

Table S1 The frequently mutated genes in the 4 subtypes of the 3DMed cohort (n=735)

Gene	EBV (N=38)	MSI (N=34)	GS (N=225)	CIN (N=438)
<i>TP53</i>	12 (32%)	13 (38%)	101 (45%)	322 (73.5%)
<i>ARID1A</i>	16 (42.1%)	25 (73.5%)	45 (20%)	43 (9.8%)
<i>LRP1B</i>	5 (13%)	18 (52.9%)	17 (7.6%)	79 (18.0%)
<i>CDH1</i>	2 (5.3%)	6 (18%)	53 (23.6%)	47 (11%)
<i>KMT2C</i>	5 (13%)	29 (85.3%)	21 (9.3%)	33 (7.5%)
<i>FAT4</i>	8 (21%)	15 (44%)	10 (4.4%)	51 (11.6%)
<i>KMT2D</i>	5 (13%)	29 (85.3%)	18 (8.0%)	30 (6.8%)
<i>AR</i>	9 (24%)	11 (32%)	17 (7.6%)	38 (8.7%)
<i>SPTA1</i>	3 (7.9%)	7 (21%)	15 (6.7%)	46 (10.5%)
<i>ZFH3</i>	3 (7.9%)	19 (55.9%)	16 (7.1%)	33 (7.5%)
<i>MSH3</i>	1 (2.6%)	23 (67.6%)	16 (7.1%)	29 (6.6%)
<i>PIK3CA</i>	15 (39.5%)	11 (32%)	19 (8.4%)	17 (3.9%)
<i>TGFBR2</i>	1 (2.6%)	27 (79.4%)	15 (6.7%)	15 (3.4%)
<i>APC</i>	2 (5.3%)	10 (29%)	7 (3.1%)	36 (8.2%)
<i>GLI3</i>	1 (2.6%)	11 (32%)	9 (4.0%)	34 (7.8%)
<i>PREX2</i>	4 (11%)	5 (15%)	11 (4.9%)	32 (7.3%)
<i>ERBB2</i>	2 (5.3%)	13 (38%)	11 (4.9%)	25 (5.7%)
<i>ARID1B</i>	1 (2.6%)	14 (41%)	12 (5.3%)	24 (5.5%)
<i>ATM</i>	0 (0%)	11 (32%)	12 (5.3%)	25 (5.7%)
<i>KRAS</i>	2 (5.3%)	11 (32%)	14 (6.2%)	21 (4.8%)
<i>CTNND2</i>	1 (2.6%)	8 (24%)	7 (3.1%)	28 (6.4%)
<i>NTRK3</i>	1 (2.6%)	9 (26%)	7 (3.1%)	27 (6.2%)
<i>NF1</i>	2 (5.3%)	11 (32%)	8 (3.6%)	21 (4.8%)
<i>RHOA</i>	4 (11%)	4 (12%)	17 (7.6%)	17 (3.9%)
<i>PTPRT</i>	0 (0%)	10 (29%)	2 (0.9%)	29 (6.6%)
<i>KIT</i>	1 (2.6%)	1 (2.9%)	18 (8.0%)	20 (4.6%)
<i>RNF43</i>	0 (0%)	22 (64.7%)	6 (2.7%)	12 (2.7%)
<i>NCOR2</i>	3 (7.9%)	18 (53%)	7 (3.1%)	11 (2.5%)
<i>ACVR2A</i>	0 (0%)	27 (79.4%)	7 (3.1%)	5 (1.1%)
<i>ERBB4</i>	0 (0%)	4 (12%)	7 (3.1%)	27 (6.2%)
<i>SMARCA4</i>	4 (11%)	14 (41%)	8 (3.6%)	12 (2.7%)
<i>ERBB3</i>	2 (5.3%)	9 (26%)	13 (5.8%)	13 (3.0%)
<i>FAM135B</i>	1 (2.6%)	6 (18%)	7 (3.1%)	22 (5.0%)
<i>IRS2</i>	3 (7.9%)	14 (41%)	2 (0.9%)	17 (3.9%)
<i>FAT1</i>	3 (7.9%)	17 (50%)	2 (0.9%)	14 (3.2%)
<i>COL7A1</i>	1 (2.6%)	16 (47%)	5 (2.2%)	13 (3.0%)
<i>KMT2A</i>	1 (2.6%)	13 (38%)	8 (3.6%)	13 (3.0%)
<i>SLIT2</i>	1 (2.6%)	9 (26%)	3 (1.3%)	21 (4.8%)
<i>ATRX</i>	6 (16%)	5 (15%)	9 (4.0%)	13 (3.0%)
<i>CHD4</i>	2 (5.3%)	9 (26%)	10 (4.4%)	12 (2.7%)
<i>SMAD4</i>	4 (11%)	3 (8.8%)	7 (3.1%)	18 (4.1%)
<i>PTPN13</i>	5 (13%)	5 (15%)	0 (0%)	21 (4.8%)
<i>ROS1</i>	3 (7.9%)	5 (15%)	3 (1.3%)	20 (4.6%)
<i>ATR</i>	2 (5.3%)	14 (41%)	1 (0.4%)	14 (3.2%)
<i>REV3L</i>	2 (5.3%)	6 (18%)	6 (2.7%)	16 (3.7%)
<i>NRG3</i>	1 (2.6%)	7 (21%)	7 (3.1%)	15 (3.4%)
<i>MTOR</i>	4 (11%)	7 (21%)	4 (1.8%)	15 (3.4%)
<i>FANCM</i>	2 (5.3%)	15 (44%)	0 (0%)	13 (3.0%)
<i>CTNNB1</i>	5 (13%)	5 (15%)	8 (3.6%)	12 (2.7%)
<i>RNF213</i>	1 (2.6%)	15 (44%)	3 (1.3%)	11 (2.5%)
<i>JMJD1C</i>	1 (2.6%)	16 (47%)	2 (0.9%)	11 (2.5%)
<i>SPEN</i>	3 (7.9%)	12 (35%)	5 (2.2%)	10 (2.3%)

EBV, Epstein-Barr virus; MSI, microsatellite instability; GS, genomically stable; CIN, chromosomal instability.

Table S2 The response to immunotherapy of patients with gastric cancer in the Korean cohort (n=55)

SEQ.ID	group_cluster	Patient.ID	patient	Response	MSI.type.by.pentaplex	MSI.score.(WES)	EBV.in.situ	EBV.(WES)	Number.of.SNVs	TCGA	Mesenchymal.subtype.by.ACRG	Immune.signature	Pathology	Best.of.response	BOR	DCR
PB-16-002	GS	EP-02	PB-16-002	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	P/D adeno	PD	SD/PD	PD
PB-16-003	GS	EP-03	PB-16-003	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	Low	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-004	GS	EP-04	PB-16-004	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	P/D adeno	PD	SD/PD	PD
PB-16-005	GS	EP-05	PB-16-005	1	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	P/D adeno	PR	CR/PR	CR/PR/SD
PB-16-006	GS	EP-06	PB-16-006	0	MSS	Low	Negative	Negative	Low ML	CIN	N/A	N/A	M/D adeno	SD	SD/PD	CR/PR/SD
PB-16-007	GS	EP-09	PB-16-007	NA	MSS	Low	Negative	Negative	Low ML	GS	N/A	N/A	M/D adeno	NE	NE	NE
PB-16-008	CIN	EP-08	PB-16-008	NA	MSS	Low	Negative	Negative	Mod ML	CIN	N/A	N/A	P/D adeno	NE	NE	NE
PB-16-011	CIN	EP-07	PB-16-011	0	MSS	Low	Negative	Negative	Low ML	GS	N/A	N/A	M/D adeno	PD	SD/PD	PD
PB-16-013	GS	EP-11	PB-16-013	1	MSS	Low	Negative	Negative	Low ML	GS	N/A	N/A	M/D adeno	PR	CR/PR	CR/PR/SD
PB-16-014	GS	EP-12	PB-16-014	0	MSS	Low	Negative	Negative	Low ML	GS	N/A	N/A	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-015	GS	EP-14	PB-16-015	0	MSS	Low	Negative	Negative	Low ML	CIN	N/A	N/A	P/D adeno	PD	SD/PD	PD
PB-16-016	GS	EP-13	PB-16-016	0	MSS	Low	Negative	Negative	Mod ML	CIN	N/A	N/A	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-018	CIN	EP-16	PB-16-018	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	M/D adeno	PD	SD/PD	PD
PB-16-022	GS	EP-18	PB-16-022	0	MSS	Low	Negative	Negative	Low ML	GS	Mesenchymal	High	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-023	GS	EP-17	PB-16-023	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	Low	P/D adeno	PD	SD/PD	PD
PB-16-024	CIN	EP-21	PB-16-024	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	High	P/D adeno	PD	SD/PD	PD
PB-16-025	GS	EP-20	PB-16-025	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	M/D adeno	PD	SD/PD	PD
PB-16-026	GS	EP-27	PB-16-026	0	MSS	Low	Negative	Negative	Mod ML	GS	N/A	N/A	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-029	CIN	EP-28	PB-16-029	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	M/D adeno	PD	SD/PD	PD
PB-16-030	GS	EP-22	PB-16-030	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	High	Signet ring cell	PD	SD/PD	PD
PB-16-031	CIN	EP-32	PB-16-031	1	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	High	P/D adeno with NE feature	CR	CR/PR	CR/PR/SD
PB-16-032	CIN	EP-25	PB-16-032	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	M/D adeno	PD	SD/PD	PD
PB-16-034	GS	EP-29	PB-16-034	0	MSS	Low	Negative	Negative	Mod ML	CIN	Mesenchymal	High	Signet ring cell	SD	SD/PD	CR/PR/SD
PB-16-035	GS	EP-30	PB-16-035	0	MSS	Low	Negative	Negative	Low ML	CIN	Mesenchymal	High	P/D adeno	PD	SD/PD	PD
PB-16-037	GS	EP-31	PB-16-037	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-039	GS	EP-33	PB-16-039	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	High	P/D adeno	PD	SD/PD	PD
PB-16-040	GS	EP-34	PB-16-040	0	MSS	Low	Negative	Negative	Low ML	GS	Mesenchymal	High	M/D adeno	SD	SD/PD	CR/PR/SD
PB-16-041	GS	EP-37	PB-16-041	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	High	Signet ring cell	PD	SD/PD	PD
PB-16-042	GS	EP-35	PB-16-042	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	Low	W/D adeno	SD	SD/PD	CR/PR/SD
PB-16-043	GS	EP-38	PB-16-043	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	Signet ring cell	PD	SD/PD	PD
PB-16-047	GS	EP-42	PB-16-047	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	Low	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-049	GS	EP-41	PB-16-049	0	MSS	Low	Negative	Negative	Mod ML	CIN	Non-mesenchymal	Low	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-051	GS	EP-44	PB-16-051	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	High	M/D adeno	PD	SD/PD	PD
PB-16-052	GS	EP-50	PB-16-052	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	High	Signet ring cell	SD	SD/PD	CR/PR/SD
PB-16-054	GS	EP-47	PB-16-054	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	Low	M/D adeno	SD	SD/PD	CR/PR/SD
PB-16-055	GS	EP-48	PB-16-055	0	MSI	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	Low	Signet ring cell	PD	SD/PD	PD
PB-16-056	GS	EP-45	PB-16-056	0	MSS	Low	Negative	Negative	Low ML	GS	Non-mesenchymal	High	M/D adeno	SD	SD/PD	CR/PR/SD
PB-16-057	CIN	EP-46	PB-16-057	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	Adenoneuro-endocrine	PD	SD/PD	PD
PB-16-059	GS	EP-54	PB-16-059	1	MSS	Low	Positive	Negative	Low ML	GS	Non-mesenchymal	High	P/D adeno	PR	CR/PR	CR/PR/SD
PB-16-060	GS	EP-53	PB-16-060	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	P/D adeno	PD	SD/PD	PD
PB-16-062	GS	EP-57	PB-16-062	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	High	Signet ring cell	SD	SD/PD	CR/PR/SD
PB-16-064	GS	EP-55	PB-16-064	0	MSS	Low	Negative	Negative	Low ML	CIN	Non-mesenchymal	Low	P/D adeno	SD	SD/PD	CR/PR/SD
PB-16-066	GS	EP-58	PB-16-066	0	MSS	Low	Negative	Negative	High ML	GS	Mesenchymal	Low	Signet ring cell	SD	SD/PD	CR/PR/SD
PB-16-067	CIN	EP-59	PB-16-067	0	MSS	Low	Negative	Negative	Mod ML	GS	Non-mesenchymal	Low	P/D adeno	PD	SD/PD	PD
PB-16-069	GS	EP-61	PB-16-069	0	MSS	Low	Negative	Negative	Low ML	GS	Mesenchymal	High	M/D adeno	SD	SD/PD	CR/PR/SD

Number of non-synonymous SNVs ≥ 400 was defined as high mutational load (ML); 100–400, intermediate ML; <100, low ML. MSI, microsatellite instability; WES, whole-exome sequencing; EBV, Epstein-Barr virus; SNVs, single nucleotide variants; TCGA, The Cancer Genome Atlas Project; ACRG, Asian Cancer Research Group; BOR, best of response; DCR, disease control rate; GS, genomically stable; MSS, microsatellite stable; CIN, chromosomal instability; M/D adeno, moderately differentiated adenocarcinoma; P/D adeno, poorly differentiated adenocarcinoma; W/D adeno, well differentiated adenocarcinoma; PD, progressive disease; SD, stable disease; CR, complete response; PR, partial response; NE, not evaluable.