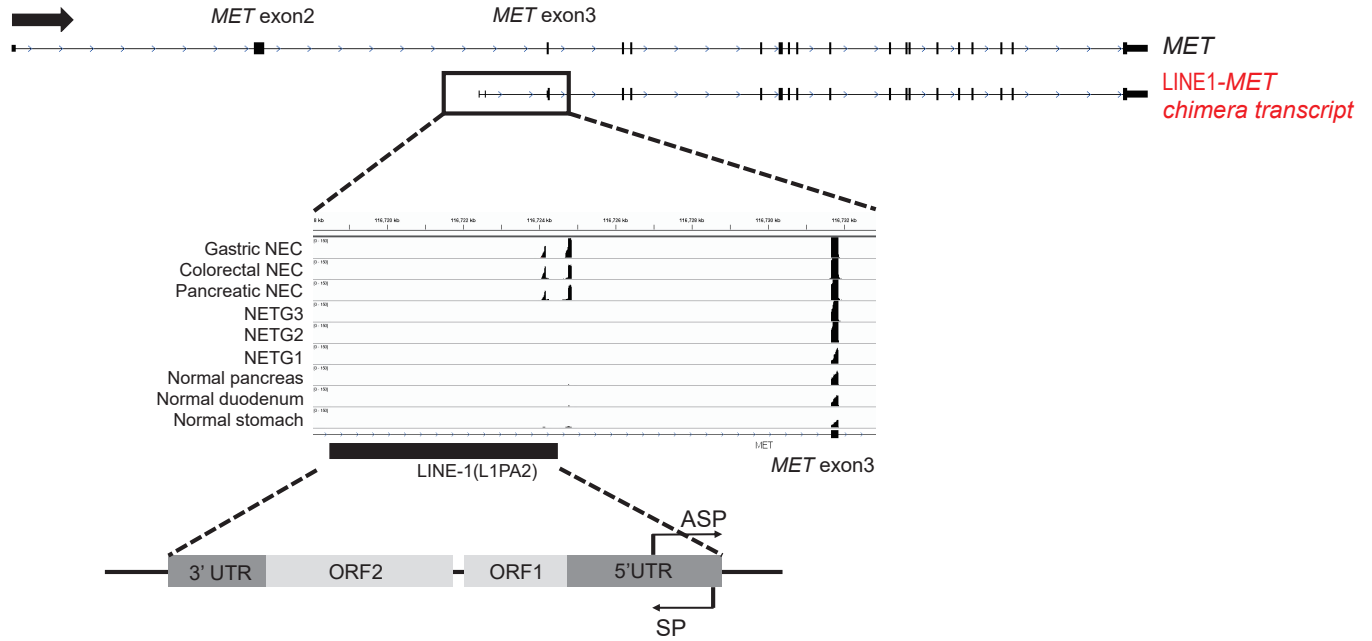
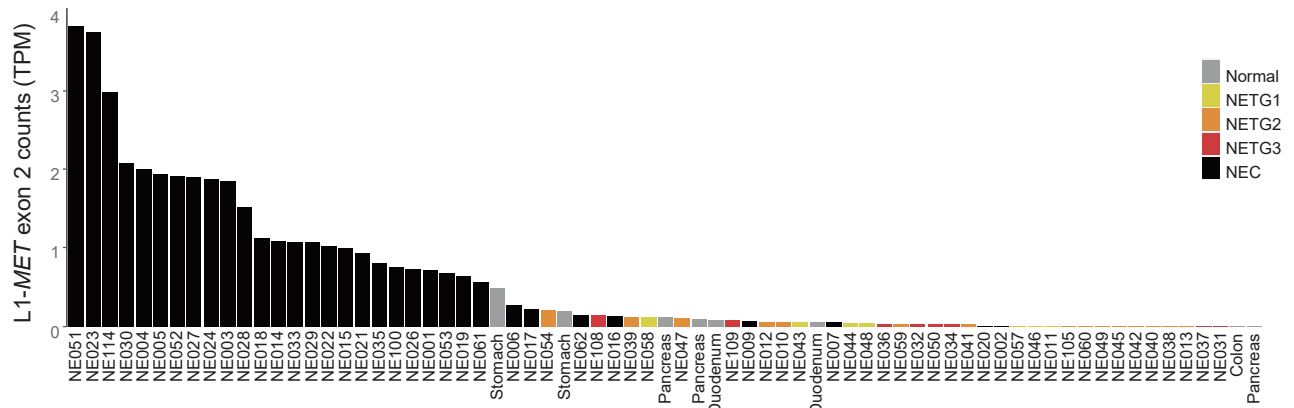


Supplementary Figure S12. LINE1-MET chimeric transcripts in GIS-NENs.

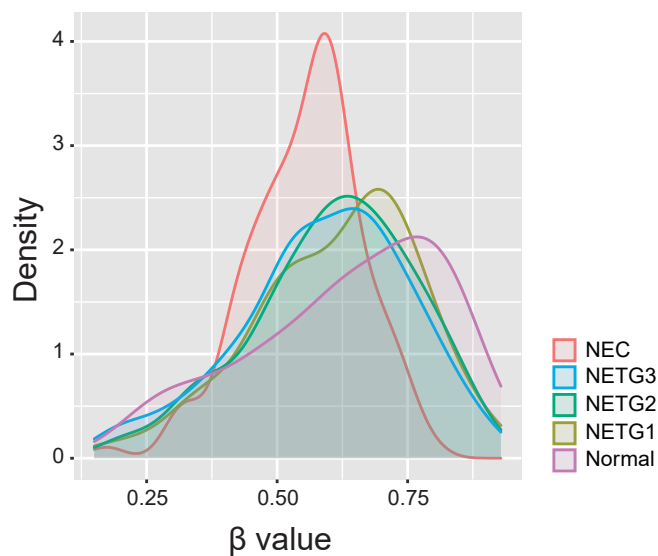
A



B



C



A, Integrative Genomic Viewer (IGV) visualized RNA-seq data for the intron 2 locus of *MET* in representative GIS-NEC/NET/normal tissues. LINE1-*MET* transcription starts from 5' UTR inside of LINE1 (L1PA2) in only NEC samples and is controlled by the LINE1 antisense promoter (ASP). **B**, Box plot showing read counts (TPM, Transcripts Per Kilobase Million) for LINE1 (L1)-*MET* exon2 in GIS-NEC/NET/normal tissues. With a two-fold higher TPM of the average value of all normal tissues as a threshold, most GIS-NECs (74.3%, 26/35) featured LINE1-*MET* chimeric transcripts, not observed in GIS-NETs (0%, 0/30). **C**, Density plot of 111 probes with large fluctuations of β values (standard deviation > 0.18) within the genome-wide LINE-1 locus among GIS-NENs shows differences in methylation status, particularly in GIS-NECs (GIS-NECs versus GIS-NETG3s, $P = 7.31 \times 10^{-45}$; GIS-NECs versus GIS-NETG2s, $P = 5.75 \times 10^{-40}$; GIS-NECs versus GIS-NETG1s, $P = 3.67 \times 10^{-42}$; GIS-NECs versus normal tissues, $P = 2.35 \times 10^{-148}$). These findings suggest demethylation of LINE-1 antisense promoter could induce LINE1-*MET*, as previously reported (12).