

Materials and Methods

Reduced intensity conditioning with busulfan in the macaque. Two macaques were treated with intravenous busulfan to observe the hematological effects of such treatment and to obtain pharmacokinetic data (e.g., area under the curve [AUC] and concentration at steady-state [C_{ss}], which is AUC divided by the dosing interval see **Supplemental Table 3**). For busulfan analysis, 3 mL of whole blood was collected prior to infusion, at the end of infusion, 15 minutes after the end of infusion, and also at 4, 5, 6, and 8 hours after the start of infusion on both treatment days. Blood samples were centrifuged at 450×g for 15 minutes to collect serum. Serum samples were stored at negative 80°C until transportation to the Pharmacokinetics Laboratory at Seattle Cancer Care Alliance for analysis. Each specimen subsequently underwent derivatization and extraction processes carried out by using sodium iodide solution and ethyl acetate, respectively. After 30 minutes of incubation and agitation, the parts of organic phase were transferred to individual vials for gas chromatography-mass spectrometry device (GC-MSD) quantification (Agilent Technologies, GC: 6890N; MSD: 5973). The concentration versus time data is plotted by using the pharmacokinetics program WinNonLin (Pharsight Corp. Mountain View, CA). Both non-compartmental and compartmental models were used to find the best fit of the data set and estimate the AUC and C_{ss} of busulfan exposures of the animals. The first monkey (K03232) was given a dose of busulfan of 4 mg/kg on two consecutive mornings and as a result there was pronounced neutropenia and thrombocytopenia (data not shown). K03232 was euthanized 18 days after the first dose of busulfan due to pronounced cytopenia. Due to the neutropenia and thrombocytopenia observed in K03232, the second monkey (M05181) was given a decreased dose of busulfan of 2 mg/kg on two consecutive mornings. In M05181 there was again pronounced cytopenia, but not as severe as that observed in M05181 (data not shown).

The first experimental monkey K05079 weighed 6.0 kg at treatment and was given a busulfan dose of 4 mg/kg on two consecutive mornings (total dose = 24.0 mg each day). The first and second doses of busulfan produced an AUC of 4842 $\mu\text{M}\cdot\text{min}$ and 4977 $\mu\text{M}\cdot\text{min}$, and a

C_{ss} of 828 ng/ml and 851 ng/ml, respectively. The median busulfan clearance was 3.57 ml/min/kg (range: 3.26–3.92) and median half-life was 2.35 hours (range: 2.17–2.97).

Supplemental Table 1. Gene marking before first drug treatment

Monkey	Conditioning	Vector	Days After Transplantation of 1st Drug Treatment	PBL Gene Marking (%) Before 1st Drug Treatment
M00228	1020cGy TBI	Gammaretrovirus (MND- MFG)	251	10.5
M01044	1020cGy TBI	Gammaretrovirus (MSCV)	221	14.8
M01277	1020cGy TBI	Gammaretrovirus (MND- MFG)	434	8.5
J02370	800cGy TBI	HIV-derived lentivirus	510	14.1
T04228	800cGy TBI	HIV-derived lentivirus	574	17.2
M05189	900cGy TBI	HIV-derived lentivirus	253	5.2
J02043	1020cGy TBI	HIV-derived lentivirus	177	65.6*
M02426	800cGy TBI	Gammaretrovirus (MND)	140	4.4*
K05079	Busulfan 4 mg/kg/day (2 days)	HIV-derived lentivirus	56	4.4*

PBL=peripheral blood

TBI=total body irradiation

*percent gene marking approximated from provirus copy number

Supplemental Table 2. Drug Treatment in Nonhuman Primates

Animal	DPT	O⁶BG mg/m²	BCNU mg/m²	TMZ mg/m²
Baboons-<i>Papio cynocephalus</i>				
M01044	221	120	--	400
	250	120	--	600
	290	120	--	800
	326	120*	--	800
	382	120*	--	1000
	438	120*	--	1100
	894	120*	30 [†]	--
M00228	251	120	--	600
	303	120*	--	800
	318	120*	--	1000
	355	120*	--	1200
	383	120*	--	1400
	411	120*	40 [†]	--
M01277	434	120*	40 [†]	--
	677	120*	20	--
Macaque-<i>Macaca nemestrina</i>				
J02043	177	120*	20 [†]	--
	292	120*	30 [†]	--
J02370	510	120*	15	--
	888	120*	20	--
T04228	574	120*	20	--
M05189	253	120*	17.5	--
	322	120*	25	--

	510	120*	25	--
K05079	56	120*	25	--
M02426	140	120*	15	--
	264	120*	20	--
	449	120*	30	--
	588	120*	30	--

DPT= days post-transplant

*Fractionated dose of 120 mg/m² O⁶BG (O⁶BG-2X) given prior to and 7-8 hours after BCNU or TMZ

†BCNU purchased from Bristol-Myers Squibb

Supplemental Table 3. Pharmacokinetics of conditioning with busulfan

Monkey	Weight	Dose	Weight-	AUC #1	Css #1	AUC #2	Css #2
	(kg)	(mg/kg/day)	Adjusted Dose	($\mu\text{M}\cdot\text{min}$)	(ng/ml)	($\mu\text{M}\cdot\text{min}$)	(ng/ml)
			(mg/day)				
K03232	6.8	4	27.2	4122	705	4297	735
M05181	4.1	2	8.2	2268	388	2276	389
K05079	6.0	4	24	4842	828	4977	851

*AUC and Css values from the last (4th) dose of busulfan

Supplemental Table 4. Closest proto-oncogene promoter to unique RIS before drug treatment

Gene Abbreviation	RefSeq	Monkey	Distance (bp)
MCL1	NM_021960	J02370	380
ZNF384	NM_001039917	J02043	854
ZNF644	NM_032186	J02043	2666
FGFR1OP	NM_007045	T04228	3083
PTTG1IP	NM_004339	J02043	4965
STK11	NM_000455	T04228	7726
FSTL3	NM_005860	J02370	8510
GPX1	NM_000581	J02043	8778
PTPN6	NM_080548	J02043	11538
NCAPD2	NM_014865	J02043	12639
ICAM1	NM_000201	T04228	14061
ZDHHC18	NM_032283	J02043	15290
NOTCH1	NM_017617	J02370	15728
RUNX3	NM_004350	J02043	16085
CREBBP	NM_001079846	J02043	21765
PTMA	NM_002823	T04228	22291
LYL1	NM_005583	J02370	23015
SET	NM_003011	T04228	24248
CUTL1	NM_001913	J02043	24418
NCAPD2	NM_014865	J02043	24513
USP39	NM_006590	J02043	24718
IL6ST	NM_002184	J02043	25186
LTB	NM_002341	T04228	25659
PPP1R14B	NM_138689	J02370	28747
GNA12	NM_007353	K05079	29511
LTB	NM_002341	J02043	31621
PPP1R14B	NM_138689	J02043	31889
STAT5A	NM_003152	T04228	31950
CCR1	NM_001295	M05189	33635
SHC1	NM_003029	J02043	35297
MPL	NM_005373	J02370	35530
DDX6	NM_004397	J02043	36637
TCIRG1	NM_006019	T04228	37903
USP3	NM_006537	J02043	39056
TAP2	NM_018833	J02043	42638
FAM117A	NM_030802	J02043	45188
TCIRG1	NM_006019	T04228	45354
FRMD8	NM_031904	J02370	45817
CNR2	NM_001841	J02043	48273
ARNT	NM_001668	T04228	51599
GPX1	NM_000581	J02043	51957
TPM4	NM_003290	J02043	53448
DTX2	NM_020892	J02370	53724
SNX5	NM_152227	J02370	55429
DDX10	NM_004398	T04228	55928
MYH9	NM_002473	M05189	58446
CHD3	NM_001005271	J02043	61021
NSD1	NM_172349	T04228	61286
NFATC3	NM_004555	J02043	61713
LYL1	NM_005583	J02043	62057
NFAT5	NM_006599	J02370	62489
GFI1B	NM_004188	J02043	63754
TP53	NM_000546	T04228	66853
PDXK	NM_003681	M05189	67616
SSBP4	NM_001009998	T04228	67652
SPECC1	NM_001033553	J02043	71152
BRD2	NM_005104	T04228	72728
SMG6	NM_017575	J02043	73359
ARHGEF12	NM_015313	J02043	73620
AKAP13	NM_006738	J02043	73984
RARG	NM_000966	M05189	74125
BLM	NM_000057	J02043	75073
RUNX1	NM_001754	J02043	75664

TREML2	NM_024807	T04228	78370
RGS19	NM_001039467	J02370	78622
BRD2	NM_005104	J02043	79315
GABPB2	NM_005254	J02370	80867
HMGCR	NM_000859	J02370	81310
CCR7	NM_001838	J02370	82911
JUNB	NM_002229	J02043	88158
DNAL4	NM_005740	M05189	89053
DNAL4	NM_005740	J02043	92022
TRAF1	NM_005658	J02370	92876
CIRBP	NM_001280	J02370	93373
NSD1	NM_172349	T04228	98631
PEAR1	NM_001080471	J02370	102865
COX19	NM_001031617	T04228	107217
PTBP1	NM_002819	M05189	112017
EDG6	NM_003775	M05189	112861
SEPT5	NM_002688	J02043	114973
POU2F2	NM_002698	J02043	125232
RHOF	NM_019034	T04228	125728
RUNX2	NM_001015051	J02043	130327
TIAM1	NM_003253	J02370	130370
RHOF	NM_019034	J02043	136355
MCL1	NM_021960	J02370	137498
TNFRSF8	NM_001243	T04228	138632
NFIC	NM_205843	J02370	141024
ENC1	NM_003633	J02370	141104
ICAM1	NM_000201	M05189	141544
PTBP1	NM_002819	J02043	149750
CRIP2	NM_001312	T04228	156540
TCL1A	NM_001098725	T04228	157736
RGS19	NM_001039467	J02370	160136
DST	NM_183380	J02043	164786
GSPT1	NM_002094	J02043	165311
PPP1R1A	NM_006741	J02370	167005
STX4	NM_004604	J02370	171589
RARA	NM_000964	J02043	172490
MAP4K2	NM_004579	J02370	179693
GRAP2	NM_004810	J02370	180905
SLAMF6	NM_052931	J02043	181188
SCAMP4	NM_079834	T04228	182585
FANCE	NM_021922	J02370	185956
SYDE1	NM_033025	M05189	199033
MUC1	NM_001018016	J02043	201224
FLT3	NM_004119	J02043	206900
DHRS3	NM_004753	J02043	210661
RNF216	NM_207111	J02043	212299
MAFB	NM_005461	T04228	212752
MUC1	NM_001018016	J02043	216651
FBXL10	NM_032590	J02043	217561
CRIP2	NM_001312	M05189	218041
DHRS3	NM_004753	J02043	218367
ACSL6	NM_001009185	J02043	221094
BATF	NM_006399	J02043	221653
LTB	NM_002341	M05189	222159
SCAMP4	NM_079834	J02370	222289
DTX3	NM_178502	J02370	227049
DNAL4	NM_005740	J02043	228971
GRAP2	NM_004810	J02043	230784
RARG	NM_000966	T04228	233756
CCR1	NM_001295	J02043	237606
NFKB2	NM_002502	J02370	243019
EPHA2	NM_004431	J02370	244865
SYDE1	NM_033025	J02043	245870
HIST1H4I	NM_003495	J02043	247255
NCKIPSD	NM_016453	J02043	259535
SLC19A1	NM_194255	J02043	260195

CCND2	NM_001759	J02043	265576
RARG	NM_000966	J02043	266797
PPP1R1A	NM_006741	J02043	271180
LTB	NM_002341	J02370	271368
RGS19	NM_001039467	J02043	271631
PFN1	NM_005022	J02043	275444
BATF	NM_006399	J02370	275789
ICAM1	NM_000201	J02043	279483
SYDE1	NM_033025	J02043	282568
TPM3	NM_001043351	J02370	283644
RHOF	NM_019034	J02043	286323
MYH9	NM_002473	J02370	305218
RGS19	NM_001039467	J02370	309950
NFIC	NM_205843	J02370	312115
NFIC	NM_205843	J02043	312358
NSD1	NM_172349	J02043	317920
LTB	NM_002341	J02043	318399
LTB	NM_002341	M05189	328198
IFNGR2	NM_005534	J02043	330324
RNF216	NM_207111	J02043	342825
RHCG	NM_016321	J02043	343117
TAP2	NM_018833	J02043	345372
PDXK	NM_003681	J02043	352855
EPOR	NM_000121	J02370	355413
RHOF	NM_019034	J02043	357782
CLTC	NM_004859	J02043	358070
SFPQ	NM_005066	M05189	361885
SLC16A3	NM_004207	J02043	364570
MCL1	NM_021960	J02043	364738
E2F3	NM_001949	J02370	375535
TFAP4	NM_003223	J02043	386881
FANCA	NM_000135	J02370	386981
PIM3	NM_001001852	J02043	393400
ICAM1	NM_000201	K05079	393422
BCL10	NM_003921	J02043	397632
NFATC3	NM_004555	J02043	402153
FGR	NM_005248	J02043	405654
SCAMP4	NM_079834	T04228	409291
FANCG	NM_004629	J02370	409475
TCIRG1	NM_006019	J02043	421180
TOB2	NM_016272	J02370	423194
DST	NM_183380	M05189	427228
RAP1A	NM_001010935	J02043	427471
GPX1	NM_000581	J02043	431627
MYST4	NM_012330	J02043	435425
PPP1CC	NM_002710	M05189	438875
RGS19	NM_001039467	J02043	455836
EML4	NM_019063	J02370	456961
E2F3	NM_001949	J02043	457207
BMI1	NM_005180	J02370	458658
TCIRG1	NM_006019	K05079	463651
WHSC1L1	NM_023034	J02043	465229
SUSD3	NM_145006	K05079	465922
FBXW4	NM_022039	J02043	476946
MAF	NM_001031804	J02043	478709
SLC38A1	NM_030674	T04228	478909
PLEKHG2	NM_022835	J02043	485928
PPP1R14B	NM_138689	T04228	500201
CORO2B	NM_006091	J02043	500834
GLB1	NM_000404	J02043	503196
BRD2	NM_005104	J02043	504009
MLLT1	NM_005934	J02043	505034
ICAM1	NM_000201	T04228	506700
SLC26A11	NM_173626	J02043	510013
PIM3	NM_001001852	M05189	510847
EPS15	NM_001981	M05189	513310

MAP3K8	NM_005204	J02043	521694
FLI1	NM_002017	J02043	525858
MYCN	NM_005378	J02043	528945
LMO1	NM_002315	J02370	530143
MEF2D	NM_005920	J02043	532490
WHSC1L1	NM_023034	J02043	535767
MMP14	NM_004995	J02043	539760
PPP1R14B	NM_138689	J02043	541053
MAP3K8	NM_005204	T04228	542414
TP53	NM_000546	M05189	554625
TFRC	NM_001128148	J02043	558546
GNAI2	NM_002070	J02043	561612
LTB	NM_002341	T04228	565093
MCL1	NM_021960	J02043	567554
MLL1	NM_005934	J02370	572359
SCYL1	NM_020680	J02043	573318
FANCG	NM_004629	M05189	574866
SMG6	NM_017575	J02043	579496
SMG6	NM_017575	J02370	582565
TP53RK	NM_033550	T04228	587288
KCTD2	NM_015353	J02043	592625
BMI1	NM_005180	J02043	595134
NFKB1	NM_003998	J02043	601000
UBL7	NM_201265	J02043	604135
JUNB	NM_002229	T04228	608894
JUNB	NM_002229	T04228	609360
MUC1	NM_001018016	J02043	638094
RPL22	NM_000983	J02043	638452
KCTD2	NM_015353	J02370	638677
KCTD2	NM_015353	J02370	638706
FBXW4	NM_022039	J02043	644185
COTL1	NM_021149	J02043	658602
EDG6	NM_003775	M05189	663446
FANCG	NM_004629	T04228	666065
HSP90AB1	NM_007355	J02043	666129
HEXIM1	NM_006460	M05189	677456
RSPH10B	NM_173565	J02043	684037
SOX8	NM_014587	J02043	684283
SEPT9	NM_006640	J02043	697616
EBF1	NM_024007	T04228	708688
POU2AF1	NM_006235	J02043	714430
MLL1	NM_005934	J02370	715135
ARHGAP25	NM_001007231	T04228	715281
FBXW4	NM_022039	T04228	723954
CASC5	NM_144508	T04228	726288
FANCG	NM_004629	J02370	726905
GADD45G	NM_006705	J02370	728813
ZDHHC14	NM_024630	K05079	737861
PTPN11	NM_002834	T04228	756104
KDSR	NM_002035	T04228	757712
SOX8	NM_014587	J02043	761903
BCL9	NM_004326	J02043	766373
PECAM1	NM_000442	J02043	773445
SOX8	NM_014587	J02043	774519
HSP90AA1	NM_001017963	J02370	777422
ICAM1	NM_000201	J02370	784406
SEPT9	NM_006640	J02043	787437
IER2	NM_004907	K05079	792458
PIM3	NM_001001852	J02043	794159
NAPA	NM_003827	J02370	798767
MALT1	NM_006785	T04228	805220
NAPA	NM_003827	J02043	815374
SEPT9	NM_006640	J02043	815678
SLC38A1	NM_030674	J02043	829307
PAX5	NM_016734	J02370	835828
SPI1	NM_003120	T04228	840973

FGR	NM_005248	J02043	847366
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CD6	NM_006725	J02043	871926
FGR	NM_005248	J02043	883396
FGR	NM_005248	J02043	883619
RRAS2	NM_012250	J02043	888848
NRAS	NM_002524	J02370	929078
ID2	NM_002166	J02370	946866
TNFRSF13B	NM_012452	J02043	950724
RNASE10	NM_001012975	J02370	951591
BMI1	NM_005180	J02043	964757
KCTD2	NM_015353	J02043	965183
NCOR2	NM_006312	J02043	976503
NAPA	NM_003827	J02043	1039390
TOB2	NM_016272	J02043	1041368
WAS	NM_000377	J02043	1043798
LTB	NM_002341	J02043	1044887
SH3GL1	NM_003025	J02043	1056748
C1orf164	NM_018150	J02370	1058046
TTL	NM_153712	T04228	1064771
RHOH	NM_004310	T04228	1069871
RASGRP1	NM_005739	J02043	1076992
PLCH2	NM_014638	J02043	1078481
SEPT9	NM_006640	J02370	1080373
UBE2D2	NM_003339	T04228	1080558
ERC2	NM_015576	J02043	1086927
CORO1A	NM_007074	J02043	1097035
FBXL10	NM_032590	J02043	1097086
BCL3	NM_005178	J02043	1107870
FANCE	NM_021922	J02043	1145032
SEPT9	NM_006640	J02370	1146250
NUMA1	NM_006185	J02370	1153668
FANCE	NM_021922	J02043	1157073
NCOR2	NM_006312	T04228	1158654
CASC5	NM_144508	J02043	1159104
PPP1R14B	NM_138689	J02043	1181011
ZMYM2	NM_003453	J02043	1190481
MLL1	NM_005934	J02043	1206080
RPN1	NM_002950	J02043	1207945
HMGCR	NM_000859	J02043	1213376
RGS19	NM_001039467	J02370	1214677
CARS	NM_001014437	J02043	1235088
WAS	NM_000377	J02043	1238956
PPP1R14B	NM_138689	J02370	1243903
ME3	NM_006680	J02043	1244190
FBXL10	NM_032590	J02043	1276196
C1orf164	NM_018150	J02043	1313600
DTX3	NM_178502	J02043	1319037
TNFRSF13B	NM_012452	J02370	1364503
FBXW7	NM_033632	J02043	1364809
ABTB2	NM_145804	J02370	1364881
NAPA	NM_003827	J02043	1386731
DTX3	NM_178502	J02043	1398288
DTX3	NM_178502	J02043	1403172
DTX3	NM_178502	J02043	1415300
CUTL1	NM_001913	T04228	1437059
BTG1	NM_001731	J02043	1456517
BCL11A	NM_018014	K05079	1479747
PRRX1	NM_006902	J02043	1530512
TOB2	NM_016272	J02043	1577482
IL17RB	NM_018725	J02043	1592046
LTB	NM_002341	J02043	1596292
CUTL1	NM_001913	J02043	1609750
RSPH10B	NM_173565	T04228	1613042
MN1	NM_002430	T04228	1630808
ICAM1	NM_000201	J02043	1634080

ICAM1	NM_000201	J02043	1634706
SMAD3	NM_005902	J02370	1636727
TNFRSF8	NM_001243	J02043	1643631
CUTL1	NM_001913	J02370	1674049
BTG1	NM_001731	J02370	1712697
ICAM1	NM_000201	J02043	1724005
RAP1GDS1	NM_021159	T04228	1737565
MAF	NM_001031804	J02043	1739020
TP53RK	NM_033550	J02370	1750268
PECAM1	NM_000442	T04228	1760122
MCM5	NM_006739	M05189	1771183
MLLT1	NM_005934	J02370	1774585
ALK	NM_004304	J02043	1794811
NIN	NM_020921	J02043	1845583
ABL1	NM_007313	J02043	1949350
CEBPA	NM_004364	J02043	2014678
PTPRE	NM_006504	J02370	2085839
RUNX2	NM_001015051	J02043	2105132
NAPA	NM_003827	J02043	2137493
JAK1	NM_002227	T04228	2209324
BSPRY	NM_017688	J02370	2279735
PLAG1	NM_002655	J02043	2288295
TFPT	NM_013342	J02370	2376014
TCF12	NM_003205	J02043	2393628
MAP4K2	NM_004579	J02043	2399581
PLEK2	NM_016445	T04228	2419107
AFF3	NM_002285	J02043	2474963
CASC5	NM_144508	T04228	2492856
SATB1	NM_002971	J02043	2512699
LACTB	NM_032857	J02043	2515612
MN1	NM_002430	T04228	2591239
MLLT3	NM_004529	T04228	2599475
SATB1	NM_002971	J02043	2601088
TAF15	NM_003487	J02043	2661779
ID3	NM_002167	J02370	2662457
SBDS	NM_016038	J02370	2698466
SNX5	NM_152227	J02043	2739503
CAPG	NM_001747	J02370	2775089
NAPA	NM_003827	J02043	2785759
CASC5	NM_144508	J02043	2947860
HOXD13	NM_000523	J02043	2959221
PTPRE	NM_006504	J02370	2961991
UBL7	NM_201265	J02370	3030562
IL16	NM_172217	J02043	3123307
SDCCAG8	NM_006642	J02043	3168672
PRLR	NM_000949	T04228	3193481
RMND5B	NM_022762	J02043	3247589
HPSE	NM_006665	J02043	3314913
RAP1B	NM_001010942	J02043	3342824
RPN1	NM_002950	J02043	3380153
HOXD13	NM_000523	J02370	3429695
SLC30A5	NM_022902	T04228	3474112
NUMA1	NM_006185	M05189	3513139
RAMP1	NM_005855	J02043	3553548
ANKRD44	NM_153697	J02370	3558174
MAP3K8	NM_005204	T04228	3875729
DST	NM_183380	T04228	3886361
FBXW7	NM_033632	J02043	3909063
RBL2	NM_005611	J02043	3918750
SOX3	NM_005634	J02043	3921430
LCP1	NM_002298	J02043	4030154
ZNF521	NM_015461	J02370	4043640
EVI1	NM_005241	T04228	4059047
STK38L	NM_015000	J02043	4084454
CASC5	NM_144508	J02043	4093159
PIM3	NM_001001852	J02370	4152731

BTG1	NM_001731	T04228	4222852
STK38L	NM_015000	J02043	4290683
FBXW7	NM_033632	J02043	4436121
BCL2L1	NM_001191	J02043	4504022
ZNF239	NM_005674	T04228	4520568
DTX3	NM_178502	J02043	4542471
BRCA2	NM_000059	T04228	4579789
BRCA2	NM_000059	T04228	4629285
PICALM	NM_001008660	J02043	4691893
LRMP	NM_006152	J02043	4759913
ALG14	NM_144988	T04228	4776080
NFKBIA	NM_020529	J02043	4779531
GPHN	NM_001024218	J02043	4830033
EIF1B	NM_005875	J02043	5467136
TNFSF13B	NM_006573	J02043	5536031
SLC9A9	NM_173653	J02043	6085508
EIF1B	NM_005875	J02370	6256067
ACTB	NM_001101	T04228	6310717
MID1	NM_000381	J02043	6335276
RPN1	NM_002950	M05189	6507292
ZNF521	NM_015461	J02043	6669656
ZNF608	NM_020747	M05189	6893948
C1orf55	NM_152608	J02043	6903820
MYB	NM_005375	J02370	7387566
RUNX1T1	NM_175635	M05189	7438854
FHIT	NM_002012	J02043	7650505
NCOR2	NM_006312	J02043	7735542
MYB	NM_005375	J02370	8007257
RPN1	NM_002950	J02370	8667764
EIF1B	NM_005875	J02043	8848950
ZNF521	NM_015461	J02043	9205895
TFG	NM_001007565	J02043	9385358
JAKMIP1	NM_144720	T04228	9966752
RPN1	NM_002950	T04228	10002836
CDK6	NM_001259	J02043	10025440
SEPT6	NM_145800	J02043	11128848
LNPEP	NM_005575	M05189	12112950
PRLR	NM_000949	M05189	16430660
LCP1	NM_002298	J02043	19246341
CDK6	NM_001259	J02043	21520851
PRLR	NM_000949	J02043	34639751
Average Distance (bp)			1578937

Bold and italic are unique RIS within proto-oncogenes

All unique RIS are listed once with only the nearest proto-oncogene TSS

Supplemental Table 5 Closest proto-oncogene promoter to unique RIS after drug treatment

Gene Abbreviation	RefSeq	Monkey	Distance (bp)
MCL1	NM_021960	J02370	380
PIM1	NM_002648	J02043	4786
EP300	NM_001429	K05079	16046
FRMD8	NM_031904	J02370	21869
LYL1	NM_005583	J02370	23015
GPX1	NM_000581	J02370	25875
ETS1	NM_005238	K05079	28589
PPP1R14B	NM_138689	J02370	28747
DDX6	NM_004397	J02043	36637
USP3	NM_006537	J02043	39056
JUNB	NM_002229	J02370	49332
MRV11	NM_130385	J02043	55508
NOTCH1	NM_017617	J02370	101980
CLP1	NM_006831	J02043	138987
RGS19	NM_001039467	J02370	160136
MEF2B	NM_005919	K05079	162150
NAPA	NM_003827	J02043	170266
FANCE	NM_021922	J02370	185956
STK11	NM_000455	J02370	195126
EPS15L1	NM_021235	K05079	208527
CLTCL1	NM_007098	J02043	243358
HIST1H4I	NM_003495	J02043	247255
LTB	NM_002341	J02043	253332
NAPA	NM_003827	J02370	258013
NCKIPSD	NM_016453	J02043	259535
TPM3	NM_001043351	K05079	274434
PFN1	NM_005022	J02043	275444
MSN	NM_002444	K05079	365233
FANCA	NM_000135	J02370	386981
EPOR	NM_000121	J02043	393360
PIM3	NM_001001852	J02043	393400
FANCG	NM_004629	J02370	409475
TCIRG1	NM_006019	K05079	423973
TRAF1	NM_005658	K05079	432949
MAP3K8	NM_005204	J02043	521694
MEF2D	NM_005920	J02043	532490
WHSC1L1	NM_023034	J02043	535767
SOX8	NM_014587	K05079	622387
RPL22	NM_000983	J02043	638452
NFATC3	NM_004555	J02043	662723
KCTD2	NM_015353	J02043	670505
MEF2B	NM_005919	J02043	721937
SOX8	NM_014587	J02370	747171
SOX8	NM_014587	J02043	774519
MTCP1	NM_001018024	J02370	777797
IER2	NM_004907	K05079	792458
NAPA	NM_003827	J02043	815374
FGR	NM_005248	J02043	883619
CCR1	NM_001295	K05079	886547
ID2	NM_002166	J02370	946866
SEPT6	NM_145800	J02043	947784
RSPH10B	NM_173565	J02370	1082616
EPS15	NM_001981	J02370	1188761
SOX8	NM_014587	J02043	1220786
PPP1R14B	NM_138689	J02370	1243903
SPI1	NM_003120	K05079	1305473
C1orf164	NM_018150	J02043	1313600
TNFRSF13B	NM_012452	J02370	1364503
ABTB2	NM_145804	J02370	1364881
ABTB2	NM_145804	J02043	1365033
DTX3	NM_178502	K05079	1484576
IL17RB	NM_018725	J02043	1592046
IL17RB	NM_018725	K05079	1716350

MARCH3	NM_178450	J02370	2033162
PTPRE	NM_006504	J02370	2085839
PADI2	NM_007365	J02370	2134869
PADI2	NM_007365	J02043	2391959
LEF1	NM_016269	J02370	2710566
ARHGEF12	NM_015313	J02043	2722424
SNX5	NM_152227	J02043	2739503
NAPA	NM_003827	K05079	2769916
RMND5B	NM_022762	K05079	2959576
ANKRD44	NM_153697	J02370	3429361
MN1	NM_002430	J02043	3783174
RBL2	NM_005611	J02043	3918750
SLC9A9	NM_173653	J02043	5306035
SEPT6	NM_145800	J02043	11128848
TIAM1	NM_003253	J02043	11426350
Average Distance (bp)			1237573

Bold and italic are unique RIS within proto-oncogenes

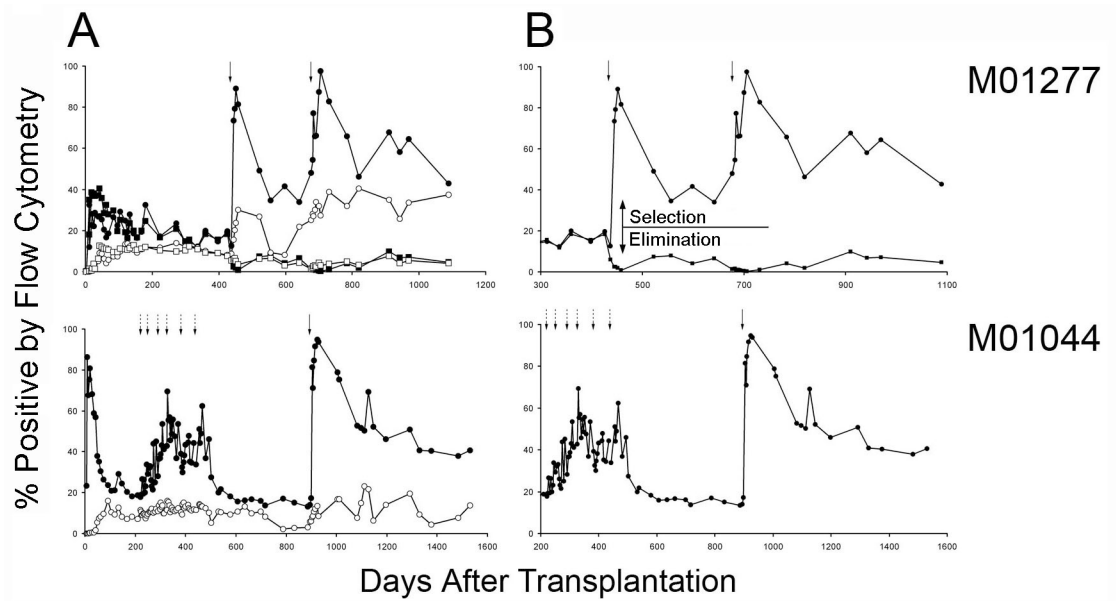
All unique RIS are listed once with only the nearest proto-oncogene TSS

Supplemental Table 6 Unique RIS isolated both before and after drug treatment

Gene Abbreviation	RefSeq	Monkey	Distance (bp)
MCL1	NM_021960	J02370	380
LYL1	NM_005583	J02370	23015
PPP1R14B	NM_138689	J02370	28747
DDX6	NM_004397	J02043	36637
<i>USP3</i>	<i>NM_006537</i>	<i>J02043</i>	<i>39056</i>
RGS19	NM_001039467	J02370	160136
FANCE	NM_021922	J02370	185956
HIST1H4I	NM_003495	J02043	247255
NCKIPSD	NM_016453	J02043	259535
PFN1	NM_005022	J02043	275444
FANCA	NM_000135	J02370	386981
PIM3	NM_001001852	J02043	393400
FANCG	NM_004629	J02370	409475
MAP3K8	NM_005204	J02043	521694
MEF2D	NM_005920	J02043	532490
WHSC1L1	NM_023034	J02043	535767
RPL22	NM_000983	J02043	638452
SOX8	NM_014587	J02043	774519
IER2	NM_004907	K05079	792458
NAPA	NM_003827	J02043	815374
FGR	NM_005248	J02043	883619
ID2	NM_002166	J02370	946866
PPP1R14B	NM_138689	J02370	1243903
C1orf164	NM_018150	J02043	1313600
TNFRSF13B	NM_012452	J02370	1364503
ABTB2	NM_145804	J02370	1364881
IL17RB	NM_018725	J02043	1592046
PTPRE	NM_006504	J02370	2085839
SNX5	NM_152227	J02043	2739503
RBL2	NM_005611	J02043	3918750
SEPT6	NM_145800	J02043	11128848
Average Distance (bp)			1149649

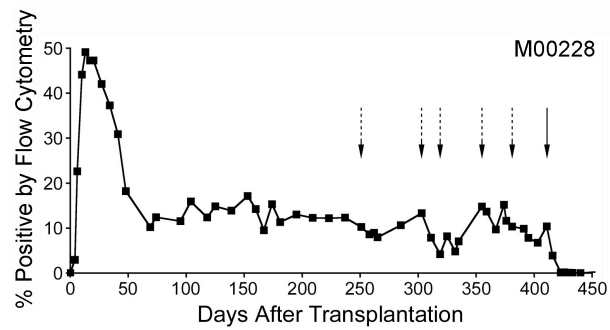
Bold and italic are unique RIS within proto-oncogenes

Supplemental Figure 1



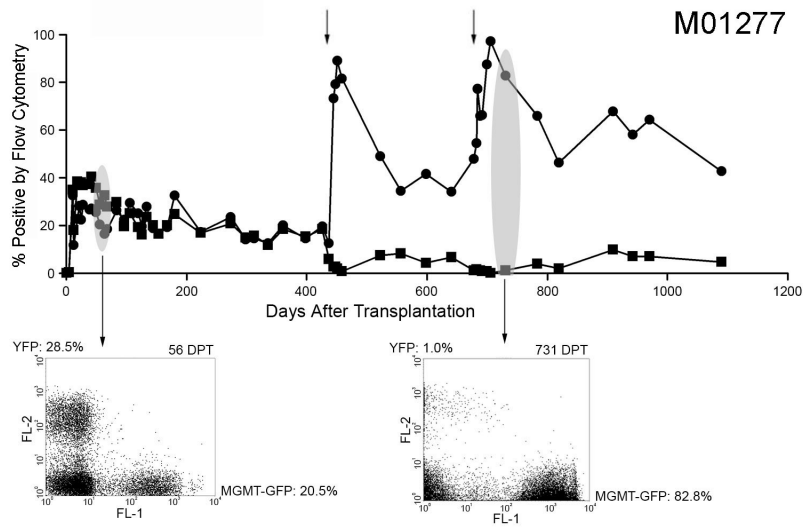
Supplemental Figure 1. Efficient MGMP140K-mediated in vivo selection in the baboon (M01277 and M01044). The left panels (A) show gene marking in MGMP140K-GFP granulocytes (closed circle), MGMP140K-GFP lymphocytes (open circle), YFP granulocytes (closed square), and YFP lymphocytes (open square) before and after in vivo selection with either O⁶BG and TMZ (dashed arrow) or BCNU (solid arrow). The right panels (B) show a truncated representation of the time following in vivo selection with O⁶BG-2X and TMZ or BCNU. Granulocytes are the only subset represented for clarity of selection (MGMP140K-GFP) and elimination (YFP).

Supplemental Figure 2



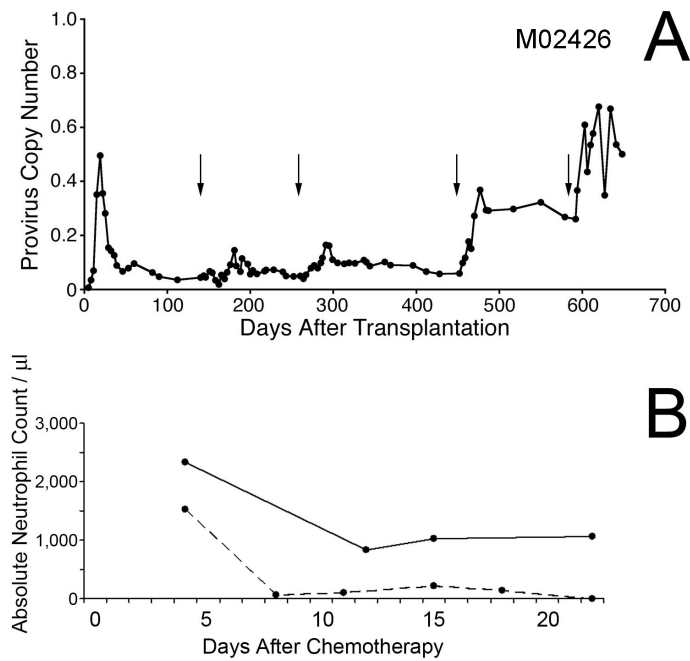
Supplemental Figure 2. Pronounced elimination of unprotected YFP-only gene modified cells after O⁶BG and BCNU, but not multiple doses of O⁶BG and TMZ (M00228). Truncated gene marking plot of the YFP-only granulocytes pictured in Figure 1A and 1B. Gene marking in YFP-only granulocytes (closed square), before and after in vivo selection with either O⁶BG and TMZ (dashed arrows) or O⁶BG-2X and BCNU (solid arrow).

Supplemental Figure 3



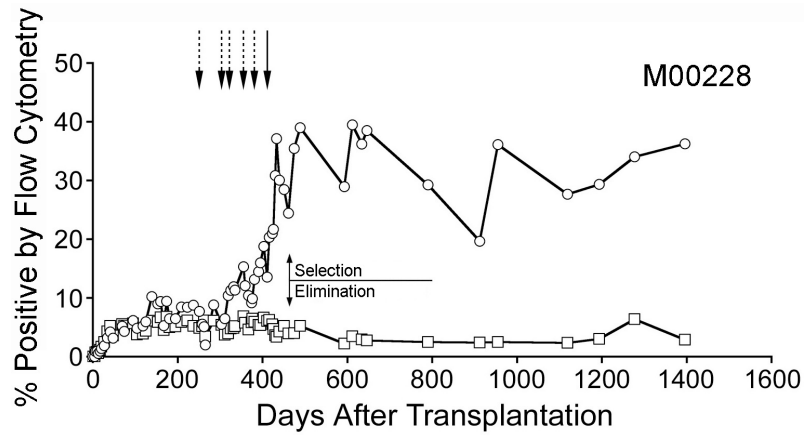
Supplemental Figure 3. Representative flow cytometry of gene marked cells before and after MGMTP140K-mediated in vivo selection (M01277). The upper panel (A) is gene marking in MGMT-GFP granulocytes (closed circle) and YFP-only granulocytes (closed squares). Gray shaded ovals correspond to time points of the representative flow cytometry plots showing GFP and YFP gene marking before and after in vivo selection with O⁶BG-2X and BCNU (solid arrow).

Supplemental Figure 4



Supplemental Figure 4. Efficient MGMP140K-mediated in vivo selection and chemoprotection in the macaque (M02426). Panel (A) Gene marking plotted as provirus copy number from whole white blood cells before and after in vivo selection of MGMP140K-GFP gene-marked cells in a macaque. Treatment with O⁶BG-2X and BCNU denoted by solid arrows. Panel (B) is a representation of the absolute neutrophil count plotted as days after **drug treatment** in the macaque represented in panel A following the final O⁶BG and BCNU treatment (day 588). Gene marking in the macaque was 0.27 provirus copies and the **drug** dose was 120 mg/m² O⁶BG-2X and 30 mg/m² BCNU (black solid line). There was no MGMP140K gene marking in the control macaque and the **drug** dose was 120 mg/m² O⁶BG-2X and 25 mg/m² BCNU (black dashed line).

Supplemental Figure 5



Supplemental Figure 5. Efficient MGMTP140K-mediated in vivo selection of gene marked lymphocytes in the baboon (M00228). Gene marking in MGMTP140K-GFP lymphocytes (open circle) and YFP lymphocytes (open square) before and after in vivo selection with either O⁶BG and TMZ (dashed arrows) or O⁶BG-2X and BCNU (solid arrow).