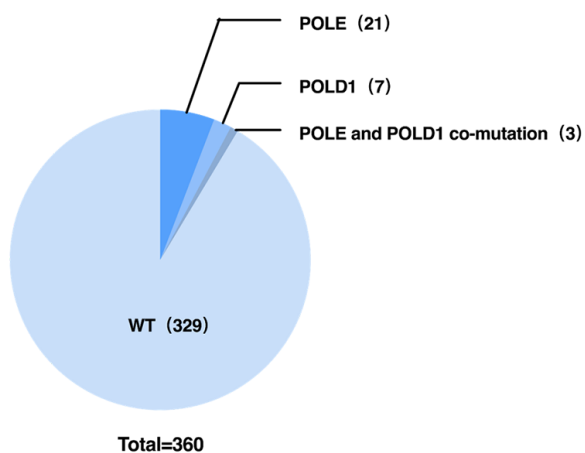
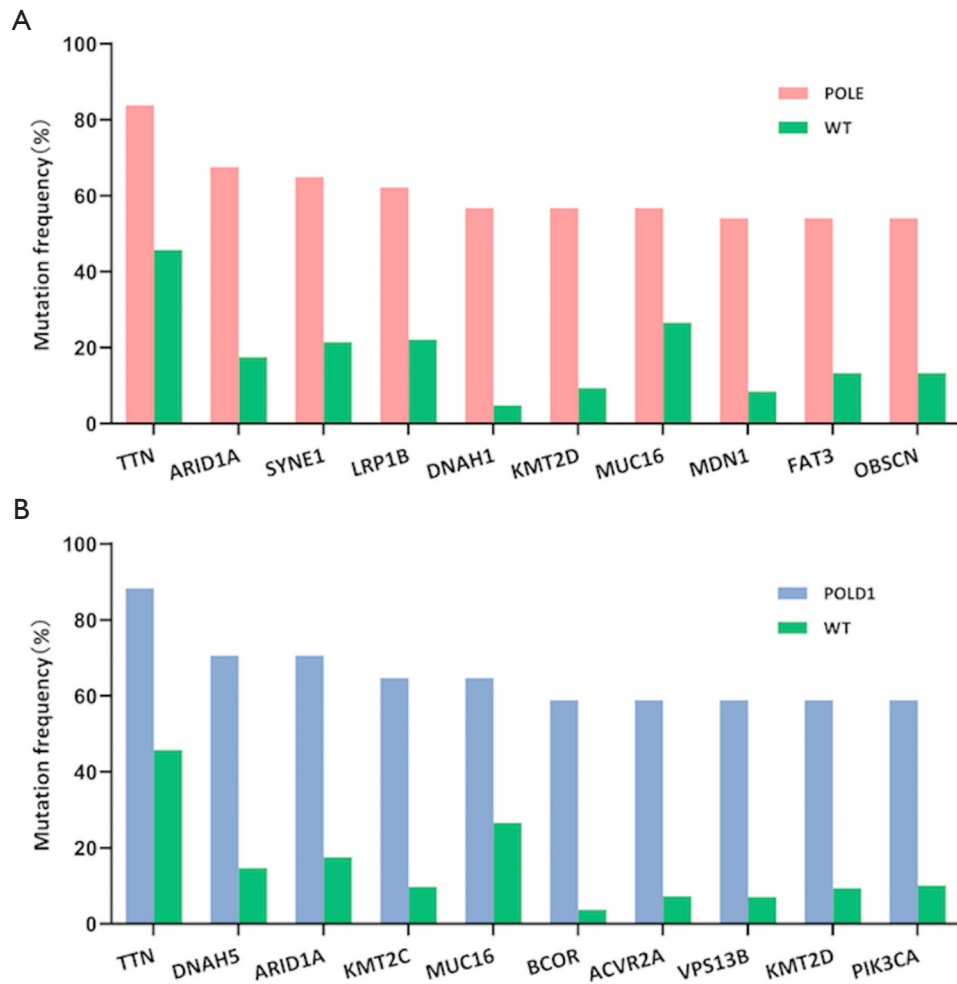


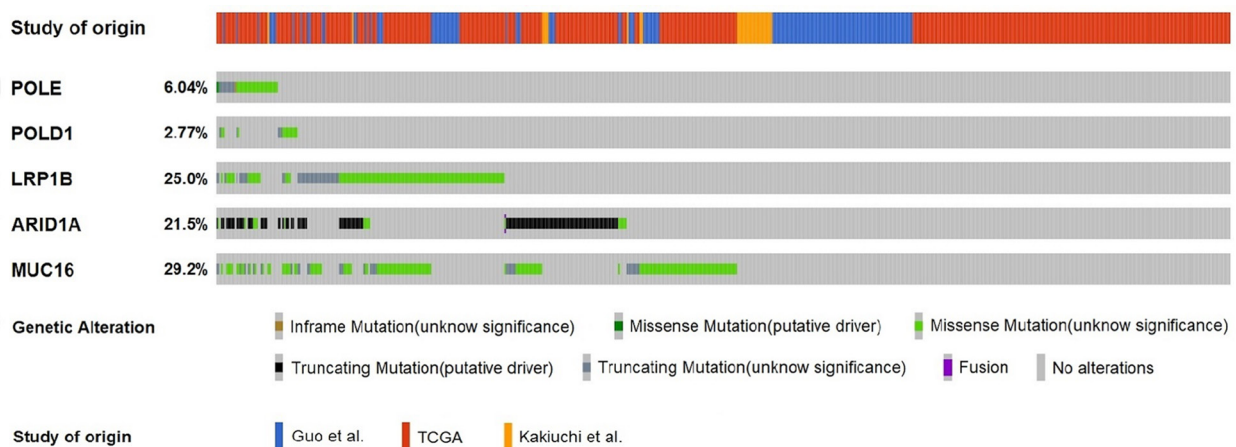
**Figure S1** Sample composition and size of the study cohort. The percentages represented the mutation frequency of *POLE/POLD1* in these three groups.



**Figure S2** The distribution of *POLE/POLD1* mutations in 360 samples selected. Among the 360 samples, 31 cases had *POLE/POLD1* mutations, of which 24 had *POLE* mutations, 10 had *POLD1* mutations, and 3 had both *POLE* and *POLD1* mutations. WT = *POLE* and *POLD1* wild-type.



**Figure S3** Related genes with high mutation frequency in mutant groups. Top ten genes with high mutation frequency in the *POLE* (A) and *POLD1* (B) mutation groups. WT = *POLE* and *POLD1* wild-type. Fisher's exact test was used to statistically compare the *POLE* or *POLD1* mutants with the wild-type group.



**Figure S4** The oncoprint showing gene mutation status and distribution of *POLE*, *POLD1*, *LRP1B*, *ARID1A* and *MUC16* in the cohort. The percentages represented the proportion of mutations in each gene in the entire population. Most samples with *POLE/POLD1* mutations also had *LRP1B*, *ARID1A* or *MUC16* mutations.

**Table S1** Sites and predicted consequences of POLE and POLD1 mutations

Nucleotide change	Amino acid change	Mutation type	Site	SIFT score	Polyphen-2 score
POLE					
c.70G>C	p.G24R	Missense Mutation	Other	0.01	0.813
c.207C>T	p.T69=	Splice Region	Splice Region	-	-
c.208G>A	p.E70K	Missense Mutation	Other	0.04	0.98
c.331-2A>G	p.X111_splice	Splice Site	Splice Site	-	-
c.335G>T	p.C112F	Missense Mutation	Other	0.7	0.002
c.557C>T	p.A186V	Missense Mutation	Other	0.51	0.03
c.630G>C	p.K210N	Missense Mutation	Other	0.14	0.003
c.673G>A	p.D225N	Missense Mutation	Other	0	1
c.727dupA	p.W243Lfs*20	Frameshift Ins	Other	-	-
c.857C>T	p.P286L	Missense Mutation	Exo.	0	1
c.1231G>T	p.V411L	Missense Mutation	Exo.	0	1
c.1346C>T	p.T449M	Missense Mutation	Exo.	0.21	0.01
c.1420G>A	p.V474I	Missense Mutation	Other	0.06	0.987
c.1516A>G	p.M506V	Missense Mutation	Other	0	0.989
c.1651delC	p.V551Ffs*12	Frameshift Del	Pol.	-	-
c.1741G>C	p.A581P	Missense Mutation	Pol.	0.01	0.921
c.2041A>C	p.S681R	Missense Mutation	Pol.	0.01	0.614
c.1993C>T	p.R665W	Missense Mutation	Pol.	0	1
c.2091dupC	p.F699Vfs*11	Frameshift Ins	Pol.	-	-
c.2134C>T	p.R712C	Missense Mutation	Pol.	0	0.995
c.2377C>T	p.R793C	Missense Mutation	Pol.	0.01	0.992
c.2461C>T	p.R821C	Missense Mutation	Pol.	0	1
c.2485A>G	p.M829V	Missense Mutation	Pol.	0.01	1
c.2539C>T	p.R847W	Missense Mutation	Pol.	0	1
c.2743G>A	p.E915K	Missense Mutation	Pol.	0.06	0.003
c.2865-4_2865-3insC	p.X955_splice	Splice Site	Splice Site	-	-
c.3109C>T	p.R1037C	Missense Mutation	Pol.	0	0.996
c.3332G>A	p.R1111Q	Missense Mutation	Pol.	0.04	0.998
c.3970C>T	p.R1324C	Missense Mutation	Other	0	0.999
c.3989C>T	p.P1330L	Missense Mutation	Other	0.08	0.914
c.4162C>A	p.L1388I	Missense Mutation	Other	0	0.999
c.4193_4194delAT	p.Y1398*	Frameshift Del	Other	-	-
c.4247C>T	p.A1416V	Missense Mutation	Other	0.07	0.032
c.4555C>T	p.R1519C	Missense Mutation	Other	0	1
c.4556G>A	p.R1519H	Missense Mutation	Other	0.01	0.999
c.4647delG	p.K1550Nfs*12	Frameshift Del	Other	-	-
c.5096C>A	p.A1699D	Missense Mutation	Other	0.27	0.015
c.5213C>A	p.T1738N	Missense Mutation	Other	0	0.98
c.5239G>A	p.D1747N	Missense Mutation	Other	0	0.998
c.5333C>A	p.A1778D	Missense Mutation	Other	0.63	0.003
c.5539_5541delCTT	p.K1847del	Inframe Del	Other	-	-
c.5666A>G	p.Y1889C	Missense Mutation	Other	0	0.999
c.5842G>T	p.D1948Y	Missense Mutation	Other	0.01	0
c.5867A>G	p.E1956G	Missense Mutation	Other	0.08	0.001
c.5900C>T	p.A1967V	Missense Mutation	Other	0.27	0.001
c.6008A>G	p.Y2003C	Missense Mutation	Other	0	1
c.6049C>T	p.R2017C	Missense Mutation	Other	0.02	0.024
c.6349A>G	p.N2117D	Missense Mutation	Other	0.43	0.012
c.6446G>A	p.R2149H	Missense Mutation	Other	0.12	0
c.6676G>A	p.G2226R	Missense Mutation	Other	0.4	0.066
c.6748-2A>C	p.X2250_splice	Splice Site	Splice Site	-	-
POLD1					
c.-2G>T	p.X1_splice	Splice Site	Splice Site	-	-
c.347delC	p.P116Hfs*53	Frameshift Del	Other	-	-
c.377G>A	p.R126H	Missense Mutation	Other	0.01	0.993
c.537dupG	p.R180Efs*72	Frameshift Ins	Other	-	-
c.931C>T	p.R311C	Missense Mutation	Exo.	0	0.999
c.971G>T	p.G324V	Missense Mutation	Exo.	0	1
c.997C>A	p.P333T	Missense Mutation	Exo.	0	0.944
c.1504G>A	p.D502N	Missense Mutation	Exo.	0.2	0.081
c.1520G>A	p.R507H	Missense Mutation	Exo.	0	0.996
c.1573C>T	p.R525W	Missense Mutation	Exo.	0	0.994
c.1762G>A	p.E588K	Missense Mutation	Pol	0	0.99
c.1837G>T	p.A613S	Missense Mutation	Pol.	0	0.99
c.2182A>C	p.I728L	Missense Mutation	Pol.	0.07	0.514
c.2251-1G>T	p.X751_splice	Splice Site	Splice Site	-	-
c.2414G>A	p.S805N	Missense Mutation	Pol.	1	0.001
c.2489A>G	p.E830G	Missense Mutation	Pol.	0	1
c.2629G>A	p.D877N	Missense Mutation	Pol.	0	1
c.3315G>T	p.E1105D	Missense Mutation	Other	0.31	0.012

**Table S2** Demographic and clinicopathological characteristics in STAD cohort according to *POLE/POLD1* mutation status

	<i>POLE/POLD1</i>	WT	p value
Number	49	564	
Age	70.5 [44-90]	67 [30-90]	0.042 <sup>†</sup>
Sex			
Female	21 (42.86%)	177 (31.38%)	0.201
Male	26 (53.06%)	338 (59.93%)	
Unknown	2 (4.08%)	49 (8.69%)	
Stage			
I	8 (16.33%)	60 (10.64%)	0.326
II	8 (16.33%)	135 (23.94%)	
III	19 (38.78%)	209 (37.06%)	
IV	10 (20.41%)	81 (14.36%)	
Unknown	4 (8.16%)	79 (14.01%)	
Grade			
G1	0	12 (2.13%)	0.802
G2	15 (30.61%)	140 (24.82%)	
G3	25 (51.02%)	235 (41.67%)	
Unknown	9 (18.37%)	177 (31.38%)	
pT stage			
T1	3 (6.12%)	31 (5.50%)	0.079
T2	8 (16.33%)	111 (19.68%)	
T3	15 (30.61%)	239 (42.38%)	
T4	20 (40.82%)	133 (23.58%)	
Unknown	3 (6.12%)	50 (8.87%)	
pN stage			
N0	17 (34.69%)	133 (23.58%)	0.444
N1	12 (24.49%)	138 (24.47%)	
N2	8 (16.33%)	126 (22.34%)	
N3	9 (18.37%)	109 (19.33%)	
Unknown	3 (6.12%)	58 (10.28%)	
pM stage			
M0	39 (79.59%)	462 (81.91%)	0.403
M1	5 (10.20%)	41 (7.27%)	
Unknown	5 (10.20%)	61 (10.82%)	
Anatomic subdivision			
Antrum	24 (48.98%)	177 (31.38%)	0.047*
Cardia	5 (10.20%)	132 (23.40%)	
Fundus / body	14 (28.57%)	162 (28.72%)	
Other	1 (2.04%)	16 (2.84%)	
Unknown	5 (10.20%)	77 (13.65%)	
Residual tumor			
R0	33 (67.35%)	313 (55.50%)	0.897
R1	2 (4.08%)	16 (2.84%)	
R2	1 (2.04%)	16 (2.84%)	
Unknown	13 (26.53%)	219 (38.83%)	
Radiation therapy			
Yes	8 (16.33%)	67 (11.88%)	0.343
No	23 (24.49%)	293 (51.95%)	
Unknown	18 (36.73%)	204 (36.17%)	
Targeted therapy			
Yes	13 (26.53%)	161 (28.55%)	0.851
No	18 (36.73%)	195 (34.57%)	
Unknown	18 (36.73%)	208 (36.88%)	

Data are n (%) or median [range]. WT = *POLE* and *POLD1* wild-type. <sup>†</sup>, determined by Mann-Whitney test. Other statistical comparisons between groups were made by Fisher exact test. \*, P<0.05.