

Supplementary table S1 The optional parameters of the tools in the bioinformatics analysis

Tools	Optional parameters
fastp (v0.20.0)	-f 10 -t 0 -F 10 -T 0 -w 8 --length_required 35 -q 15 -u 40 -n 5 -3 1
BWA mem2(v2.1)	mem -Y -M -R "@RG\tID:"..."tSM:"..."tLB:"..."tPU:"..."tPL:"ILLUMINA"
SAMtools (v1.9)	sort --reference hs37d5.fa
MarkDuplicates (packed in GATK 4.1.2.0)	--VALIDATION_STRINGENCY SILENT --OPTICAL_DUPLICATE_PIXEL_DISTANCE 2500 --ASSUME_SORT_ORDER "coordinate" --CLEAR_DT false --CREATE_MD5_FILE true
BaseRecalibrator (packed in GATK 4.1.2.0)	-R hs37d5.fa --use-original-qualities --known-sites Mills_and_1000G_gold_standard.indels.b37.vcf --known-sites dbsnp_138.b37.del100.vcf.gz --known-sites 1000G_phase1.indels.b37.vcf.gz
ApplyBQSR (packed in GATK 4.1.2.0)	-R hs37d5.fa --add-output-sam-program-record --use-original-qualities
Mutect2 (packed in GATK 4.1.2.0)	--germline-resource af-only-gnomad.raw.sites.b37.vcf.gz --af-of-alleles-not-in-resource 0.0000025 -A ClippingRankSumTest

Supplementary table S2 The distribution of *TP53* status in 92 GI-NENs

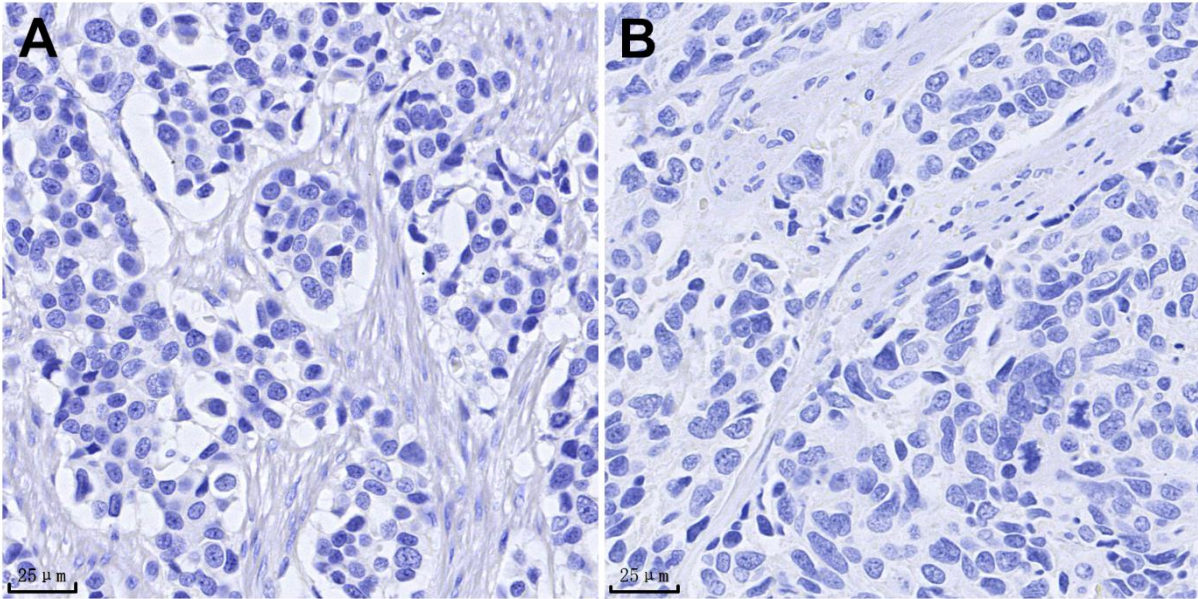
	<i>TP53 Mutations</i>	NET	NECs
	Nonsense	0	8
LOF	Frameshift indels	0	4
	Splicing	0	5
	Wild type	34	4
GOF	Missense	1	31
	In-frame indels	0	5

Supplementary table S3 Comparison between the percentage of p53 positive cells and *TP53* mutation status in 92 GI-NEN cases

Percentage of p53 positive cells (%)	Mutational Analysis						Total
	LOF			Wild Type	GOF		
	Nonsense	Frameshift	Splicing		Missense	In-Frame	
0	5	3	3	2	0	0	13
1-10	1	0	1	28	0	0	30
11-20	0	0	0	5	0	0	5
21-30	1	0	1	0	2	0	4
31-40	0	0	0	0	0	0	0
41-50	0	0	0	0	1	1	2
51-60	0	0	0	0	0	0	0
61-70	0	1	0	1	1	0	3
71-80	0	0	0	1	2	0	3
81-90	0	0	0	1	3	2	6
91-100	1	0	0	0	23	2	26

Supplementary table S4 The inter-pathologist concordance for p53 IHC patterns in GI-NENs

Original interpretation	Interpretation from the third pathologist			
	Pattern A	Pattern B	Pattern C1	Pattern C2
Pattern A	13	0	0	0
Pattern B	1	34	0	0
Pattern C1	0	1	5	0
Pattern C2	0	0	0	38



Supplementary figure S1. The examples of uninterpretable cases. p53 expression was completely absent throughout the entire section including both tumor cells and non-tumor internal control cells (40×) in one case with wild-type *TP53* (A) and another case with *TP53* missense mutation (B).