

**Supplementary Table 1. Collapsed burden testing for 114 cancer susceptibility genes**

Gene	T1 variant counts			T2 variant counts			T3 variant counts		
	Cases	Controls	P value	Cases	Controls	P value	Cases	Controls	P value
ABCB11	0	0	1.00	8	13	0.64	19	44	0.79
ALK	0	0	1.00	5	6	0.35	12	12	0.08
APC	1	1	0.54	25	44	0.51	59	76	0.00
ATM	0	6	0.19	10	24	0.85	37	84	0.76
AXIN2	0	0	1.00	0	2	1.00	4	18	0.18
BAP1	0	0	1.00	1	2	1.00	3	6	1.00
BLM	0	1	1.00	11	14	0.20	21	39	0.67
BMPR1A	0	0	1.00	0	5	0.18	1	7	0.45
BRCA1	0	3	0.56	8	18	1.00	27	58	1.00
BRCA2	4	5	0.48	44	67	0.10	72	141	0.59
BRIP1	2	4	1.00	25	36	0.16	40	59	0.08
BUB1B	1	0	0.32	2	0	0.10	11	20	0.70
CBL	0	0	1.00	0	0	1.00	5	7	0.54
CDC73	0	1	1.00	0	7	0.10	2	9	0.52
CDH1	0	0	1.00	7	5	0.06	18	33	0.65
CDK4	0	1	1.00	0	2	1.00	2	13	0.17
CDKN1B	0	0	1.00	0	0	1.00	5	5	0.31
CDKN2A	0	0	1.00	0	0	1.00	0	0	1.00
CEBPA	0	0	1.00	0	0	1.00	0	0	1.00
CHEK2	1	2	1.00	4	7	0.75	8	15	0.82
COL7A1	1	2	1.00	3	6	1.00	57	101	0.29
CYLD	0	0	1.00	0	2	1.00	2	5	1.00
DDB2	0	0	1.00	0	1	1.00	9	12	0.35
DICER1	0	1	1.00	1	2	1.00	8	23	0.56
DIS3L2	0	0	1.00	6	19	0.52	6	21	0.31
DKC1	0	0	1.00	0	0	1.00	0	0	1.00
DOCK8	0	2	1.00	14	35	0.65	26	65	0.49
EGFR	0	0	1.00	0	0	1.00	0	0	1.00
ELANE	0	0	1.00	1	0	0.32	1	0	0.32
ERCC2	0	0	1.00	4	10	1.00	7	17	0.83
ERCC3	3	1	0.10	6	10	0.60	7	27	0.19
ERCC4	1	0	0.32	14	21	0.36	20	38	0.67
ERCC5	0	0	1.00	10	18	0.69	26	35	0.09
EXT1	0	0	1.00	0	1	1.00	1	8	0.29
EXT2	0	0	1.00	7	21	0.54	24	59	0.55
FAH	2	5	1.00	4	9	1.00	7	12	0.63
FANCA	0	2	1.00	7	18	0.83	39	77	0.76
FANCC	0	4	0.31	20	49	0.60	24	60	0.55
FANCG	0	2	1.00	1	4	1.00	4	9	1.00
FAS	0	0	1.00	0	3	0.56	9	15	0.66
FH	0	1	1.00	1	4	1.00	2	6	1.00
FLCN	0	0	1.00	2	5	1.00	7	18	0.83
GATA2	0	0	1.00	0	0	1.00	1	0	0.32
GBA	0	0	1.00	1	3	1.00	2	5	1.00
GJB2	0	0	1.00	0	1	1.00	1	2	1.00
GPC3	0	0	1.00	0	0	1.00	0	0	1.00
HFE	0	0	1.00	2	3	0.66	5	9	0.78

HMBS	0	0	1.00	1	4	1.00	6	10	0.60
HRAS	0	0	1.00	0	0	1.00	1	2	1.00
ITK	0	0	1.00	0	1	1.00	4	21	0.09
KIT	0	0	1.00	0	2	1.00	5	13	0.80
MAX	0	0	1.00	0	0	1.00	0	0	1.00
MEN1	0	0	1.00	0	0	1.00	2	1	0.24
MET	0	0	1.00	0	0	1.00	0	0	1.00
MLH1	0	0	1.00	5	4	0.16	10	12	0.25
MSH2	0	0	1.00	5	10	1.00	11	21	0.85
MSH6	0	1	1.00	12	26	1.00	27	48	0.45
MTAP	0	1	1.00	1	1	0.54	1	3	1.00
MUTYH	0	2	1.00	9	13	0.37	26	28	0.02
NBN	0	2	1.00	13	18	0.25	18	24	0.14
NF1	0	0	1.00	2	6	1.00	21	33	0.30
NF2	0	0	1.00	4	2	0.09	5	7	0.54
PALB2	0	1	1.00	14	28	0.87	18	35	0.77
PDGFRA	0	0	1.00	3	2	0.34	9	25	0.58
PHOX2B	0	0	1.00	0	0	1.00	0	0	1.00
PMS2	0	0	1.00	0	0	1.00	0	0	1.00
POLD1	1	1	0.54	2	6	1.00	4	20	0.13
POLE	2	1	0.24	5	13	0.80	28	42	0.16
POLH	0	0	1.00	12	12	0.08	15	21	0.21
PRKAR1A	0	0	1.00	1	1	0.54	3	1	0.10
PRSS1	0	0	1.00	0	0	1.00	0	0	1.00
PTCH1	0	0	1.00	5	5	0.31	10	28	0.49
PTEN	1	0	0.32	1	0	0.32	2	1	0.24
PTPN11	0	0	1.00	0	1	1.00	3	7	1.00
RAD51C	1	2	1.00	2	5	1.00	14	46	0.16
RAD51D	2	1	0.24	3	3	0.39	10	14	0.38
RB1	0	0	1.00	6	9	0.58	10	16	0.53
RECQL4	0	6	0.19	3	22	0.03	38	96	0.39
RET	0	1	1.00	5	3	0.12	6	11	0.80
RHBDF2	1	0	0.32	15	41	0.47	19	46	0.69
RUNX1	0	0	1.00	1	1	0.54	1	1	0.54
SBDS	0	0	1.00	0	0	1.00	0	0	1.00
SDHA	0	2	1.00	3	10	0.57	5	15	0.63
SDHAF2	0	1	1.00	0	2	1.00	1	6	0.44
SDHB	0	0	1.00	1	1	0.54	1	3	1.00
SDHC	0	0	1.00	0	0	1.00	0	0	1.00
SDHD	0	1	1.00	1	1	0.54	2	2	0.60
SDHD	0	0	1.00	0	0	1.00	1	0	0.32
SERPINA1	0	0	1.00	11	17	0.42	12	20	0.57
SH2D1A	0	0	1.00	0	0	1.00	0	0	1.00
SLC25A13	0	0	1.00	0	0	1.00	0	0	1.00
SMAD4	0	0	1.00	0	0	1.00	1	7	0.45
SMARCA4	0	0	1.00	0	1	1.00	0	3	0.56
SMARCB1	0	0	1.00	0	0	1.00	1	1	0.54
SMARCE1	0	1	1.00	0	1	1.00	1	3	1.00
SOS1	0	1	1.00	1	2	1.00	4	12	0.79
STAT3	0	0	1.00	0	0	1.00	2	2	0.60

STK11	0	0	1.00	0	0	1.00	5	22	0.15
SUFU	0	0	1.00	0	1	1.00	2	3	0.66
TERT	0	0	1.00	0	1	1.00	15	12	0.01
TGFBR1	0	0	1.00	1	1	0.54	10	12	0.25
TMEM127	0	0	1.00	1	1	0.54	1	2	1.00
TP53	0	0	1.00	0	1	1.00	1	2	1.00
TRIM37	0	1	1.00	1	5	0.67	7	23	0.33
TSC1	0	0	1.00	0	1	1.00	23	28	0.05
TSC2	3	9	0.76	16	34	1.00	35	61	0.37
UROD	1	0	0.32	1	2	1.00	13	23	0.59
VHL	0	0	1.00	1	2	1.00	1	2	1.00
WAS	0	0	1.00	0	0	1.00	0	0	1.00
WRN	8	11	0.34	29	63	1.00	50	100	0.79
WT1	0	0	1.00	2	6	1.00	3	8	1.00
XPA	0	1	1.00	0	4	0.31	2	6	1.00
XPC	2	0	0.10	11	14	0.20	16	18	0.07