

Supplementary material

Mutability of druggable kinases and pro-inflammatory cytokines by their proximity to telomeres and A+T content

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Table s1. Two factor characteristics of 129 druggable kinases

Kinases	gene ID	chr*	gene locus	telomere locus	gene to telomere	A, T ** (%)	A + T (%)	FL*** (bp)
1	PRKAG1	12	49 Mb	133 Mb	133-49 = 84	25,28	53%	1657
2	PRKAB1	12	119 Mb	133 Mb	133-119 = 14	23,27	50%	2219
3	ADCK5	8	144 Mb	145 Mb	145 - 144 = 1	17,19	36%	1960
4	ALPK3	15	84 Mb	100 Mb	100 - 84 = 16	22,23	45%	10238
5	ADCK4	19	40 Mb	58 Mb	58 - 40 = 18	18, 20	38	2443
6	ALPK2	18	58 Mb	80 Mb	80 - 58 = 22	30, 23	53	7437
7	BCKDK	16	31 Mb	0	31	19, 21	40	2036
8	CAMKV	3	49 Mb	0	49	21,22	43	2998
9	CDKL3	5	134 Mb	181 Mb	181-134=47	34,28	62	1717
10	CDKL4	2	39 Mb	0	39	33,30	63	1623
11	CDKL1	14	50 Mb	107 Mb	107 - 50=57	29,31	60	5402
12	CDKL2	4	75 Mb	190 Mb	190-75 =115	30,32	62	4704
13	CDK15	2	201 Mb	242 Mb	242-201=41	29,29	58	3587
14	CDK17	12	96 Mb	133 Mb	133-96=37	28,32	60	4036
15	CDK14	7	90 Mb	159 Mb	159-90=69	29,32	61	4970
16	CDK18	1	205 Mb	248 Mb	248-205=43	20,20	40	3068
17	CLK4	5	178 Mb	181 Mb	181-178=3	32,32	64	2504
18	CDK10	16	89 Mb	90 Mb	90-89=1	19,22	41	1595
19	CLK3	15	74 Mb	101 Mb	101-74=27	24,21	45	1846
20	CSNK2A2	16	58 Mb	90 Mb	90-58=32	24,22	46	1887
21	DGKH	13	42 Mb	114 Mb	114-42=72	30,33	63	17366
22	DYRK3	1	206 Mb	248 Mb	248-206=42	26,32	58	8128
23	DYRK1B	19	39 Mb	58 Mb	58-39=19	17,20	37	2496
24	DYRK4	12	4 Mb	0 Mb	4-0=4	28,24	52	1845
25	EEF2K	16	22 Mb	90 Mb	90-22=68	23,28	51	7398
26	DYRK2	12	67 Mb	133 Mb	133-67=66	28,33	61	8739
27	ERN2	16	23 Mb	0 Mb	23-0=23	20,20	40	3337
28	FASTK	7	151 Mb	159 Mb	159-151=8	16,22	38	1794
29	GK2	4	79 Mb	190 Mb	190-79=111	29,29	58	1868
30	HIPK4	19	40 Mb	58 Mb	58-40=18	19,20	39	2446
31	ITPKA	15	41 Mb	101 Mb	101-41=60	17,17	34	1825
32	CSNK1G3	5	123 Mb	181 Mb	181-123=58	30,33	63	4360
33	CSNK1G2	19	1.9 Mb	0 Mb	1.9-0=1.9	19,17	36	2895
34	PRKACG	9	69 Mb	138 Mb	138-69=69	22,22	44	1610
35	CSNK1G1	15	64 Mb	101 Mb	101-64=37	27,29	56	8085
36	ITPK1	14	93 Mb	107 Mb	107-93=14	19,23	42	6188
37	PSKH2	8	86 Mb	145 Mb	145-86=59	31,31	62	2557
38	CAMK1D	10	12 Mb	0 Mb	12-0=12	26,23	49	2085
39	TK2	16	66 Mb	90 Mb	90-66=24	22,28	50	4824
40	PRKACB	1	84 Mb	248 Mb	248-84=164	29,35	64	4496
41	PNCK	X	153 Mb	156 Mb	156-153=3	19,20	39	1888
42	CAMK1G	1	209 Mb	249 Mb	249-209=40	23,24	47	2456
43	CAMKK1	17	3.8 Mb	0 Mb	3.8-0=3.8	21,21	42	3572
44	PSKH1	16	67 Mb	90 Mb	90-67=23	18,23	41	3497
45	PHKA1	X	72 Mb	155 Mb	155-72=83	26,29	55	6286

* chr, chromosome; ** A, adenine; T, thymine; *** FL, full-length; bp, base pair

Table s1. Two factor characteristics of 129 druggable kinases (continued)

Kinases	gene ID	chr	gene locus	telomere locus	gene to telomere	A, T (%)	A + T (%)	FL (bp)
46	RPS6KC1	1	213 Mb	248 Mb	248-213=35	29,30	59	5505
47	PRKCQ	10	6.3 MB	0 Mb	6.3-0=6.3	28,26	54	3255
48	LMTK3	19	48 Mb	58 Mb	58-48=10	16,15	31	4945
49	MARK4	19	45 Mb	58 Mb	58-45=13	21,21	42	5231
50	MAST3	19	18 Mb	0 Mb	18-0=18	19,21	40	5906
51	LRRK1	15	101 Mb	101.5 Mb	0.5	23,25	48	15674
52	MAP3K14	17	45 Mb	83 Mb	83-45=38	22,20	42	4442
53	LTK	15	41 Mb	101 Mb	101-41=60	17,20	37	3072
54	MAP3K10	19	40 Mb	58 Mb	58-40=18	16,15	31	3754
55	MAST4	5	66 Mb	181 Mb	181-66=115	26,25	51	9918
56	MAST2	1	45 Mb	0 Mb	45-0=45	22,21	43	5737
57	MAPK15	8	143 MB	145 Mb	145-143=2	17,19	36	1871
58	MAPK4	18	50 Mb	79 Mb	79-50=29	23,22	45	4763
59	MKNK2	19	2 Mb	0 Mb	2-0=2	20,20	40	1758
60	CDC42BPG	11	64 Mb	135 Mb	135-64=71	20,18	38	6161
61	CDC42BPB	14	103 Mb	107 Mb	107-103=4	24,21	45	6844
62	NEK11	3	131 Mb	198 Mb	198-131=67	31,26	57	2926
63	NEK5	13	52 Mb	114 Mb	114-52=62	31,27	58	2913
64	NEK10	3	27 Mb	0 Mb	27-0=27	31,31	62	8543
65	NIM1K	5	43 MB	0 Mb	43-0=43	27,22	49	2313
66	NEK4	3	52 Mb	0 Mb	52-0=52	27,30	57	6053
67	NEK6	9	124 Mb	138 Mb	138-124=14	24,25	49	3468
68	NRK	X	105 MB	154 Mb	154-105=49	31,28	59	8066
69	NEK7	1	198 Mb	248 Mb	248-198=50	30,36	66	4114
70	SCYL1	11	65 MB	133 MB	133-65=68	21,18	39	2636
71	NRBP2	8	143 Mb	145 Mb	145-143=2	22,22	44	3724
72	PIK3C2G	12	18 Mb	0 Mb	18-0=18	32,31	63	4864
73	PAK7	20	9.5 Mb	0 Mb	9.5-0=9.5	29,26	55	4834
74	PANK3	5	168 MB	181 Mb	181-168=13	30,34	64	10274
75	PIK3C2B	1	204 Mb	247 Mb	247-204=43	21,26	47	8457
76	PAK3	X	111 Mb	155 MB	155-111=44	30,31	61	9126
77	PAK6	15	40 Mb	99 Mb	99-40=59	20,21	41	3872
78	SCYL3	1	169 Mb	248 Mb	248-169=79	30,30	60	6308
79	PDIK1L	1	26 Mb	0 Mb	26-0=26	31,33	64	4113
80	PIP4K2C	12	57 Mb	133 Mb	133-57=76	22,29	51	3176
81	PIP5K1A	1	151 Mb	246 Mb	246-151=95	24,30	54	3761
82	PLK5	19	1.5 Mb	0 Mb	1.5	19,20	39	3760
83	PHKG1	7	56 Mb	0 Mb	56	23,20	43	2074
84	PI4KA	22	20 Mb	50 Mb	30	22,24	46	6751
85	PIP5K1B	9	68 MB	138 Mb	138-68=70	27,27	54	3115
86	PKMYT1	16	2.9 Mb	0 Mb	2.9	15,19	34	2061
87	PKN3	9	128 Mb	138 Mb	10	18,19	37	3393
88	PRPF4B	6	4 Mb	0 Mb	4	32,32	64	7517
89	TP53RK	20	46 Mb	64 Mb	18	25,33	58	3180
90	PRKRA	2	242 Mb	178 Mb	242-178=64	30,28	58	1770

Table s1. Two factor characteristics of 129 druggable kinases (continued)

Kinases	gene ID	chr	gene locus	telomere locus	gene to telomere	A, T (%)	A + T (%)	FL (bp)
91	PRKY	Y	7.2 MB	0 Mb	7.2	27,28	55	7240
92	PXK	3	58 Mb	0 MB	58-0=58	29,29	58	3001
93	RIOK1	6	7.3 Mb	0 Mb	7.3	31,28	59	2498
94	RIOK3	18	23 Mb	79 MB	79-23=56	31,30	61	3574
95	RPS6KL1	14	74 Mb	106 Mb	32	22,23	45	5322
96	SBK2	19	55 MB	58 Mb	3	15,22	37	2251
97	SCYL2	12	100 Mb	133 Mb	33	30,33	63	5977
98	SBK3	19	55 Mb	58 MB	3	17,17	34	1270
99	SGK494	17	28 MB	80 MB	52	25,31	56	3772
100	POMK	8	43 Mb	0 Mb	43	23,27	50	1868
101	SGK223	8	8.3 Mb	0 Mb	8.3	20,18	38	4845
102	SRPK3	X	153 Mb	156 Mb	3	20,18	38	1960
103	STK32C	10	132 Mb	133 Mb	1	18,18	36	2096
104	STK33	11	8.3 Mb	0 Mb	8.3	31,28	59	2728
105	STK32B	4	5 MB	0 Mb	5	24,25	49	3535
106	STK40	1	36 Mb	0 Mb	36	20,22	42	3882
107	STK17A	7	43 Mb	0 Mb	43	30,32	62	3918
108	STK36	2	241 Mb	218 Mb	241-218=23	21,26	47	4873
109	STK32A	5	147 Mb	181 Mb	181-147=34	27,26	53	878
110	STK38L	12	27 Mb	0 Mb	27-0=27	32,34	66	4957
111	STKLD1	9	133 Mb	138 MB	138-133=5	21,23	44	2826
112	STK3	8	98 Mb	145 Mb	145-98=47	32,31	63	2833
113	STK31	7	23 Mb	0 Mb	23	32,29	61	3274
114	TESK2	1	45 Mb	0 MB	45	23,26	49	3071
115	TBCK	4	106 Mb	190 Mb	190-106=84	30,31	61	7772
116	TLK1	2	171 MB	242 MB	242-171=71	30,31	61	5723
117	TPK1	7	144 Mb	159 MB	159-144=15	29,31	60	2439
118	TLK2	17	62 Mb	83 MB	83-62=21	28,27	55	5640
119	TSSK6	19	19 MB	58 MB	58-19=39	17,18	35	1330
120	TSSK1B	5	113 MB	181 Mb	181-113=68	25,24	49	2437
121	TTBK2	2	42 Mb	101 Mb	101-42=59	29,30	59	11208
122	TSSK4	14	24 Mb	107 Mb	107-24=83	25,26	51	1317
123	TTBK1	6	43 Mb	0 Mb	43	19,17	36	7130
124	TSSK3	1	32 MB	0 Mb	32	25,21	46	1026
125	UCK1	9	131 MB	138 Mb	138-131=7	21,21	42	2162
126	UCK2	1	165 Mb	248 Mb	248-165=85	22,27	49	4801
127	WNK2	9	93 MB	138 Mb	138-93=45	18,17	35	7080
128	VRK2	2	57 MB	0 Mb	57-0=57	33,28	61	1773
129	WEE2	7	141 Mb	159 Mb	159-141=18	29,30	59	3061

Table s2. Two factor characteristics of 73 pro-inflammatory cytokines of the MIS-C*

Cytokines ¹	gene ID	chr	gene locus	telomere locus	gene to telomere	A, T (%)	A + T (%)	FL (bp)
1	IL-18	11q	112Mb	134 Mb	134-112=22	32, 27	59	1115
2	IL-6	7p	22Mb	0 Mb	22-0=22	30, 29	59	1127
3	CCL-3	17q	36Mb	83 Mb	83-36=47	21,28	49	780
4	CCL-4	17q	36Mb	82 Mb	82-36=47	23,31	56	660
5	CDCP1	3p	45Mb	0 Mb	45-0=45	24,26	50	5963
6	IL-17A	6p	52Mb	0 Mb	52-0=52	30,30	60	1871
7	CCL20	2q	227 Mb	241 Mb	241-227=14	31,35	66	834
8	CCL28	5p	43 Mb	0	43-0=43	28,33	61	3126
9	HGF	7q	81 Mb	158 Mb	158-81=77	32,33	65	5834
10	CXCL10	4q	76 Mb	189 Mb	189-76=113	32,32	64	1175
11	FGF-21	19q	48 Mb	58 Mb	58-48=10	16,22	38	2292
12	IFN-gamma	12q	68 Mb	132 Mb	132-68=64	33,33	66	1211
13	CCL19	9p	34 Mb	0	34-0=34	22,21	43	683
14	OPG	8q	118 Mb	145 Mb	145-118=27	32,29	61	2087
15	LIF-R	5p	38 Mb	0	38-0=38	30,35	65	10385
16	CSF-1	1p	109 Mb	0	109-0=109	21,21	42	3994
17	CCL23	17q	36 Mb	83 Mb	83-36=47	25,26	51	628
18	CX3CL1	16q	57 Mb	90 Mb	90-57=33	19 22	41	3285
19	PD-L1	9p	5 Mb	0	5-0=5	28 32	60	3634
20	EN-RAGE	1q	153 Mb	248 Mb	248-153=95	28 27	55	485
21	CXCL9	4q	76 Mb	189	189-76=113	30 31	61	2761
22	IL-10	1q	206 Mb	246 Mb	246-206=40	27 28	55	1630
23	MCP-3	17q	34 Mb	83	83-34=49	30 31	61	810
24	MCP-2	17q	34 Mb	83	83-34=49	29 32	61	862
25	OSM	22q	30 Mb	50 Mb	50-20=30	20 22	42	1865
26	TNFSF14	19p	6 Mb	0	6-0=6	27 23	50	4778
27	TGF-alpha	2p	70 Mb	0	70-0=70	26 31	57	4117
28	IL8	4q	73 Mb	144	144-73=71	33 35	68	1642
29	TGF b1	19q	41 Mb	51 Mb	51-41=10	18 19	37	2780
30	VEGFA	6p	43 Mb	0	43-0=43	24 26	50	3609
31	IL7	8q	78 Mb	142	142-78=64	33 30	63	2016
32	MMP1	11q	102 Mb	134 Mb	134-102=32	29 29	58	1971
33	MCP1	17q	34 Mb	83	83-34=49	29 31	60	741
34	Flt3L	19q	49 Mb	58 Mb	58-49=9	18 20	38	1050
35	CD8A	2p	86 Mb	0	86-0=86	23 26	49	2106
36	TNF	6p	31 Mb	0	31-0=31	23 23	46	1678
37	CCL28	5p	43 Mb	0	43-0=43	28 33	61	3126

* multisystem inflammatory syndrome in children, MIS-C

Table s2. Two factor characteristics of 73 pro-inflammatory cytokines of MIS-C (con'd)

Cytokines	gene ID	chr	gene locus	telomere locus	gene to telomere	A, T (%)	A + T (%)	FL (bp)
38	IL10RB	21q	33 Mb	46 Mb	46-33=13	27 26	53	1941
39	CD40	20q	46 Mb	64 Mb	64-46=18	26 24	50	1682
40	TWEAK	17p	7 Mb	0	7-0=7	18 21	39	1377
41	MMP10	11q	102 Mb	134	134-102=32	27 31	58	1759
42	CCL25	19p	8 Mb	0	8-0=8	19 25	44	1002
43	IL-10RA	11q	117 Mb	135	135-117=18	22 23	45	3653
44	NT-3	12p	5 Mb	0	5-0=5	27 27	54	1168
45	TRAIL	3q	172 Mb	198	198-172=26	33 28	61	1876
46	FGF-23	12p	4 Mb	0	4-0=4	27 27	54	3002
47	IL-15RA	10p	5 Mb	0	5-0=5	23 22	45	1566
48	uPA	10q	73 Mb	133	133-73=60	23 25	48	2343
49	ADA	20q	44 Mb	64	64-44=20	24 19	43	1496
50	TNFRSF9	1p	7 Mb	0	7-0=7	27 30	57	5872
51	IL-18A	11q	112 Mb	134	134-112=22	26 26	52	628
52	CD5	11q	61 Mb	134	134-61=73	22 22	44	3127
53	FGF-19	11q	69 Mb	134	134-69=65	20 25	45	1821
54	IL-12B	5q	159 Mb	181	181-159=22	29 28	57	2364
55	CST5	20p	23 Mb	0	23-0=23	21 25	46	755
56	TNFB	6p	31 Mb	0	31-0=31	22 22	44	1416
57	SIRT2	19q	38 Mb	58	58-38=20	22 20	42	1862
58	STAMBP	2p	73 Mb	0	73-0=73	26 31	57	6412
59	4E-BP1	8p	38 Mb	0	38-0=38	21 17	38	827
60	CD244	1q	160 Mb	248	248-160=148	25 28	53	2495
61	DNER	2q	229 Mb	241	241-229=12	23 28	51	3257
62	CCL11	17q	34 Mb	83	83-34=49	27 30	57	1005
63	AXIN1	16q	0	0	0-0=0	20 17	37	3707
64	TRANCE	13q	42 Mb	114	114-42=72	28 30	58	2201
65	SCF	12q	88 Mb	132	132-88=44	23 24	47	3168
66	CD6	11q	60 Mb	134	134-60=74	19 20	39	3252
67	CASP-8	2q	201 Mb	241	241-201=40	28 29	57	2914
68	CXCL11	4q	76 Mb	189	189-76=113	34 32	66	1479
69	MCP-4	17q	34 Mb	83	83-34=49	26 30	56	823
70	CXCL1	4q	73 Mb	189	189-73=116	26 30	56	1174
71	CXCL6	4q	73 Mb	189	189-73=116	27 35	62	1537
72	ST1A1	16p	28 Mb	0	28-0=28	26 20	46	1254
73	CXCL5	4q	73 Mb	189	189-73=116	28 36	64	2436

Table s3. Two factor characteristics of druggable kinases and select approved drugs

Class of druggable proteins	Druggable kinase candidates	Approved kinase drugs	Approved cytokine drugs
Less mutable target (proportion); = Factor-disease no match	18 % (23 of 129)	33 % (1 of 3)	17 % (1 of 6)
Resulting top list	GK2 PIP5K1A UCK2 PRKAG1 PHKA1	EGFR (Certain mutant forms of which are irreversibly targeted by osimertinib)	IL-23 (By guselkumab)
More mutable target (proportion); = Factor-disease match	82 % (106 of 129)	67 % (2 of 3)	83 % (5 of 6)
Resulting top list	CLK5 PRPF4B PANK3 PDIK1L PIK3C2G	PDGFR (By imatinib)	TNF (by golimumab) IL-17A (by secukinumab) IL-6 (by siltuximab) GDF8 (by Luspatercept) VEGF (by bevacizumab/lucentis)
No. of genes	n=129	n=3	n=6
Size-proximity correlation (Pearson)	NS*	-	NS
Size-A+T correlation (Pearson)	Sig.**	-	NS
Relative size of genes (class-wise)	Longer	Longer	Shorter

* Not significant, NS; ** significant, Sig.

Table s4. Two factor characteristics of genetic loci in mice exposed to ionizing radiation

CNV* loci ²	CNV ID	chr	gene start	gene end	P or Q arm?	CNV to telomere	A + T ** (%)	FL (bp)
1	CNVc1	11	25.9 M	25.91 M	q arm	95.10	56.00	4449
2	CNVa8	4	21.33M	21.34	q arm	134.70	55.40	15240
3	CNVa1	1	7.8 M	11.88	q arm	186.20	62.10	3989970
4	CNVa13	5	65.68 M	65.69	q arm	86.00	56.30	5687
5	CNVa7	8	18.70 M	18.76	q arm	110.24	60.10	58814
6	CNVab12	19	57.18 M	57.2	q arm	4.00	54.30	13637
7	CNVa36	16	25.33 M	25.37	q arm	71.50	50.80	40306
8	CNVa15	5	78.79 M	89.12	q arm	71.00	56.30	10334213
9	CNVb35	13	76.29 M	79.52	q arm	42.50	59.60	3235174
10	CNVb54	12	100.82 M	100.83	q arm	19.00	56.60	4453
11	CNVb14	16	40.04 M	40.04	q arm	58.00	50.80	4494
12	CNVb16	11	41.63 M	41.63	q arm	79.40	56.00	4514
13	CNVb32	1	72.27 M	72.282	q arm	121.73	62.10	9125
14	CNVb6	14	15.30 M	17.774	q arm	108.80	51.50	2468734
15	CNVb28	15	61.77 M	61.788	q arm	41.93	50.50	9491
16	CNVb31	16	72.13M	72.166	q arm	25.85	50.80	29387
17	CNVb18	4	48.96M	49.017	q arm	107.00	55.40	48214
18	CNVb57	14	114.84M	116.324	q arm	9.80	51.50	1482942
19	CNVb15	16	41.62M	41.695	q arm	57.00	50.80	66816
20	CNVab12	19	57.18M	57.202	q arm	3.90	54.30	13637

* copy number variation or de novo mutations found in mice after ionizing radiation², CNV; ** A+T content of the entire chromosome calculated

References for supplementary material

- 1 Gruber, C. N. *et al.* Mapping Systemic Inflammation and Antibody Responses in Multisystem Inflammatory Syndrome in Children (MIS-C). *Cell* **183**, 982-995 e914, doi:10.1016/j.cell.2020.09.034 (2020).
- 2 Adewoye, A. B., Lindsay, S. J., Dubrova, Y. E. & Hurles, M. E. The genome-wide effects of ionizing radiation on mutation induction in the mammalian germline. *Nat Commun* **6**, 6684, doi:10.1038/ncomms7684 (2015).