**Supplemental Data Figure legends**

Fig. 1S (A, B) DNA sequence electropherogram of RET exon 11 of normal and patient. The nucleotide sequences are depicted from 3’ to 5’ and numbered. Locations of the deletions are boxed in solid or broken line. Patient is heterozygous for the deletion and the sequence profile beyond the deletion is the superimposition of sequences of normal and mutant allele. (C) The deletion causes a frame shift and a termination codon (Stop). Translated amino acids are numbered and shown underneath the nucleotide sequences. Arrowheads indicate the starts of the mutations. (D) Schematic drawing of the normal and truncated RET. Exons of RET gene are indicated with numbered boxes. The deletion at the exon 11 causes a truncation at the TMD resulting in a mutant RET with the intact extracellular domain and part of the TMD only. Abbreviations: SP, signal peptide; Cad, cadherin domain; Cys, cysteine-rich domain TMD, transmembrane domain; TK, tyrosine kinase domains.

Fig. 2S Expression of normal and mutant RET proteins in transfected HTB11 neuroblastoma cells. (A) RT-PCR and restriction endonuclease digestion assay was performed to detect the transcription of mutant RET. PCR amplification using cDNA as a template would generate a 624 bp product from the normal RET, and a 619 bp product from the mutated
The 5 bp deletion removed the unique EarI restriction site (5’-CTCTTC-3’) of the RT-PCR product. EarI digested RT-PCR products of untransfected HTB11 cells (lane 1); cells transfected with normal RET (lane 2); and cells transfected with mutant RET (lane 3) were analyzed by agarose gel electrophoresis. PCR product of normal RET gave two fragments of 528 and 96 bp after EarI digestion. By contrast, PCR from mutant RET was not cleaved by EarI because the 5 bp deletion destroyed the EarI restriction site (italic). RT-PCR and EarI digestion showed that mutant RET construct was transcribed in transfected cells. Cleavage sites of EarI digestion were indicated with arrowheads. Locations and sequences of the forward and reverse primers were shown, sizes of digested RT-PCR products were indicated. (B) Western blotting analysis of lysates of HTB11 cells transfected with normal RET (N) or with mutant RET (Mu) using anti-RET-N antibody. The anti-RET-N antibody recognizes the N-terminal extracellular region of RET and hence detects both the normal and truncated RET products. Two protein bands of 155 and 175 kDa, which were the expected molecular weights of the non-glycosylated (NG) and glycosylated (G) forms of full length RET9 protein, respectively were detected in cells transfected normal RET (N). In the lane of cells transfected with mutant RET (Mu), the protein band (asterisk) corresponding to the truncated RET protein (the
expected molecular weight was 80 kDa) was detected. The faint protein band (arrowhead) in the lane transfected with normal \textit{RET (N)} that ran at the position above the truncated RET was the degraded product of normal RET. Positions of molecular size markers were indicated as shown. (C, D) Localization of normal and mutant RET proteins were analyzed in transfected cells with antibodies that recognized the N-terminal region (anti-RET-N), and the C-terminal region (anti-RET-C) of RET protein. Cells transfected with 1.5 μg of normal \textit{RET (C)} or mutant \textit{RET (D)}. Immuno-fluorescence staining using anti-RET-N antibody detected the translation of the normal and truncated forms of RET proteins in cells transfected with normal and mutant \textit{RET}. In contrast, anti-RET-C could detect the normal RET in cells transfected with normal \textit{RET}, but could not detect the mutant RET in cells transfected with mutant \textit{RET}. The weak immuno-reactivity of cells transfected with mutant \textit{RET} with anti-RET-C antibody was due to the transcription and translation of the genomic \textit{RET} gene.

Fig. 3S Schematic drawing showing the effects of the truncated RET protein in GFL signalling.

(A) Normal RET protein and GFL signalling in normal control. (B) Truncated RET protein is transported to the plasma membrane and form dimer with truncated RET or with the normal RET upon GFL binding. However, the truncated RET homodimer and
truncated RET/normal RET heterodimer would not elicit GFL signalling. The truncated RET would therefore compete with the normal RET receptor acting in a dominant negative manner. (C) The truncated RET receptor is not transported to the cell membrane and/or is degraded intracellularly. Half the normal level of RET receptor would be present on the cell membrane resulting in RET haploinsufficiency.