Table 6.4: Linear regression statistics performed when genome features were plotted versus histone enrichment levels. For the probability of expression statistics clones were clustered in groups of 20 and analysed as described in 6.2.3.

Histone	Feature	No. of observations	Intercept	Regression coefficient	Correlation coefficient
H3	**GC content (%)**	327	0.755	0.454	0.117
	Gene density	223	0.930	0.001	0.131
	***Alu* content**	223	0.878	0.004	0.246
	LINE content	223	1.022	-0.004	0.166
	Expression level	115	1.026	$4.53x10^{-5}$	0.074
	Prob. of Expression	-	0.872	0.308	0.663
H4	**GC content (%)**	256	0.488	0.776	0.125
	Gene density	166	0.793	0.002	0.204
	***Alu* content**	166	0.683	0.010	0.354
	LINE content	166	1.017	-0.011	0.256
	Expression level	103	0.879	0.0002	0.067
	Prob. of Expression	-	0.791	0.277	0.544

These statistics illustrate very weak correlations between levels of Histone H3 and H4 acetylation and other genome features on chromosome 22. However a stronger correlation can be seen between histone actylation and probability of transcription.

6.4: Study of the Replication Timing of Chromosomal Breakpoints using the Genomic Arrays

6.4.1: Assessment of the replication timing of a t(17q21.1:22q12.2) translocation on the chromosome 22 array.

A replication timing profile was generated for a lymphoblastoid cell line with a translocation between chromosomes 17 and 22 to investigate if the translocation affected the replication timing profile. The location of the chromosomal breakpoints had already been mapped by other members of the laboratory (Fiegler, Gribble et al. 2003), and the breakpoint on chromosome 22 had been located at approximately 11.5Mb along the q arm within clone bA46E17. The replication timing profile of

chromosome 22 was assessed on the tile path array. The average standard error of the points on the three replicates was 5.9%. The replication timing profile is shown in Figure 6.12.

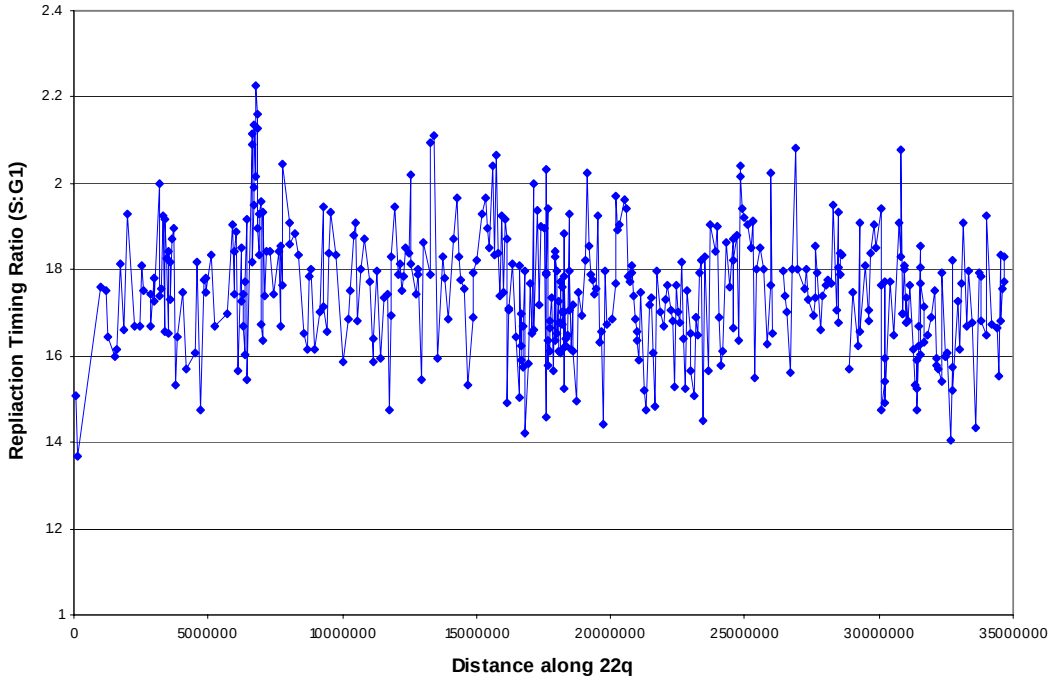

Figure 6.12: Replication timing profile of the 22 clones on the translocated cell line

The chromosome 22 replication profile for a normal lymphoblastoid cell line is described in section 5.3.1.

Comparison of the two replication timing profiles, illustrated in Figure 6.13 for the translocation and a normal cell line showed three differences. Firstly, six regions can be seen as having replication timings clearly different from the normal replication profile. The first of these is close to the breakpoint, about 430Kb (5 clones) downstream. Secondly, the data obtained from the translocated cell line displayed more local variation, with more points closer to 1:1 and 2:1, than that obtained from the normal cell line and thirdly, there are more data points over the hypothetical maximum ratio of 2:1, this is particularly noticeable at the VJ recombination region.

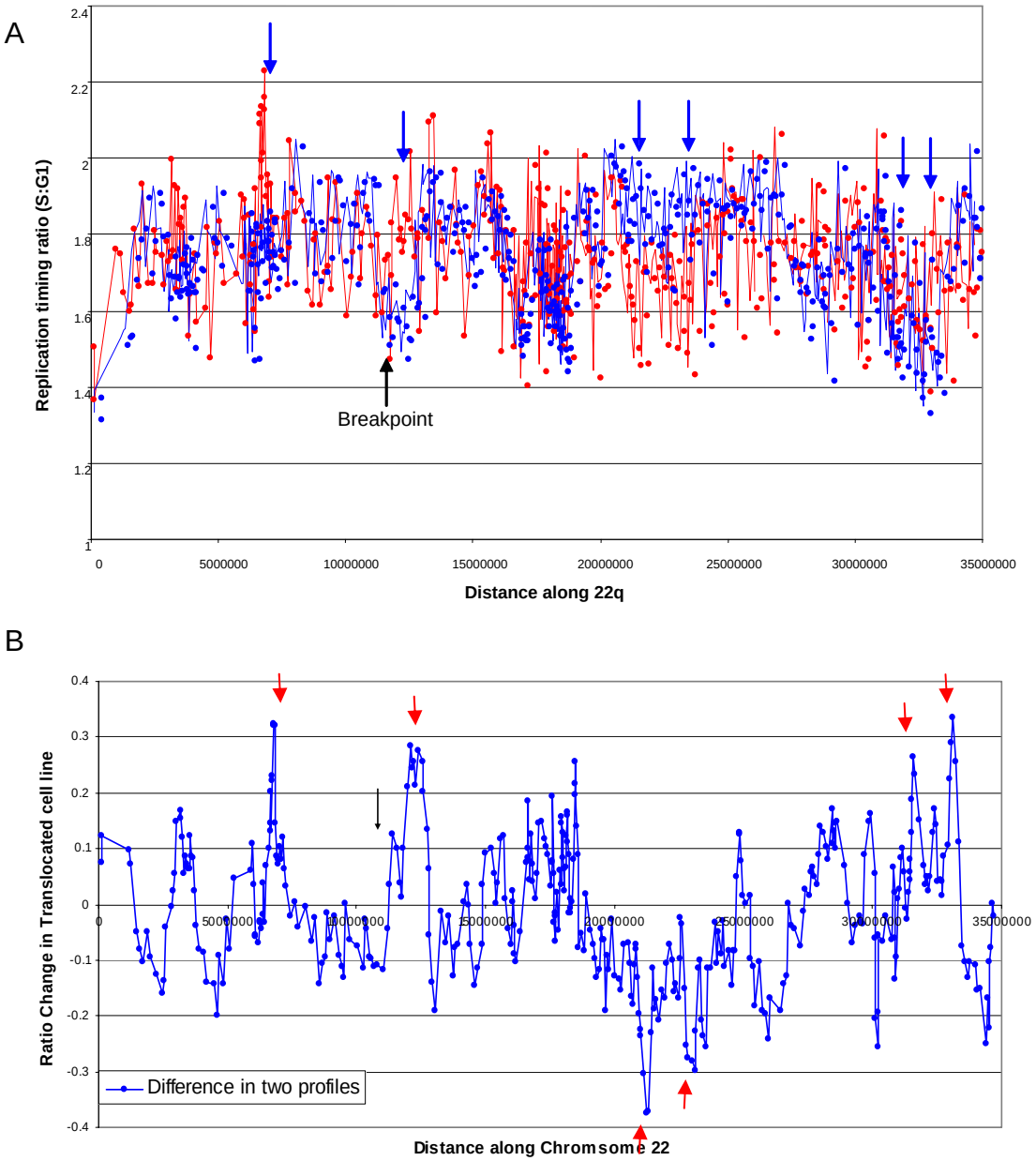

Figure 6.13: A: Comparison of the replication timing profile from a normal lymphoblastoid cell line and a lymphoblastoid cell line with a translocation between chromosomes 17 and 22. Blue: Replication profile from a normal cell line. Red: Replication profile from a translocated cell line. The breakpoint on chromosome 22 is indicated by the black arrow. Regions where there are significant changes in replication timing between the two regions are highlighted with blue arrows. B: The difference in replication timing between the translocated cell line and the normal cell line. The breakpoint is shown by the black arrow. Regions with 3 or more clones showing a greater than 0.2 difference (5 x standard deviation of a self:self