Supplementary Figure Legends

Supplementary Figure S1. Aberrant *DNMT3B* expression and global DNA methylation in primary neuroblastoma tumors

A, RT-PCR examination of aberrant *DNMT3B* transcripts expressed in neuroblastoma (NB) and ganglioneuroblastoma (GNB) patient samples were normalized to the *GAPDH* housekeeping gene, and *DNMT3B* was amplified from exons 6 and 11 to identify the wild-type and aberrant *DNTM3B* transcripts specifically. DNA sizing is shown on the left and *DNMT3B* isoforms are shown on the right. B, Southern blot of RT-PCR shown in Figure 1A of aberrant *DNMT3B* transcripts expressed in neuroblastoma (NB) and ganglioneuroblastoma (GNB) patient samples using a probe spanning exons six and seven to detect all of the known aberrant isoforms amplified in the RT-PCR. C, Southern blot of RT-PCR shown in Supplementary Figure 1A of aberrant *DNMT3B* transcripts expressed in neuroblastoma (NB) and ganglioneuroblastoma (GNB) patient samples using a probe spanning exons six and seven to detect all of the known aberrant isoforms amplified in the RT-PCR.

Supplementary Figure S2. *DNMT3B7* expression levels in primary neuroblastoma tumors and induced cells

A, Expression of *DNMT3B7* in primary ganglioneuroblastoma (GNB), ganglioneuroma (GN), and neuroblastoma tumors (NB) low, intermediate and high risk as determined by real-time RT-PCR. The data are summarized in the table on the right of the graph. B, Expression of *DNMT3B7* (RNA) as determined by real-time RT-PCR or DNMT3B7 (protein) as determined by quantitation of Western blot shown in Figure 2B using Image J in induced LA1-55n cells. The data are summarized in the table on the right of the graph.

Supplementary Figure S3. Establishment of KCNR neuroblastoma cells overexpressing DNMT3B7.

SMS-KCNR cells were transduced with a constitutive *DNMT3B7* or control vector. Parental SMS-KCNR, vector control and *DNMT3B7* expressing cells were grown and counted daily for three days.

Supplementary Figure S4. Analyses of SMS-KCNR cell xenografts

A, Microvascular Density of SMS-KCNR xenografts. B, Percent of cells in G0 in SMS-KCNR xenografts. C, Apoptosis by TUNEL assay in SMS-KCNR xenografts.

Supplementary Figure S5. DNA methylation of Satellite 2 repetitive elements. Southern blotting analysis of DNA methylation of Satellite 2 repetitive elements. *Msp*I digests DNA regardless of methylation. *Hpa*II is a methylation sensitive isoschizomer of *Msp*I. Horizontal lines are drawn to indicate the level of methylation. All three lanes digest to the same degree in the *Msp*I digested lanes. The bracket on the right of the figure indicates the level of hypermethylation in the *DNMT3B7*-expressing cell lines.

Supplementary Figure S6. *DNMT3B7* expression in LA1-55n transduced cells by RNA-Sequencing

RNA-Sequencing reads aligned to the *DNMT3B* genomic locus in the control and two *DNMT3B7*-expressing LA1-55n cells.

Supplementary Figure S7. Endogenous levels of *DNMT1, DNMT3A*, and *DNMT3B* in *DNMT3B7*-expressing LA1-55n cells

A. Relative expression of endogenous *DNMT1* in *DNMT3B7*-expressing or vector control LA1-55n cells at day 0 and day 21 determined by real-time. B, Relative

expression of endogenous *DNMT3A* in *DNMT3B7*-expressing or vector control LA1-55n cells at day 0 and day 21 determined by real-time. C, Relative expression of endogenous *DNMTB* in *DNMT3B7*-expressing or vector control LA1-55n cells at day 0 and day 21 determined by real-time.

Supplementary Figure S8. Relative DNA methylation by mass spectrometry

The methylation level of *EEA1* and *RXRB* was determined by quantitative mass spectrometry of PCR amplified bisulfite-treated DNA of *DNMT3B7*-expressing or vector control LA1-55n cells at day 21. Mass spectrometry was performed in technical duplicate. In the top panel, the average percent methylation levels are graphed +/- standard error. In the table at the bottom of the figure, the raw values from the mass spectrometry experiment are given.

Supplementary Figure S9. Effect of ATRA on global DNA methylation

Global DNA methylation by mass spectrometry of the *DNMT3B7*-expressing LA1-55n cells or control, treated with ATRA or vehicle control for seven days. Samples were normalized to vehicle controls.