Table A. Statistics of the sizes of the ERVs studied, including those in the sex chromosomes – X and Y  $\,$ 

			Standard					
ERV	Number	Mean (bp)	deviation (bp)	0%	25%	50%	75%	100%
ETn	1866	1519	2429	60	316	331	340	9776
IAP	5950	3009	2725	60	402	2722	5281	9877
HERV-K	872	1430	1704	751	965	974	1011	10368

**Table B. Univariate permutation tests for low-resolution features.** P-values obtained from univariate permutation tests with three different test statistics (sample mean difference, sample median difference, and sample variance ratio) and for three comparisons (fixed elements vs. controls, polymorphic (or *in vitro*) elements vs. controls, and fixed vs polymorphic (or *in vitro*) elements) in the study of ETns, IAPs, and HERV-Ks. Significant results (p-value<0.05) are in bold, and color coded as red when the statistics is higher in, e.g., fixed elements vs. controls, and in blue when it is lower.

ETn	Fixe	ed vs. co	ontrol	Polymo	rphic vs	. control	Fixed	vs. polyı	morphic
	Mean	Median	Variance	Mean	Median	Variance	Mean	Median	Variance
<b>Recombination rates</b>	0.00	0.00	0.96	0.32	0.22	0.13	0.00	0.00	0.11
Replication timing	0.00	0.00	0.00	0.00	0.00	0.01	0.12	0.06	0.39
Distance to telomere	0.06	0.06	0.09	0.96	0.88	0.13	0.28	0.50	0.63
Distance to centromere	0.00	0.00	0.77	0.67	0.36	0.19	0.00	0.00	0.15
				1					
IAP	Fixe	ed vs. co	ontrol	Polymo	rphic vs	. control	Fixed	vs. polyı	morphic
	Mean	Median	Variance	Mean	Median	Variance	Mean	Median	Variance
Recombination rates	0.00	0.00	0.58	0.11	0.35	0.96	0.00	0.00	0.58
Replication timing	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00
Distance to telomere	0.71	0.98	0.00	0.57	0.27	0.03	0.78	0.16	0.23
Distance to centromere	0.00	0.00	0.53	0.57	0.42	0.51	0.00	0.00	0.12
HERV-K	Fixe	ed vs. co	ontrol	In vi	trovs.c	ontrol	Fixe	ed vs. <i>in</i>	vitro
	Mean	Median	Variance	Mean	Median	Variance	Mean	Median	Variance
Recombination rates	0.01	0.00	0.26	0.22	0.98	0.32	0.00	0.00	0.06
Replication timing	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08
Distance to telomere	0.53	0.00	0.00	0.84	0.17	0.01	0.48	0.03	0.08
Distance to centromere	0.89	0.60	0.00	0.01	0.03	0.12	0.05	0.02	0.02

# Table C. Predictors that explained a deviance >20% in single logistic regression fits for the three comparisons implemented for each of type of elements – ETns, IAPs and HERV-Ks (these predictors were excluded from multiple FLR models).

The "Predictor" column reports predictors included in each single logistic regression fit. The "Coefficient" column reports coefficient estimates (a positive coefficient means that an increase in the feature increases the likelihood of, e.g., fixed vs. control; a negative coefficient means an increase in the feature decreases such likelihood). The "p-value" column reports p-values for the coefficients. They both are in bold if p-value<0.05. For functional predictors, several rows are listed corresponding to the intervals where the feature was considered – as indicated in the "Range of windows" column. The "DE" column reports the total deviance explained by each single logistic regression fit.

A. Fixed ETn vs control				
Predictor Ra	ange of windows	s Coefficient	p-value	DE (%)
Mononucleotide content	Scalar	4.5E+00	2.0E-16	26.9
Dinucleotide content	Scalar	1.0E+01	2.0E-16	88.6
Trinucleotide content	Scalar	4.8E+00	2.0E-16	32.0
Tetranucleotide content	Scalar	8.8E+00	2.0E-16	75.1
	(-32,-24)	1.6E-02	1.7E-03	
	(-24,-16)	1.1E-02	3.9E-02	
	(-16,-8)	2.2E-02	4.5E-05	
LINE content	(-8,0)	2.9E-02	6.3E-08	33.0
	(0,8)	2.6E-02	6.5E-07	55.0
	(8,16)	1.7E-02	1.3E-03	
	(16,24)	1.1E-02	3.6E-02	
	(24,32)	2.2E-02	1.3E-05	
	(-32,-16)	-1.3E-02	2.4E-01	
Intron content	(-16,0)	-8.2E-02	2.7E-09	26.4
Intron content	(0,16)	-6.9E-02	1.2E-06	20.4
	(16,32)	-4.5E-02	2.7E-05	
	(-30,-20)	-2.3E-02	1.3E-04	
	(-20,-10)	-2.0E-02	1.2E-03	
Most conserved elements	(-10,0)	-6.2E-02	2.0E-16	46.6
content	(0,10)	-5.6E-02	2.0E-16	40.0
	(10,20)	-3.5E-02	3.0E-08	
	(20,30)	-2.9E-02	1.4E-06	
	(-30,-10)	-1.0E-03	1.9E-01	
mESC expression WA	(-10,10)	-9.5E-03	2.0E-16	26.8
	(10,30)	-2.7E-03	2.1E-04	

#### A. Fixed ETn vs control

## B. Polymorphic ETn vs control

Predictor	Range of windows	Coefficient	p-value	DE (%)
Mononucleotide content	Scalar	4.5E+00	2.0E-16	24.2
Dinucleotide content	Scalar	9.3E+00	2.0E-16	85.9
Trinucleotide content	Scalar	5.3E+00	2.0E-16	33.9
Tetranucleotide content	Scalar	9.3E+00	2.0E-16	77.2
LINE content	Scalar	8.3E-01	2.0E-16	26.7
	(-28,-20)	-4.6E-02	2.6E-01	
	(-20,-12)	-3.0E-02	5.8E-01	
	(-12,-4)	-5.5E-02	3.1E-01	
Intron content	(-4,4)	-1.9E-01	2.7E-04	21.1
	(4,12)	-1.1E-02	8.4E-01	
	(12,20)	-7.0E-02	2.0E-01	
	(20,28)	7.1E-03	8.7E-01	
Most conserved elements content	Scalar	-5.8E+00	2.0E-16	28.5

Predictor Range of windows Coefficient p-value DE (%)

#### C. Fixed ETn vs polymorphic

). Fixed IAP vs control				
Predictor Ra	inge of window	s Coefficient	p-value	DE (%
Mononucleotide content	Scalar	4.9E+00	2.0E-16	27.7
Dinucleotide content	Scalar	3.5E+01	2.0E-16	86.1
Trinucleotide content	Scalar	4.7E+00	2.0E-16	30.7
Tetranucleotide content	Scalar	7.9E+00	2.0E-16	70.5
LINE content	Scalar	1.6E+00	2.0E-16	42.3
	(-30,-20)	4.6E-03	7.8E-01	
	(-20,-10)	-5.3E-02	1.5E-02	
Intron content	(-10,0)	-9.5E-02	4.3E-05	22.8
Introli content	(0,10)	-9.5E-02	5.4E-05	22.0
	(10,20)	-1.2E-02	5.9E-01	
	(20,30)	-4.7E-02	5.0E-03	
	(-28,-20)	-3.0E-02	1.0E-08	
	(-20,-12)	-2.9E-02	3.4E-07	
Mast assessed along the	(-12,-4)	-3.8E-02	2.5E-11	
Most conserved elements content	(-4,4)	-8.3E-02	2.0E-16	43.8
Content	(4,12)	-3.3E-02	6.0E-09	
	(12,20)	-3.2E-02	2.8E-08	
	(20,28)	-2.5E-02	3.7E-06	
	(-30,-10)	-1.3E-03	4.6E-02	
mESC expression WA	(-10,10)	-9.4E-03	2.0E-16	26.1
	(10,30)	-2.4E-03	1.2E-04	
	(-28,-20)	4.4E-02	5.9E-03	
	(-20,-12)	1.3E-01	9.6E-07	
	(-12,-4)	4.3E-02	9.8E-03	
H3K9me3 content	(-4,4)	3.1E-01	2.0E-16	31.9
	(4,12)	6.5E-02	2.0E-04	
	(12,20)	2.2E-02	1.6E-01	
	(20,28)	8.4E-02	4.2E-05	

#### E. Polymorphic IAP vs control

Predictor	Range of windows	Coefficient	p-value	DE (%)
Mononucleotide content	Scalar	4.6E+00	2.0E-16	27.4
Dinucleotide content	Scalar	3.8E+01	2.0E-16	89.1
Trinucleotide content	Scalar	5.1E+00	2.0E-16	36.0
Tetranucleotide content	Scalar	8.5E+00	2.0E-16	74.5
LINE content	Scalar	1.1E+00	2.0E-16	40.2
	(-28,-20)	-2.3E-03	9.2E-01	
	(-20,-12)	-6.8E-02	2.0E-02	
	(-12,-4)	-5.5E-02	6.1E-02	
Intron content	(-4,4)	-1.2E-01	7.3E-05	21.8
	(4,12)	-3.9E-02	2.1E-01	
	(12,20)	-1.2E-02	7.0E-01	
	(20,28)	-7.0E-02	2.5E-03	
Most conserved elements content	Scalar	-2.5E+00	2.0E-16	35.1
	(-30,-10)	-2.4E-03	4.6E-03	
mESC expression WA	(-10,10)	-9.4E-03	2.0E-16	22.3
	(10,30)	-2.7E-03	8.7E-04	

## F. Fixed IAP vs polymorphic

Predictor Ra	ange of window	s Coefficient	p-value	DE (%)
	(-28,-20)	-8.7E-03	2.8E-01	
	(-20,-12)	-2.1E-02	2.4E-02	
	(-12,-4)	-2.8E-02	3.0E-03	
H3K9me3 content	(-4,4)	1.7E-01	2.0E-16	21.5
	(4,12)	-1.5E-02	7.8E-02	
	(12,20)	-1.9E-02	2.5E-02	
	(20,28)	6.0E-04	9.5E-01	

#### G. Fixed HERV-K vs control

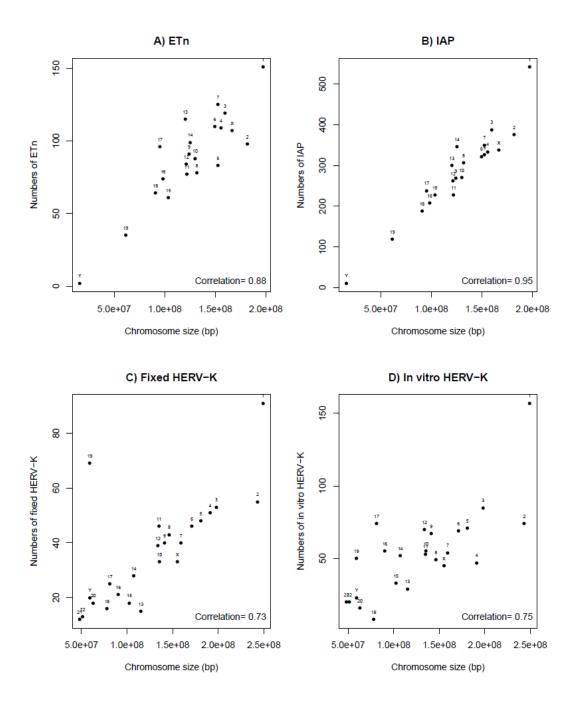
Predictor Ra	ange of window	s Coefficient	p-value	DE (%)
Mononucleotide content	Scalar	9.4E+00	2.0E-16	76.4
Dinucleotide content	Scalar	6.8E+00	2.0E-16	54.9
Trinucleotide content	Scalar	5.5E+00	2.0E-16	29.1
Tetranucleotide content	Scalar	2.5E+00	2.0E-16	60.4
	(-28,-20)	-7.7E-02	1.6E-03	
	(-20,-12)	-5.9E-02	5.4E-02	
	(-12,-4)	-2.8E-04	9.9E-01	
Intron content	(-4,4)	-1.8E-01	9.3E-10	25.7
	(4,12)	-2.4E-02	4.2E-01	
	(12,20)	-5.4E-02	6.3E-02	
	(20,28)	-6.8E-02	3.0E-03	
	(-32,-16)	-5.2E-03	1.5E-04	
H1-hESC transcript	(-16,0)	-7.5E-03	4.0E-06	26.6
expression WA	(0,16)	-9.5E-03	4.4E-09	20.0
	(16,32)	-4.5E-03	5.4E-04	

### H. In vitro HERV-K vs control

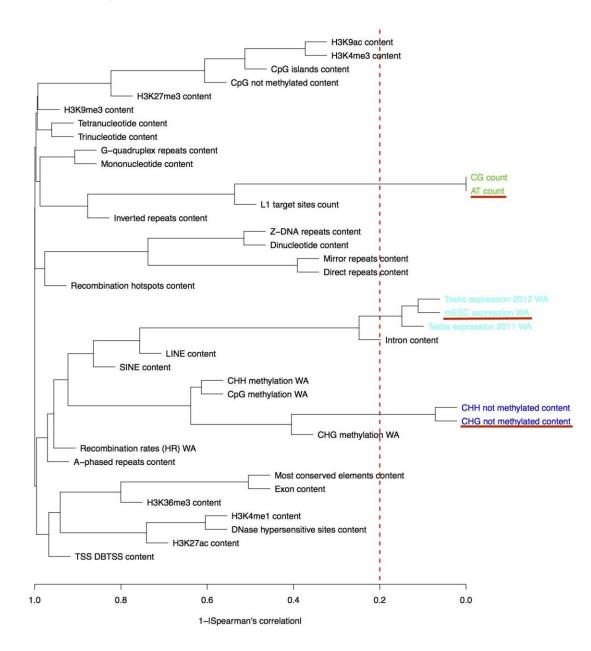
Predictor Ra	nge of windov	vs Coefficient	p-value	DE (%)
I. Fixed vs in vitro HERV-	·К			
Predictor Ra	nge of windov	vs Coefficient	p-value	DE (%)
Managements at internet	Oright	4 45 . 04		05.5

Predictor Ra	nge of windo	ws Coefficient	p-value	DE (%)
Mononucleotide content	Scalar	1.1E+01	2.0E-16	85.5
Dinucleotide content	Scalar	7.3E+00	2.0E-16	59.3
Trinucleotide content	Scalar	6.3E+00	2.0E-16	36.9
Tetranucleotide content	Scalar	1.0E+01	2.0E-16	64.6
L1 target sites count	Scalar	4.2E+00	2.0E-16	23.6
Recombination hotspots motif count	Scalar	1.6E+00	2.0E-16	26.2

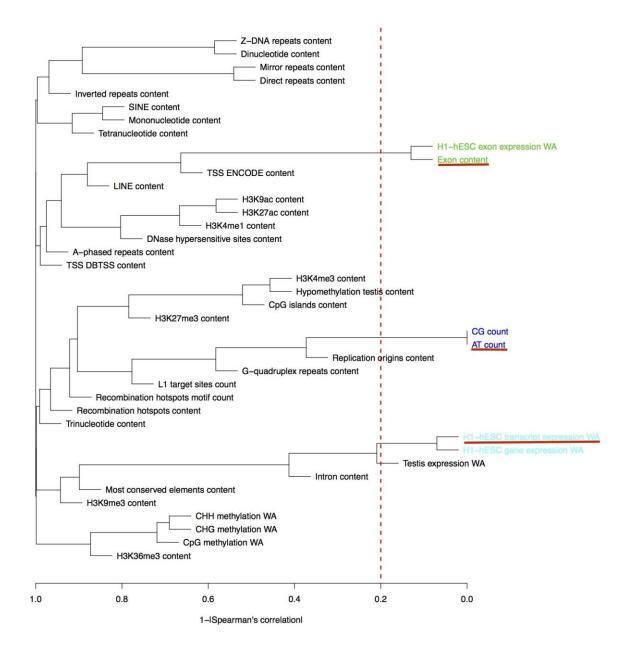
**Figure A.** Scatterplot of chromosome size versus number of ERVs integrated. Correlation is quite high for all the elements, both in human and mouse. Notably, human chromosome 19 stands out as an outlier, showing a higher concentration of fixed HERV-K.

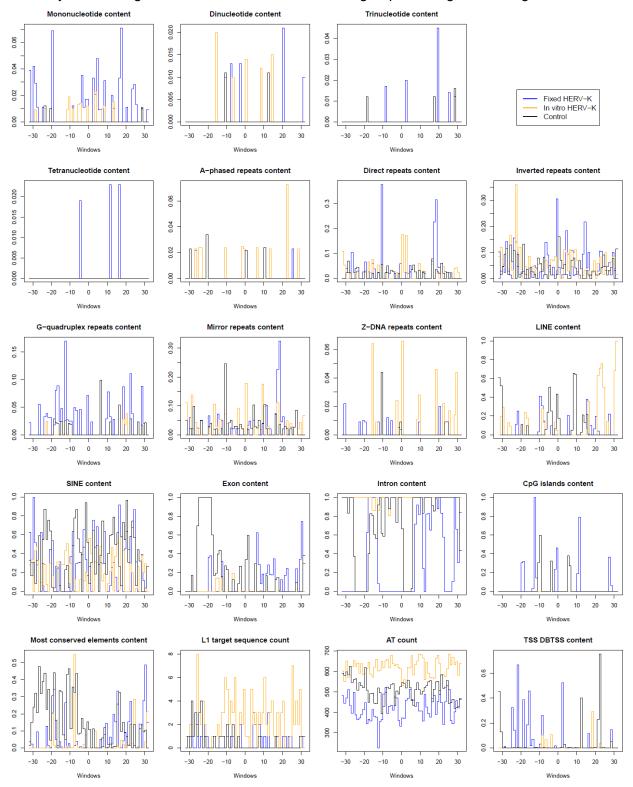


**Figure B.** Hierarchical clustering of features close to fixed ETn and control regions (polymorphic ETn, fixed and polymorphic IAP clustering is similar to fixed ETn). WA= weighted averages, bp= base pairs, TSS= transcription start sites. Underlined is the feature from each cluster that was used in the analyses.

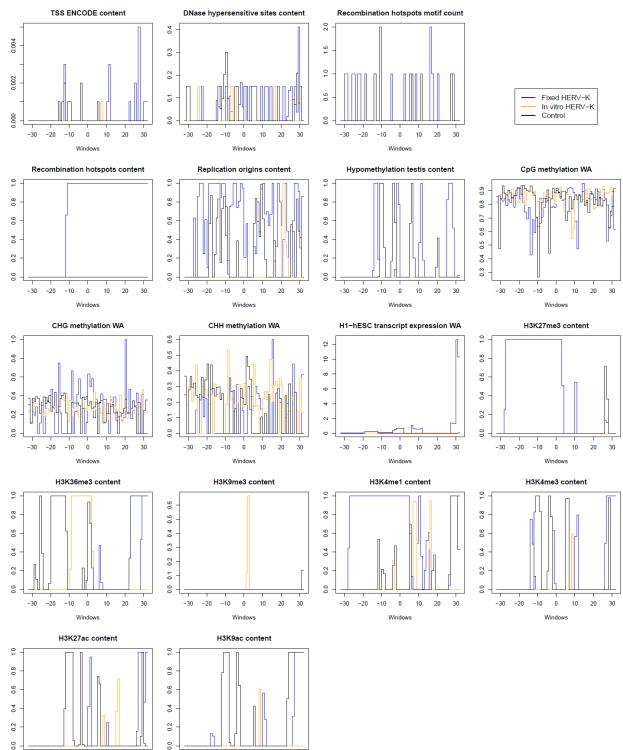


**Figure C.** Hierarchical clustering of features close to fixed HERV-K and controls regions (the clustering for *in vitro* HERV-Ks is similar to fixed HERV-K). WA= weighted averages, bp= base pairs, TSS= transcription start sites. Underlined is the feature from each cluster that was used in the analyses.





**Figure D.** Plot of features in one fixed HERV-K, one *in vitro* HERV-K and one human control randomly chosen regions. Colors indicate the different groups the regions belong to.



-30 -20 -10 0 10 20 30

Windows

30

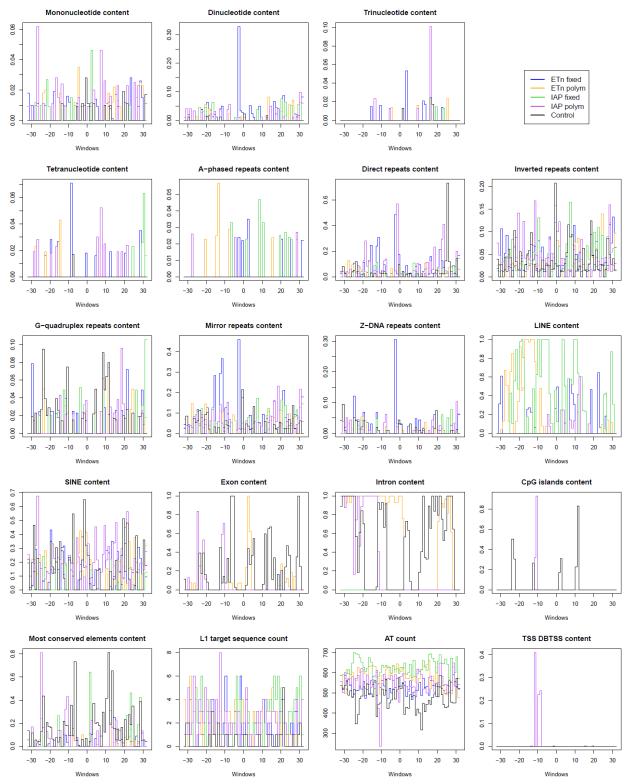
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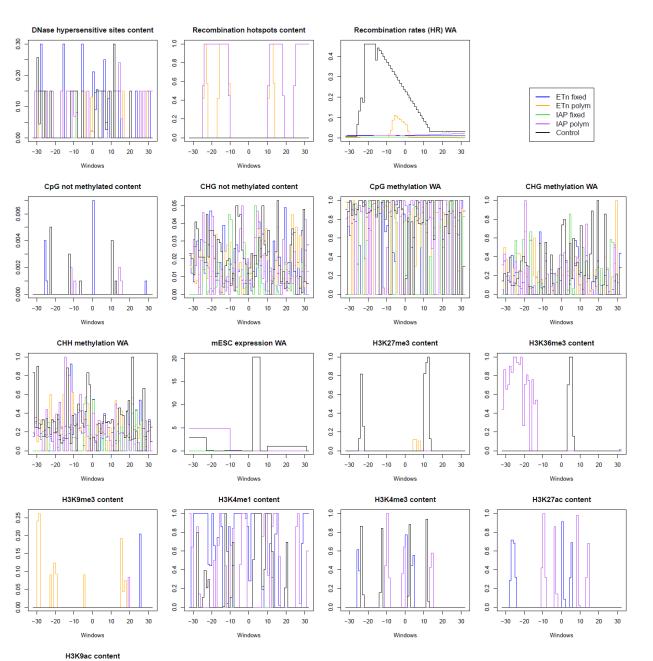
Windows

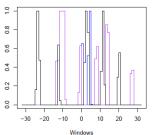
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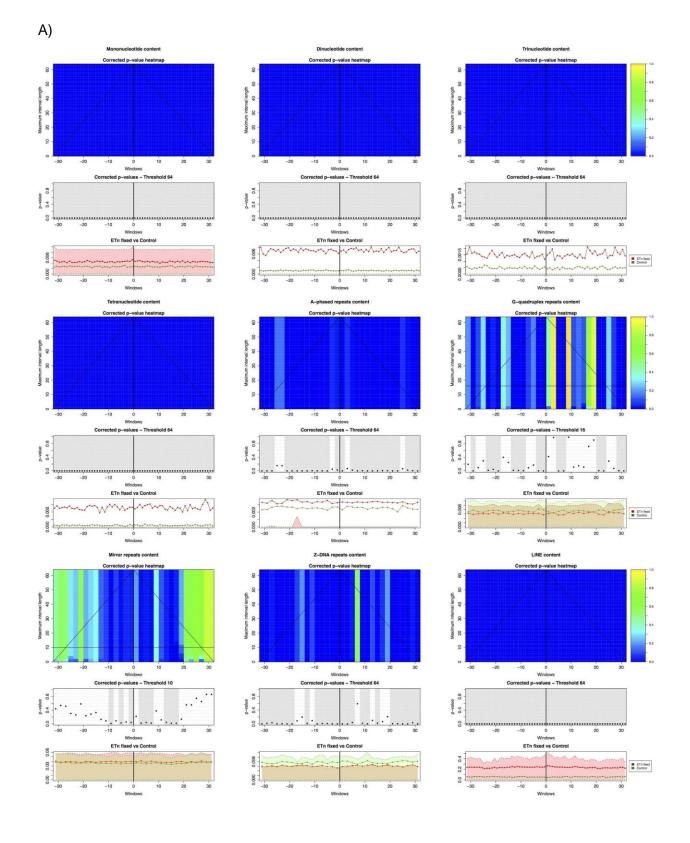
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**Figure E.** Plot of features in one fixed ETn, one polymorphic ETn, one fixed IAP, one polymorphic IAP and one mouse control randomly chosen regions. Colors indicate the different groups the regions belong to.

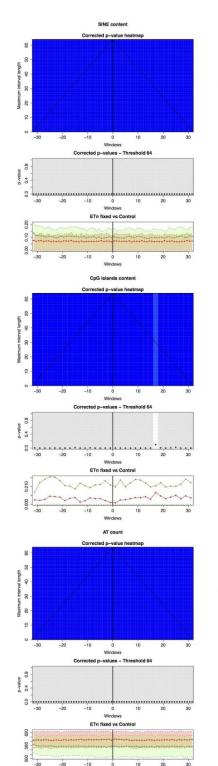






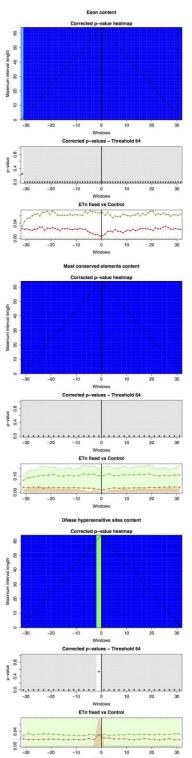


**Figure F.** Significant genomic features for ITP of comparisons fixed ETn vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.



-10 ó 10

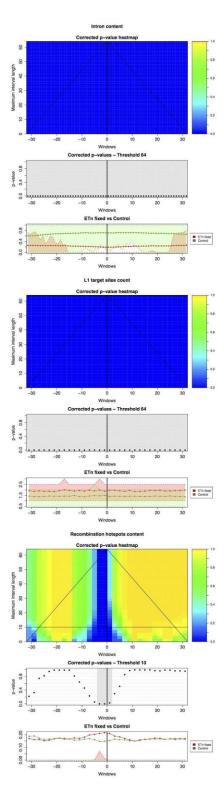
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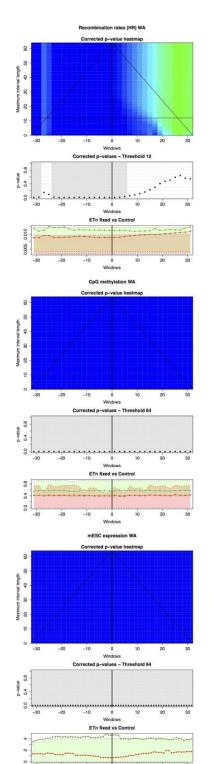


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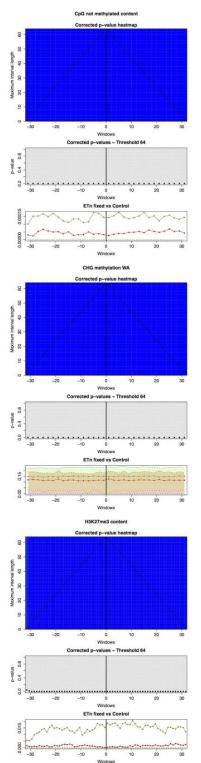
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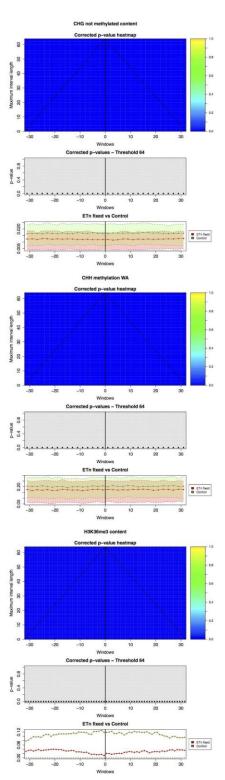


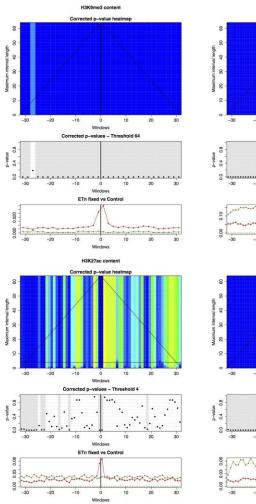


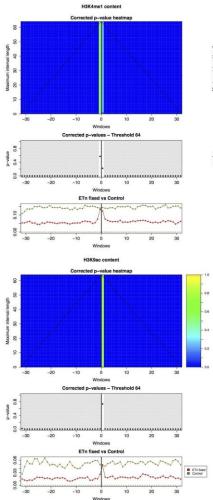
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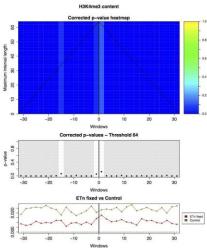
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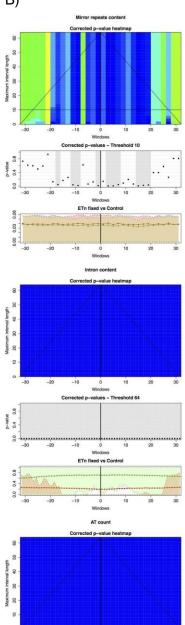


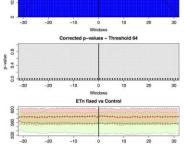


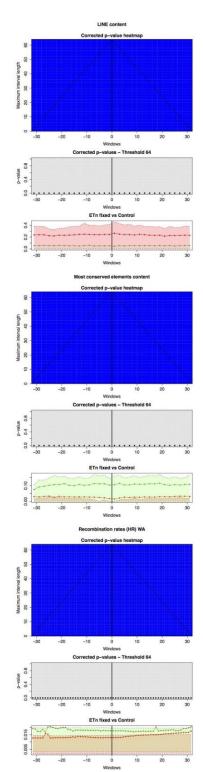


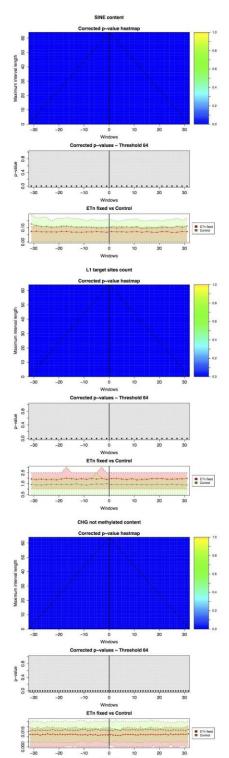




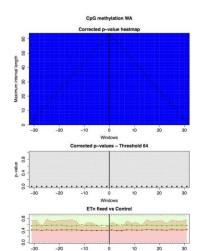


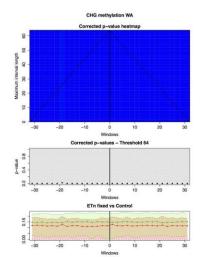


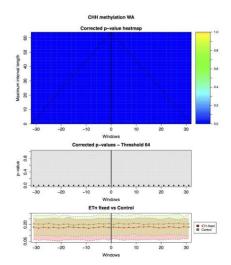


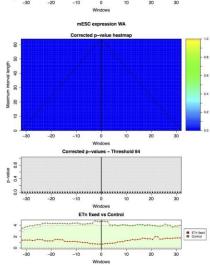


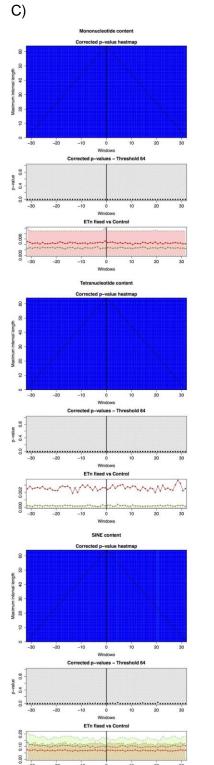
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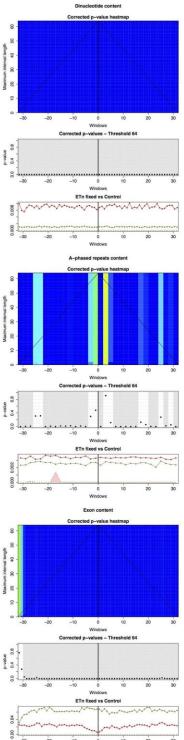


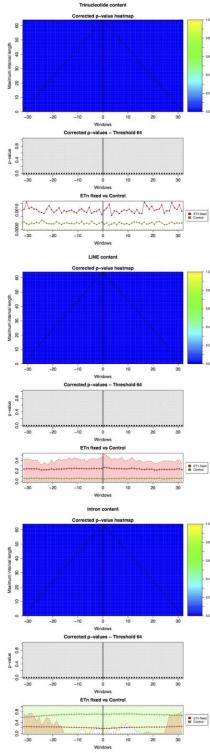


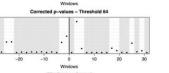
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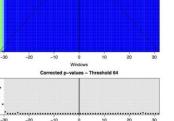
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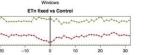
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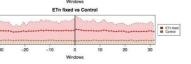


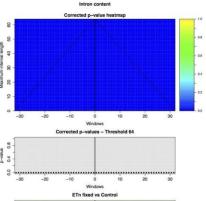


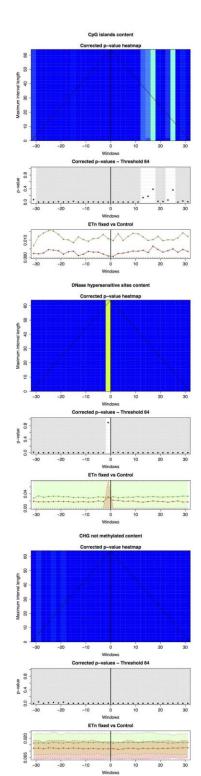


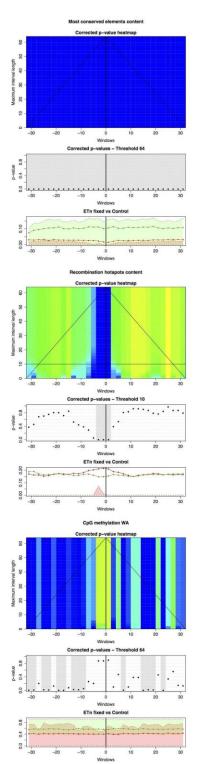


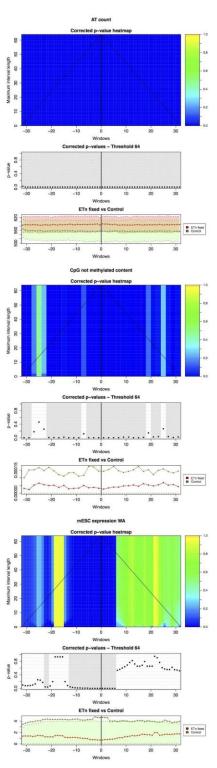
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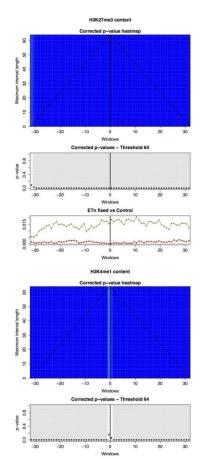












ETn fixed vs Control

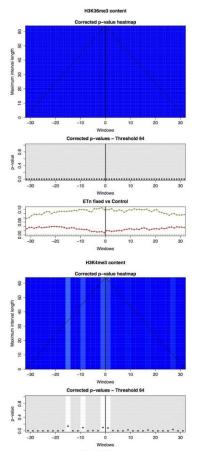
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ETn fixed vs Control

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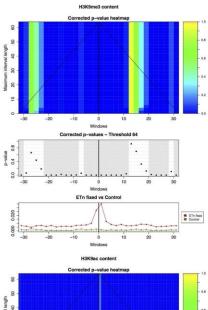
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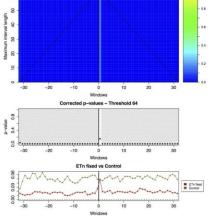
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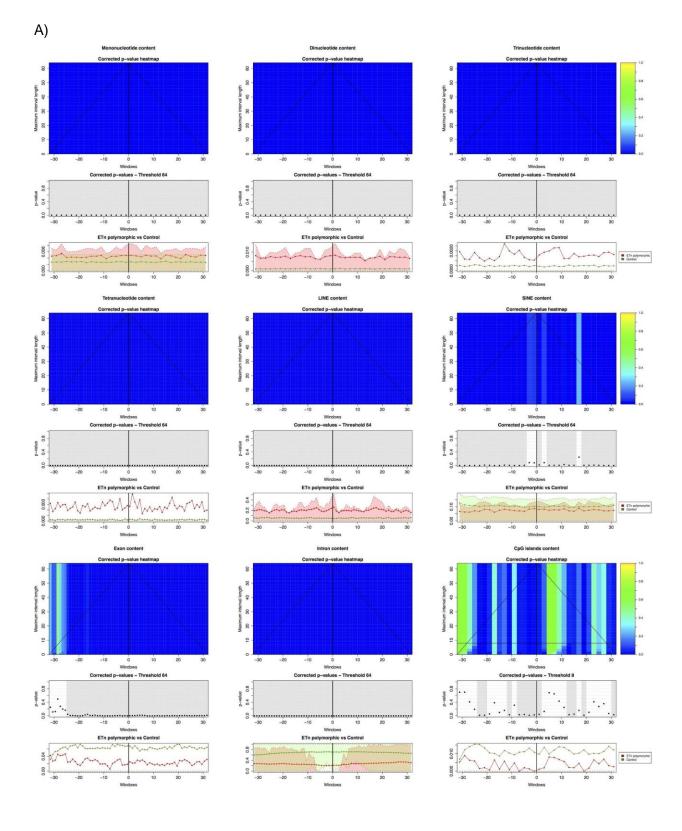
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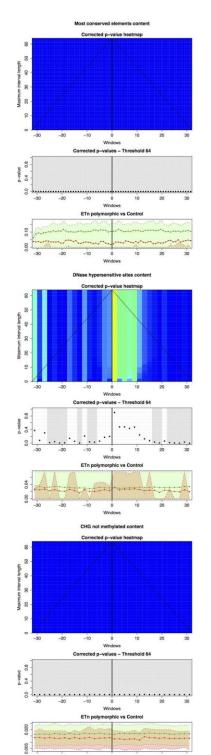
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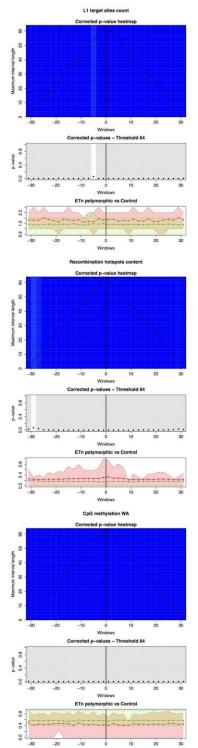


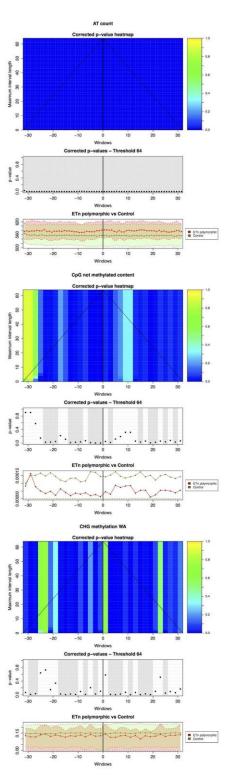
**Figure G.** Significant genomic features for ITP of comparisons polymorphic ETn vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.

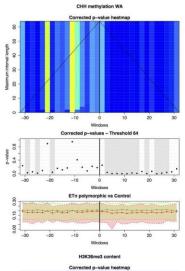


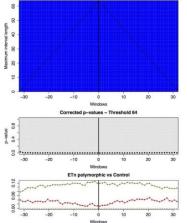


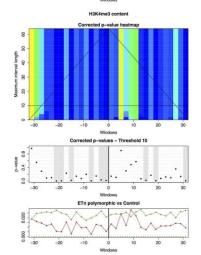
-10 0 10 20

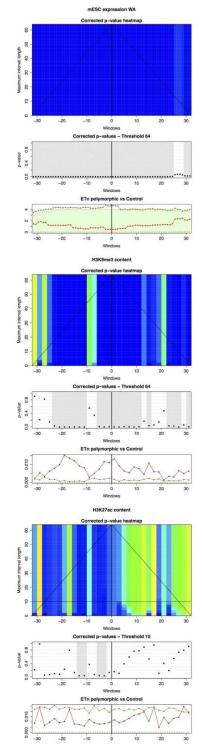








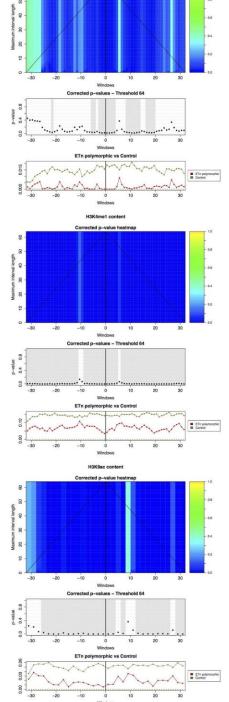




0

-20

10 20 30

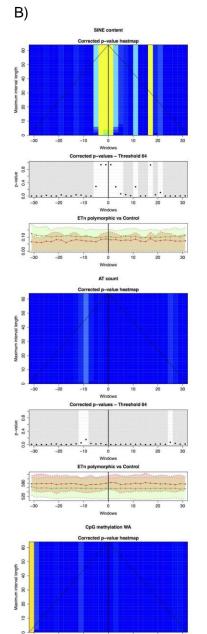


H3K27me3 content

Corrected p-value heatm

99

20



-10 0

p-value 0.4 0.8

0.0

0.8

0.4

81

-30

-20

Windows Corrected p-values - Threshold 64

-20 -10 0 10 20 30

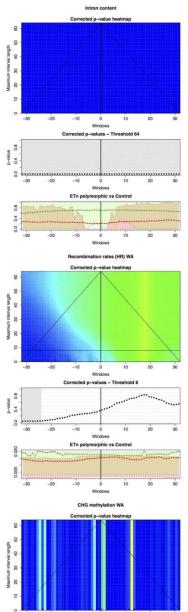
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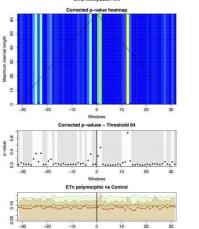
10

20 30

ETn polymorphic vs Control

Windows





-10

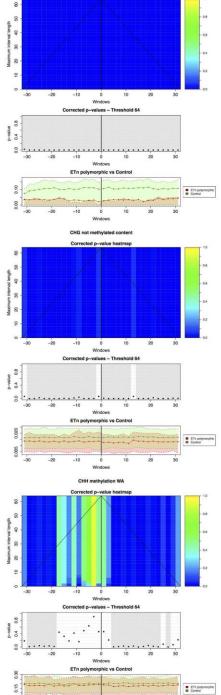
0 Windows

-20

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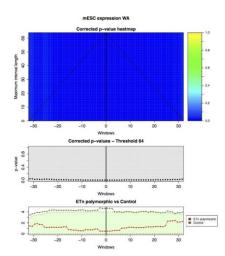
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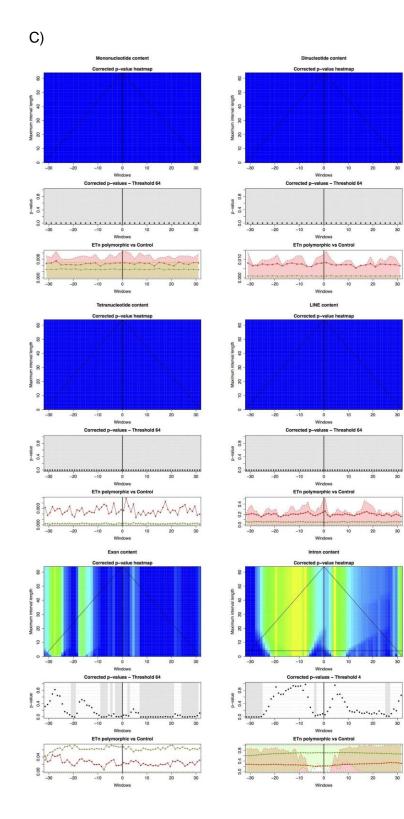
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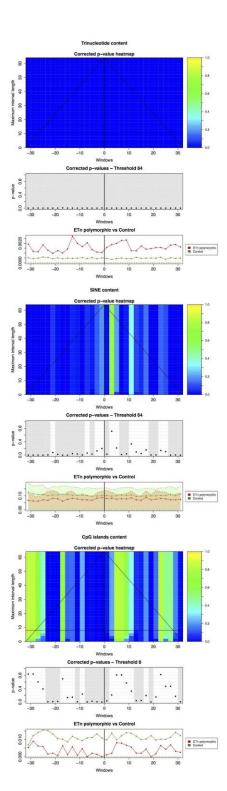


Most conserved elements content

Corrected p-value heatmap





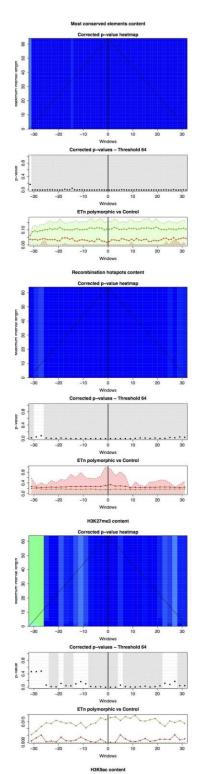


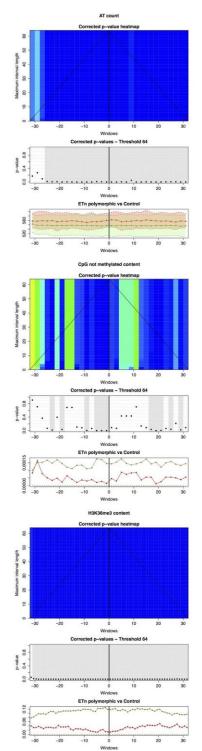
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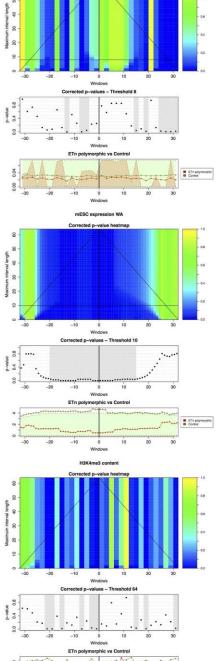
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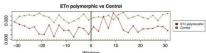


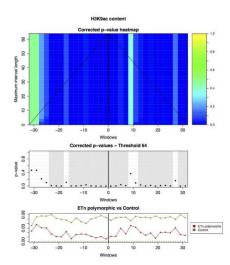


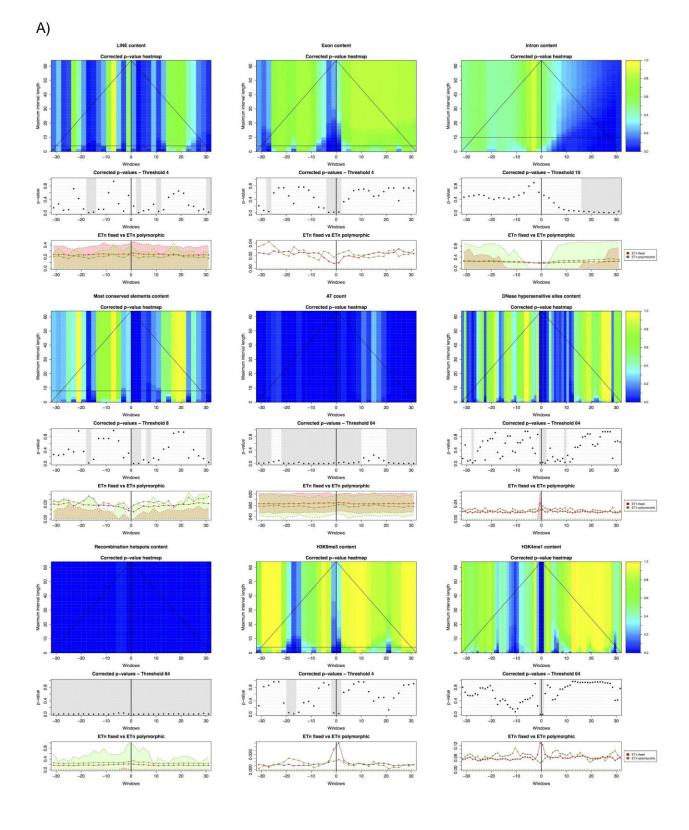


DNase hypersensitive sites content

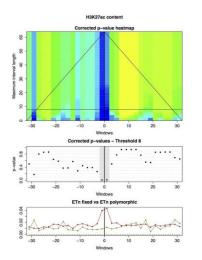
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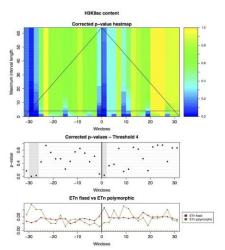


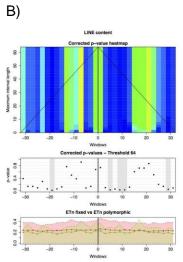


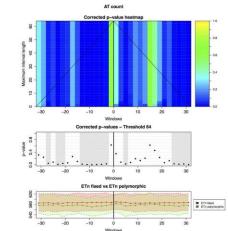


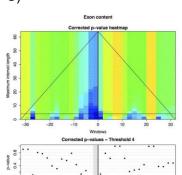
**Figure H.** Significant genomic features for ITP of comparisons fixed vs. polymorphic ETn with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.

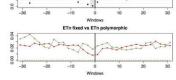


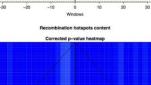


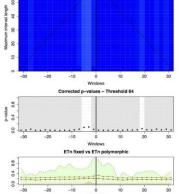


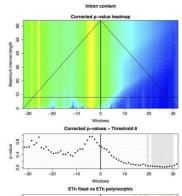


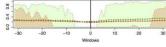




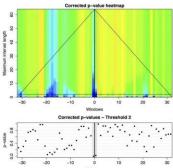






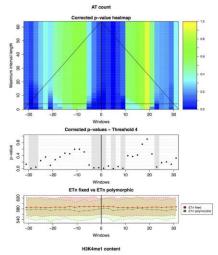


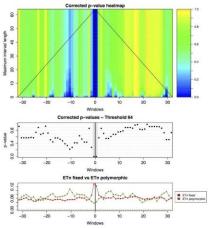
H3K9me3 content

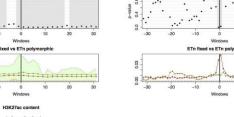


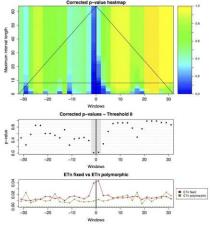
failthan

10 20





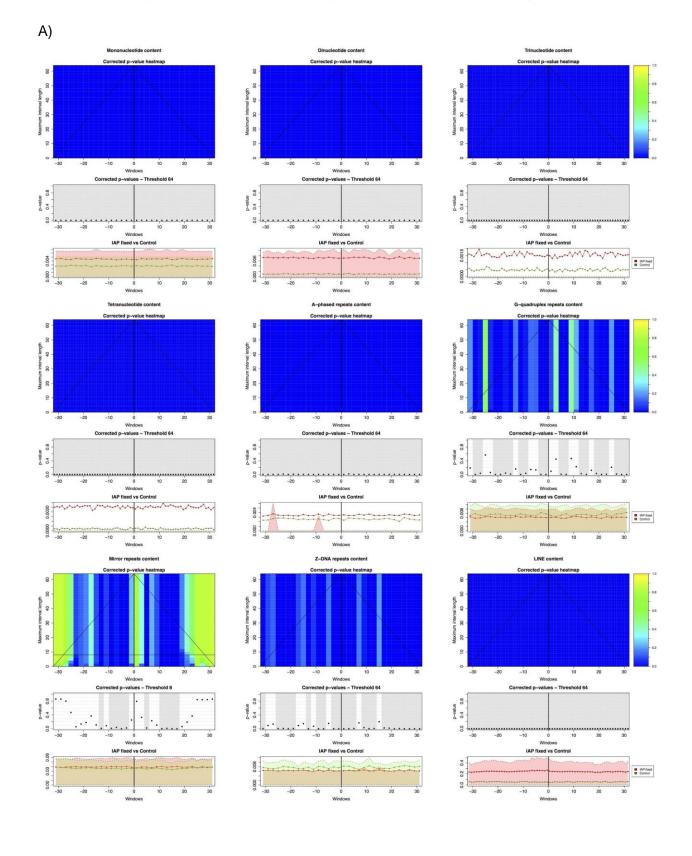




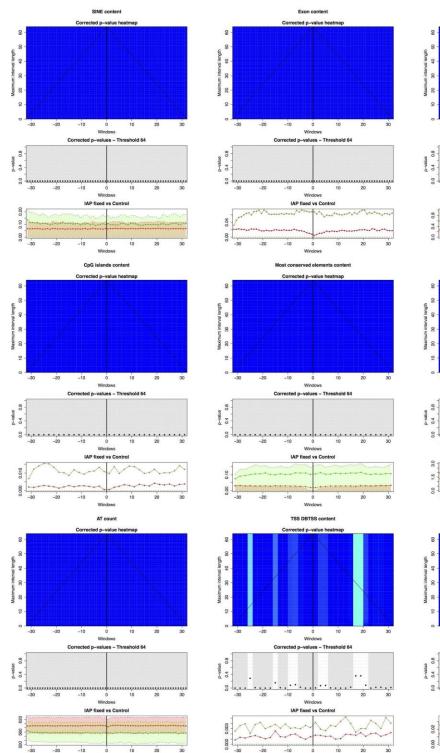
C)

60

50

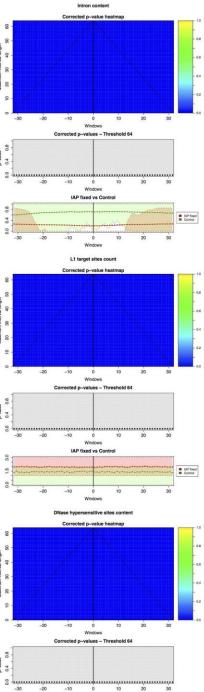


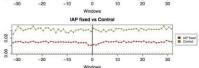
**Figure I.** Significant genomic features for ITP of comparisons fixed IAP vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.

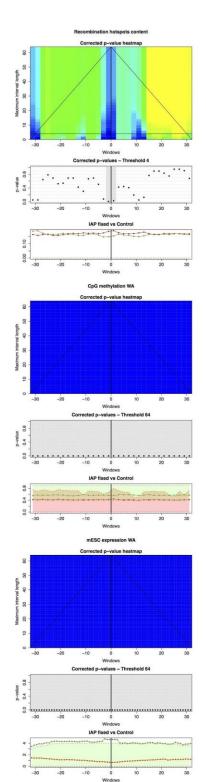


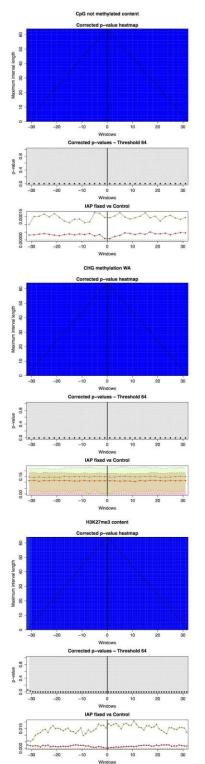
Windows

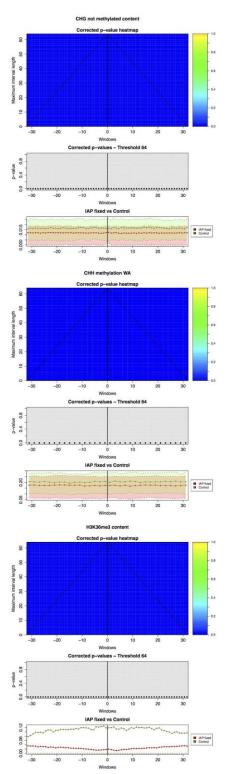
Windows

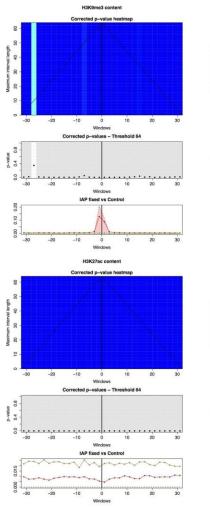


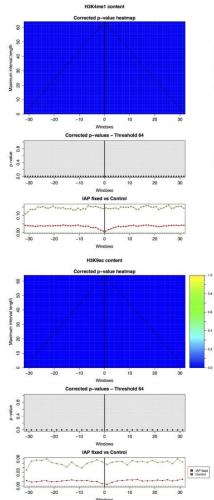


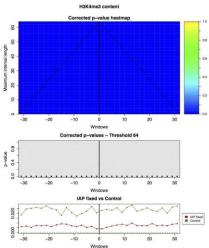


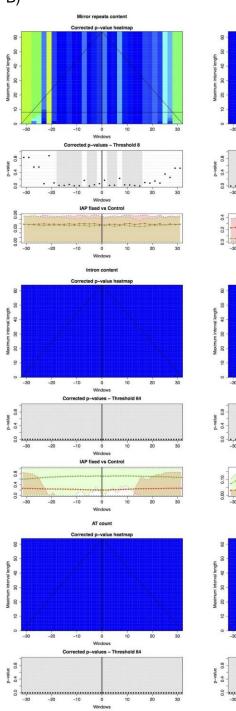












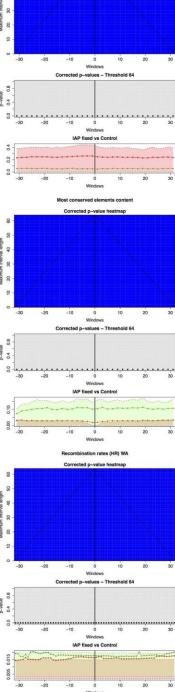
IAP fixed vs Control

-10

620

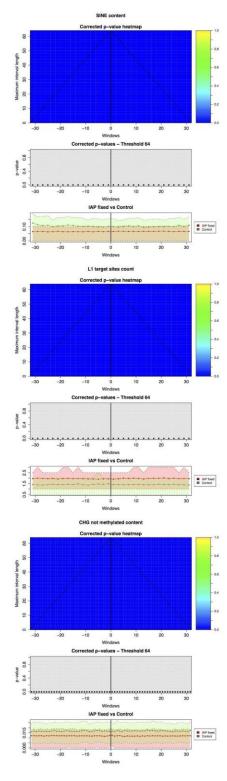
560

200

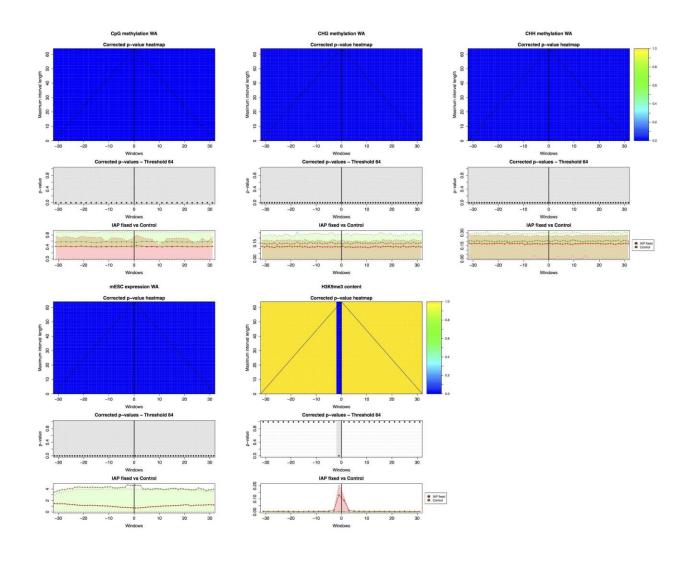


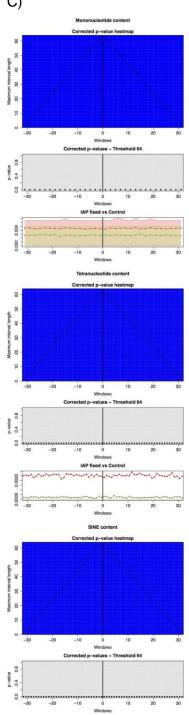
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B)





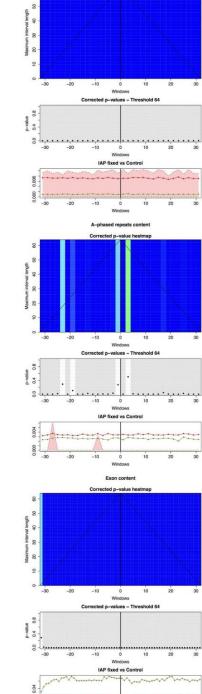
IAP fixed vs Control

-10

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0.00

-30

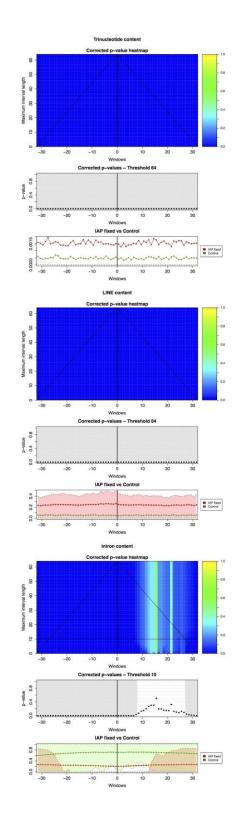
-10

20

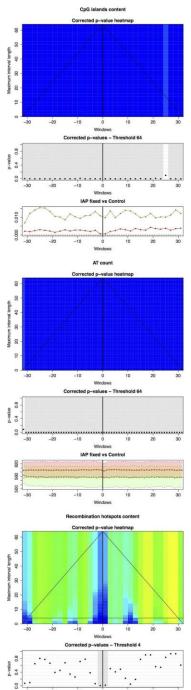
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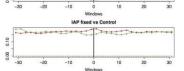
Dinu

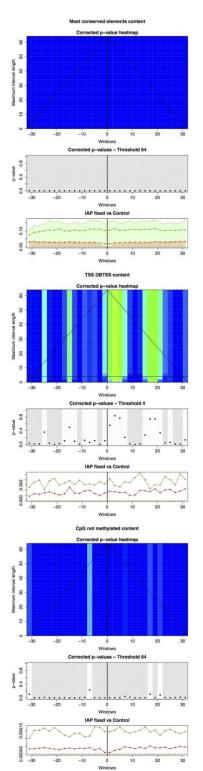
8

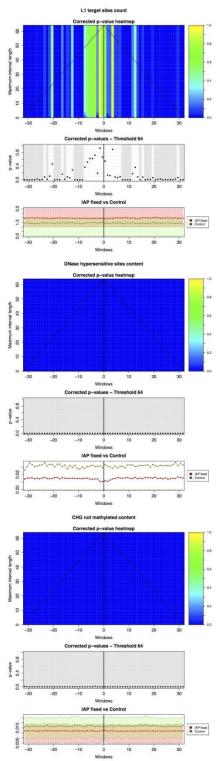


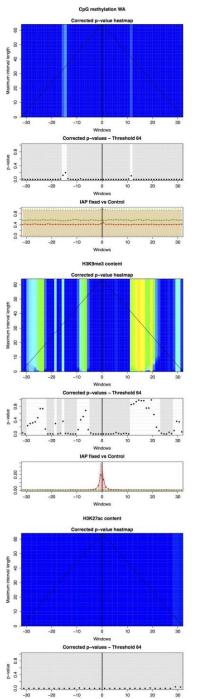
C)

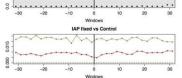


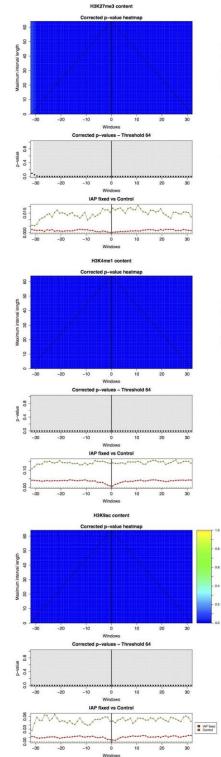


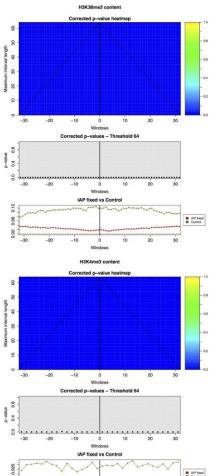


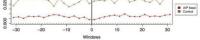




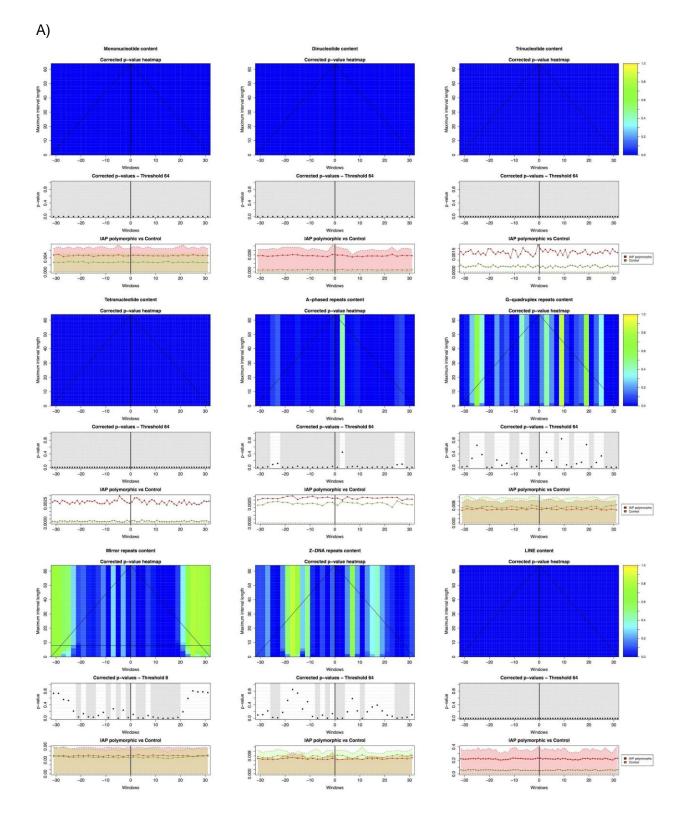


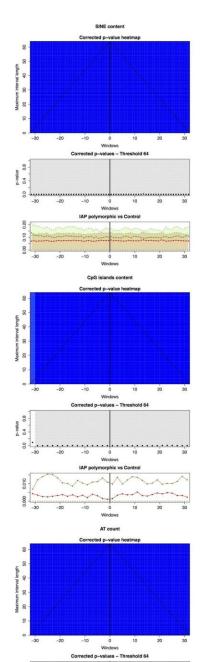






**Figure J.** Significant genomic features for ITP of comparisons polymorphic IAP vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.





0 Windows

IAP polymorphic vs Control

10 20

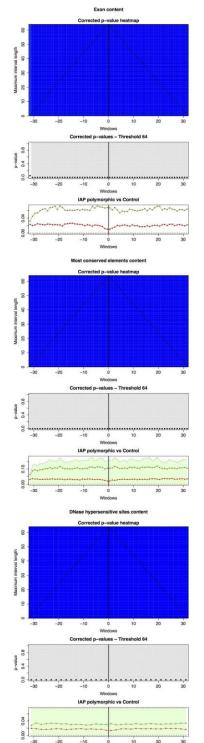
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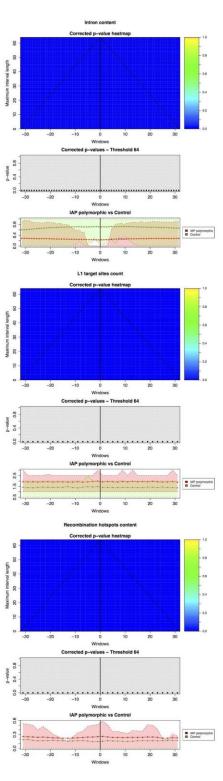
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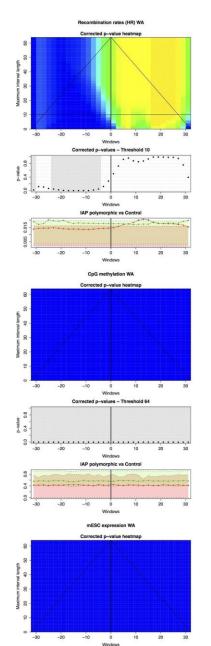
620

500 560

-30







Corrected p-values - Threshold 64

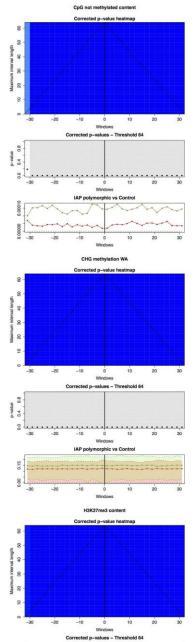
-10 0 Windows 10 20

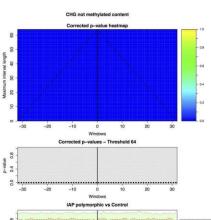
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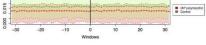
p-value 0.4 0.8

p-value 0.4 0.8

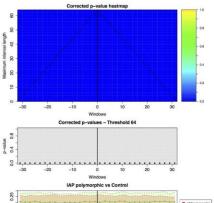
3

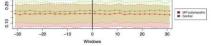


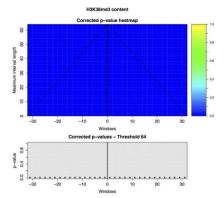


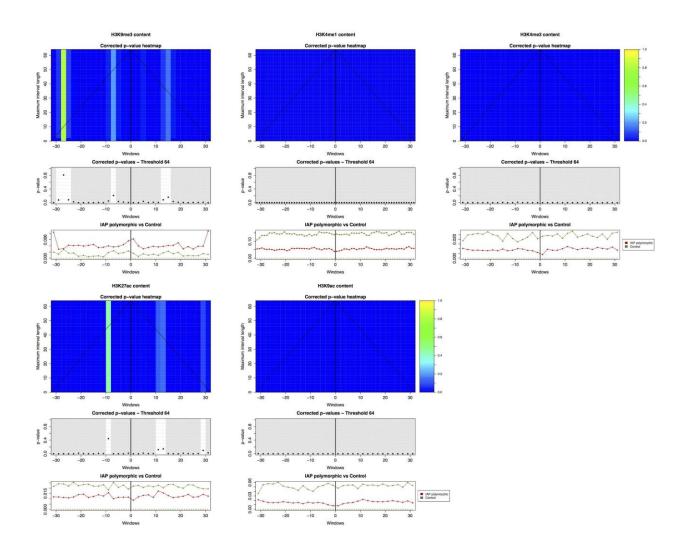


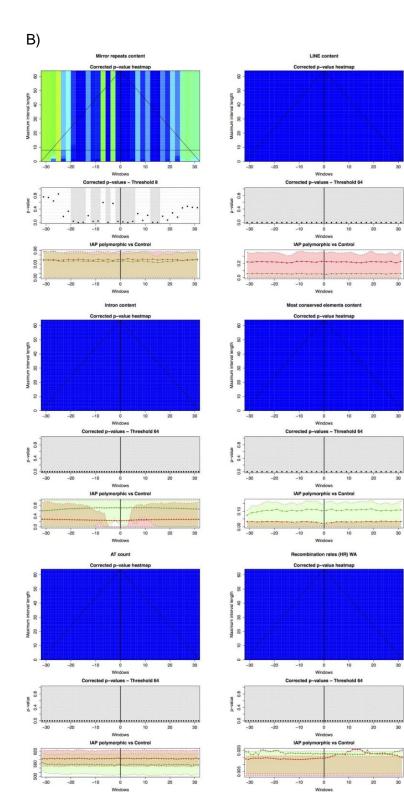


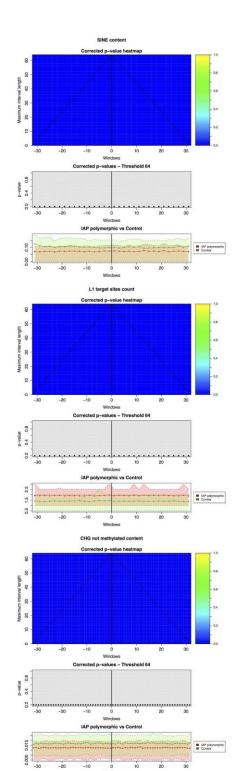


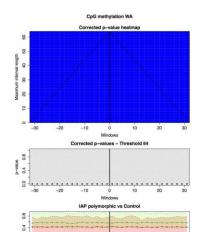






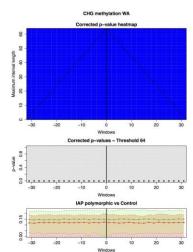


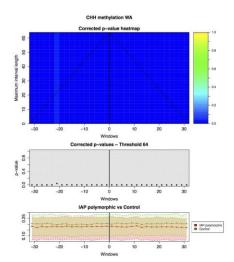


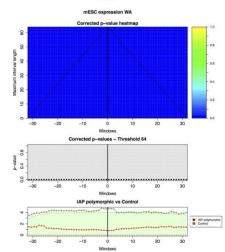


0.0

-30 -20 -10 0 10

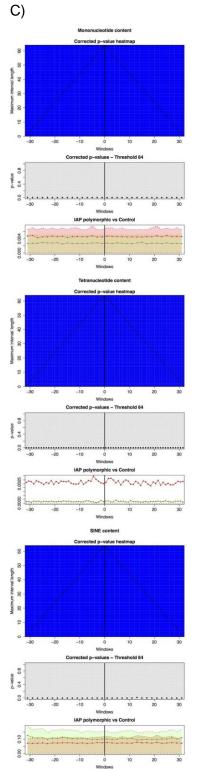


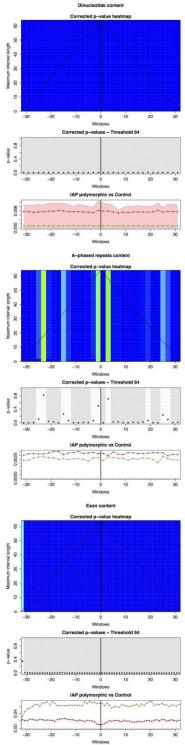


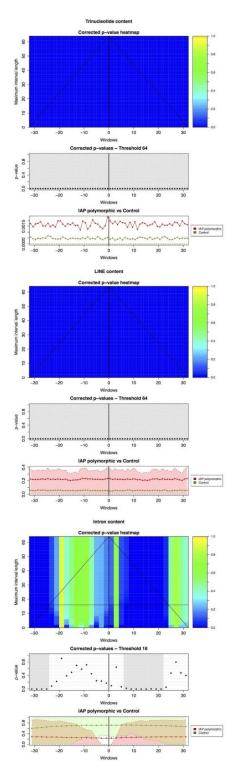


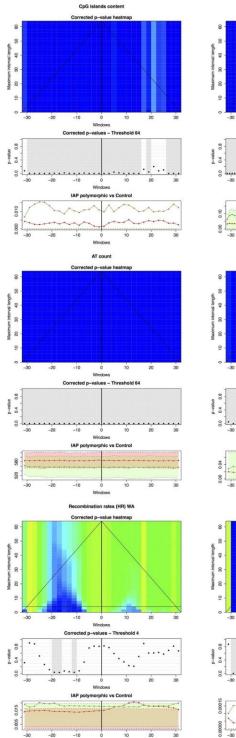
Windows

20

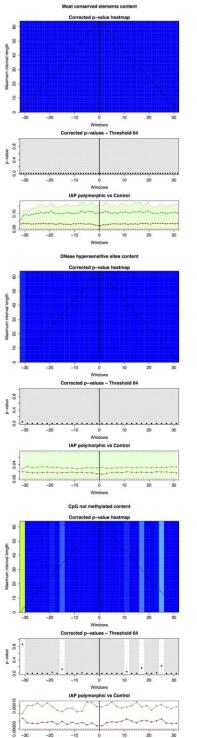


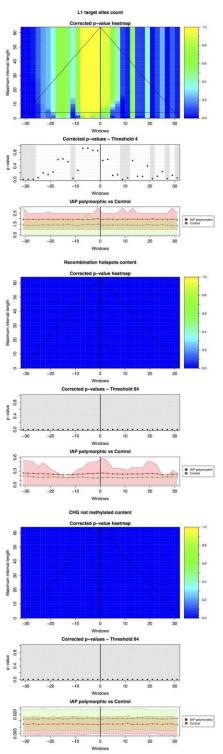


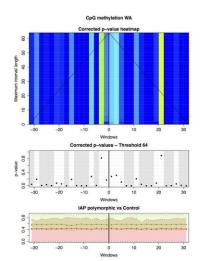




-10







H3K36me3 content

Corrected p-value heatmap

-10 0 10 Windows

Corrected p-values - Threshold 64

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AP polymorphic vs Control

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09

Maximum interval length 20 30 40 50

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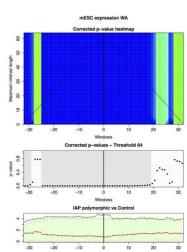
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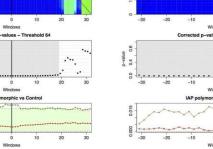
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0.06

0.0

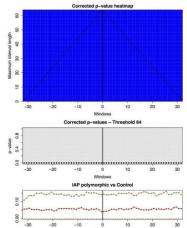
-20 -10





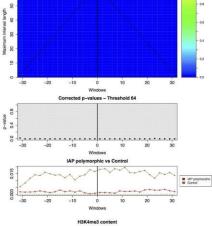
09



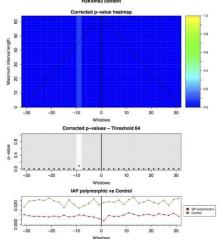


Windows

H3K9ac content

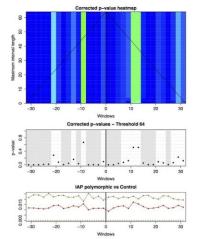


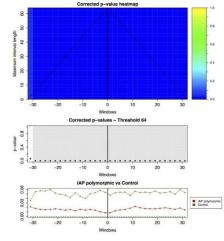
H3K27me3 content Corrected p-value heatmap



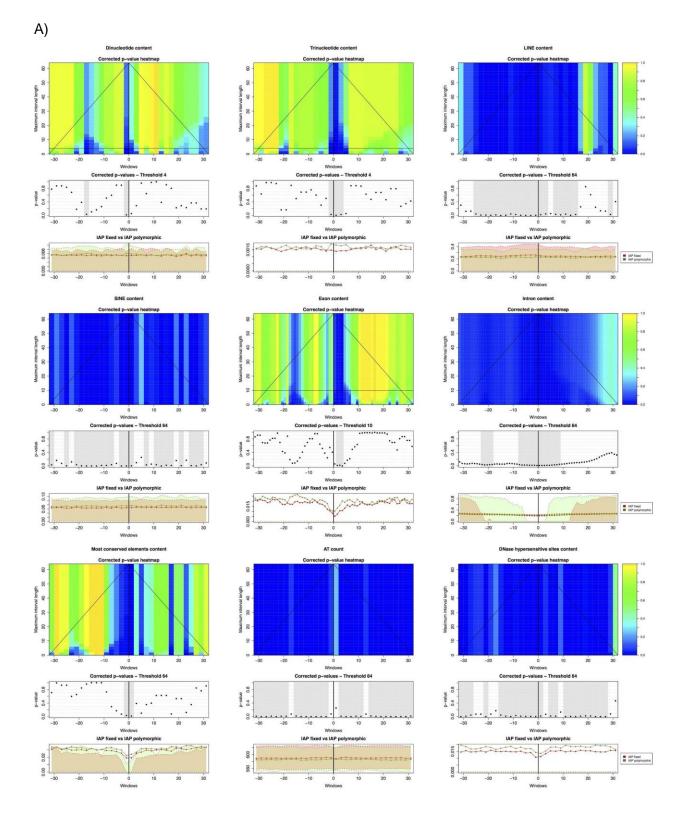


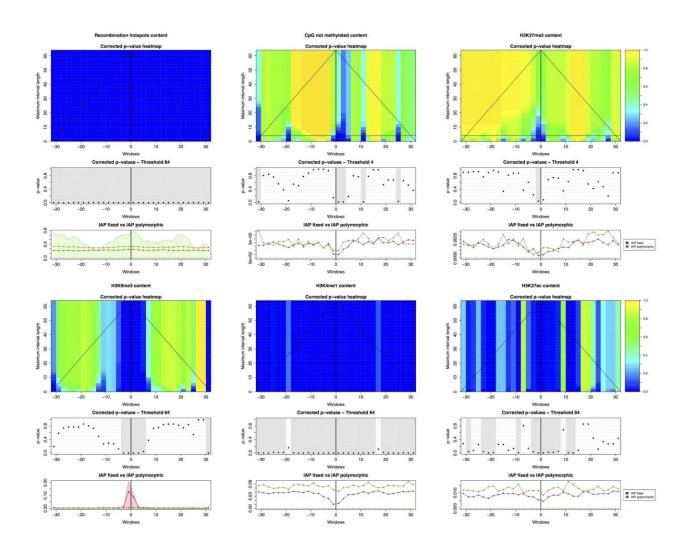
10 20 30

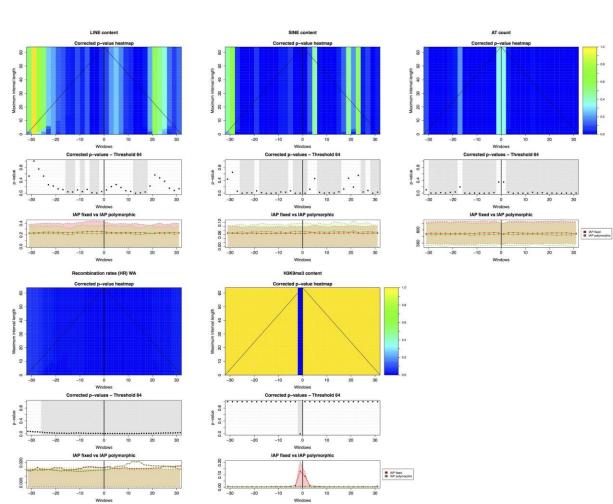




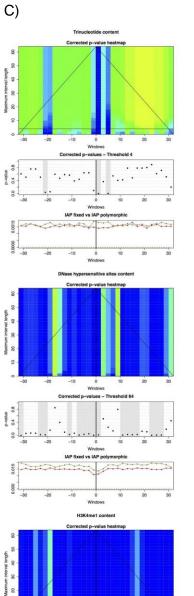
**Figure K.** Significant genomic features for ITP of comparisons fixed vs. polymorphic IAP with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.







B)



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p-value

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-10

Windows Corrected p-values - Threshold 64

0 Windows

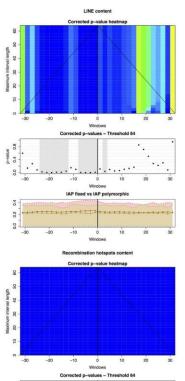
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IAP fixed vs IAP poly 

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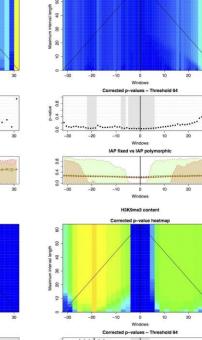
p-value 0.4 0.8

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8 1<mark>....</mark> -30

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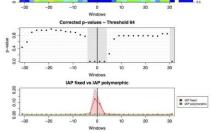
Intron content

ted p-value I

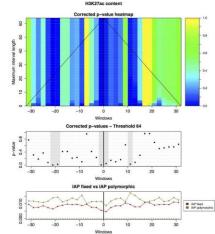
30

30

IAP fixed
 IAP polymorphic



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IAP fixed vs IAP polymorphic

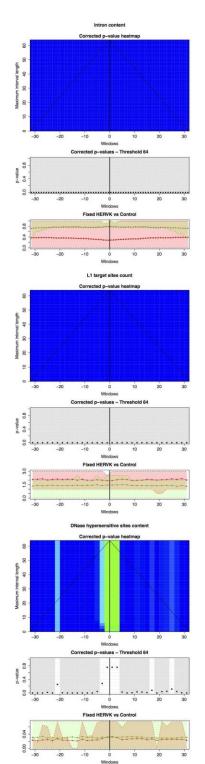
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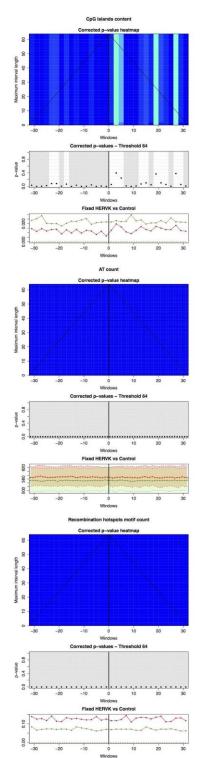
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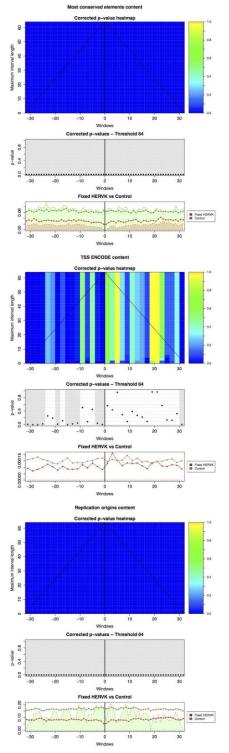
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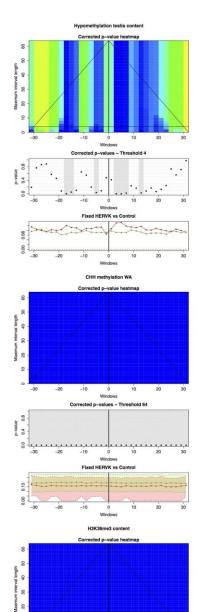
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**Figure L.** Significant genomic features for ITP of comparisons fixed HERV-K vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.









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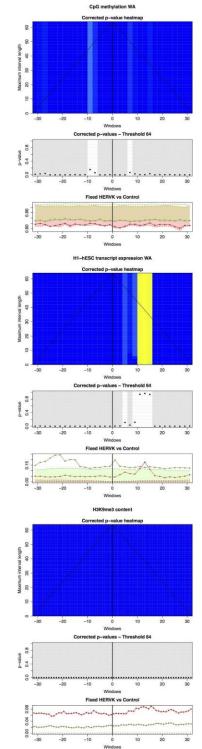
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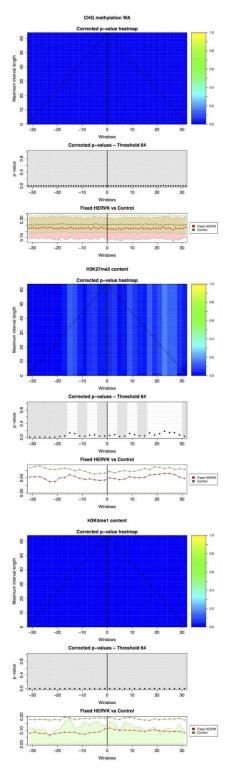
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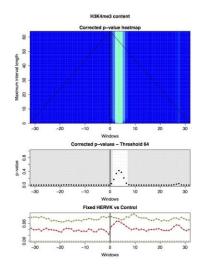
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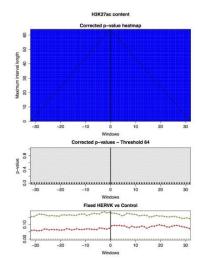
Fixed HERVK vs Control

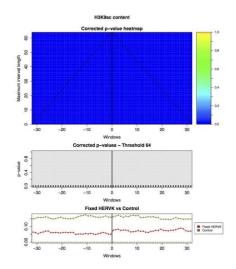
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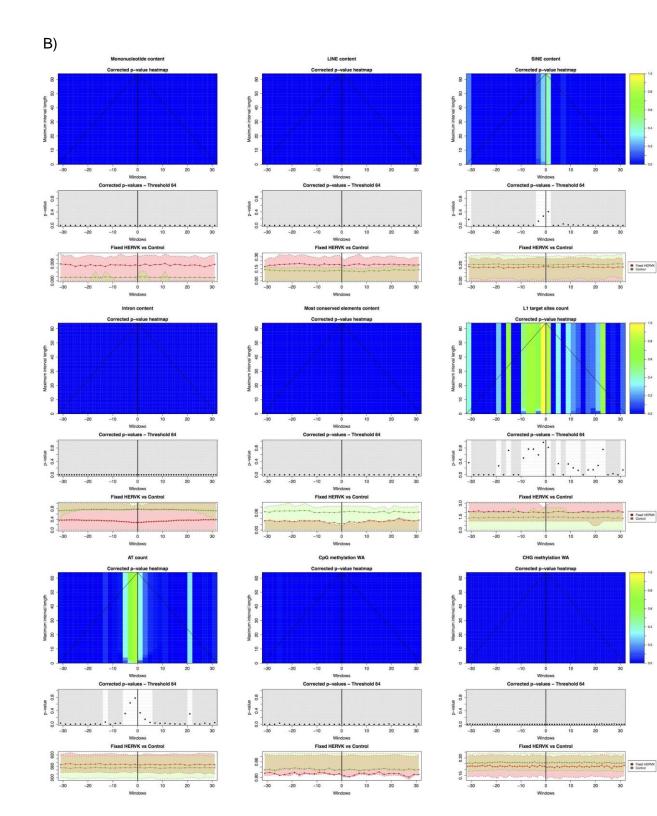




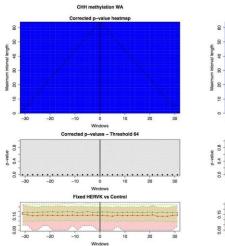


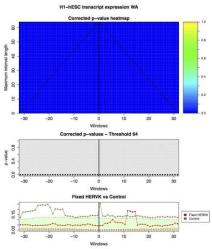


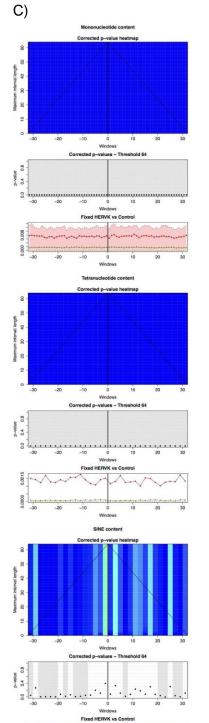




Fixed HERVK







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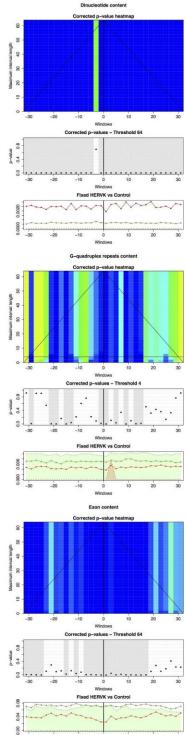
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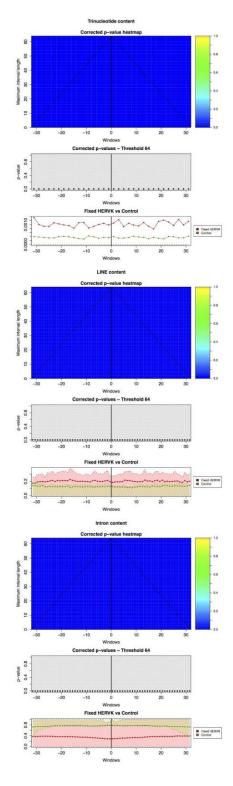
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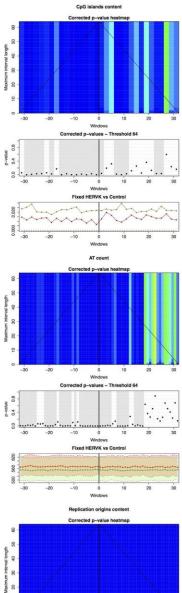
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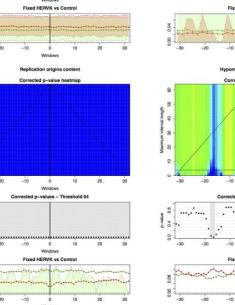
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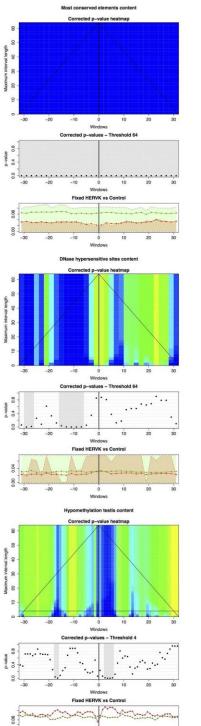
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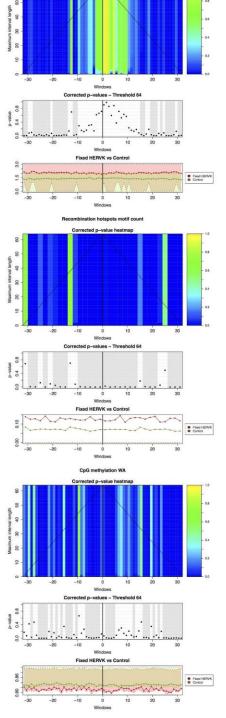
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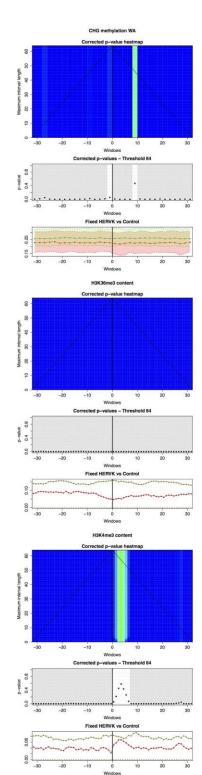


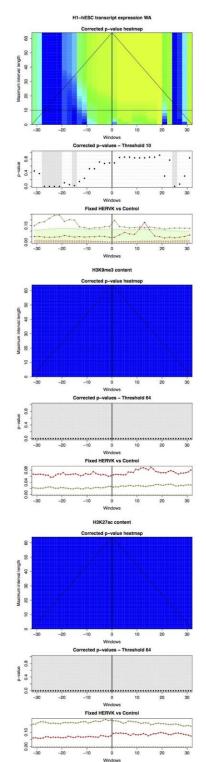
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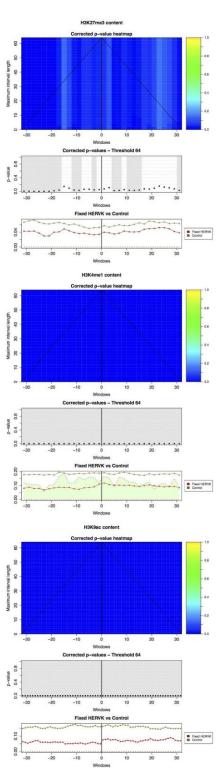
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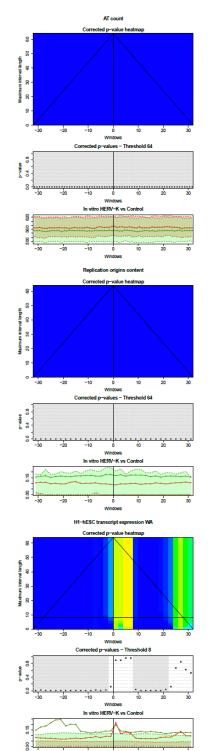


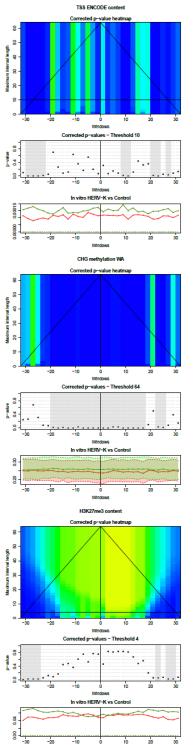


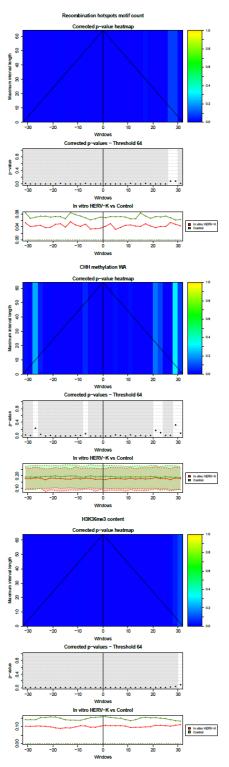


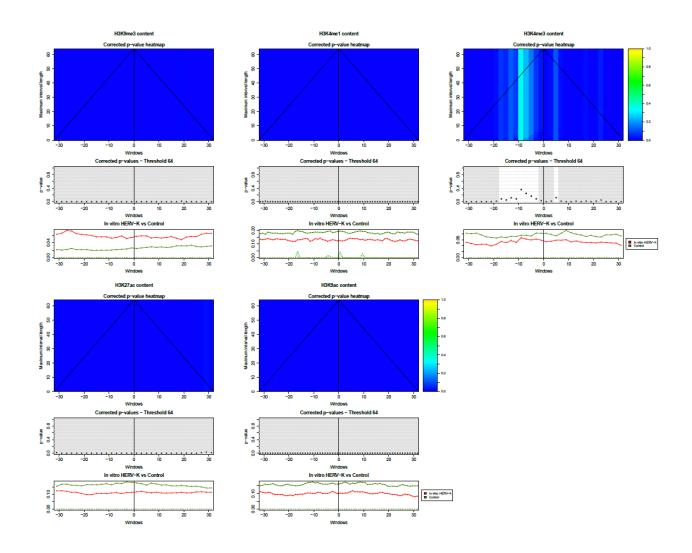
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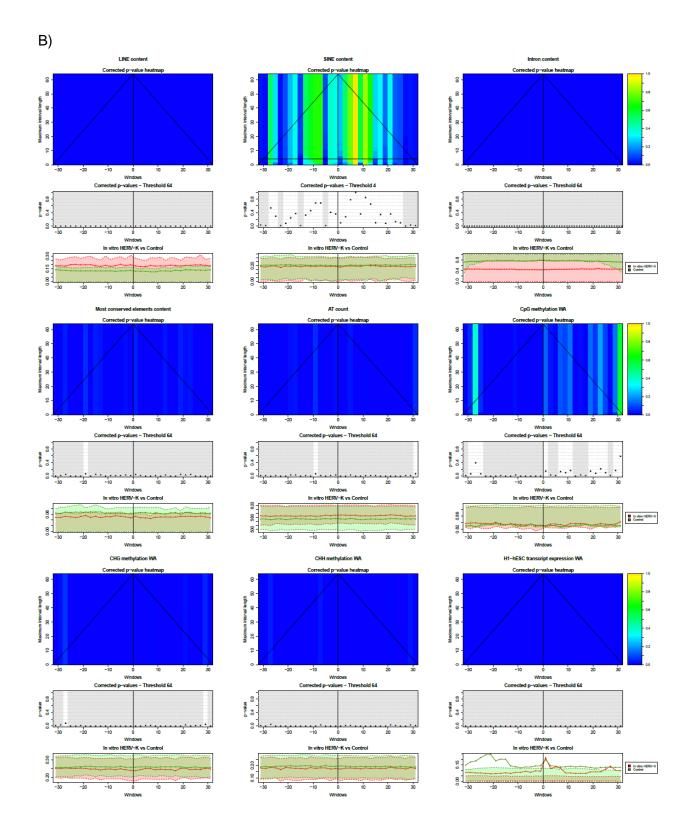
**Figure M.** Significant genomic features for ITP of comparisons *in vitro* HERV-K vs. control with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.

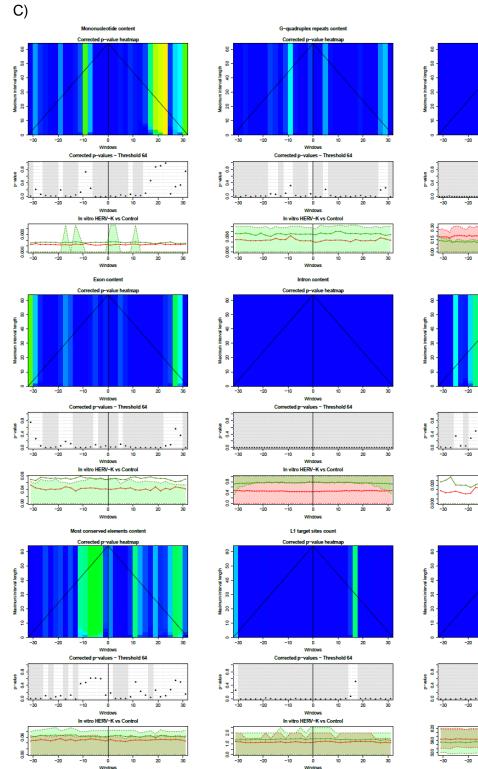


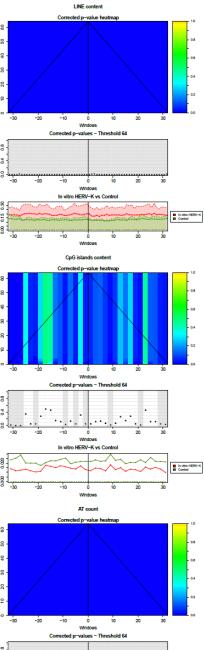


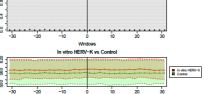


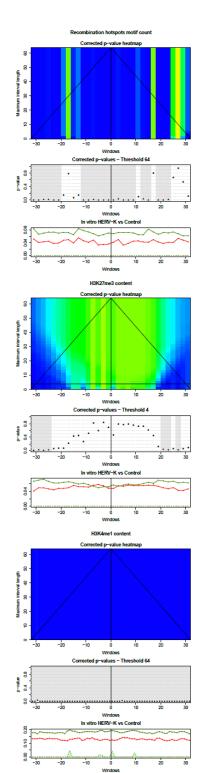


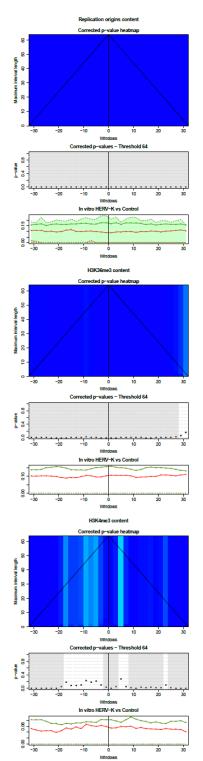


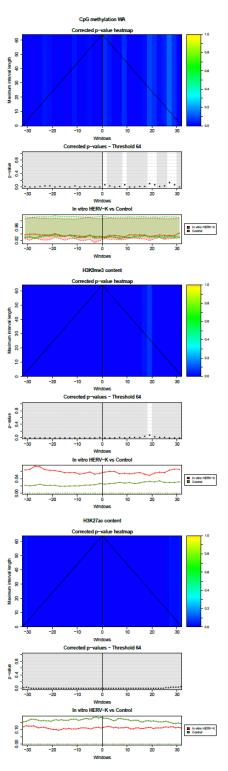


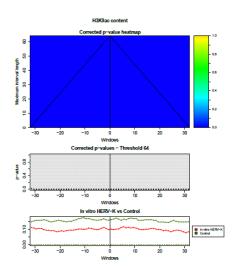




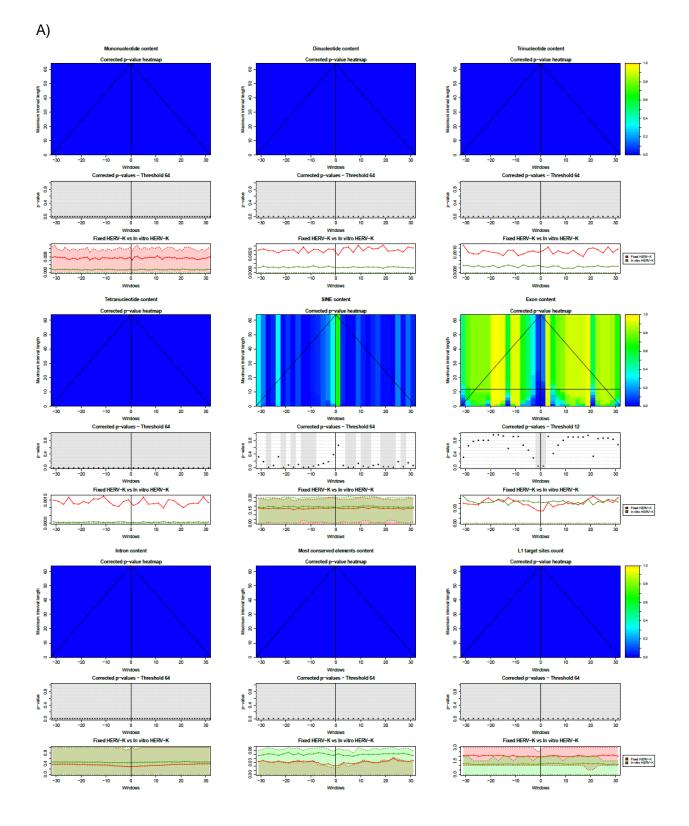


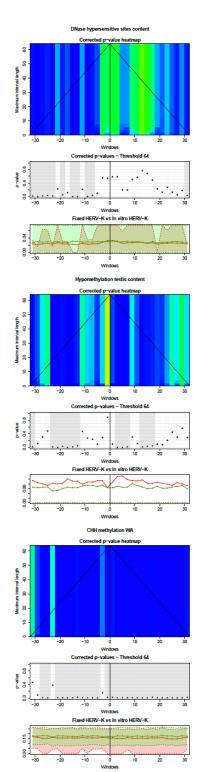


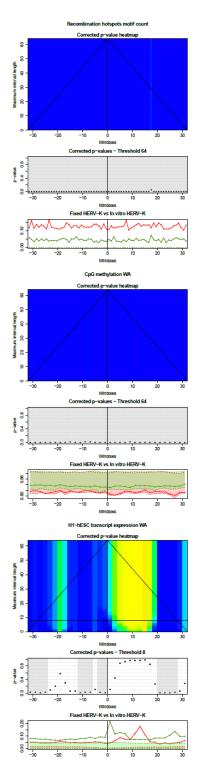


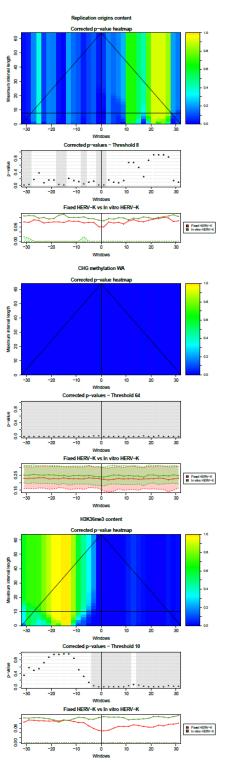


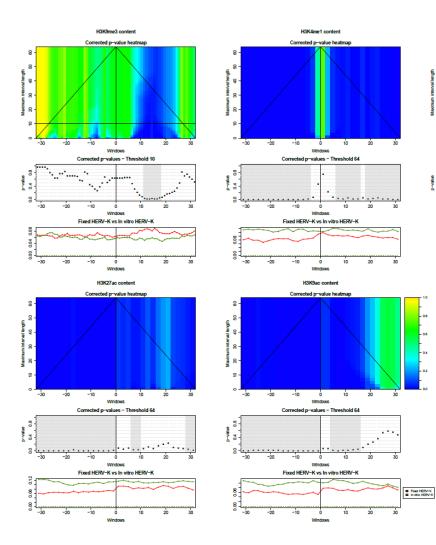
**Figure N.** Significant genomic features for ITP of comparisons fixed vs. *in vitro* HERV-K with test statistics: A) sample mean difference, B) sample median difference, C) sample variance ratio.

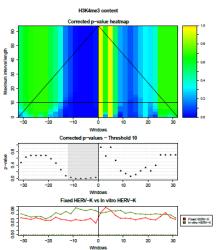


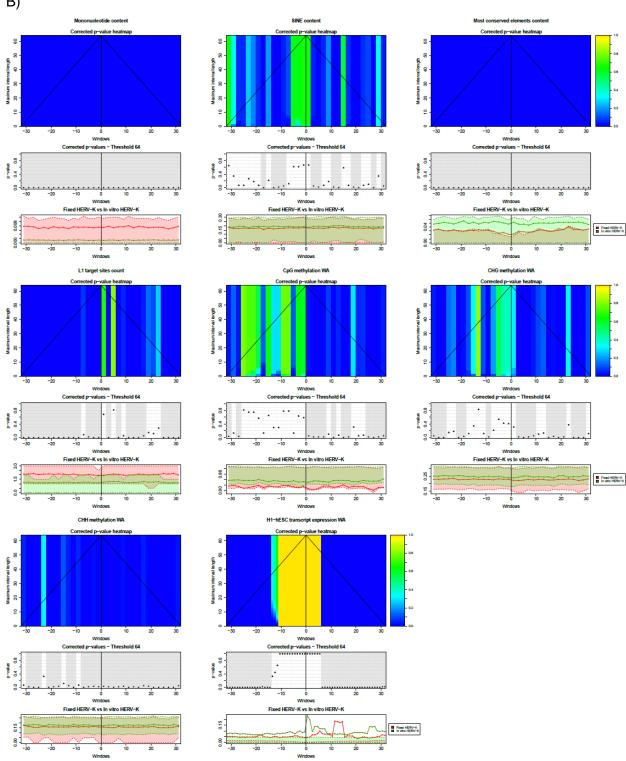








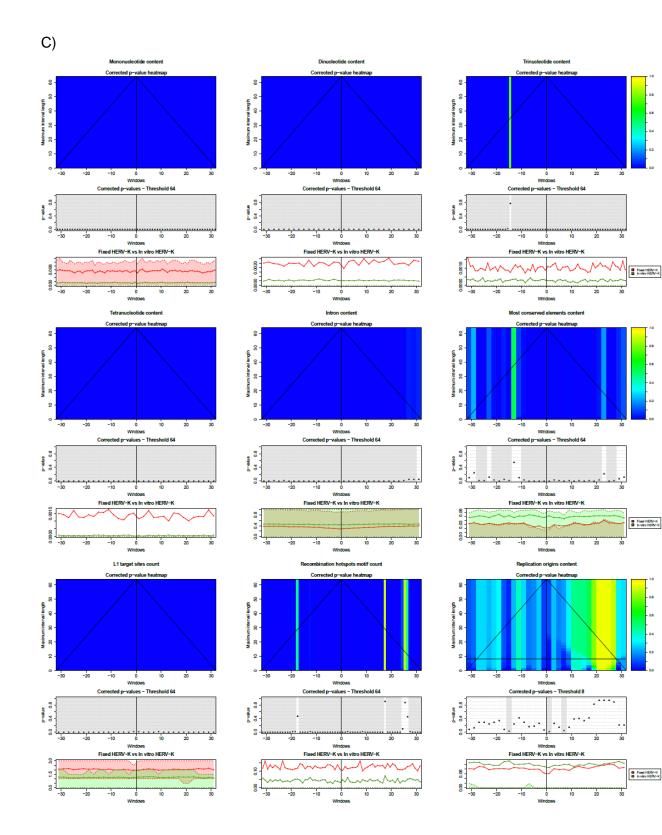




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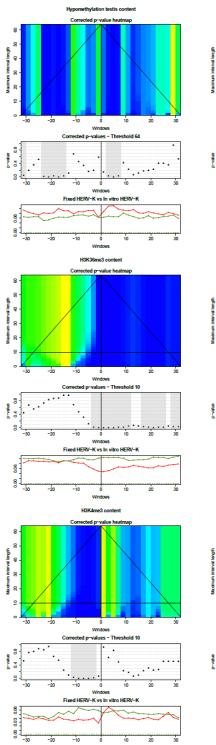


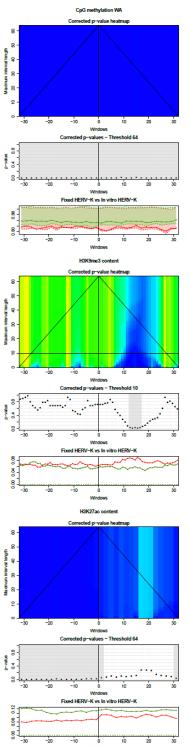
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Fixed HERV-K In vitro HERV-K

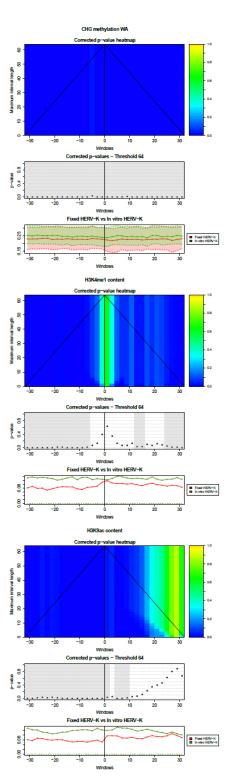
Fixed HERV-K
In vitro HERV-K





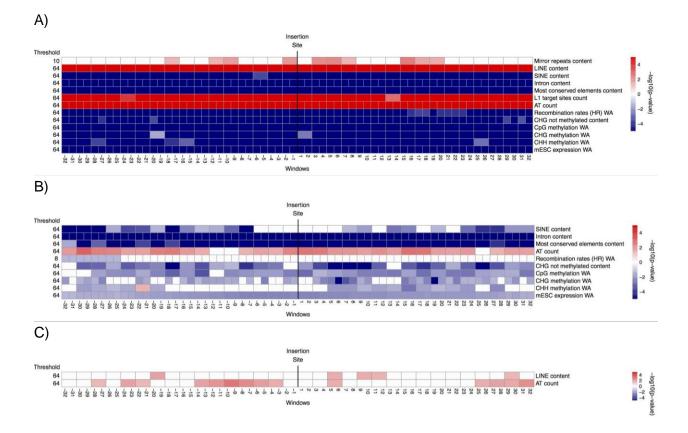
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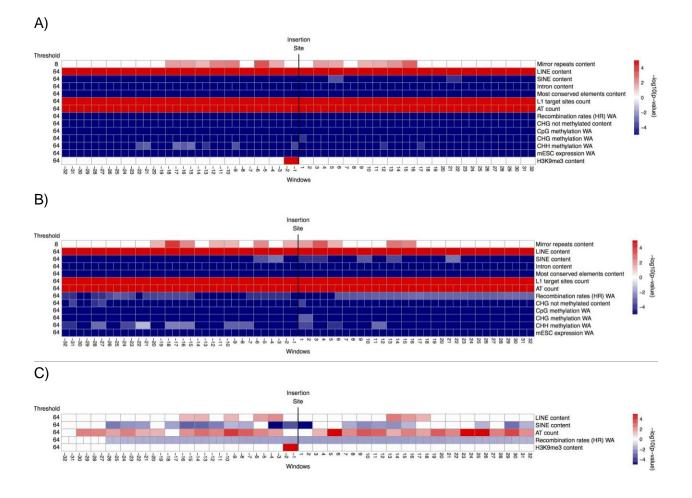
**Figure O.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **median** difference as test statistics: (A) fixed ETns vs. controls, (B) polymorphic ETns vs. controls, and (C) fixed vs. polymorphic ETns. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

White cells: not significant (p-value >0.05), red cells: significant with higher median in the flanking regions of ETns vs. controls (or in the flanking regions of fixed vs. polymorphic ETns), blue cells: significant with lower median in the flanking regions of ETns vs. controls (or in the flanking regions of fixed vs. polymorphic ETns). Color intensity is proportional to significance (more intense colors correspond to lower corrected p-values).



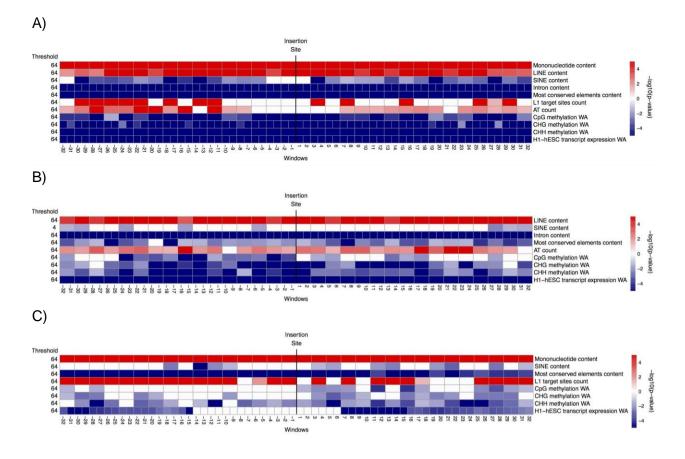
**Figure P.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **median** difference as test statistics: (A) fixed IAPs vs. controls, (B) polymorphic IAPs vs. controls, and (C) fixed vs. polymorphic IAPs. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

White cells: not significant (p-value >0.05), red cells: significant with higher median in the flanking regions of IAPs vs. controls (or in the flanking regions of fixed vs. polymorphic IAPs), blue cells: significant with lower median in the flanking regions of IAPs vs. controls (or in the flanking regions of fixed vs. polymorphic IAPs). Color intensity is proportional to significance (more intense colors correspond to lower corrected p-values).



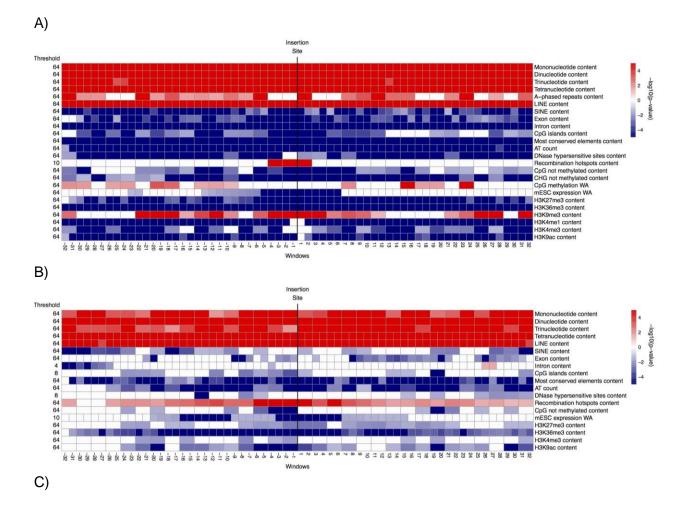
**Figure Q.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **median** difference as test statistics: (A) fixed HERV-Ks vs. controls, (B) *in vitro* HERV-Ks vs. controls, and (C) fixed vs. *in vitro* HERV-Ks. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

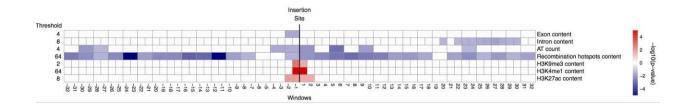
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**Figure R.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **variance** difference as test statistics: (A) fixed ETns vs. controls, (B) polymorphic ETns vs. controls, and (C) fixed vs. polymorphic ETns. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

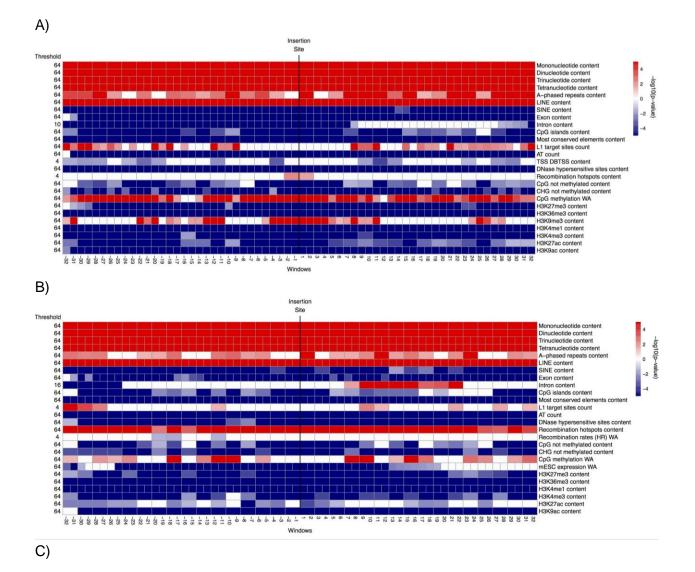
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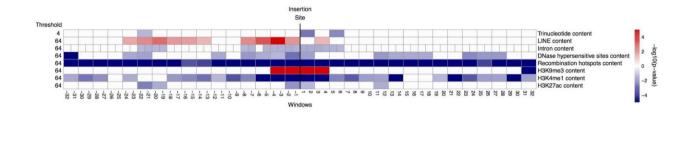




**Figure S.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **variance** difference as test statistics: (A) fixed IAPs vs. controls, (B) polymorphic IAPs vs. controls, and (C) fixed vs. polymorphic IAPs. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

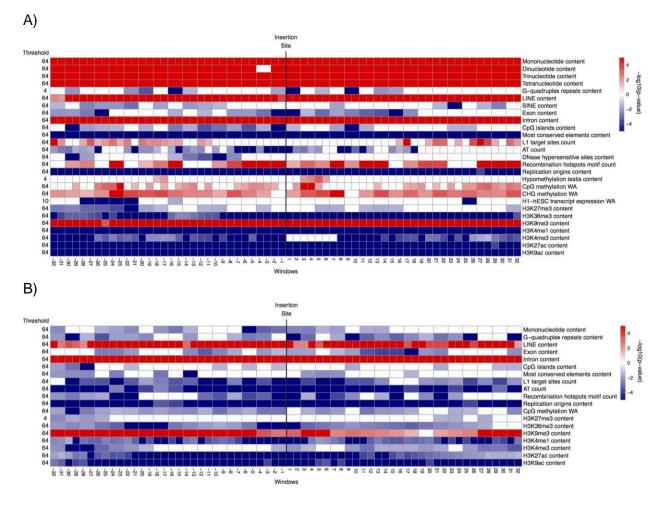
White cells: not significant (p-value >0.05), red cells: significant with higher variance in the flanking regions of IAPs vs. controls (or in the flanking regions of fixed vs. polymorphic IAPs), blue cells: significant with lower variance in the flanking regions of IAPs vs. controls (or in the flanking regions of fixed vs. polymorphic IAPs). Color intensity is proportional to significance (more intense colors correspond to lower corrected p-values).





**Figure T.** Significance (i.e. -log10(corrected p-value)) of genomic features in windows along the flanking regions, obtained from the ITP using the **variance** difference as test statistics: (A) fixed HERV-Ks vs. controls, (B) *in vitro* HERV-Ks vs. controls, and (C) fixed vs. *in vitro* HERV-Ks. In each panel, the horizontal axis represents the 64 1-kb windows. The vertical black line between window -1 kb and 1 kb marks the integration site. The thresholds reported on the left represent the maximum scale at which each feature is significant, ranging from 64 kb (coarsest) to 1 kb (finest). Each row corresponds to one feature and each cell represents one or two contiguous windows, depending on the number of nodes employed in the B-splines (we consider one value for every 1-kb window when using the raw data, and one value every two 1-kb windows when using the piecewise constant smoothed version of the data).

White cells: not significant (p-value >0.05), red cells: significant with higher variance in the flanking regions of HERV-Ks vs. controls (or in the flanking regions of fixed vs. *in vitro* HERV-Ks), blue cells: significant with lower variance in the flanking regions of HERV-Ks vs. controls (or in the flanking regions of fixed vs. *in vitro* HERV-Ks). Color intensity is proportional to significance (more intense colors correspond to lower corrected p-values).



C)

