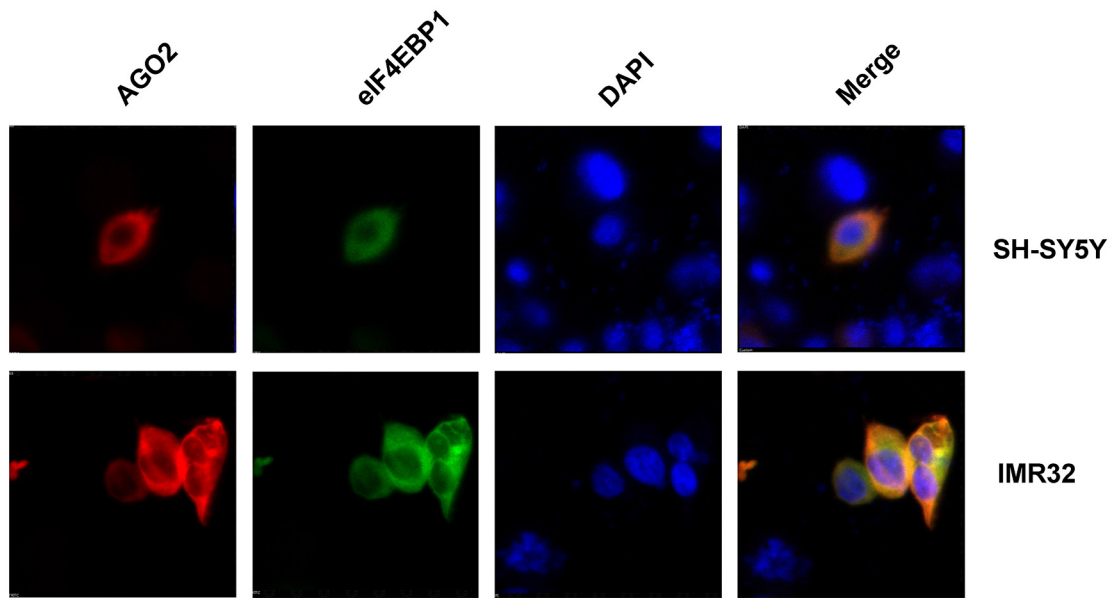


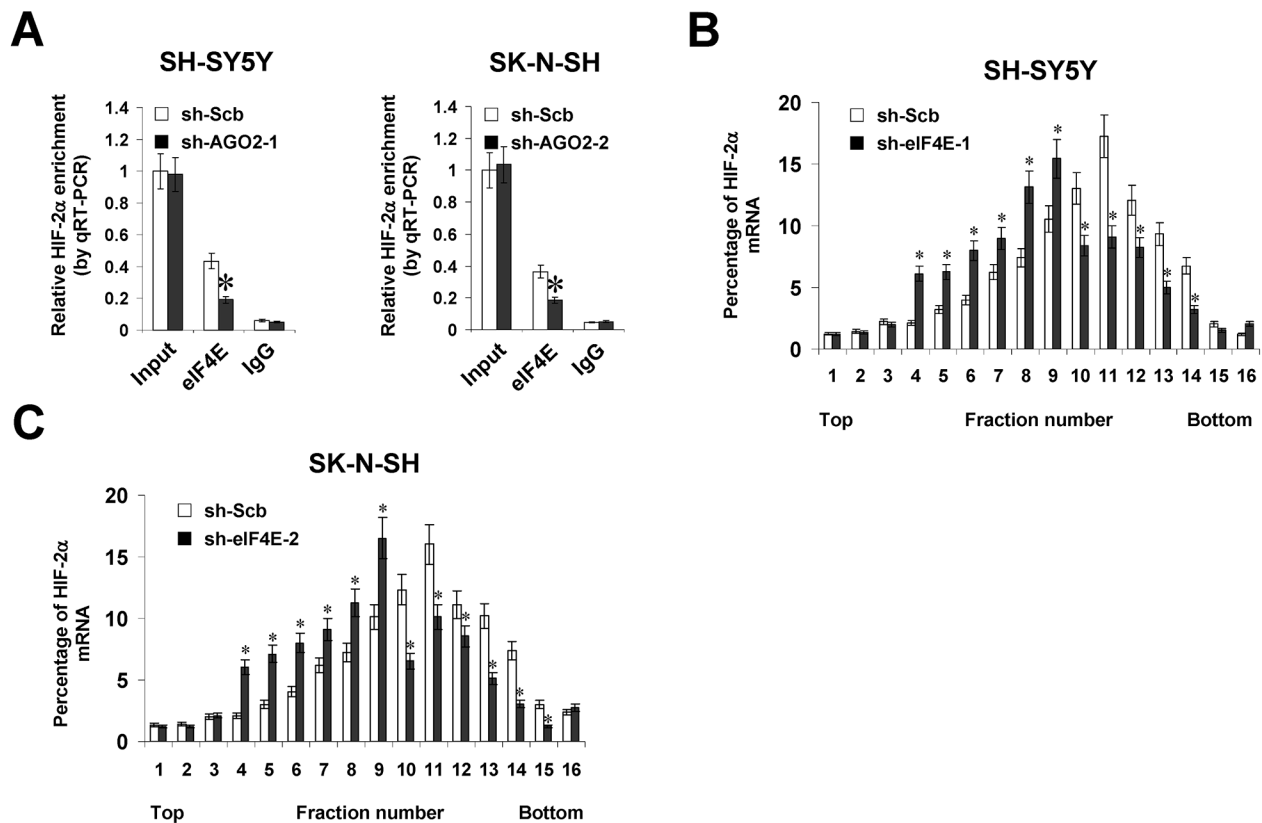
## SUPPLEMENTARY FIGURES AND TABLES



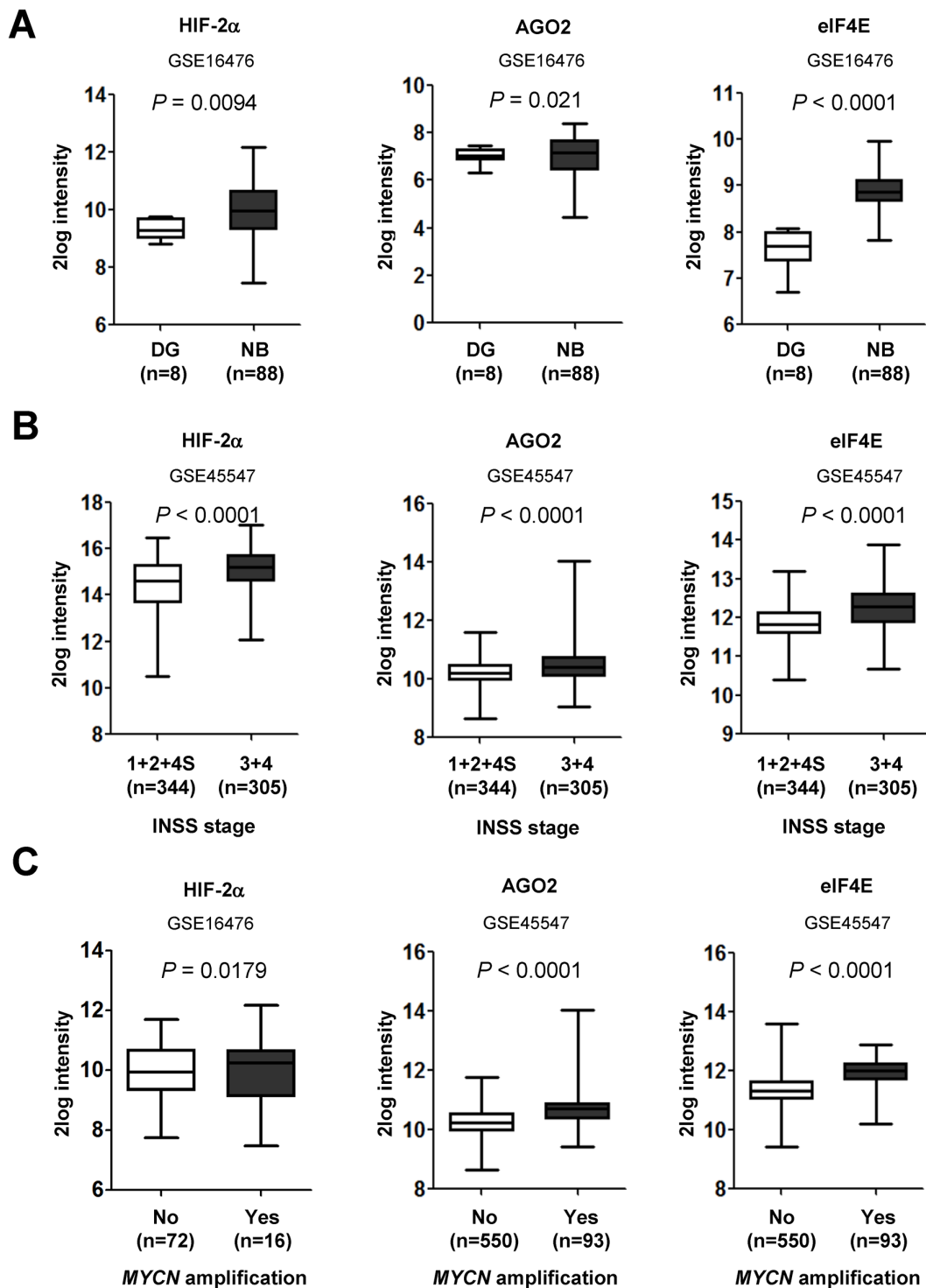
**Supplementary Figure S1: Effects of miR-558 on the 3'-UTR activity of *HIF-2α* in NB cells.** A. and B. real-time qRT-PCR showing the miR-558 levels in NB cells transfected with empty vector (mock), miR-558 precursor, anti-NC (100 nmol/L) or anti-miR-558 (100 nmol/L) inhibitors. C. and D. dual-luciferase assay indicating the activity of *HIF-2α* 3'-UTR luciferase reporter in NB cells transfected with mock, miR-558 precursor, anti-NC (100 nmol/L) or anti-miR-558 (100 nmol/L) inhibitors. \*  $P < 0.01$  vs. mock or anti-NC.



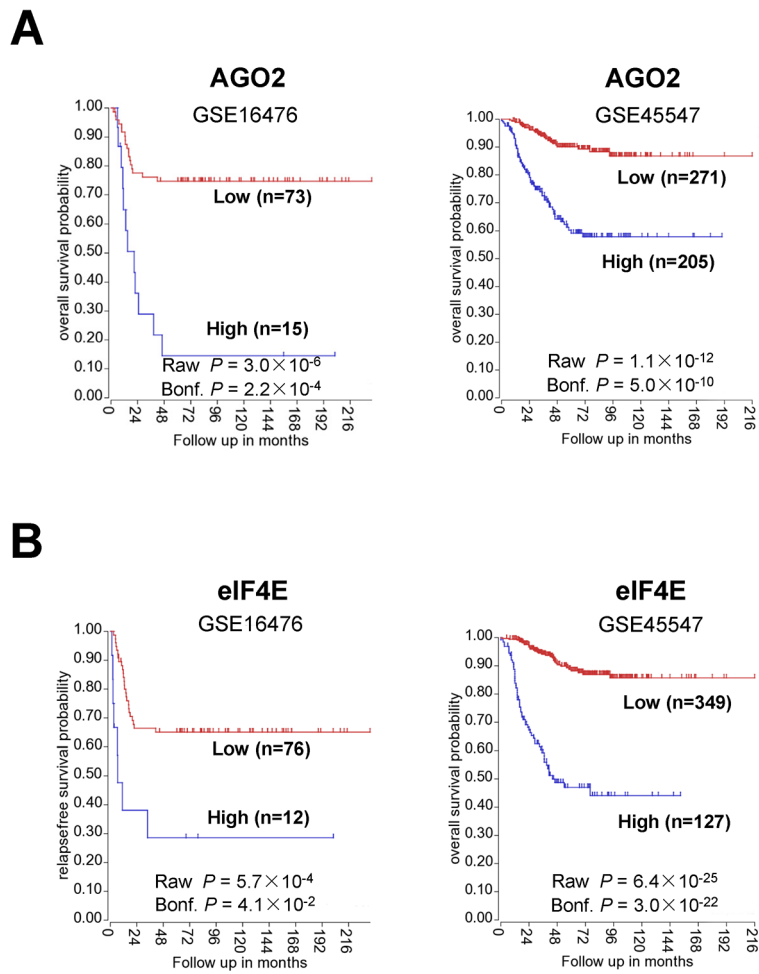
**Supplementary Figure S2: Endogenous expression of AGO2 and eIF4EBP1 in NB cells.** Immunofluorescence assay revealing the co-localization of AGO2 and eIF4EBP1 in cultured SH-SY5Y and IMR32 cells.



**Supplementary Figure S3: Effects of eIF4E on HIF-2 $\alpha$  translation in NB cells.** A. RIP and real-time qRT-PCR assay showing the binding of eIF4E to *HIF-2 $\alpha$*  5'-UTR in NB cells transfected with sh-Scb or sh-AGO2. B. and C. sucrose gradient sedimentation assay indicating the distribution of *HIF-2 $\alpha$*  transcripts to the polysome fractions in NB cells transfected with sh-Scb or sh-eIF4E. \*  $P < 0.01$  vs. sh-Scb.



**Supplementary Figure S4: Expression of HIF-2α, AGO2, and eIF4E in public datasets.** A. the expression of HIF-2α, AGO2, and eIF4E in normal dorsal ganglia (DG) and NB tissues derived from GEO database and R2 microarray analysis and visualization platform (<http://r2.amc.nl>). B. and C. mining the GEO database and R2 microarray analysis and visualization platform (<http://r2.amc.nl>) showing the expression of HIF-2α, AGO2, and eIF4E in NB tissues with different INSS stages or MYCN amplification status.



**Supplementary Figure S5: Patients' survival analysis.** Kaplan–Meier survival plots of NB cohorts (stratified by the scan method and adjusted by Bonferroni correction) derived from GEO database and R2 microarray analysis and visualization platform (<http://r2.amc.nl>) showing the survival probability of patients with high or low expression of AGO2 **A.** or eIF4E **B.**

Supplementary Table S1: Primer sets used for qRT-PCR and RIP

Primer set	Primers	Sequence	Product size (bp)	Application
HIF-2 $\alpha$	Forward	5'-AAAGCCTTGGAGGGTTTCATT-3'	292	qRT-PCR
	Reverse	5'-AGGTGGCTGACTTGAGGTTGA-3'		
HIF-2 $\alpha$ 5'-UTR	Forward	5'-AGGCGGCCGTACAATCCT-3'	187	qRT-PCR, RIP
	Reverse	5'-TGTCAGACCCGAAAAGAG-3'		
$\beta$ -actin	Forward	5'-ATCTACGAGGGGTATGCC-3'	227	qRT-PCR
	Reverse	5'-TAGCTCTTCTCCAGGGAG-3'		
miR-558	Forward	RiboBio		qRT-PCR
	Reverse	RiboBio		
U6	Forward	RiboBio		qRT-PCR
	Reverse	RiboBio		

HIF-2 $\alpha$ , hypoxia-inducible factor 2 alpha; 5'-UTR, 5'-untranslated region.

**Supplementary Table S2: Oligonucleotide sets used for constructs, inhibitors and short hairpin RNAs**

Oligo set	Sequences
pre-miR-558	5'-TGCTGTGAGCTGCTGTACCAAAATGTTTGGCCACTGACTGACATTTGGTACAGCAGCTCA-3' (sense); 5'-CCTGTGAGCTGCTGTACCAAAATGTCAGTCAGTGGCCAAAACATTTGGTACAGCAGCTCAC-3' (antisense)
pre-miR-NC	5'-TGCTGAAATGTACTGCGCGTGGAGACGTTTTGGCCACTGACTGACGTCTCCACGCAGTACATTT-3' (sense); 5'-CCTGAAATGTACTGCGTGGAGACGTCAGTCAGTGGCCAAAACGTCTCCACGCAGTACATTTTC-3' (antisense)
HIF-2 $\alpha$ 5'-UTR mut (miR-558)	5'-AGACTGTATGTTAGTACAGGCCCGCCCTCCGACTCCTTCCGACTCCCAGC-3' (sense); 5'-GGAGGCCGGCCTGTACTAACATACAGTCTCAGGACACTGCCGAGGATTG-3' (antisense)
Anti-NC	RiboBio
Anti-miR-558	RiboBio
sh-Scb	5'-CCGGGCGAACGATCGAGTAAACGGACTCGAGTCCGTTTACTCGATCGTTCGCTTTTT-3' (sense); 5'-AATTCAAAAAGCGAACGATCGAGTAAACGGACTCGAGTCCGTTTACTCGATCGTTCGCG-3' (antisense)
sh-AGO2-1	5'-CCGGGCACAGCCAGTAATCGAGTTTCTCGAGAAACTCGATTACTGGCTGTGCTTTTTG-3' (sense); 5'-AATTCAAAAAGCACAGCCAGTAATCGAGTTTCTCGAGAAACTCGATTACTGGCTGTGC-3' (antisense)
sh-AGO2-2	5'-CCGGCGTCCGTGAATTTGGAATCATCTCGAGATGATTCCAAATTCACGGACGTTTTTG-3' (sense); 5'-AATTCAAAAACGTCCGTGAATTTGGAATCATCTCGAGATGATTCCAAATTCACGGACG-3' (antisense)
sh-eIF4E-1	5'-CCGGCAGAGAGGAGGAAGGAGAAGTCTCGAGACTTCTCCTCCTCTCTGTTTTTG-3' (sense); 5'-AATTCAAAAACAGAGAGGAGGAAGGAGAAGTCTCGAGACTTCTCCTCCTCTCTG-3' (antisense)
sh-eIF4E-2	5'-CCGGCAGACCAGCAGATGGACAACCTCTCGAGAGTTGTCCATCTGCTGGTCTGTTTTG-3' (sense); 5'-AATTCAAAAACAGACCAGCAGATGGACAACCTCTCGAGAGTTGTCCATCTGCTGGTCTG-3' (antisense)
sh-HIF-2 $\alpha$ -1	5'-CCGGGCGCAAATGTACCCAATGATACTCGAGTATCATTGGGTACATTTGCGCTTTTTG-3' (sense); 5'-AATTCAAAAAGCGCAAATGTACCCAATGATACTCGAGTATCATTGGGTACATTTGCGC-3' (antisense)
sh-HIF-2 $\alpha$ -2	5'-CCGGCAGTACCCAGACGGATTTCAACTCGAGTTGAAATCCGTCTGGGTACTGTTTTTG-3' (sense); 5'-AATTCAAAAACAGTACCCAGACGGATTTCAACTCGAGTTGAAATCCGTCTGGGTACTG-3' (antisense)

pre-miR-NC, negative control miRNA precursor; HIF-2 $\alpha$ , hypoxia-inducible factor 2 alpha; 5'-UTR, 5'-untranslated region; Anti-NC, negative control inhibitor; sh-Scb, scramble short hairpin RNA; AGO2, Argonaute 2; eIF4E, eukaryotic translation initiation factor 4E.