

## **Supplemental Material**

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### **Supplemental Figure legends**

#### **Supplemental Figure 1: TRIM28 binding on ERE in the ChIP-seq replicates.**

(A) Same analysis as in Figure 1B but with cells from an independent experiment, at a different passage and with a different TRIM28 antibody.

(B) Same analysis as in Figure 1C but between hES and CD4<sup>+</sup> T-cells replicates.

#### **Supplemental Figure 2: epigenetic impact of TRIM28 recruitment on ERE.**

(A) Localisation of indicated EREs relative to TRIM28 and H3K9me3 ChIP-seq peaks, using ChIP-Cor analysis module ([http://ccg.vital-it.ch/chipseq/chip\\_cor.php](http://ccg.vital-it.ch/chipseq/chip_cor.php)). The Venn diagrams depict the number of elements bound by TRIM28 and/or bearing H3K9me3 in each case. wo, without.

(B) TRIM28, H3K9me3 and SETDB1 presence at indicated ERE in wild type and *TRIM28* KD cells, assessed by ChIP-qPCR using gene or ERE specific primers. Generic HERVK primers were previously published (Montoya-Durango et al. 2009) and potentially target 187 elements (with perfect match for the 10bp at the 3'end but 2 mismatches allowed for the rest of the sequence). Generic SVA primers and specific HERVK14CI-Gag and HERVK14CI-Pol primers were designed from Repbase consensus sequences (hs\_repbases.17.09) and potentially recognize 1139, 2 and 3 elements respectively (same

criteria as described for HERVK primers specificity). Imprinting control region H19 is a known TRIM28 binding sites in murine stem cells (Quenneville et al. 2011) and was one of the few ICRs highly enriched for TRIM28 in our ChIP-seqs. The 3' end ZNF180 also serve as positive controls (Iyengar et al. 2011). Values were normalized to their respective total inputs (IP/Ti) and to TRIM28-independent H3K9-rich loci. For H3K9 and SETDB1 ChIPs, bars represent the mean and s.d. of two independent experiments with each sample quantified in triplicates. Technical replicates (n=3) are shown for TRIM28 ChIP (\*\*p-value= $\leq 0.01$ , \*\*\*p-value= $\leq 0.001$ ).

(C) Comparison of ERE groups expression between control (E) and *TRIM28* KD (KD) hES cells. MA-plot was generated using R. Transcripts levels measured by RNA-seq (assembly hg19) reads mapped to Repbase are plotted on the x-axis and ratio on the y-axis. Of note, groups with fold changes in mRNA expression corresponding to 0 or infinite are not represented on the plot. Blue lines depict the repartition of total deregulated cellular genes (e.g., ERE transcripts present above the 95% line are in the 5% most upregulated total transcripts). A similar MA-plot was obtained by comparing control cells transduced with a LV-shNS and KD cells (not shown).

(D) Quantitative RT-PCR analysis of HERV mRNA expression in hESC 15 days after transduction with a lentivector expressing no (E) or a *TRIM28*-specific (KD) shRNA. Values are normalized for *GAPDH* and *B2M* stable expression and expressed as fold change compared to control cells. In parenthesis is the number of hits detected on the genome using UCSC In silico PCR tool for each primers pair used (<http://genome.ucsc.edu>). Mean and Standard error of the mean (SEM) of 3 independent biological replicates are shown.

**Supplemental Figure 3: Efficient TRIM28 KD is established in hES cells.**

(A) TRIM28 depletion by LV-mediated RNA interference. Serial 3-fold dilutions of protein extracts from wild-type murine ES cells (mES) or from human ES cells (hES), 7 days post transduction with a LV containing a *TRIM28*-specific (shTRIM28), no (shE, empty) or a non-specific (shNS) shRNA cassette, were loaded on an SDS-PAGE and probed with TRIM28 and PCNA antibodies.

(B) Functional validation of the *TRIM28* knockdown. Human ES cells stably expressing a *TetO*-binding, TRIM28 recruiting tTR-KRAB fusion were transduced with a LV containing a TetO-PRKG1-GFP cassette and maintained either with (ON), or without (OFF), or switched from with to without (ON/OFF) doxycycline two days after transduction with indicated shRNA-containing LV. Cells were examined by FACS 12 days after the doxycycline switch. The silencing of the TRIM28-recruiting *TetO*-containing LV is abolished in KD cells.

(C) Pluripotency gene expression is maintained in TRIM28-depleted human ES cells. mRNA levels of TRIM28 and indicated genes in KD versus control (LV-shE) human ES cells, assessed by NanoString and RNA sequencing at day 15 post LV-sh mediated transduction.

(D) Competitive assay showing TRIM28 depletion deleterious effect in hES. Cells transduced with LV-shE control (E) or LV-sh*TRIM28* (KD) are mixed in duplicates with 5% LV-shE-GFP transduced cells (E-GFP). GFP positive cells overgrowth is monitored over time.

#### **Supplemental Figure 4: TRIM28 controls HERVK expression in human stem cells.**

Human ES cells expressing or not a HA-tagged sh-resistant form of TRIM28 (TRIM28<sub>optim</sub>) were transduced in duplicates with LV-shE or LV-sh*TRIM28*. Top: TRIM28 and HERVK14CI expression was monitored 5 days after TRIM28 depletion by

quantitative RT-PCR in triplicates and normalized to stable expression of *GAPDH* and *B2M* genes. Results are representative of a duplicate experiment. Data obtained for shE-containing cells are set as 1. Bottom: parallel western blot analysis of the transduced cells using anti- TRIM28, -HA and -PCNA antibodies.

**Supplemental Figure 5: TRIM28 recruitment to Class II HERVs affects local transcriptional landscape.**

(A) Compared transcriptomes of control and TRIM28-depleted human ES cells. MA-plot was generated using R. Transcripts levels measured by RNA-seq (assembly hg19) are plotted in black dots with ratio on the y-axis and expression level on the x-axis. Blue lines depict levels of gene deregulation (e.g., only 1% of genes lie above the 99% line).

(B) Heat maps built with indicated histone marks as described in Figure 2E except that TRIM28-bound, H3K9me3-bearing, Class II HERV-close genes are considered here.

**Supplemental Figure 6: HERVK-mediated TRIM28 repression does not occur in 293T and murine stem cells.**

LV.HERVK.NR or R as described in Figure 4A , were used to transduce in duplicates and at the same multiplicity of infection, 293T (left) or murine stem cells (right). GFP expression was monitored over time by FACS. NT, non-transduced.

**Supplemental Figure 7: SVA bound by TRIM28 are highly methylated in hES**

(A) SVA expression is not upregulated in TRIM28-depleted human ES cells 14 days after LV-sh transduction (as assessed by quantitative RT-PCR). Data are normalized to the two most stable genes *B2M* and *UBIQUITIN* (UBC). Values obtained for shE-containing cells are set as 1.

(B) Representative example of UCSC Genome Browser screenshot showing ENCODE Project methylation data (Bisulfite-sequencing, Me-DIP sequencing and RRBS) of a SVA element bound by TRIM28 in our ChIP-seq.

**Supplemental Figure 8: SVA methylation is necessary for irreversible silencing.**

(A) Same conditions as in Figure 5CD except that methylation of the SVA-CVI sequence overlapping with the 5'-PRKG1 sequence was monitored in indicated vectors by pyrosequencing. Each dot represents a CpG (n=6).

(B) 293T cells expressing tTR-KRAB were not transduced (-) or transduced in duplicates with lentivectors containing only TetO (TetO-Empty), only SVA (SVACVI or SVAFV) or both sequences upstream of the pRKG1-GFP cassette. Cells were maintained off dox (-dox), on dox (+dox), or 14 days off dox followed by 14 days on dox (-/+ dox) and GFP was monitored by FACS analysis over time. In these cells the silencing of the promoter is reverted in -/+ dox conditions and GFP expression returns to levels similar to +dox conditions, no matter if a SVA element is present in CIS or not in the lentivector.

**Supplemental methods**

**DNA methylation**

Bisulfite quantitative pyrosequencing: genomic DNA was converted (1-2 µg/sample) using EpiTect Bisulfite Kit (Qiagen) as recommended by the manufacturer, PCR amplified and pyrosequenced using PyroMark Gold Q96 reagent (Qiagen) and a PyroMark Q96 ID platform. Primers overlapping the PRKG1-GFP or SVACVI-PRKG1 junctions were designed on the converted antisense and sense strand respectively using PyroMark Assay Design 2.0 software (see primers list in supplemental data). Results were analyzed using Pyro Q-CpG Software. Public data sets from the ENCODE Project

were used to obtain CpG islands and examine whole-genome bisulfite sequencing (Lister et al. 2009) as previously described (Quenneville et al. 2012). Me-DIP sequences (Hs1376 and Hs1303) were downloaded from the Human Epigenome Atlas (<http://www.genboree.org/epigenomeatlas>) (Bernstein et al. 2010).

### **Immunoblotting**

Proteins extracted with radioimmunoprecipitation RIPA buffer were loaded on SDS-PAGE and transferred on membranes probed with rabbit anti-TRIM28 (Tronolab, SY 3267-68, 1/500), mouse anti-PCNA (Oncogene, 1/500) or rat anti-HA-HRPO 3F10 antibodies (Roche, 1/1000).

### **Primers list**

#### *Sh-Dnmt3A/3B cloning:*

shDnmt3A.666(f):

GATCCCCGGAATGAATGCTGTGGAAGTTCAAGAGACTTCCACAGCATTCATTCCTTTTAA

shDnmt3A.666(b):

AGCTTAAAAAGGAATGAATGCTGTGGAAGTCTCTTGAAGTTCCACAGCATTCATTCCGGG

shDnmt3B.3(f):

GATCCCAGATCAGAGCCGAGAACAATTCAAGAGATTGTTCTCGGCTCTGATCTTTTTTA

shDnmt3B.3(b):

AGCTTAAAAAAGATCAGAGCCGAGAACAATCTCTTGAATTGTTCTCGGCTCTGATCTGGG

#### *HERVK 5'UTR cloning*

HERVK14Cl.7(f): GCAGCTACGCGTGCTTATTCTGTCTCTTTCTAACTCC

HERVK14Cl.8(b): CGACCATCTCGAGGGTTCACCTTGCTGATCATCAGAC

#### *HERVK.PBS.R cloning:*

HERVK.20(f): ATCCAACATCTGGCACCCAACACGGGGCTCCCTGTAATC

HERVK.21(b): TCGAGATTACAGGGAGCCCCGTGTTGGGTGCCAGATGTTGGAT

*HERVK.PBS.NR cloning:*

HERVK.22(f): ATCCAACATCTGGTGCCCAATGCGGGGCTCCACATAATC

HERVK.23(b): TCGAGATTATGTGGAGCCCCGCATTGGGCACCAGATGTTGGAT

*ERE RT-qPCR and/or ChIP:*

HERVK (f): AGAGGAAGGAATGCCTCTTGACAG

HERVK (b): TTACAAAGCAGTATTGCTGCCCCGC

HERVK14Cl.Gag (f): TGGGTCAGGCTGAAAGTAAG

HERVK14Cl.Gag (b): TCCATATTCCGGGAACCAAG

HERVK14Cl.Pol (f): CCATTGTGCTCCATTGGAAG

HERVK14Cl.Pol (b): CCCTCTGTGCCGATTGAAAG

HERVE (f): CACAGAGCCTACATTCGGTTAC

HERVE (b): GGGCCACTCATTATCTTTCCAG

HERVH (f): TTGGTGCCTTGACTCGGATT

HERVH (b): GGATCCTTTTTCACGGAGCAA

HERVK9 (f): GGCTGGCAATAATACCTGGATG

HERVK9 (b): CACCTCTGACTGTTCTGCAATG

SVA (f): CTCGTTCACTCAGTGCTCAATG

SVA (f): CTGGGAGGTGGAGGTTGTAG

SVA.LV/PRKG1 (f): CTGGGAGGTGGAGGTTGTAG

SVA.LV/PRKG1 (b): GCTGCCTTGGAAGGCGCAACC

LV.HERVK.R (f): GGGTATTCTGAGTCCAGCGTAG

LV.HERVK.R (b): CGTGGAATTCGATATCAAGC

LV.HERVK.NR (f): GCGTCCTCCACTTTCCACTC

LV.HERVK.NR (b): CGTGGAATTCGATATCAAGC

LV.Empty (f): GCCGACCCAGCTTTCTTGTA

LV.Empty (b): AGGGCTGCCTTGAAAAAG

*Cellular genes RT-qPCR and/or ChIP:*

TRIM28 (f): AAGGACCATACTGTGCGCTCTAC

TRIM28 (b): ACGTTGCAATAGACAGTACG TTCAC

hH19 (f): GGC TCG GGC TGT GAT GTG

hH19 (b): GAA TTG GTT GTA GTT GTG GAA TCG

H3K9rich (f): CAGCCCTCACATATGATCCC

H3K9rich (b): TCTCCGTCACATGCTTCC

ZNF180 (f): TGATGCACAATAAGTCGAGC

ZNF180 (b): TGCAGTCAATGTGGGAAGTC

NANOG (f): AAATAAGGTAGGTGCTGAAAACAAGT

NANOG (b): TTCCTCTTTCATTCACTCTGAGGTT

POU5F1 (f): CACCCTCTCAGCTCCTCAAATT

POU5F1 (b): TGCTTATGGCTGTTGATGCATT

PRKG1 (f): TCTCGCACATTCTTCACGTC

PRKG1 (b): AGGAACCTTCCCGACTTAGG

TetO (f): GAGAAAAGTGAAAGTCGAGC

TetO (b): CGTCGACAAGCTTATCGATG

EVX1 (f): CTGGGTGTCTCCCTCTCTCA

EVX1 (b): AAAGGAAACCCGCAGCTAAT

hGAPDH (f): CACCGTCAAGGCTGAGAACG

hGAPDH (b): ATACCCAAGGGAGCCACACC

*Pyrosequencing:*

GFP-5': AGATTAGGATGGGTATTATTT

Biot.hPRKG1-3': AATATAAACCTATTCCTACCC



Seq.hPRKG1-GFP: GTGGATTTTTTTTGGGGAGAGAGG

SVACVI-3': TGGGTAATATTGAGTATTGAGTGAA

Biot.hPRKG1-5': CAAACCCAAAACCTTAAAAAA

Seq.SVACVI-hPRKG1: GAGTATTGAGTGAATAAGATTT

### **Supplemental references**

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- Quenneville S, Turelli P, Bojkowska K, Raclot C, Offner S, Kapopoulou A, Trono D. 2012. The KRAB-ZFP/KAP1 system contributes to the early embryonic establishment of site-specific DNA methylation patterns maintained during development. *Cell Rep* **2**(4): 766-773.
- Quenneville S, Verde G, Corsinotti A, Kapopoulou A, Jakobsson J, Offner S, Baglivo I, Pedone PV, Grimaldi G, Riccio A et al. 2011. In embryonic stem cells, ZFP57/KAP1 recognize a methylated hexanucleotide to affect chromatin and DNA methylation of imprinting control regions. *Mol Cell* **44**(3): 361-372.

### **Supplemental tables**

Supplemental Table 1

|                                      | ChIP-seq hES-1      | ChIP-seq hES-2 |
|--------------------------------------|---------------------|----------------|
| Ab species                           | rabbit              | mouse          |
| reads length                         | 80bp                | 100bp*         |
| total nb of reads                    | 49.922.785          | 261.791.048    |
| total KAP1 peak counts               | 57806               | 25300          |
| p-value threshold of the peaks       | 0.00005             | 0.00005        |
| mean peak length                     | 950.5               | 703.9          |
| peaks fold enrichment compared to Ti | mean                | 4.5            |
|                                      | std                 | 9.3            |
|                                      | 10% quantile        | 1.0            |
|                                      | 50% quantile        | 2.4            |
|                                      | 90% quantile        | 8.8            |
|                                      | max fold enrichment | 555.5          |
|                                      |                     | 4766.3         |

\* paired-end reads

Supplemental Table 2

| chromosome | start    | end      |
|------------|----------|----------|
| chr1       | 13458304 | 13460029 |
| chr1       | 13679140 | 13680865 |
| chr1       | 19867970 | 19874189 |
| chr1       | 20323903 | 20329707 |
| chr1       | 30188535 | 30189162 |
| chr1       | 33529116 | 33530711 |
| chr1       | 33530726 | 33534293 |
| chr1       | 47370408 | 47373744 |
| chr1       | 55095959 | 55100210 |
| chr1       | 55100243 | 55101426 |
| chr1       | 68646099 | 68646501 |
| chr1       | 75842770 | 75849143 |
| chr1       | 87453925 | 87454694 |
| chr1       | 91683159 | 91686881 |
| chr1       | 94910375 | 94916345 |
| chr1       | 1.03E+08 | 1.03E+08 |
| chr1       | 1.03E+08 | 1.03E+08 |
| chr1       | 1.05E+08 | 1.05E+08 |
| chr1       | 1.07E+08 | 1.07E+08 |
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| chr1       | 1.1E+08  | 1.1E+08  |
| chr1       | 1.43E+08 | 1.43E+08 |
| chr1       | 1.51E+08 | 1.51E+08 |
| chr1       | 1.51E+08 | 1.51E+08 |
| chr1       | 1.54E+08 | 1.54E+08 |
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| chr1       | 1.81E+08 | 1.81E+08 |

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| chr1 | 2.12E+08 | 2.12E+08 |
| chr1 | 2.23E+08 | 2.23E+08 |
| chr1 | 2.25E+08 | 2.25E+08 |
| chr1 | 2.25E+08 | 2.25E+08 |
| chr1 | 2.25E+08 | 2.25E+08 |
| chr1 | 2.38E+08 | 2.38E+08 |
| chr1 | 2.42E+08 | 2.42E+08 |
| chr1 | 2.43E+08 | 2.43E+08 |
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| chr1 | 2.47E+08 | 2.47E+08 |
| chr1 | 2.47E+08 | 2.47E+08 |
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| chr11 | 67469942 | 67472882 |

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| chr12 | 58721241 | 58730698 |
| chr12 | 63370962 | 63371495 |
| chr12 | 69722716 | 69723473 |
| chr12 | 69723493 | 69724221 |
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| chr12 | 84495964 | 84500337 |
| chr12 | 88573348 | 88578315 |
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| chr12 | 95839264 | 95840213 |
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| chr12 | 1.03E+08 | 1.03E+08 |
| chr12 | 1.06E+08 | 1.06E+08 |
| chr12 | 1.08E+08 | 1.08E+08 |
| chr12 | 1.12E+08 | 1.12E+08 |
| chr12 | 1.12E+08 | 1.12E+08 |
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| chr13 | 85443677 | 85446068 |

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| chr13 | 78630688 | 78633131 |
| chr13 | 81233365 | 81233467 |
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| chr14 | 1.06E+08 | 1.06E+08 |
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| chr14 | 1.07E+08 | 1.07E+08 |
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| chr14 | 24480599 | 24484985 |
| chr14 | 42776305 | 42778955 |

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| chr14 | 81431178 | 81431712 |
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| chr16 | 35090133 | 35091581 |
| chr16 | 2710262  | 2718374  |

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| chr17 | 29960126 | 29966038 |
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| chr17 | 41951727 | 41952180 |
| chr17 | 73018670 | 73019192 |
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| chr17 | 41413585 | 41415766 |
| chr17 | 41415783 | 41422672 |
| chr17 | 41425278 | 41426994 |

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| chr18 | 36115400 | 36115948 |
| chr18 | 10220415 | 10225968 |
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| chr18 | 74366291 | 74366862 |
| chr19 | 261710   | 262048   |
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| chr19 | 9564579  | 9570158  |
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| chr19 | 58826016 | 58826633 |
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| chr19 | 9822184  | 9827591  |
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| chr19 | 11971120 | 11971799 |
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| chr19 | 14999509 | 15000134 |
| chr19 | 20430855 | 20433161 |

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| chr19 | 21521183 | 21528092 |
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| chr19 | 21854930 | 21856204 |
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| chr19 | 28194361 | 28203119 |
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| chr19 | 43404575 | 43405028 |
| chr19 | 43508920 | 43509931 |
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| chr2  | 20122507 | 20124043 |
| chr2  | 20124334 | 20128272 |
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| chr2  | 1.17E+08 | 1.17E+08 |
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| chr2  | 1.5E+08  | 1.5E+08  |
| chr2  | 1.67E+08 | 1.67E+08 |
| chr2  | 1.67E+08 | 1.67E+08 |
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| chr2  | 1.73E+08 | 1.73E+08 |
| chr2  | 1.81E+08 | 1.81E+08 |
| chr2  | 1.86E+08 | 1.86E+08 |
| chr2  | 1.87E+08 | 1.87E+08 |



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| chr2  | 99893563 | 99895036 |
| chr2  | 1.01E+08 | 1.01E+08 |
| chr2  | 1.09E+08 | 1.09E+08 |
| chr2  | 1.2E+08  | 1.2E+08  |
| chr2  | 1.28E+08 | 1.28E+08 |
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| chr2  | 1.53E+08 | 1.53E+08 |
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| chr20 | 23447561 | 23448779 |

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| chr20 | 23736503 | 23737884 |
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| chr21 | 19933658 | 19941962 |
| chr22 | 18926186 | 18935361 |
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| chr3  | 46470884 | 46472189 |
| chr3  | 46472596 | 46474652 |
| chr3  | 49256572 | 49257777 |
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| chr3 | 94366022 | 94370037 |
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| chr3 | 1.11E+08 | 1.11E+08 |
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| chr3 | 1.26E+08 | 1.26E+08 |
| chr3 | 1.26E+08 | 1.26E+08 |
| chr3 | 1.29E+08 | 1.29E+08 |
| chr3 | 1.29E+08 | 1.29E+08 |
| chr3 | 1.3E+08  | 1.3E+08  |
| chr3 | 1.3E+08  | 1.3E+08  |
| chr3 | 1.42E+08 | 1.42E+08 |
| chr3 | 1.51E+08 | 1.51E+08 |
| chr3 | 1.65E+08 | 1.65E+08 |
| chr3 | 1.71E+08 | 1.71E+08 |
| chr3 | 1.72E+08 | 1.72E+08 |
| chr3 | 1.72E+08 | 1.72E+08 |
| chr3 | 1.85E+08 | 1.85E+08 |
| chr3 | 1.85E+08 | 1.85E+08 |
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| chr3 | 32128675 | 32130594 |
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| chr3 | 1.04E+08 | 1.04E+08 |
| chr3 | 1.13E+08 | 1.13E+08 |

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| chr3 | 1.21E+08 | 1.21E+08 |
| chr3 | 1.29E+08 | 1.29E+08 |
| chr3 | 1.3E+08  | 1.3E+08  |
| chr3 | 1.64E+08 | 1.64E+08 |
| chr3 | 1.67E+08 | 1.67E+08 |
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| chr3 | 1.71E+08 | 1.71E+08 |
| chr3 | 1.75E+08 | 1.75E+08 |
| chr3 | 1.75E+08 | 1.75E+08 |
| chr3 | 1.85E+08 | 1.85E+08 |
| chr3 | 1.85E+08 | 1.85E+08 |
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| chr4 | 9659579  | 9669174  |
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| chr4 | 32647980 | 32648448 |
| chr4 | 35141359 | 35146833 |
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| chr4 | 79249818 | 79252276 |
| chr4 | 87381676 | 87382283 |
| chr4 | 87382651 | 87385693 |
| chr4 | 1E+08    | 1E+08    |

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| chr4 | 1.27E+08 | 1.27E+08 |
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| chr4 | 1.62E+08 | 1.62E+08 |
| chr4 | 1.66E+08 | 1.66E+08 |
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| chr4 | 1.77E+08 | 1.77E+08 |
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| chr4 | 10171538 | 10176220 |
| chr4 | 10298155 | 10305094 |
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| chr4 | 65489461 | 65491305 |
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| chr4 | 80745556 | 80748497 |

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| chr4 | 88214721 | 88216944 |
| chr4 | 88323862 | 88329947 |
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| chr4 | 92107102 | 92108177 |
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| chr4 | 95453310 | 95453858 |
| chr4 | 98018056 | 98023755 |
| chr4 | 1E+08    | 1E+08    |
| chr4 | 1E+08    | 1E+08    |
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| chr4 | 1.37E+08 | 1.37E+08 |
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| chr4 | 1.61E+08 | 1.61E+08 |
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| chr4 | 1.86E+08 | 1.86E+08 |
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| chr5 | 19702820 | 19708569 |
| chr5 | 20595457 | 20595901 |

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| chr5 | 23689884 | 23690654 |
| chr5 | 24650469 | 24654569 |
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| chr5 | 44986925 | 44990434 |
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| chr5 | 51601655 | 51606062 |
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| chr5 | 86806147 | 86811943 |
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| chr5 | 1.72E+08 | 1.72E+08 |
| chr5 | 1.72E+08 | 1.72E+08 |
| chr5 | 1578461  | 1585502  |
| chr5 | 8037210  | 8038116  |
| chr5 | 18782500 | 18786031 |
| chr5 | 21282578 | 21284147 |
| chr5 | 24308706 | 24310427 |
| chr5 | 24311201 | 24313452 |
| chr5 | 24748286 | 24749069 |
| chr5 | 24750539 | 24751821 |
| chr5 | 30486759 | 30496205 |
| chr5 | 31393989 | 31394399 |
| chr5 | 31394577 | 31395238 |

|      |          |          |
|------|----------|----------|
| chr5 | 31397957 | 31399103 |
| chr5 | 34461062 | 34463834 |
| chr5 | 34464138 | 34468642 |
| chr5 | 34784230 | 34787330 |
| chr5 | 41474633 | 41475198 |
| chr5 | 45914967 | 45915372 |
| chr5 | 46000158 | 46008123 |
| chr5 | 53794048 | 53798148 |
| chr5 | 53798397 | 53801236 |
| chr5 | 54670666 | 54672436 |
| chr5 | 69958434 | 69959919 |
| chr5 | 92792379 | 92793912 |
| chr5 | 1.03E+08 | 1.03E+08 |
| chr5 | 1.13E+08 | 1.13E+08 |
| chr5 | 1.14E+08 | 1.14E+08 |
| chr5 | 1.21E+08 | 1.21E+08 |
| chr5 | 1.28E+08 | 1.28E+08 |
| chr5 | 1.36E+08 | 1.36E+08 |
| chr5 | 1.45E+08 | 1.45E+08 |
| chr5 | 1.45E+08 | 1.45E+08 |
| chr5 | 1.5E+08  | 1.5E+08  |
| chr5 | 1.54E+08 | 1.54E+08 |
| chr5 | 1.54E+08 | 1.54E+08 |
| chr5 | 1.56E+08 | 1.56E+08 |
| chr5 | 1.66E+08 | 1.66E+08 |
| chr6 | 3055033  | 3055742  |
| chr6 | 23161171 | 23168440 |
| chr6 | 25999458 | 26000425 |
| chr6 | 26259300 | 26260689 |
| chr6 | 27155299 | 27158595 |
| chr6 | 28652000 | 28660735 |
| chr6 | 45203466 | 45209437 |
| chr6 | 48841312 | 48843677 |



|      |          |          |
|------|----------|----------|
| chr6 | 48843680 | 48845450 |
| chr6 | 48845769 | 48847362 |
| chr6 | 56934670 | 56939560 |
| chr6 | 57622733 | 57626916 |
| chr6 | 58726259 | 58730234 |
| chr6 | 61943454 | 61944732 |
| chr6 | 61944836 | 61950455 |
| chr6 | 65654352 | 65655016 |
| chr6 | 69094994 | 69095901 |
| chr6 | 78842189 | 78842758 |
| chr6 | 78843276 | 78850428 |
| chr6 | 79563834 | 79567847 |
| chr6 | 1.01E+08 | 1.01E+08 |
| chr6 | 1.01E+08 | 1.01E+08 |
| chr6 | 1.11E+08 | 1.11E+08 |
| chr6 | 1.11E+08 | 1.11E+08 |
| chr6 | 1.21E+08 | 1.21E+08 |
| chr6 | 1.27E+08 | 1.27E+08 |
| chr6 | 1.32E+08 | 1.33E+08 |
| chr6 | 1.46E+08 | 1.46E+08 |
| chr6 | 1.51E+08 | 1.51E+08 |
| chr6 | 1.66E+08 | 1.66E+08 |
| chr6 | 1.67E+08 | 1.67E+08 |
| chr6 | 1.67E+08 | 1.67E+08 |
| chr6 | 6065194  | 6068827  |
| chr6 | 27793623 | 27794468 |
| chr6 | 29787379 | 29787614 |
| chr6 | 29843941 | 29849606 |
| chr6 | 31199877 | 31203347 |
| chr6 | 31952468 | 31958829 |
| chr6 | 31985206 | 31991567 |
| chr6 | 32527864 | 32534667 |
| chr6 | 35074061 | 35075352 |

|      |          |          |
|------|----------|----------|
| chr6 | 47280427 | 47281566 |
| chr6 | 47281631 | 47284511 |
| chr6 | 49468990 | 49475767 |
| chr6 | 49854631 | 49859163 |
| chr6 | 54582362 | 54582530 |
| chr6 | 58738973 | 58745464 |
| chr6 | 61959215 | 61963177 |
| chr6 | 62206614 | 62207808 |
| chr6 | 67040989 | 67041671 |
| chr6 | 71155061 | 71158754 |
| chr6 | 77197057 | 77201753 |
| chr6 | 78426661 | 78436083 |
| chr6 | 87208030 | 87212055 |
| chr6 | 93907907 | 93909620 |
| chr6 | 1.06E+08 | 1.06E+08 |
| chr6 | 1.14E+08 | 1.14E+08 |
| chr6 | 1.14E+08 | 1.14E+08 |
| chr6 | 1.23E+08 | 1.23E+08 |
| chr6 | 1.26E+08 | 1.26E+08 |
| chr6 | 1.31E+08 | 1.31E+08 |
| chr6 | 1.35E+08 | 1.35E+08 |
| chr6 | 1.35E+08 | 1.35E+08 |
| chr6 | 1.59E+08 | 1.59E+08 |
| chr6 | 1.59E+08 | 1.59E+08 |
| chr6 | 1.67E+08 | 1.67E+08 |
| chr6 | 1.67E+08 | 1.67E+08 |
| chr6 | 1.71E+08 | 1.71E+08 |
| chr7 | 9056333  | 9057075  |
| chr7 | 9059465  | 9060102  |
| chr7 | 30575775 | 30576884 |
| chr7 | 30584513 | 30585046 |
| chr7 | 35949888 | 35952238 |
| chr7 | 38199588 | 38203686 |

|      |          |          |
|------|----------|----------|
| chr7 | 43848620 | 43849805 |
| chr7 | 43864939 | 43865195 |
| chr7 | 44592277 | 44592494 |
| chr7 | 48179626 | 48183803 |
| chr7 | 50637488 | 50638538 |
| chr7 | 50644673 | 50646523 |
| chr7 | 50648481 | 50651651 |
| chr7 | 51912832 | 51913840 |
| chr7 | 54516531 | 54522873 |
| chr7 | 56220245 | 56221144 |
| chr7 | 56384632 | 56390474 |
| chr7 | 99574768 | 99577185 |
| chr7 | 1.07E+08 | 1.07E+08 |
| chr7 | 1.18E+08 | 1.18E+08 |
| chr7 | 1.27E+08 | 1.27E+08 |
| chr7 | 1.38E+08 | 1.38E+08 |
| chr7 | 1.38E+08 | 1.38E+08 |
| chr7 | 1.5E+08  | 1.5E+08  |
| chr7 | 1.5E+08  | 1.5E+08  |
| chr7 | 4622056  | 4640031  |
| chr7 | 14479521 | 14480107 |
| chr7 | 16718325 | 16719016 |
| chr7 | 23414354 | 23414597 |
| chr7 | 30757871 | 30759205 |
| chr7 | 43899297 | 43904584 |
| chr7 | 45765857 | 45766484 |
| chr7 | 46077805 | 46083429 |
| chr7 | 46083486 | 46084750 |
| chr7 | 67346519 | 67346631 |
| chr7 | 87361715 | 87362736 |
| chr7 | 93499175 | 93500069 |
| chr7 | 94351604 | 94358621 |
| chr7 | 1.09E+08 | 1.09E+08 |

|      |          |          |
|------|----------|----------|
| chr7 | 1.2E+08  | 1.2E+08  |
| chr7 | 1.36E+08 | 1.36E+08 |
| chr7 | 1.36E+08 | 1.36E+08 |
| chr7 | 1.41E+08 | 1.41E+08 |
| chr7 | 1.49E+08 | 1.49E+08 |
| chr7 | 1.5E+08  | 1.5E+08  |
| chr7 | 1.5E+08  | 1.5E+08  |
| chr7 | 1.5E+08  | 1.5E+08  |
| chr7 | 1.52E+08 | 1.52E+08 |
| chr7 | 1.52E+08 | 1.52E+08 |
| chr7 | 1.54E+08 | 1.54E+08 |
| chr7 | 1.55E+08 | 1.55E+08 |
| chr8 | 7985162  | 7992200  |
| chr8 | 8054699  | 8064221  |
| chr8 | 9657336  | 9660492  |
| chr8 | 9666807  | 9669918  |
| chr8 | 12387739 | 12388401 |
| chr8 | 23277605 | 23279629 |
| chr8 | 39727903 | 39730273 |
| chr8 | 39730581 | 39731342 |
| chr8 | 39731347 | 39733525 |
| chr8 | 43748767 | 43754508 |
| chr8 | 47189665 | 47196171 |
| chr8 | 47492993 | 47494757 |
| chr8 | 47497269 | 47501113 |
| chr8 | 47563592 | 47565800 |
| chr8 | 47566094 | 47568323 |
| chr8 | 47789258 | 47792900 |
| chr8 | 49874847 | 49876121 |
| chr8 | 49876178 | 49880047 |
| chr8 | 54529631 | 54536146 |
| chr8 | 54986820 | 54989573 |
| chr8 | 58370481 | 58374202 |

|      |          |          |
|------|----------|----------|
| chr8 | 58376313 | 58378059 |
| chr8 | 58378205 | 58378574 |
| chr8 | 58378576 | 58379198 |
| chr8 | 61406020 | 61408650 |
| chr8 | 61408946 | 61410388 |
| chr8 | 67159415 | 67162348 |
| chr8 | 69800912 | 69807358 |
| chr8 | 75956286 | 75962342 |
| chr8 | 79564310 | 79566911 |
| chr8 | 91696140 | 91698074 |
| chr8 | 93248770 | 93249945 |
| chr8 | 93250042 | 93254946 |
| chr8 | 1.07E+08 | 1.07E+08 |
| chr8 | 1.13E+08 | 1.13E+08 |
| chr8 | 1.27E+08 | 1.27E+08 |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr8 | 5656032  | 5660684  |
| chr8 | 5710040  | 5715082  |
| chr8 | 5731715  | 5735786  |
| chr8 | 7010301  | 7017357  |
| chr8 | 7355396  | 7364859  |
| chr8 | 7992312  | 7992974  |
| chr8 | 12073969 | 12083497 |
| chr8 | 12316491 | 12326007 |
| chr8 | 12388513 | 12395551 |
| chr8 | 24244307 | 24245788 |
| chr8 | 29976040 | 29976903 |
| chr8 | 30004581 | 30009408 |
| chr8 | 43549161 | 43557724 |

|      |          |          |
|------|----------|----------|
| chr8 | 43737632 | 43741934 |
| chr8 | 47395592 | 47402537 |
| chr8 | 49157074 | 49163077 |
| chr8 | 53892422 | 53896628 |
| chr8 | 89682682 | 89686973 |
| chr8 | 1.1E+08  | 1.1E+08  |
| chr8 | 1.38E+08 | 1.38E+08 |
| chr8 | 1.4E+08  | 1.4E+08  |
| chr8 | 1.46E+08 | 1.46E+08 |
| chr9 | 5228601  | 5231041  |
| chr9 | 28059062 | 28059468 |
| chr9 | 31770534 | 31778847 |
| chr9 | 31908887 | 31909189 |
| chr9 | 35583261 | 35585340 |
| chr9 | 85727996 | 85730082 |
| chr9 | 93663726 | 93668611 |
| chr9 | 1.32E+08 | 1.32E+08 |
| chr9 | 1.35E+08 | 1.35E+08 |
| chr9 | 1.4E+08  | 1.4E+08  |
| chr9 | 1.4E+08  | 1.4E+08  |
| chr9 | 11254386 | 11260606 |
| chr9 | 29658985 | 29660158 |
| chr9 | 29775510 | 29775915 |
| chr9 | 29779505 | 29780675 |
| chr9 | 32743383 | 32744038 |
| chr9 | 83610428 | 83610966 |
| chr9 | 96513345 | 96517550 |
| chr9 | 98032052 | 98032467 |
| chr9 | 1.03E+08 | 1.03E+08 |
| chr9 | 1.03E+08 | 1.03E+08 |
| chr9 | 1.04E+08 | 1.04E+08 |
| chr9 | 1.04E+08 | 1.04E+08 |
| chr9 | 1.15E+08 | 1.15E+08 |

|      |          |          |
|------|----------|----------|
| chr9 | 1.25E+08 | 1.25E+08 |
| chr9 | 1.4E+08  | 1.4E+08  |
| chr9 | 1.4E+08  | 1.4E+08  |
| chr9 | 1.4E+08  | 1.4E+08  |
| chr9 | 1.4E+08  | 1.4E+08  |
| chrX | 34814140 | 34821556 |
| chrX | 41504422 | 41507947 |
| chrX | 56350413 | 56351397 |
| chrX | 56968854 | 56975163 |
| chrX | 56980257 | 56981768 |
| chrX | 57129873 | 57135383 |
| chrX | 57903595 | 57904729 |
| chrX | 64417417 | 64418096 |
| chrX | 73397833 | 73398472 |
| chrX | 73399332 | 73401850 |
| chrX | 74543028 | 74544902 |
| chrX | 74547837 | 74549696 |
| chrX | 76298059 | 76298690 |
| chrX | 76298958 | 76302348 |
| chrX | 77584433 | 77585120 |
| chrX | 79298598 | 79303771 |
| chrX | 1.15E+08 | 1.15E+08 |
| chrX | 1.27E+08 | 1.27E+08 |
| chrX | 1.35E+08 | 1.35E+08 |
| chrX | 1.46E+08 | 1.46E+08 |
| chrX | 1.49E+08 | 1.49E+08 |
| chrX | 1.54E+08 | 1.54E+08 |
| chrX | 26236941 | 26238062 |
| chrX | 42020595 | 42024055 |
| chrX | 44176066 | 44176181 |
| chrX | 46345951 | 46349117 |
| chrX | 53188840 | 53192540 |
| chrX | 57229973 | 57235484 |

|      |          |          |
|------|----------|----------|
| chrX | 61927086 | 61931686 |
| chrX | 61931802 | 61936569 |
| chrX | 61973104 | 61979195 |
| chrX | 62577888 | 62582846 |
| chrX | 62583286 | 62584508 |
| chrX | 64001101 | 64003526 |
| chrX | 64003532 | 64005376 |
| chrX | 64046497 | 64046560 |
| chrX | 64658332 | 64659930 |
| chrX | 64660048 | 64662402 |
| chrX | 64662459 | 64663729 |
| chrX | 72538156 | 72543637 |
| chrX | 72879215 | 72881767 |
| chrX | 76256525 | 76257368 |
| chrX | 77468789 | 77473628 |
| chrX | 88097312 | 88097706 |
| chrX | 88097709 | 88103837 |
| chrX | 94358647 | 94360236 |
| chrX | 94362994 | 94364259 |
| chrX | 97763108 | 97763684 |
| chrX | 1E+08    | 1E+08    |
| chrX | 1.01E+08 | 1.01E+08 |
| chrX | 1.05E+08 | 1.05E+08 |
| chrX | 1.17E+08 | 1.17E+08 |
| chrX | 1.35E+08 | 1.35E+08 |
| chrX | 1.49E+08 | 1.49E+08 |
| chrX | 1.54E+08 | 1.54E+08 |
| chrX | 1.55E+08 | 1.55E+08 |
| chrX | 1.55E+08 | 1.55E+08 |
| chrY | 6768013  | 6768647  |
| chrY | 8864103  | 8868826  |
| chrY | 9075656  | 9076939  |
| chrY | 9078948  | 9082181  |



|      |          |          |
|------|----------|----------|
| chrY | 9811446  | 9818753  |
| chrY | 14445833 | 14446302 |
| chrY | 14446991 | 14447966 |
| chrY | 15364406 | 15368317 |
| chrY | 15368343 | 15371245 |
| chrY | 15719227 | 15724298 |
| chrY | 17512199 | 17514143 |
| chrY | 18986990 | 18990701 |
| chrY | 19065549 | 19066729 |
| chrY | 19067439 | 19071821 |
| chrY | 19443925 | 19445167 |
| chrY | 19446032 | 19446131 |
| chrY | 19446809 | 19447414 |
| chrY | 19447721 | 19448428 |
| chrY | 19796396 | 19800054 |
| chrY | 20220759 | 20221448 |
| chrY | 20396110 | 20398075 |
| chrY | 20828354 | 20834260 |
| chrY | 20855921 | 20859760 |
| chrY | 20922750 | 20926406 |
| chrY | 21455136 | 21460165 |
| chrY | 22032206 | 22035528 |
| chrY | 22121336 | 22121982 |
| chrY | 22122293 | 22123825 |
| chrY | 22819620 | 22820138 |
| chrY | 22963286 | 22964067 |
| chrY | 22964071 | 22967968 |
| chrY | 23129463 | 23136722 |
| chrY | 23346198 | 23347885 |
| chrY | 23742488 | 23747930 |
| chrY | 23818158 | 23820082 |
| chrY | 23874894 | 23880453 |
| chrY | 24177732 | 24178555 |

|      |          |          |
|------|----------|----------|
| chrY | 24178615 | 24181915 |
| chrY | 24763515 | 24764905 |
| chrY | 24856026 | 24858557 |
| chrY | 25091359 | 25093293 |
| chrY | 25787021 | 25787844 |
| chrY | 25787904 | 25791204 |
| chrY | 25866598 | 25869191 |
| chrY | 26725117 | 26727051 |
| chrY | 27348671 | 27352978 |
| chrY | 27799494 | 27800183 |
| chrY | 27935163 | 27935888 |
| chrY | 28237934 | 28239325 |
| chrY | 28330444 | 28332975 |
| chrY | 2753247  | 2755438  |
| chrY | 6827459  | 6833384  |
| chrY | 7486740  | 7489270  |
| chrY | 7731816  | 7733303  |
| chrY | 7733969  | 7735271  |
| chrY | 7820601  | 7829912  |
| chrY | 7859941  | 7865753  |
| chrY | 7990466  | 7994809  |
| chrY | 8342880  | 8343620  |
| chrY | 8983383  | 8988936  |
| chrY | 9045462  | 9047889  |
| chrY | 9111316  | 9116737  |
| chrY | 13391712 | 13397257 |
| chrY | 14168807 | 14169133 |
| chrY | 15111507 | 15113006 |
| chrY | 15281634 | 15287744 |
| chrY | 15726922 | 15730495 |
| chrY | 16486767 | 16492388 |
| chrY | 16980402 | 16986834 |
| chrY | 18085225 | 18094568 |

|      |          |          |
|------|----------|----------|
| chrY | 18789713 | 18793121 |
| chrY | 18793181 | 18794487 |
| chrY | 19781704 | 19783669 |
| chrY | 19958328 | 19959017 |
| chrY | 20379725 | 20383383 |
| chrY | 20717767 | 20721423 |
| chrY | 20784411 | 20788250 |
| chrY | 21314799 | 21315650 |
| chrY | 21820791 | 21822192 |
| chrY | 23181933 | 23182973 |
| chrY | 23223788 | 23224828 |
| chrY | 23248997 | 23254418 |
| chrY | 23609523 | 23614256 |
| chrY | 23786493 | 23789892 |
| chrY | 23991618 | 23997097 |
| chrY | 24113774 | 24115164 |
| chrY | 24394455 | 24401792 |
| chrY | 24696773 | 24700073 |
| chrY | 24700133 | 24700956 |
| chrY | 24975675 | 24979982 |
| chrY | 25629926 | 25632457 |
| chrY | 25723064 | 25724454 |
| chrY | 26026512 | 26027237 |
| chrY | 26162247 | 26162936 |
| chrY | 26609423 | 26613730 |
| chrY | 27235336 | 27237270 |
| chrY | 28093178 | 28095771 |
| chrY | 28171167 | 28174467 |
| chrY | 28174527 | 28175350 |
| chrY | 59317781 | 59317904 |
| chrY | 59319095 | 59319917 |

Supplemental Table 3

## Class I

|              | Counts | % in the Class | bound by kap1<br>(counts) | bound by<br>kap1( %) |
|--------------|--------|----------------|---------------------------|----------------------|
| TOTAL        | 4985   | 100            | 1518                      | 30.5                 |
| HERVH-int    | 1994   | 40.0           | 892                       | 44.7                 |
| MER41-int    | 464    | 9.3            | 59                        | 12.7                 |
| MER57-int    | 313    | 6.3            | 30                        | 9.6                  |
| HERV17-int   | 291    | 5.8            | 97                        | 33.3                 |
| HERV9-int    | 274    | 5.5            | 97                        | 35.4                 |
| MER57A-int   | 222    | 4.5            | 16                        | 7.2                  |
| HUERS-P3-int | 183    | 3.7            | 50                        | 27.3                 |
| MER50-int    | 160    | 3.2            | 20                        | 12.5                 |
| MER66-int    | 124    | 2.5            | 15                        | 12.1                 |
| MER52-int    | 105    | 2.1            | 38                        | 36.2                 |
| PABL_A-int   | 104    | 2.1            | 25                        | 24.0                 |
| HERVE_a-int  | 75     | 1.5            | 37                        | 49.3                 |
| HERVP71A-int | 73     | 1.5            | 9                         | 12.3                 |
| PRIMA41-int  | 66     | 1.3            | 3                         | 4.5                  |
| HERV3-int    | 65     | 1.3            | 21                        | 32.3                 |
| LTR19-int    | 61     | 1.2            | 21                        | 34.4                 |
| HERVH48-int  | 56     | 1.1            | 13                        | 23.2                 |
| HERVE-int    | 51     | 1.0            | 22                        | 43.1                 |
| HERVS71-int  | 50     | 1.0            | 5                         | 10.0                 |
| HERVFH21-int | 43     | 0.9            | 9                         | 20.9                 |
| LTR46-int    | 36     | 0.7            | 3                         | 8.3                  |
| HERVFH19-int | 35     | 0.7            | 10                        | 28.6                 |
| MER84-int    | 35     | 0.7            | 1                         | 2.9                  |
| HERV30-int   | 29     | 0.6            | 1                         | 3.4                  |
| HERV15-int   | 28     | 0.6            | 10                        | 35.7                 |
| HERVI-int    | 24     | 0.5            | 14                        | 58.3                 |
| PABL_B-int   | 16     | 0.3            | 0                         | 0.0                  |

|            |   |     |   |     |
|------------|---|-----|---|-----|
| MER110-int | 5 | 0.1 | 0 | 0.0 |
| THE1C-int  | 1 | 0.0 | 0 | 0.0 |
| MLT-int    | 1 | 0.0 | 0 | 0.0 |
| THE1B-int  | 1 | 0.0 | 0 | 0.0 |

#### Class II

|              | Counts | % in the Class | bound by kap1<br>(counts) | bound by<br>kap1( %) |
|--------------|--------|----------------|---------------------------|----------------------|
| TOTAL        | 924    | 100            | 485                       | 52.5                 |
| HERVK9-int   | 286    | 31.0           | 206                       | 72.0                 |
| HERVK22-int  | 139    | 15.0           | 73                        | 52.5                 |
| HERVK11-int  | 118    | 12.8           | 70                        | 59.3                 |
| HERVK14-int  | 107    | 11.6           | 41                        | 38.3                 |
| HERVK-int    | 100    | 10.8           | 37                        | 37.0                 |
| HERVK3-int   | 68     | 7.4            | 17                        | 25.0                 |
| HERVK14C-int | 32     | 3.5            | 9                         | 28.1                 |
| HERVK13-int  | 31     | 3.4            | 15                        | 48.4                 |
| HERVK11D-int | 31     | 3.4            | 12                        | 38.7                 |
| HERVKC4-int  | 11     | 1.2            | 4                         | 36.4                 |
| THE1D-int    | 1      | 0.1            | 1                         | 100.0                |

#### Class III

|             | Counts | % in the Class | bound by kap1<br>(counts) | bound by<br>kap1( %) |
|-------------|--------|----------------|---------------------------|----------------------|
| TOTAL       | 1521   | 100            | 93                        | 6.1                  |
| HERVL-int   | 1079   | 70.9           | 73                        | 6.8                  |
| HERVL40-int | 140    | 9.2            | 4                         | 2.9                  |
| HERV16-int  | 132    | 8.7            | 7                         | 5.3                  |
| HERVL74-int | 66     | 4.3            | 4                         | 6.1                  |
| LTR52-int   | 36     | 2.4            | 2                         | 5.6                  |
| MER70-int   | 35     | 2.3            | 1                         | 2.9                  |

|           |    |     |   |     |
|-----------|----|-----|---|-----|
| LTR57-int | 33 | 2.2 | 2 | 6.1 |
|-----------|----|-----|---|-----|