Supplementary data for

DNA damage and Repair Modify DNA methylation and Chromatin Domain of the Targeted Locus.

Mechanism of allele methylation polymorphism

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Supplemental Methods

Cell culture, transfections and plasmids. Transfection efficiency was measured by assaying β-galactosidase activity of an included pSVbGal vector (Promega). Normalization by FACS was performed using antibodies to β-gal or pCMV-DsRed-Express (Clontech). pEGFP (Clontech) was used as GFP control vector.

Vectors. pDR-GFP plasmid was 14,735 bp containing (see Fig. 2): CMV IE enhancer (1–385); chicken beta actin promoter (386-751); chicken beta-actin first intron (752-1,622); rabbit beta-globin second intron (1,623-1,670); rabbit beta-globin third exon (1,671-1,724); EGFP with a STOP (7) codon at I-SceI site (1,740-2,756, I-SceI at 2,135); SV40 splice/polyadenylation signal (2,757-3,023); polyadenylation signal from phosphoglycerate kinase gene (3,025-3,607) for the puromycin resistance gene (3,600-4,200); a truncated EGFP gene sequence (5,609-6,138); and 6,450 bp of mouse genome *(6 and A. Porcellini, unpublished data)*.

siRNA against TDG: cat.# SR304768; OriGene Technologies, Inc., USA

shRNA of APE1 and APE1WT plasmids: The following oligonucleotides were used for the short hairpin RNA (shRNA) of APE1: sense, 5'-GATCCCC <u>CCTGCCACACTCAAGATCTGC</u>TTCAAGAGA<u>GCAGATCTTGAGTGTGGCA</u> GGTTTTTGGAAA-3'; and antisense, 5'-AGCTTTTCCAAAAA<u>CCTGCCACA CTCAAGATCTGC</u>TCTCTTGAAG<u>CAGATCTTGAGTGTGGCAGGGGG</u>-3'. These sequences were drawn following the empirical rules of Mittal *(Mittal, V. 2004)* and were designed to recognize and bind to a 21-base sequence (underlined) placed 175 nucleotides after the AUG initiation codon of the APE1 gene. As a control, we used the following scrambled oligonucleotide sequences: sense, 5'-GATCCCCAGTCTAACTCGCCACCCCGTATTCAAGA GATACGGGGGTGGCGAGTTAGACTTTTTTGGAAA-3'; antisense, 5'-AGCTT TTCCAAAAAGTCTAACTCGCCACCCCGTATCTCTTGAATACGGGGGTGG CGAGTTAGACTGGG-3'. These sequences were checked with BLAST (http://www.ncbi.nlm.nih.gov/blast/) for their inability to pair with any human cDNA sequence. The sequences were cloned into Bgl II and Hind III restriction sites of pSUPER vector (Oligoengine) to form the so-called pSUPER-APE1 vector.

The pFLAG-CMV-5.1/APE1-M2 expression vector was generated by modifing the pFLAG-CMV-5.1/APE1 *(Vascotto et al. 2009)*. To avoid the degradation of the ectopic APE1 mRNA by the specific siRNA sequence described above, two nucleotides of the APE1-cDNA coding sequence were mutated with site-directed mutagenesis kits (Stratagene), leaving the APE1 amino acid sequence unaffected: siRNA, 5'-CCTGCCACACTCAAGATCTGC-3'; and APE1, 5'-CCTGCAACGCTCAAGATCTGC-3'.

The expression vectors for OGG1WT ad for the K338R/K341R OGG1 mutant was the FLG-Tagged vectors previously described by Bhakat *(31)*.

RNA and DNA extraction. Total RNA was extracted using Triazol (Gibco/Invitrogen). Genomic DNA extraction was performed with following protocol: cellular pellet was resuspended in 10 mM TRIS (pH 7.8) and 50 mM NaCl solution (2×10^7 cells/ml). After addition of 1% SDS the sample was gently mixed. Proteinase K, at a final concentration of 200 µg/ml, was added

and the mixture was incubated at 55 °C overnight. The following day, hot NaCl solution (70 °C) was added to the mixture at final concentration of 1.5 M and the DNA was extracted by chloroform. DNA was ethanol precipitated, dried, and resuspended in TE buffer. Total RNA was extracted using TRIzol (Gibco/Invitrogen). cDNA was synthesized in a 20 µl reaction containing 1 µg of total RNA, 100 U of Superscript III Reverse Transcriptase (Invitrogen), and 2 µl random hexamer (20 ng/µl) (Invitrogen). mRNA was reverse-transcribed for 1 h at 50 °C, and the reaction was heat inactivated for 15 min at 70 °C. The products were stored at-20 °C.

Antibodies used for the experiments. Pol II 05-623 (Upstate); H3K4me2 ab32356 (Abcam); H3K4me3 ab1012 (Abcam); H3K9me2 ab1220 (Abcam); H3K9me3 ab8898 (Abcam); Total H3 ab1791 (Abcam); APE1 ab-194 (Abcam); Anti-5-methylcytosine (5-mC) antibody [EP4694] ab124936 (Abcam); GAPD ab9482 (Abcam); TDG sc-292440 (Santa Cruz Biotechnology); MCM7 sc-9966 (Santa Cruz Biotechnology); Normal rabbit IgG sc-2027 (Santa Cruz Biotechnology); Normal mouse IgG sc-2025 (Santa Cruz Biotechnology).

Chromatin Immuno-Precipitation (ChIP). Cells were transfected and/or treated as indicated in the legends of the figures. The cells (~2.5 x10^6 for each antibody) were fixed for 10 min at room temperature by adding 1 volume of 2% formaldehyde to a final concentration of 1%; the reaction was quenched by addition of glycine to a final concentration of 125 mM. Fixed cells were harvested and the pellet was resuspended in 1 ml of Lysis Buffer (See Below) containing 1X protease inhibitor cocktail (Roche Applied Science). The lysates were sonicated to have DNA fragments 300 to 600 bp. Sonicated samples were centrifuged and supernatants diluted 2 fold in the ChIP Buffer (See Below). An aliquot (1/10) of sheared chromatin was further treated with proteinase K, extracted with phenol/chloroform and precipitated to determine DNA concentration and shearing efficiency (input DNA). The ChIP reaction was set up according to the manufacturer's instructions. Briefly, the sheared chromatin was precleared for 2 h with 1 µg of non-immune IgG and 20 µl of Protein A/G PLUS-Agarose (Santa Cruz Biotechnology) saturated with salmon sperm (1 mg/ml). Precleared chromatin was divided in aliquots and incubated at 4 °C for 16 h with 1 µg of the specific antibody (see above) and non-immune IgG respectively. The immuno-complexes were recovered by incubation for 3 h at 4 °C with 20 µl of protein-A/G agarose, beads were washed with wash buffers according to the manufacturer's instructions and immunoprecipitated DNA was recovered and subjected to qPCR using the primers indicated in the legend of the specific figures, primers sequences are described in Supplemental Table S1.

Chromosome conformation capture (3C). The actual position of oligonucleotides and Hae III restriction sites are shown in Figs. 3A and 3BB.
A total of 5x10^6 cells were crosslinked in 20 ml of serum-free medium with 1% formaldehyde for 10 min at room temperature. The reaction was quenched by the addition of glycine to a final concentration of 125 mM. Fixed cells were harvested and the pellet resuspended in 0.5 ml of ice cold lysis buffer (10 mM Tris pH 8.0, 10 mM NaCl, 0.2% NP40 and protease inhibitors),

and incubated on ice for 15 min. Nuclei were washed with 0.25 ml of restriction enzyme buffer and pelleted. Nuclei were then resuspended in 180 µl of restriction enzyme buffer. SDS was added to a final concentration of 0.1%, and nuclei were incubated at 37 °C for 15 min. Triton X-100 was then added to the final concentration of 1% to sequester SDS. Digestion was performed with 150 U of restriction enzyme at 37 °C for 16 h. The restriction enzyme was inactivated by the addition of SDS to 2% and incubation at 65 °C for 30 min. The reaction was diluted into 4 ml ligation reaction buffer containing 50 U of T4 DNA Ligase (Roche Applied Science). Ligations were incubated at 16 °C for 18 h. EDTA (to a concentration of 10 mM) was added to stop the reactions. Samples were treated with Proteinase K (200 µg/ml) and incubated for 2 h at 50 °C, and then overnight at 65 °C to reverse the formaldehyde crosslinks. The following day, the DNA was purified by phenol/chloroform extraction and ethanol precipitation. Samples were redissolved in 20 µl of TE buffer. To prepare a control template, we used pDR-GFP plasmid. Five micrograms of plasmid DNA were digested with Hae III in 50 µl of 1x buffer for 8 h at 37 °C and then ligated in 20 µl with 5 U of T4 Ligase at 16 °C for 4 h. The efficiency of digestion after the entire 3C treatment was quantified by realtime PCR, amplifying a fragment spanning two Hae III sites (uncut) in different 3C DNA preparations. A total of 35 rounds of PCR amplification were used. The efficiency of ligation was assayed as follow: a linear Hind III-digested pUC18 plasmid was added to all the preparations before ligation. The ligated plasmid was quantified by real-time PCR, amplifying a fragment spanning the Hind III site (M13/pUC Forward and Reverse primers were used). An appropriate amount of DNA that would amplify within the linear range was subsequently used for the experiments. The efficiency of digestion was quantified by realtime PCR, amplifying three fragments spanning three different Hae III sites. The presence of the amplified products indicated the efficiency of digestion, and was expressed as ratio between cleaved/un-cleaved band. Experiments with a cutting Ratio >0.03 (ΔCT≥4, 97% digestion) were discarded. Primers *m* and *e*; *p* and *Rec2* and *Sce/Bcg* and *q* were used.

Bisulfite treatment and amplicon library preparation. 2 µg of genomic DNA were converted with "C/T conversion reagent" according EZ DNA Methylation Kit (Zymo Research, USA) and eluted in 50 µl of H_2O following the manufacturer's instruction. We generated an amplicon library of bisulfite treated DNA using a double step PCR strategy. In the first PCR reaction, we amplified amplicons ranging in size between 300-450bp (all primers pairs are reported in Supplemental Table S1). The 5' end of these primers contained overhang adapter sequences (Fw: 5'-TCGTCGGCAGCGTCAGATGTGTA TAAGAGACAG-3', RV: 5'-GTCTCGTGGGCTCGGAGATGTGTATAAGAG ACAG-3') that were used in the second step of PCR to add multiplexing indices and illumina sequencing adapters. First PCR products was performed using a "FastStart High Fidelity PCR System"(Roche) at the following thermo cycle condition: one cycle at 95°C for 2 min followed by 30 cycles at 95°C for 30 sec, at TM °C for 40 sec, at 72°C for 60 sec , followed by a final extension step at 72°C for 5 min. Reactions were performed in 30 µl total volumes: 3 µl 10x reaction buffer, 0.6 µl of 10 mM dNTP mix, 1 µl of 4 µM forward and reverse primers, 3.6 µl $MgCl_2$ 25 mM, 2-4 µl bisulfite template DNA, 0.25 µl FastStart Taq, and H_2O up to a final volume of 30 µl. Five microliters of first

PCRs were used to check product size on 1.5% agarose gel. To eliminate small DNA fragments (primers dimers), we used 20 µl of AMPure purification magnetic Beads (Beckman-Coulter, Brea, CA, USA) following the manufacturer's protocol. Second PCR step was performed in 50 µl total volumes: 5 µl 10x reaction buffer, 1 µl dNTP mix, 5 µl forward and reverse "Nextera XT" primers (Illumina, SanDiego, CA, USA), 6 µl MgCl$_2$ 25 mM, 5 µl of first PCR product, 0.4 µl FastStart Taq, and H$_2$O up to a final volume of 50 µl. Thermo-cycle settings were: one cycle at 95°C for 2 min followed by 8 cycles at 95°C for 30 sec, 55°C for 40 sec, 72°C for 40 sec, followed by a final extension step at 72°C for 5 min. Another purification step with 50.8 µl of AMPure Beads , was performed and all amplicons were quantified using Qubit® 2.0 Fluorometer. The quality of each amplicon was checked by Agilent 2100 Bioanalyzer using DNA 1000 Kit (Agilent Technologies, Santa Clara, CA, U.S.) according to the manufacturer's instructions. Amplicons were pooled at equimolar ratio and then diluted to final concentration of 8 picomolar. 15% (v/v) of Phix control libraries (Illumina, San Diego, CA, USA) was combined with normalized library to increase diversity of base calling during sequencing. Amplicons library was subjected to sequencing using V3 reagents kits on Illumina MiSeq system (Illumina, San Diego, CA, U.S.A). Pair-end sequencing was carry out in 281 cycles per read (281 x 2). An average of 25,607.875 reads/sample was used to further analysis.

Sequence analysis. First, FASTQC software (http://www.bioinformatics.bbsrc.ac.uk/projects/fastqc) was used to quality check FastQ files obtained from Illumina Miseq sequencer. Paired-end reads from sequencer platform were merged together using PEAR tool (*Zhang J.)* with a minimum of 40 overlapping residues as threshold and quality filtered was obtained using as threshold a mean PHREAD score of at least 33. Finally, FASTQ assembled reads were converted to FASTA format using PRINSEQ tool (Schmieder R). To analyze the methylation status of each amplicon, we used a homemade pipeline (Amplimethprofiler) specifically designed for deep targeted bisulfite amplicon sequencing of multiple genomic regions. This pipeline was made freely available at https://sourceforge.net/projects/amplimethprofiler. "Amplimethprofiler" recognizes corresponding target region discarding PCR artifacts and reads that do not match expected lengths. Next, reads were aligned to the corresponding bisulphite-converted reference using BLASTn (Camacho C). A filter of 99% bisulfite conversion efficiency was used. The pipeline output format reports the methylation status for each CpG dinucleotide coded 0 if the site is recognized as unmethylated, 1 if the site is recognized as methylated, and 2 if the methylation state could not be assessed. Quantitative methylation average for each site are then computed as sum of the number of non-converted bases mapped on that site over the total number of mapped reads (quantitative methylation analysis) for both strands.

Buffers Formulation.
3C Buffer 1: 10 mM Tris pH 8.0, 10 mM NaCl, 0.2% NP40 and protease inhibitors.
3C Ligation Buffer: 66 mM Tris-HCl, 5 mM MgCl$_2$, 5 mM DTT, 1 mM ATP, pH 7.5.
ChIP Lysis Buffer: 10 mM Tris-HCl pH 8.0, 10 mM NaCl, 0.2 % NP40.
ChIP Buffer: 1% Triton X-100, 2 mM EDTA, 150 mM NaCl, 20 mM Tris-HCl pH 8.0.

Supplemental References:

Mittal, V. (2004). Improving the efficiency of RNA interference in mammals. Nat. Rev. Genet. 5, 355–365.

Vascotto C, Fantini D, Romanello M, Cesaratto L, Deganuto M et al. (2009) APE1/Ref-1 interacts with NPM1 within nucleoli and plays a role in the rRNA quality control process. Mol Cell Biol 29, 1834-1854.

Table S1. Complete list of DNA oligonucleotides used for PCR.

Table S2. Inhibition of BER during repair reduces transcription and increases methylation of the repaired DNA.

Table S3. Summary of the analyzed sequences.

Figure S1. Recruitment of RNA polymerase II large subunit (A) and the apurinic nuclease APE1 (B) along the GFP gene in H and L cells.

Figure S2. Silencing APE1, TDG or inactivating OGG1 reduces GFP expression.

Figure S3. Rescue of GFP expression in cells in which the activity of OGG1 and APE1 has been altered by expressing the dominant negative mutants.

Statistical Table 1. Statistical analysis of data presented in Figure 1, panel B

Statistical Table 2. Statistical analysis of data presented in Figure 1, panel C

Statistical Table 3. Statistical analysis of data presented in Figure 2, panel B

Statistical Table 4. Statistical analysis of data presented in Figure 2, panel C

Table S1

ID	PRIMERS	Locus
3C Primer a	5'-GGCGGGGCGAGGCGGAGA-3'	pDR-GFP
3C Primer b	5'-GAGTCGCTGCGTTGCCTTC-3'	pDR-GFP
3C/ChIP Primer c	5'-CGCCCGCAGCGCTCACAGC-3'	pDR-GFP
3C/ChIP Primer d	5'-ACGTGCTGGTTATTGTGCTGTC-3'	pDR-GFP
3C/ChIP Primer e	5'-TCCTGCTCCTGGGCTTCTCG-3'	pDR-GFP
3C Primer f	5'-AAGATGGTGCGCTCCTGGACGTA-3'	pDR-GFP
3C Primer g	5'-GGTGAAGTTCGAGGGCGACAC-3'	pDR-GFP
3C/ChIP Primer h	5'-TGCACGCTGCCGTCCTCG-3'	pDR-GFP
Primer Rec2	5'-CGGCGGCGGTCACGAACTC-3'	pDR-GFP
3C Primer i	5'-GCTGATCTCGTTCTTCAGGC-3'	pDR-GFP
3C Primer l	5'-GGTACTCTGTTCTCACCCTTC-3'	pDR-GFP
3C Primer m	5'-GAAAGCGAAGGAGCAAAGCTG-3'	pDR-GFP
ChIP Primer a	5'-CGTTACTCCCACAGGTGAGC-3'	pDR-GFP
SS3/ChIP Primer r	5'-AGTTCATCTGCACCACCG-3'	pDR-GFP
ChIP Primer p	5'-GGCGTAAATTGTAAGCGTTA-3'	pDR-GFP
ChIP Primer q	5'-GCCTGAAGAACGAGATCAGC-3'	pDR-GFP
SS2/ChIP Primer s	5'-CAGGGTAATACCTACGGC-3'	pDR-GFP
SS1/ChIP Primer t	5'-AACGGCCACAAGTTCAGC-3'	pDR-GFP
AS3/ChIP Primer u	5'-ATGAACTTCAGGGTCAGC-3'	pDR-GFP
AS2/ChIP Primer v	5'-ATCCCTAGCCGGACACGC-3'	pDR-GFP
AS1/ChIP Primer z	5'-TTGTGGCCGTTTACGTCG-3'	pDR-GFP
Primer I-SceI	5'-GCTAGGGATAACAGGGTAAT-3'	pDR-GFP
Primer Bcg	5'-GAGGGCGAGGGCGATGCC-3'	pDR-GFP
Bisulfite E01F	5'-GTGTGATTGGTGGTTTTAGAGT-3'	pDR-GFP
Bisulfite E02R	5'-CCATCCTCAATATTATAACAAAT-3'	pDR-GFP
Bisulfite EN01F	5'-GGAGTTGTTTATTGGGGTGGTGTTTATTTTGGT-3'	pDR-GFP
Bisulfite EN02R	5'-GTTTGTGTTTTAGGATGTTGTTG-3'	pDR-GFP
Minus/Bisulfite E3F	5'-GTATTTTAGTTTGTGTTTTAGGATG -3'	pDR-GFP
Minus/Bisulfite E4R	5'-CACCTAAAACTAAAACACT-3'	pDR-GFP
Plus/Bisulfite E5F	5'-AGGAGGTATTTGGAGTTGAGGTA-3'	pDR-GFP
Plus/Bisulfite E6R	5'-TACTCCAACTTATACCCCAAAATAT -3'	pDR-GFP
MEDIP I F	5'-TGTTTTGGTTGGCGTAAGGC-3'	Mouse Rosa26
MEDIP I R	5'-CGGCGGGTAAAACGACTCC-3'	Mouse Rosa26
MEDIP II F	5'-AGAAAACTGGCCCTTGCCAT-3'	Mouse Rosa26
MEDIP II R	5'-TTGAGGCAACTCAAGTCGGAA-3'	Mouse Rosa26
18S F	5'-TCCCCATGAACGAGGAATTC-3'	h18S
18S R	5'-GTGTACAAAGGGCAGGGACTT-3'	h18S

Supplementary Table S1. Complete list of DNA oligonucleotides used for PCR.
On the left is shown the primer identification tag and the specific experiments (ID); on the center, the DNA sequence; on the right, the genes or loci corresponding to the specific primers.

Matched Pairs Days= 5 d

Difference: OGG1 DN-OGG1 DN+wt

OGG1 DN	122.889	t-Ratio	-10.2524
OGG1 DN+wt	227.333	DF	8
Mean Difference	-104.44	Prob > |t|	<.0001*
Std Error	10.1873	Prob > t	1.0000
Upper95%	-80.953	Prob < t	<.0001*
Lower95%	-127.94		
N	9		
Correlation	-0.4037		

Difference: CTRL-OGG1 DN+wt

CTRL	231.111	t-Ratio	0.40279
OGG1 DN+wt	227.333	DF	8
Mean Difference	3.77778	Prob > |t|	0.6977
Std Error	9.37902	Prob > t	0.3488
Upper95%	25.4058	Prob < t	0.6512
Lower95%	-17.85		
N	9		
Correlation	-0.1658		

Difference: CTRL-OGG1 DN

CTRL	231.111	t-Ratio	10.52973
OGG1 DN	122.889	DF	8
Mean Difference	108.222	Prob > |t|	<.0001*
Std Error	10.2778	Prob > t	<.0001*
Upper95%	131.923	Prob < t	1.0000
Lower95%	84.5216		
N	9		
Correlation	-0.0179		

Matched Pairs Days= 7 d

Difference: OGG1 DN-OGG1 DN+wt

OGG1 DN	156.8	t-Ratio	-9.92706
OGG1 DN+wt	266.2	DF	9
Mean Difference	-109.4	Prob > |t|	<.0001*
Std Error	11.0204	Prob > t	1.0000
Upper95%	-84.47	Prob < t	<.0001*
Lower95%	-134.33		
N	10		
Correlation	0.34277		

Difference: CTRL-OGG1 DN+wt

CTRL	256.4	t-Ratio	-0.93338
OGG1 DN+wt	266.2	DF	9
Mean Difference	-9.8	Prob > |t|	0.3750
Std Error	10.4995	Prob > t	0.8125
Upper95%	13.9516	Prob < t	0.1875
Lower95%	-33.552		
N	10		
Correlation	0.51943		

Difference: CTRL-OGG1 DN

CTRL	256.4	t-Ratio	15.29114
OGG1 DN	156.8	DF	9
Mean Difference	99.6	Prob > |t|	<.0001*
Std Error	6.51358	Prob > t	<.0001*
Upper95%	114.335	Prob < t	1.0000
Lower95%	84.8653		
N	10		
Correlation	0.74403		

Difference: OGG1 DN+wt-OGG1 DN+AZA

OGG1 DN+wt	266.2	t-Ratio	0.597845
OGG1 DN+AZA	259	DF	9
Mean Difference	7.2	Prob > |t|	0.5647
Std Error	12.0433	Prob > t	0.2823
Upper95%	34.4437	Prob < t	0.7177
Lower95%	-20.044		
N	10		
Correlation	0.27873		

Difference: OGG1 DN-OGG1 DN+AZA

OGG1 DN	156.8	t-Ratio	-11.6538
OGG1 DN+AZA	259	DF	9
Mean Difference	-102.2	Prob > |t|	<.0001*
Std Error	8.76964	Prob > t	1.0000
Upper95%	-82.362	Prob < t	<.0001*
Lower95%	-122.04		
N	10		
Correlation	0.20697		

Difference: CTRL-OGG1 DN+AZA

CTRL	256.4	t-Ratio	-0.29417
OGG1 DN+AZA	259	DF	9
Mean Difference	-2.6	Prob > |t|	0.7753
Std Error	8.8383	Prob > t	0.6124
Upper95%	17.3936	Prob < t	0.3876
Lower95%	-22.594		
N	10		
Correlation	0.49977		

Matched Pairs Days=14 d

Difference: OGG1 DN-OGG1 DN+wt

OGG1 DN	103.667	t-Ratio	-15.3342
OGG1 DN+wt	273	DF	8
Mean Difference	-169.33	Prob > |t|	<.0001*
Std Error	11.0428	Prob > t	1.0000
Upper95%	-143.87	Prob < t	<.0001*
Lower95%	-194.8		
N	9		
Correlation	0.20163		

Difference: CTRL-OGG1 DN+wt

CTRL	260.222	t-Ratio	-0.79638
OGG1 DN+wt	273	DF	8
Mean Difference	-12.778	Prob > |t|	0.4488
Std Error	16.0449	Prob > t	0.7756
Upper95%	24.2218	Prob < t	0.2244
Lower95%	-49.777		
N	9		
Correlation	-0.6602		

Difference: CTRL-OGG1 DN

CTRL	260.222	t-Ratio	19.6073
OGG1 DN	103.667	DF	8
Mean Difference	156.556	Prob > |t|	<.0001*
Std Error	7.98455	Prob > t	<.0001*
Upper95%	174.968	Prob < t	1.0000
Lower95%	138.143		
N	9		
Correlation	0.18311		

Difference: OGG1 DN+wt-OGG1 DN+AZA

OGG1 DN+wt	273	t-Ratio	0.158416
OGG1 DN+AZA	270.333	DF	8
Mean Difference	2.66667	Prob > |t|	0.8781
Std Error	16.8333	Prob > t	0.4390
Upper95%	41.4844	Prob < t	0.5610
Lower95%	-36.151		
N	9		
Correlation	-0.1769		

Difference: OGG1 DN-OGG1 DN+AZA

OGG1 DN	103.667	t-Ratio	-13.8171
OGG1 DN+AZA	270.333	DF	8
Mean Difference	-166.67	Prob > |t|	<.0001*
Std Error	12.0623	Prob > t	1.0000
Upper95%	-138.85	Prob < t	<.0001*
Lower95%	-194.48		
N	9		
Correlation	0.09455		

Difference: CTRL-OGG1 DN+AZA

CTRL	260.222	t-Ratio	-1.20104
OGG1 DN+AZA	270.333	DF	8
Mean Difference	-10.111	Prob > |t|	0.2641
Std Error	8.41864	Prob > t	0.8680
Upper95%	9.3023	Prob < t	0.1320
Lower95%	-29.525		
N	9		
Correlation	0.66404		

Matched Pairs Days= 5 d

Difference: shAPE1-shAPE1+wt

APE1 DN	104.111	t-Ratio	-15.5904
APE1 DN+wt	229.778	DF	8
Mean Difference	-125.67	Prob > |t|	<.0001*
Std Error	8.06053	Prob > t	1.0000
Upper95%	-107.08	Prob < t	<.0001*
Lower95%	-144.25		
N	9		
Correlation	0.23618		

Difference: ctrl-shAPE1+wt

CTRL	231.111	t-Ratio	0.110919
APE1 DN+wt	229.778	DF	8
Mean Difference	1.33333	Prob > |t|	0.9144
Std Error	12.0208	Prob > t	0.4572
Upper95%	29.0534	Prob < t	0.5428
Lower95%	-26.387		
N	9		
Correlation	-0.2593		

Difference: ctrl-shAPE1

CTRL	231.111	t-Ratio	11.56805
APE1 DN	104.111	DF	8
Mean Difference	127	Prob > |t|	<.0001*
Std Error	10.9785	Prob > t	<.0001*
Upper95%	152.316	Prob < t	1.0000
Lower95%	101.684		
N	9		
Correlation	-0.8002		

Matched Pairs Days= 7 d

Difference: shAPE1-shAPE1+wt

APE1 DN	75.4	t-Ratio	-19.0401
APE1 DN+wt	264.4	DF	9
Mean Difference	-189	Prob > |t|	<.0001*
Std Error	9.9264	Prob > t	1.0000
Upper95%	-166.54	Prob < t	<.0001*
Lower95%	-211.46		
N	10		
Correlation	0.56666		

Difference: ctrl-shAPE1+wt

CTRL	256.4	t-Ratio	-0.80521
APE1 DN+wt	264.4	DF	9
Mean Difference	-8	Prob > |t|	0.4415
Std Error	9.93535	Prob > t	0.7793
Upper95%	14.4753	Prob < t	0.2207
Lower95%	-30.475		
N	10		
Correlation	0.58801		

Difference: ctrl-shAPE1

CTRL	256.4	t-Ratio	16.12618
APE1 DN	75.4	DF	9
Mean Difference	181	Prob > |t|	<.0001*
Std Error	11.224	Prob > t	<.0001*
Upper95%	206.39	Prob < t	1.0000
Lower95%	155.61		
N	10		
Correlation	-0.1029		

Difference: shAPE1-shAPE1+wt   -AZA

APE1 DN+wt	264.4	t-Ratio	-0.16374
APE1 DN+AZA	265	DF	9
Mean Difference	-0.6	Prob > |t|	0.8736
Std Error	3.66424	Prob > t	0.5632
Upper95%	7.68909	Prob < t	0.4368
Lower95%	-8.8891		
N	10		
Correlation	0.95124		

Difference: ctrl-shAPE1+wt   A

APE1 DN	75.4	t-Ratio	-18.0409
APE1 DN+AZA	265	DF	9
Mean Difference	-189.6	Prob > |t|	<.0001*
Std Error	10.5095	Prob > t	1.0000
Upper95%	-165.83	Prob < t	<.0001*
Lower95%	-213.37		
N	10		
Correlation	0.40383		

Difference: ctrl-shAPE1

CTRL	256.4	t-Ratio	-0.86094
APE1 DN+AZA	265	DF	9
Mean Difference	-8.6	Prob > |t|	0.4116
Std Error	9.98911	Prob > t	0.7942
Upper95%	13.9969	Prob < t	0.2058
Lower95%	-31.197		
N	10		
Correlation	0.5621		

Matched Pairs Days=14 d

Difference: shAPE1-shAPE1+wt

APE1 DN	65.1111	t-Ratio	-13.3976
APE1 DN+wt	273.222	DF	8
Mean Difference	-208.11	Prob > |t|	<.0001*
Std Error	15.5335	Prob > t	1.0000
Upper95%	-172.29	Prob < t	<.0001*
Lower95%	-243.93		
N	9		
Correlation	-0.6172		

Difference: ctrl-shAPE1+wt

CTRL	260.222	t-Ratio	-0.7595
APE1 DN+wt	273.222	DF	8
Mean Difference	-13	Prob > |t|	0.4693
Std Error	17.1164	Prob > t	0.7653
Upper95%	26.4706	Prob < t	0.2347
Lower95%	-52.471		
N	9		
Correlation	-0.5867		

Difference: ctrl-shAPE1

CTRL	260.222	t-Ratio	22.21317
APE1 DN	65.1111	DF	8
Mean Difference	195.111	Prob > |t|	<.0001*
Std Error	8.78358	Prob > t	<.0001*
Upper95%	215.366	Prob < t	1.0000
Lower95%	174.856		
N	9		
Correlation	-0.1412		

Difference: shAPE1-shAPE1+wt   -AZA

APE1 DN+wt	273.222	t-Ratio	0.088475
APE1 DN+AZA	272.889	DF	8
Mean Difference	0.33333	Prob > |t|	0.9317
Std Error	3.76755	Prob > t	0.4658
Upper95%	9.02132	Prob < t	0.5342
Lower95%	-8.3547		
N	9		
Correlation	0.95503		

Difference: ctrl-shAPE1+wt   A

APE1 DN	65.1111	t-Ratio	-13.4153
APE1 DN+AZA	272.889	DF	8
Mean Difference	-207.78	Prob > |t|	<.0001*
Std Error	15.4881	Prob > t	1.0000
Upper95%	-172.06	Prob < t	<.0001*
Lower95%	-243.49		
N	9		
Correlation	-0.4774		

Difference: ctrl-shAPE1

CTRL	260.222	t-Ratio	-0.69451
APE1 DN+AZA	272.889	DF	8
Mean Difference	-12.667	Prob > |t|	0.5070
Std Error	18.2384	Prob > t	0.7465
Upper95%	29.3911	Prob < t	0.2535
Lower95%	-54.724		
N	9		
Correlation	-0.7219		

Supplementary Table S2. Inhibition of BER during repair reduces transcription and increases methylation of the repaired DNA. Cytofluorimetric analysis of GFP expression in cells transfected with I-SceI and OGG1 dominant negative variant or shRNA targeting APE1 (figure S4B and S4C). 5azadC treatment was performed as indicated in Materials and Methods. Rec H and Rec L are indicated in Fig. S4.

		# of reads			
Samples	Strand	Total	BcgI	I-SceI	% BcgI
CTRL	*PLUS*	54,210	28,174	26,036	52.0
I-SceI	*PLUS*	13,642	8,567	5,075	62.8
I-SceI +shAPE1	*PLUS*	7,268	5,606	1,662	77.1
I-SceI +shAPE1+wt	*PLUS*	2,389	1,812	577	75.8
CTRL	*MINUS*	81,923	39,508	42,415	48.2
I-SceI	*MINUS*	29,002	16,945	12,057	58.4
I-SceI +shAPE1	*MINUS*	10,929	7,722	3,207	70.7
I-SceI +shAPE1+wt	*MINUS*	5,500	3,657	1,843	66.5

# of reads (Both Strands)					
Samples	Total	BcgI	I-SceI	% BcgI	Recombination index
CTRL	136,133	67,682	68,451	49.7	0 %
I-SceI	42,644	25,512	17,132	59.8	17 %
I-SceI +shAPE1	18,197	13,328	4,869	73.2	32 %
I-SceI +shAPE1+wt	7,889	5,469	2,420	69.3	28 %

Supplementary Table S3. Summary of the analyzed sequences. Bisulfite-DNA derived from the samples shown on the left column were subjected to deep sequence analysis of the DSB region (Table S1) 7 days after the transfection with the various constructs indicated. BcgI and I-SceI represent the number of sequences corresponding to the recombinant (BcgI) and unrecombinant (I-SceI) cassette. Hela cells contain a single copy of DRGFP integrated randomly in the genome and 1 copy of the I-SceI and BcgI cassettes (50% in the Control). The DSB (I-SceI), repaired by HR generates new BcgI cassettes. The increase of the fraction of sequences containing the BcgI represents an accurate measure of the recombination index. Methylation analysis expressed as percent methylated CpG when compared to control cells has been normalized to the recombination index.

Supplementary Figure 1. Recruitment of RNA polymerase II large subunit and APE1 at the GFP gene in Rec H and Rec L cells.

ChIP analysis with specific antibodies to the large fragment of RNA polymerase II (A) or APE1 (B) was carried out as described in Methods in control or H and L clones. GFP regions indicated as Prom, ATG, GFP3' and Poly-A correspond to the primers shown in Fig. 1A. The brackets and the * represent the comparison between different groups. *p<0.01 (*Wilcoxon rank-sum test*).

Supplementary Figure 2. Silencing APE1, TDG or inactivating OGG1 reduces GFP expression and changes the Rec H/Rec L ratio. A and B.

Cytofluorimetric analysis of cells exposed to OGG1 dominant negative expression vector, shRNA targeting APE1 or siRNA targeting TDG with or without a wild type TDG expressing vector, 2 days after transfection with I-SceI vector. The analysis was performed at days 5, 7, 14 after transfection with the constructs indicated. Aliquots taken at day 14 had been exposed 2 days prior (12th day following silencing) to 5-azadC as described in Methods. The fraction of RecH and RecL cells is shown by horizontal lines in each panel. The histograms on the right show the fraction of Rec H and Rec L clones in cells expressing the dominant-negative OGG1 or shAPE1. Statistical significant differences are indicated by horizontal lines using Student's matched pairs *t* test: *p<0.01 (*Wilcoxon rank-sum test*).

C. Immunoblot with antibodies recognizing human TDG or APE1 in total cell extracts from samples (indicated at the top of the panel) 48 h or 14 days after transfection with I-SceI and the various constructs indicated.

Supplementary Figure 3. OGG1 and APE1 expression vectors restore GFP expression reduced by OGG1 or APE1 dominant negative variants.

A. Cytofluorimetric analysis of cells exposed to human OGG1 or APE1 dominant-negative mutants with or without vectors expressing the wild type proteins, 2 days after exposure to I-SceI. The analysis was performed at days 5, 7, 14 after OGG1 or APE1 transfection. Aliquots taken at day 12 after silencing were exposed to 5-azadC as described in Methods. The fraction of RecH and RecL cells is shown by horizontal lines in each panel

B and C. Quantitative analysis of the intensity of fluorescence derived from A. The brackets and the * represent the comparison between different groups. *p<0.01 (*Wilcoxon rank-sum test*).
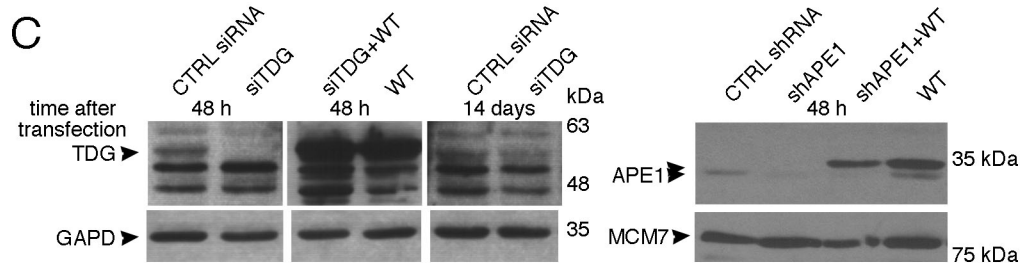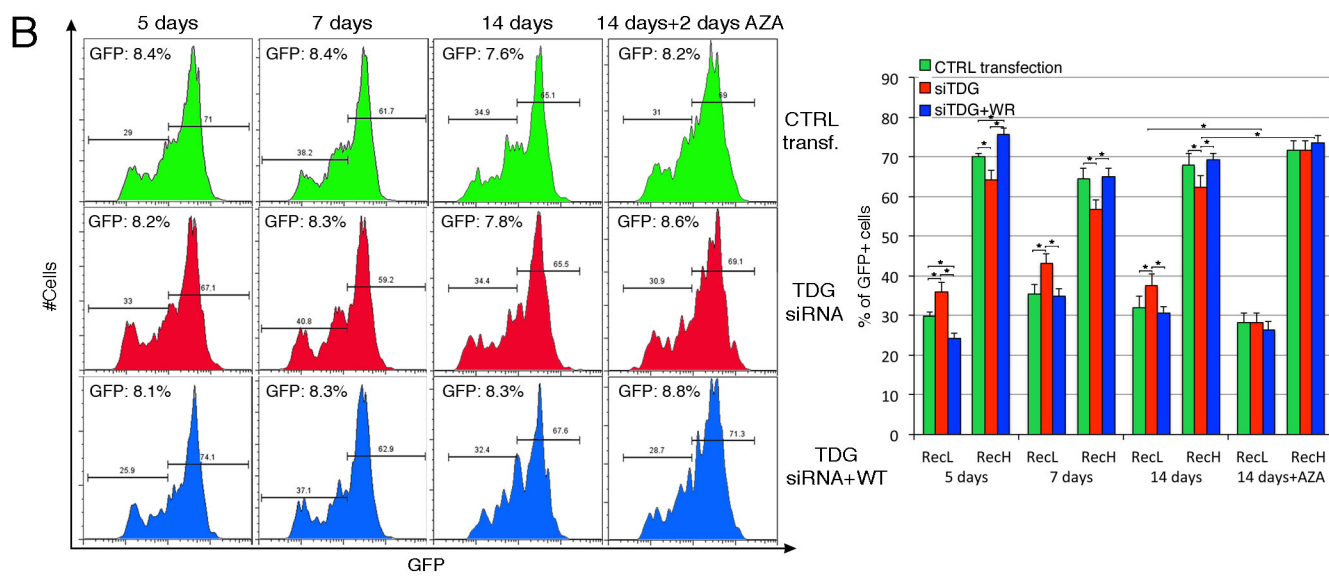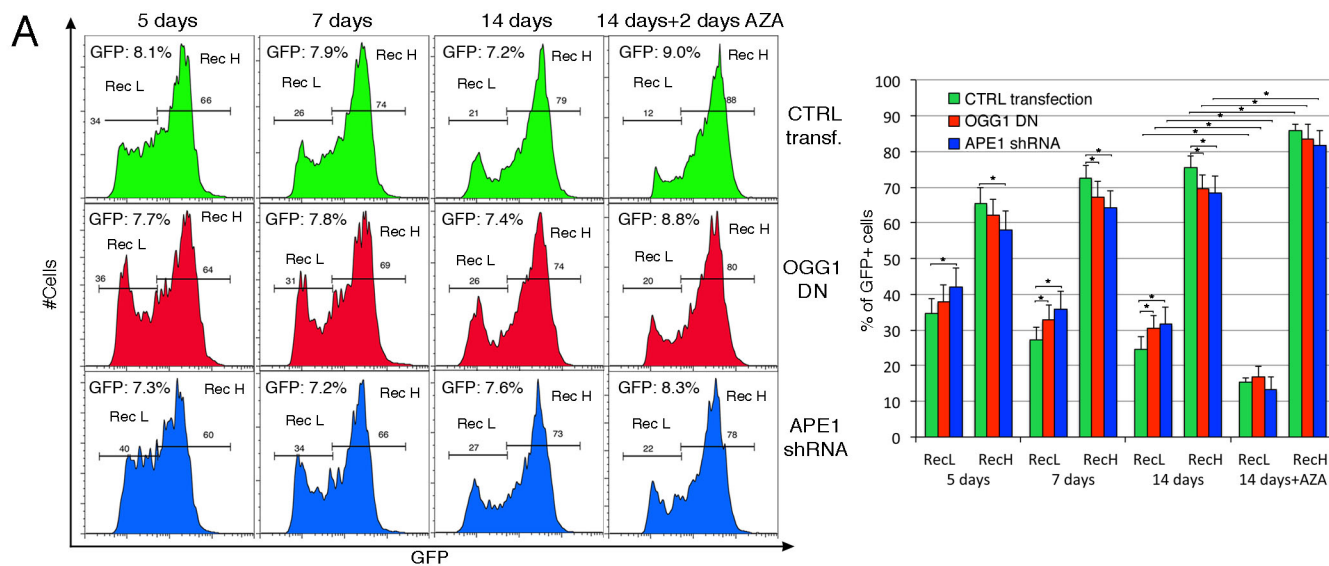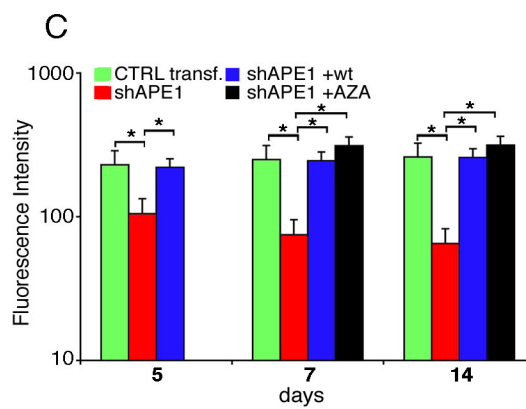
A ChIP RNA Pol II

B ChIP APE I

Fig. S3

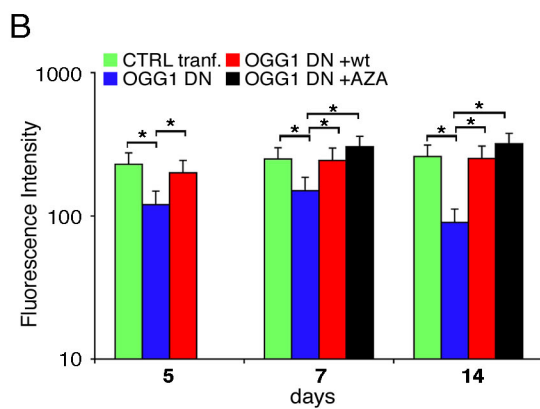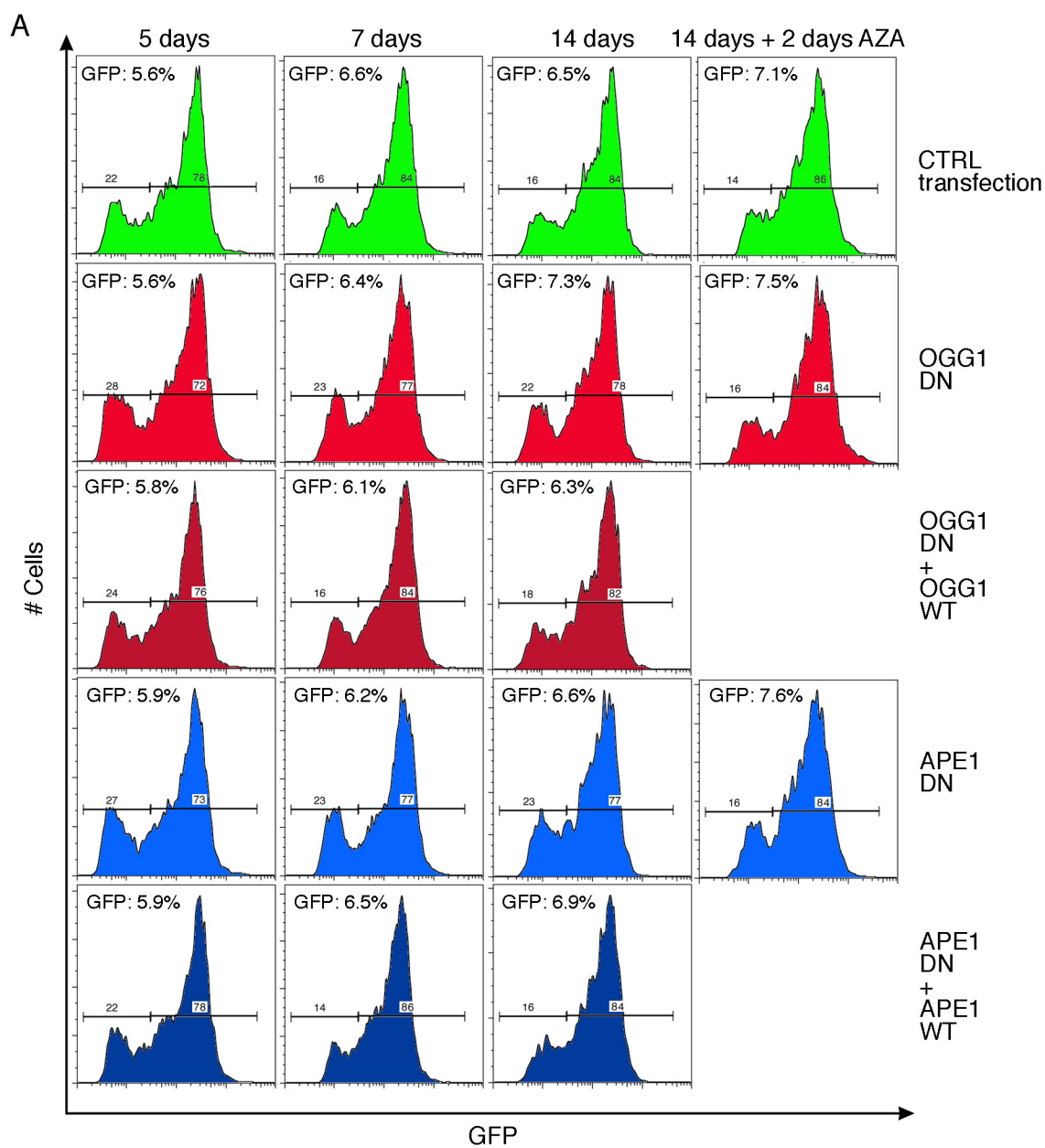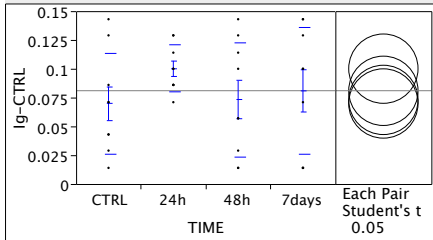Fig 1 panel B stat: Oneway   Page 1 of 12
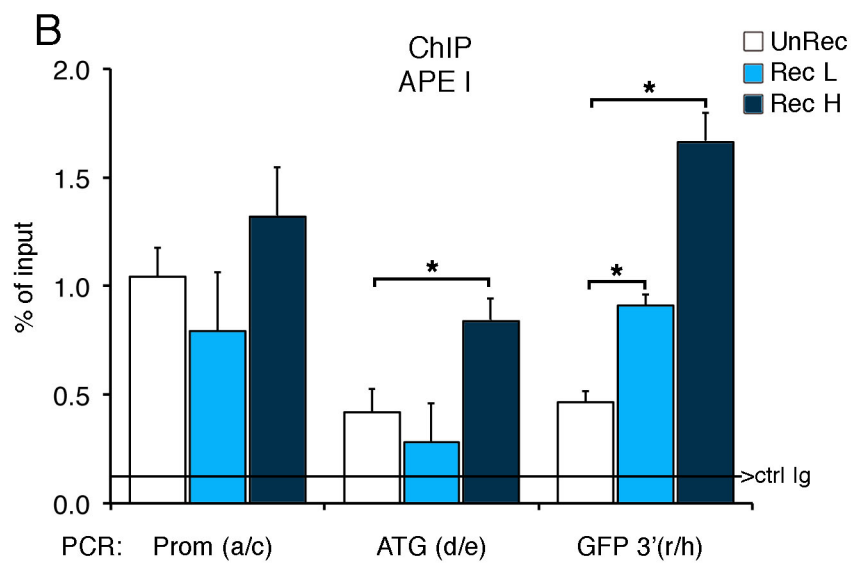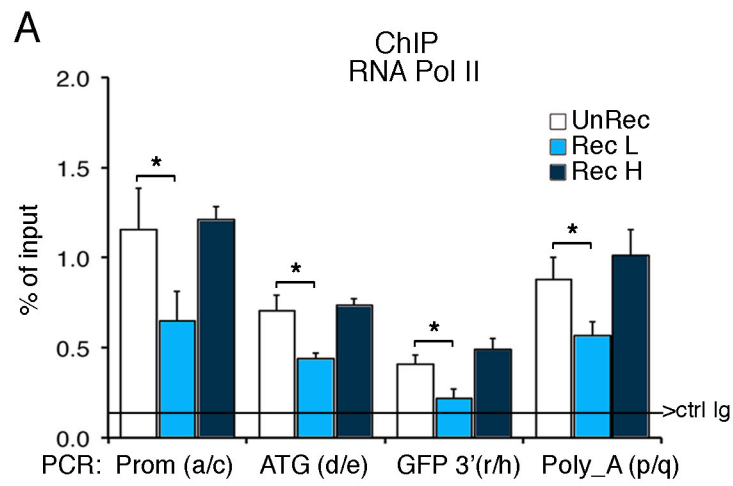
Fit Y by X Group

Oneway Analysis of Ig-CTRL By TIME PCR=d/e

Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.069889	0.043793	0.01460	0.03623	0.10355
24h	9	0.100111	0.020331	0.00678	0.08448	0.11574
48h	9	0.073000	0.049820	0.01661	0.03471	0.11129
7days	9	0.080889	0.055092	0.01836	0.03854	0.12324

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	142.000	15.7778	−0.883
24h	9	202.500	22.5000	1.306
48h	9	151.500	16.8333	−0.533
7days	9	170.000	18.8889	0.110

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
2.1660	3	0.5387

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
24h	CTRL	0.0302222	−0.012311	0.0727555	0.1575
24h	48h	0.0271111	−0.015422	0.0696444	0.2034
24h	7days	0.0192222	−0.023311	0.0617555	0.3642
7days	CTRL	0.0110000	−0.031533	0.0535333	0.6020
7days	48h	0.0078889	−0.034644	0.0504222	0.7081
48h	CTRL	0.0031111	−0.039422	0.0456444	0.8825

Power Details

Test TIME
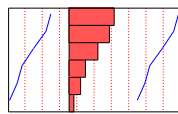
Power

α	σ	δ	Number	Power
0.0500	0.044295	0.011755	36	0.2124

Oneway Analysis of H3 By TIME PCR=d/e
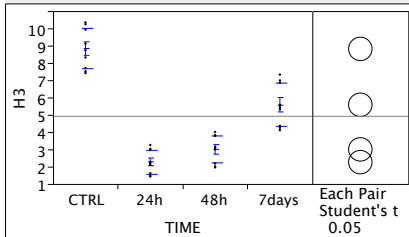
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	8.81422	1.16470	0.38823	7.9190	9.7095
24h	9	2.26211	0.69051	0.23017	1.7313	2.7929
48h	9	3.00067	0.79748	0.26583	2.3877	3.6137
7days	9	5.58200	1.23262	0.41087	4.6345	6.5295

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	288.000	32.0000	4.421
24h	9	66.000	7.3333	−3.653
48h	9	105.000	11.6667	−2.229
7days	9	207.000	23.0000	1.461

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
30.3153	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
CTRL	24h	6.552111	5.59325	7.510970	<.0001*
CTRL	48h	5.813556	4.85470	6.772415	<.0001*
7days	24h	3.319889	2.36103	4.278748	<.0001*
CTRL	7days	3.232222	2.27336	4.191082	<.0001*
7days	48h	2.581333	1.62247	3.540193	<.0001*
48h	24h	0.738556	−0.22030	1.697415	0.1265
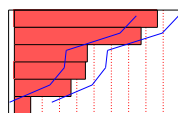
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.998583	2.566677	36	1.0000

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Fit Y by X Group

Oneway Analysis of H3K9m3 By TIME PCR=d/e
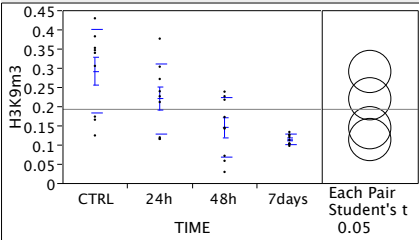
Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.290556	0.108546	0.03618	0.20712	0.37399
24h	9	0.219444	0.091209	0.03040	0.14934	0.28955
48h	9	0.144111	0.077158	0.02572	0.08480	0.20342
7days	9	0.113333	0.013048	0.00435	0.10330	0.12336

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	250.000	27.7778	3.033
24h	9	194.500	21.6111	1.005
48h	9	134.500	14.9444	−1.151
7days	9	87.000	9.6667	−2.886

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
15.1195	3	0.0017*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
CTRL 7days	0.1772222	0.099473	0.2549717	<.0001*	
CTRL 48h	0.1464444	0.068695	0.2241939	0.0006*	
24h 7days	0.1061111	0.028362	0.1838606	0.0090*	
24h 48h	0.0753333	−0.002416	0.1530828	0.0571	
CTRL 24h	0.0711111	−0.006638	0.1488606	0.0717	
48h 7days	0.0307778	−0.046972	0.1085273	0.4260	

Power Details

Test TIME
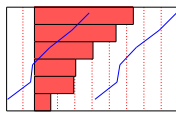
Power

α	σ	δ	Number	Power
0.0500	0.080971	0.068826	36	0.9884

Oneway Analysis of H3K9m2 By TIME PCR=d/e
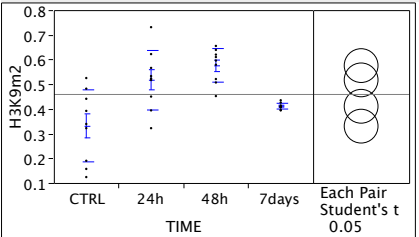
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.330222	0.145518	0.04851	0.21837	0.44208
24h	9	0.517556	0.121014	0.04034	0.42454	0.61057
48h	9	0.575444	0.067888	0.02263	0.52326	0.62763
7days	9	0.410667	0.013086	0.00436	0.40061	0.42073

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	88.500	9.8333	−2.832
24h	9	204.000	22.6667	1.352
48h	9	257.000	28.5556	3.289
7days	9	116.500	12.9444	−1.809

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.2057	3	0.0004*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
48h CTRL	0.2452222	0.148483	0.3419614	<.0001*	
24h CTRL	0.1873333	0.090594	0.2840725	0.0004*	
48h 7days	0.1647778	0.068039	0.2615169	0.0015*	
24h 7days	0.1068889	0.010150	0.2036280	0.0314*	
7days CTRL	0.0804444	−0.016295	0.1771836	0.1000	
48h 24h	0.0578889	−0.038850	0.1546280	0.2318	

Power Details

Test TIME
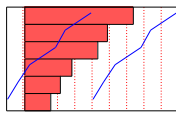
Power

α	σ	δ	Number	Power
0.0500	0.100747	0.094745	36	0.9971

Fit Y by X Group

Oneway Analysis of H3K4m3 By TIME PCR=d/e
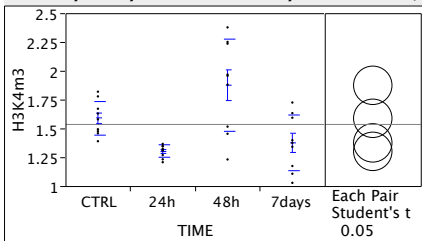
Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.58800	0.148401	0.04947	1.4739	1.7021
24h	9	1.30122	0.054295	0.01810	1.2595	1.3430
48h	9	1.87433	0.396826	0.13228	1.5693	2.1794
7days	9	1.37478	0.242618	0.08087	1.1883	1.5613

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean–Mean0)/Std0
CTRL	9	210.000	23.3333	1.571
24h	9	83.000	9.2222	–3.032
48h	9	246.000	27.3333	2.886
7days	9	127.000	14.1111	–1.425

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
16.7618	3	0.0008*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
48h	24h	0.5731111	0.337268	0.8089546	<.0001*	
48h	7days	0.4995556	0.263712	0.7353990	0.0001*	
CTRL	24h	0.2867778	0.050934	0.5226212	0.0187*	
48h	CTRL	0.2863333	0.050490	0.5221768	0.0189*	
CTRL	7days	0.2132222	–0.022621	0.4490657	0.0748	
7days	24h	0.0735556	–0.162288	0.3093990	0.5298	

Power Details

Test TIME
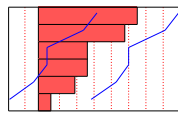
Power

α	σ	δ	Number	Power
0.0500	0.245614	0.222642	36	0.9950

Oneway Analysis of H3K4m2 By TIME PCR=d/e
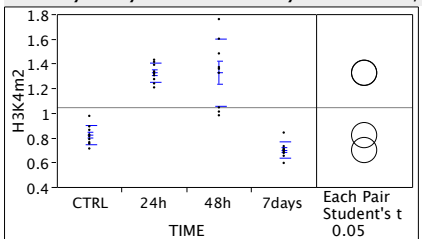
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.82022	0.080526	0.02684	0.7583	0.8821
24h	9	1.32422	0.077320	0.02577	1.2648	1.3837
48h	9	1.32600	0.271242	0.09041	1.1175	1.5345
7days	9	0.69944	0.066099	0.02203	0.6486	0.7503

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean–Mean0)/Std0
CTRL	9	119.000	13.2222	–1.717
24h	9	244.000	27.1111	2.813
48h	9	251.000	27.8889	3.069
7days	9	52.000	5.7778	–4.165

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
28.5415	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
48h	7days	0.6265556	0.482200	0.7709115	<.0001*	
24h	7days	0.6247778	0.480422	0.7691338	<.0001*	
48h	CTRL	0.5057778	0.361422	0.6501338	<.0001*	
24h	CTRL	0.5040000	0.359644	0.6483560	<.0001*	
CTRL	7days	0.1207778	–0.023578	0.2651338	0.0980	
48h	24h	0.0017778	–0.142578	0.1461338	0.9801	
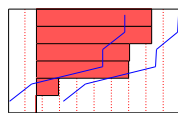
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.150336	0.285847	36	1.0000

Fit Y by X Group

Fig 1 panel B stat: Oneway　　　　　　　　　　　　　　　　　　　　　　　　**Page 4 of 12**

Fit Y by X Group

Oneway Analysis of Ig-CTRL By TIME PCR=p/q
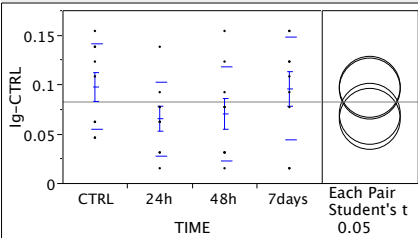
Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.097444	0.043385	0.01446	0.06410	0.13079
24h	9	0.065000	0.037376	0.01246	0.03627	0.09373
48h	9	0.070111	0.047480	0.01583	0.03361	0.10661
7days	9	0.095667	0.052235	0.01741	0.05552	0.13582

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	196.500	21.8333	1.084
24h	9	132.500	14.7222	-1.231
48h	9	143.500	15.9444	-0.827
7days	9	193.500	21.5000	0.974

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
3.3562	3	0.3399

Means Comparisons

Comparisons for each pair using Student's t

Level - Level	Difference	Lower CL	Upper CL	p-Value	
CTRL 24h	0.0324444	-0.011196	0.0760847	0.1397	
7days 24h	0.0306667	-0.012974	0.0743069	0.1620	
CTRL 48h	0.0273333	-0.016307	0.0709735	0.2112	
7days 48h	0.0255556	-0.018085	0.0691958	0.2417	
48h 24h	0.0051111	-0.038529	0.0487513	0.8130	
CTRL 7days	0.0017778	-0.041862	0.0454180	0.9344	
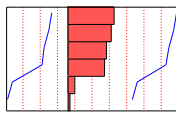
Power Details Dialog

TIME
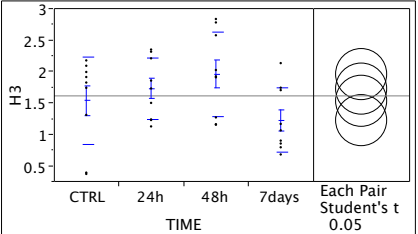Click and Enter 1, 2 or a sequence of values
for each:

	α	σ	δ	Number
From:	0.050	0.045448	0.014626	36
To:	.	.	.	.
By	.	.	.	.

☐ Solve for Power
☐ Solve for Least Significant Number
☐ Solve for Least Significant Value
☐ Adjusted Power and Confidence Interval

(Done)　(Cancel)　(Help)

Calculations will be done on all combinations
of sequences.

Oneway Analysis of H3 By TIME PCR=p/q

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.52589	0.699425	0.23314	0.9883	2.0635
24h	9	1.71967	0.485177	0.16173	1.3467	2.0926
48h	9	1.95044	0.670150	0.22338	1.4353	2.4656
7days	9	1.21811	0.509412	0.16980	0.8265	1.6097

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	166.000	18.4444	-0.000
24h	9	185.000	20.5556	0.658
48h	9	213.000	23.6667	1.681
7days	9	102.000	11.3333	-2.338

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
6.6717	3	0.0831

Means Comparisons

Comparisons for each pair using Student's t

Level - Level	Difference	Lower CL	Upper CL	p-Value	
48h 7days	0.7323333	0.157565	1.307102	0.0141*	
24h 7days	0.5015556	-0.073213	1.076324	0.0850	
48h CTRL	0.4245556	-0.150213	0.999324	0.1422	
CTRL 7days	0.3077778	-0.266991	0.882546	0.2835	
48h 24h	0.2307778	-0.343991	0.805546	0.4195	
24h CTRL	0.1937778	-0.380991	0.768546	0.4972	
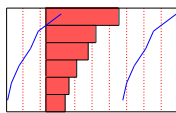
Power Details Dialog

TIME
Click and Enter 1, 2 or a sequence of values
for each:

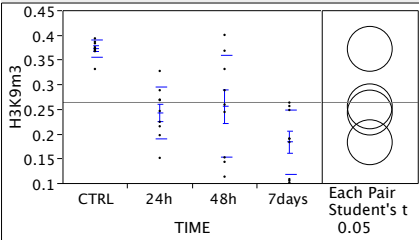|	α	σ	δ	Number
From:	0.050	0.59858	0.268521	36
To:	.	.	.	.
By	.	.	.	.

☐ Solve for Power
☐ Solve for Least Significant Number
☐ Solve for Least Significant Value
☐ Adjusted Power and Confidence Interval

(Done)　(Cancel)　(Help)

Calculations will be done on all combinations
of sequences.

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Fig 1 panel B stat: Oneway   **Page 5 of 12**

Fit Y by X Group

Oneway Analysis of H3K9m3 By TIME PCR=p/q

Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.371778	0.017655	0.00588	0.35821	0.38535
24h	9	0.242778	0.052578	0.01753	0.20236	0.28319
48h	9	0.255333	0.102538	0.03418	0.17652	0.33415
7days	9	0.182667	0.065654	0.02188	0.13220	0.23313

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	275.500	30.6111	3.965
24h	9	144.500	16.0556	−0.786
48h	9	161.000	17.8889	−0.183
7days	9	85.000	9.4444	−2.960

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
19.0639	3	0.0003*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
CTRL	7days	0.1891111	0.124876	0.2533466	<.0001*	
CTRL	24h	0.1290000	0.064765	0.1932355	0.0003*	
CTRL	48h	0.1164444	0.052209	0.1806799	0.0008*	
48h	7days	0.0726667	0.008431	0.1369021	0.0278*	
24h	7days	0.0601111	−0.004124	0.1243466	0.0656	
48h	24h	0.0125556	−0.051680	0.0767910	0.6932	
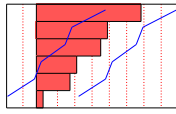
Power Details Dialog

TIME
Click and Enter 1, 2 or a sequence of values
for each:

	α	σ	δ	Number
From:	0.050	0.066897	0.068472	36
To:	.	.	.	.
By	.	.	.	.

☐ Solve for Power
☐ Solve for Least Significant Number
☐ Solve for Least Significant Value
☐ Adjusted Power and Confidence Interval

(Done) (Cancel) (Help)

Calculations will be done on all combinations
of sequences.

Oneway Analysis of H3K9m2 By TIME PCR=p/q
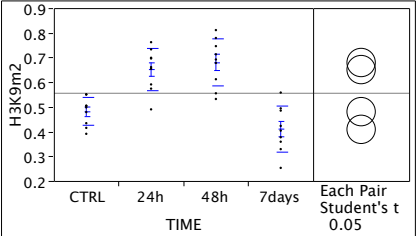
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.480778	0.056705	0.01890	0.43719	0.52437
24h	9	0.651111	0.085829	0.02861	0.58514	0.71709
48h	9	0.679778	0.096636	0.03221	0.60550	0.75406
7days	9	0.409111	0.093329	0.03111	0.33737	0.48085

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	113.000	12.5556	−1.936
24h	9	233.000	25.8889	2.411
48h	9	251.000	27.8889	3.069
7days	9	69.000	7.6667	−3.544

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
23.9550	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
48h	7days	0.2706667	0.189429	0.3519044	<.0001*	
24h	7days	0.2420000	0.160762	0.3232377	<.0001*	
48h	CTRL	0.1990000	0.117762	0.2802377	<.0001*	
24h	CTRL	0.1703333	0.089096	0.2515711	0.0002*	
CTRL	7days	0.0716667	−0.009571	0.1529044	0.0818	
48h	24h	0.0286667	−0.052571	0.1099044	0.4775	
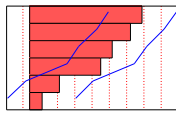
Power Details Dialog

TIME
Click and Enter 1, 2 or a sequence of values
for each:

	α	σ	δ	Number
From:	0.050	0.084603	0.113577	36
To:	.	.	.	.
By	.	.	.	.

☐ Solve for Power
☐ Solve for Least Significant Number
☐ Solve for Least Significant Value
☐ Adjusted Power and Confidence Interval

(Done) (Cancel) (Help)

Calculations will be done on all combinations
of sequences.

Fig 1 panel B stat: Oneway   **Page 6 of 12**

Fit Y by X Group

Oneway Analysis of H3K4m3 By TIME PCR=p/q

Statistical Table 1.

Statistical analysis of data presented in Figure 1, panel B
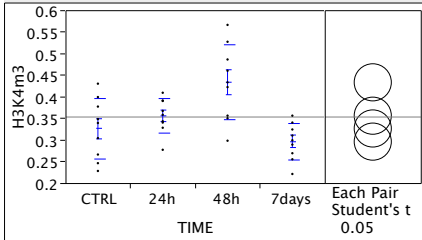
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.326333	0.070255	0.02342	0.27233	0.38034
24h	9	0.355889	0.039945	0.01332	0.32518	0.38659
48h	9	0.433111	0.087483	0.02916	0.36587	0.50036
7days	9	0.295889	0.042733	0.01424	0.26304	0.32874

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	139.000	15.4444	−0.987
24h	9	184.500	20.5000	0.639
48h	9	250.500	27.8333	3.051
7days	9	92.000	10.2222	−2.704

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
13.7037	3	0.0033*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
48h	7days	0.1372222	0.076472	0.1979724	<.0001*
48h	CTRL	0.1067778	0.046028	0.1675280	0.0011*
48h	24h	0.0772222	0.016472	0.1379724	0.0144*
24h	7days	0.0600000	−0.000750	0.1207502	0.0527
CTRL	7days	0.0304444	−0.030306	0.0911946	0.3150
24h	CTRL	0.0295556	−0.031195	0.0903057	0.3291

Power Details

Test TIME
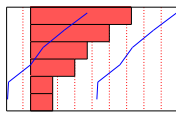
Power

α	σ	δ	Number	Power
0.0500	0.063267	0.050987	36	0.9788

Oneway Analysis of H3K4m2 By TIME PCR=p/q
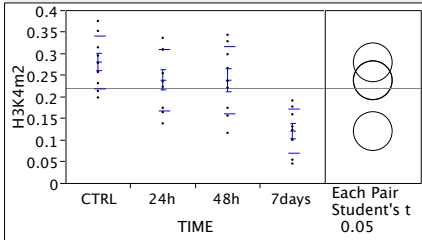
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.279222	0.060963	0.02032	0.23236	0.32608
24h	9	0.238000	0.070488	0.02350	0.18382	0.29218
48h	9	0.237556	0.078664	0.02622	0.17709	0.29802
7days	9	0.120111	0.050846	0.01695	0.08103	0.15920

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	232.000	25.7778	2.375
24h	9	186.500	20.7222	0.712
48h	9	185.500	20.6111	0.676
7days	9	62.000	6.8889	−3.800

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
15.9916	3	0.0011*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
CTRL	7days	0.1591111	0.095674	0.2225480	<.0001*
24h	7days	0.1178889	0.054452	0.1813258	0.0006*
48h	7days	0.1174444	0.054008	0.1808813	0.0007*
CTRL	48h	0.0416667	−0.021770	0.1051036	0.1904
CTRL	24h	0.0412222	−0.022215	0.1046591	0.1950
24h	48h	0.0004444	−0.062992	0.0638813	0.9887
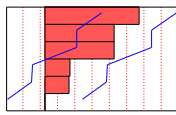
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.066065	0.059394	36	0.9944

Fit Y by X Group

Fig 1 panel B stat: Oneway   **Page 7 of 12**
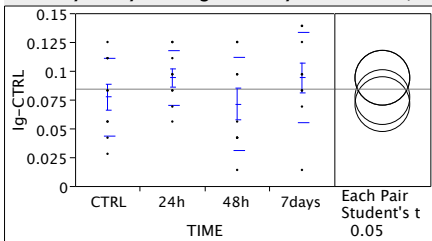
Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B

Fit Y by X Group

Oneway Analysis of Ig-CTRL By TIME PCR=r/h

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.077222	0.033903	0.01130	0.05116	0.10328
24h	9	0.094000	0.023822	0.00794	0.07569	0.11231
48h	9	0.071111	0.040591	0.01353	0.03991	0.10231
7days	9	0.094000	0.039205	0.01307	0.06386	0.12414

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	146.000	16.2222	−0.737
24h	9	190.000	21.1111	0.847
48h	9	135.500	15.0556	−1.124
7days	9	194.500	21.6111	1.013

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
2.7672	3	0.4289

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
7days	48h	0.0228889	−0.010724	0.0565019	0.1750
24h	48h	0.0228889	−0.010724	0.0565019	0.1750
7days	CTRL	0.0167778	−0.016835	0.0503908	0.3169
24h	CTRL	0.0167778	−0.016835	0.0503908	0.3169
CTRL	48h	0.0061111	−0.027502	0.0397241	0.7136
7days	24h	1.388e−17	−0.033613	0.0336130	1.0000

Power Details

Test TIME
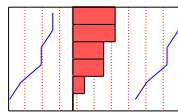
Power

α	σ	δ	Number	Power
0.0500	0.035006	0.010149	36	0.2483

Oneway Analysis of H3 By TIME PCR=r/h
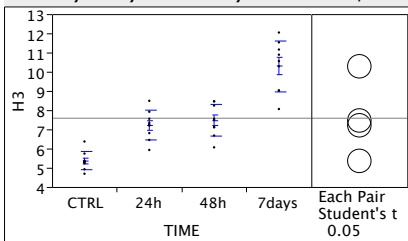
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	5.3603	0.47795	0.15932	4.9930	5.728
24h	9	7.2130	0.76281	0.25427	6.6267	7.799
48h	9	7.4640	0.82288	0.27429	6.8315	8.097
7days	9	10.2850	1.32165	0.44055	9.2691	11.301

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	47.000	5.2222	−4.347
24h	9	162.000	18.0000	−0.146
48h	9	173.000	19.2222	0.219
7days	9	284.000	31.5556	4.274

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
28.1772	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
7days	CTRL	4.924667	4.06124	5.788091	<.0001*
7days	24h	3.072000	2.20858	3.935424	<.0001*
7days	48h	2.821000	1.95758	3.684424	<.0001*
48h	CTRL	2.103667	1.24024	2.967091	<.0001*
24h	CTRL	1.852667	0.98924	2.716091	0.0001*
48h	24h	0.251000	−0.61242	1.114424	0.5579
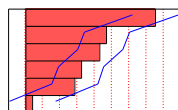
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.899195	1.76012	36	1.0000

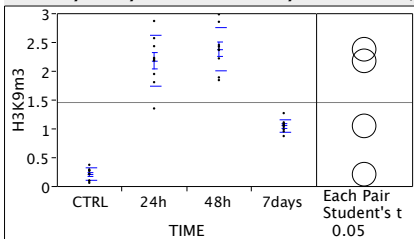**Fig 1 panel B stat: Oneway**   **Page 8 of 12**

Fit Y by X Group

Oneway Analysis of H3K9m3 By TIME PCR=r/h

Statistical Table 1.

Statistical analysis of data presented in Figure 1, panel B

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.20600	0.105134	0.03504	0.1252	0.2868
24h	9	2.17356	0.443556	0.14785	1.8326	2.5145
48h	9	2.37478	0.379631	0.12654	2.0830	2.6666
7days	9	1.04444	0.111220	0.03707	0.9590	1.1299

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	45.000	5.0000	−4.421
24h	9	237.000	26.3333	2.557
48h	9	258.000	28.6667	3.325
7days	9	126.000	14.0000	−1.461

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
29.7748	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
48h	CTRL	2.168778	1.87900	2.458553	<.0001*	
24h	CTRL	1.967556	1.67778	2.257331	<.0001*	
48h	7days	1.330333	1.04056	1.620108	<.0001*	
24h	7days	1.129111	0.83934	1.418886	<.0001*	
7days	CTRL	0.838444	0.54867	1.128219	<.0001*	
48h	24h	0.201222	−0.08855	0.490997	0.1669	

Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.30178	0.879028	36	1.0000
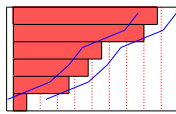
Oneway Analysis of H3K9m2 By TIME PCR=r/h
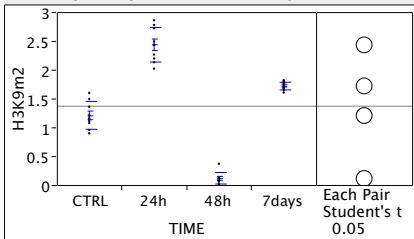
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.20578	0.236716	0.07891	1.0238	1.3877
24h	9	2.43189	0.302574	0.10086	2.1993	2.6645
48h	9	0.11289	0.101718	0.03391	0.0347	0.1911
7days	9	1.71922	0.070892	0.02363	1.6647	1.7737

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	126.000	14.0000	−1.461
24h	9	288.000	32.0000	4.421
48h	9	45.000	5.0000	−4.421
7days	9	207.000	23.0000	1.461

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
32.8421	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
24h	48h	2.319000	2.125189	2.512811	<.0001*	
7days	48h	1.606333	1.412522	1.800144	<.0001*	
24h	CTRL	1.226111	1.032300	1.419922	<.0001*	
CTRL	48h	1.092889	0.899078	1.286700	<.0001*	
24h	7days	0.712667	0.518856	0.906478	<.0001*	
7days	CTRL	0.513444	0.319633	0.707256	<.0001*	
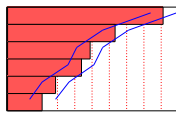
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.20184	0.845109	36	1.0000

Fit Y by X Group

Oneway Analysis of H3K4m3 By TIME PCR=r/h

Statistical Table 1.

Statistical analysis of data presented in Figure 1, panel B
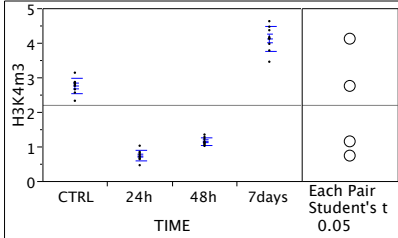
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	2.75267	0.225884	0.07529	2.5790	2.9263
24h	9	0.73600	0.156503	0.05217	0.6157	0.8563
48h	9	1.14833	0.111155	0.03705	1.0629	1.2338
7days	9	4.11833	0.357359	0.11912	3.8436	4.3930

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	207.000	23.0000	1.461
24h	9	46.000	5.1111	-4.384
48h	9	125.000	13.8889	-1.498
7days	9	288.000	32.0000	4.421

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
32.6777	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
7days 24h	3.382333	3.159416	3.605250	<.0001*	
7days 48h	2.970000	2.747083	3.192917	<.0001*	
CTRL 24h	2.016667	1.793750	2.239584	<.0001*	
CTRL 48h	1.604333	1.381416	1.827250	<.0001*	
7days CTRL	1.365667	1.142750	1.588584	<.0001*	
48h 24h	0.412333	0.189416	0.635250	0.0007*	

Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.232152	1.344827	36	1.0000
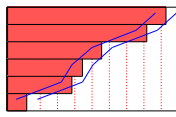
Oneway Analysis of H3K4m2 By TIME PCR=r/h
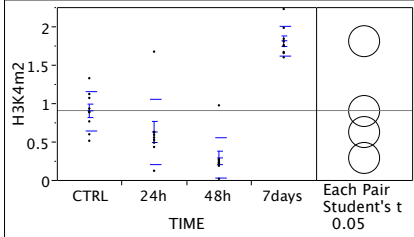
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.89789	0.255258	0.08509	0.7017	1.0941
24h	9	0.62400	0.421840	0.14061	0.2997	0.9483
48h	9	0.28689	0.267571	0.08919	0.0812	0.4926
7days	9	1.80700	0.194031	0.06468	1.6579	1.9561

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	185.000	20.5556	0.658
24h	9	130.000	14.4444	-1.315
48h	9	66.000	7.3333	-3.653
7days	9	285.000	31.6667	4.311

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
25.8428	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
7days 48h	1.520111	1.23512	1.805099	<.0001*	
7days 24h	1.183000	0.89801	1.467988	<.0001*	
7days CTRL	0.909111	0.62412	1.194099	<.0001*	
CTRL 48h	0.611000	0.32601	0.895988	0.0001*	
24h 48h	0.337111	0.05212	0.622099	0.0219*	
CTRL 24h	0.273889	-0.01110	0.558877	0.0590	
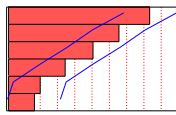
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.296794	0.564507	36	1.0000

Fit Y by X Group

Fig 1 panel B stat: Oneway Page 10 of 12

Fit Y by X Group

Oneway Analysis of Ig-CTRL By TIME PCR=Tf/Tr

Statistical Table 1.
Statistical analysis of data presented in Figure 1, panel B
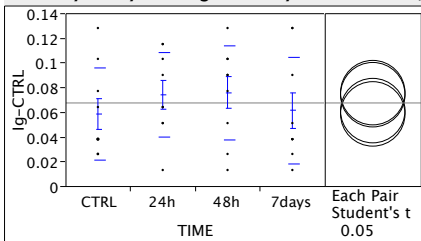
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.058444	0.037404	0.01247	0.02969	0.08720
24h	9	0.074000	0.034347	0.01145	0.04760	0.10040
48h	9	0.075667	0.038158	0.01272	0.04634	0.10500
7days	9	0.061111	0.043352	0.01445	0.02779	0.09443

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	143.500	15.9444	−0.827
24h	9	187.000	20.7778	0.735
48h	9	185.500	20.6111	0.680
7days	9	150.000	16.6667	−0.588

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
1.6026	3	0.6588

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
48h	CTRL	0.0172222	−0.019700	0.0541443	0.3492
24h	CTRL	0.0155556	−0.021367	0.0524776	0.3972
48h	7days	0.0145556	−0.022367	0.0514776	0.4279
24h	7days	0.0128889	−0.024033	0.0498110	0.4822
7days	CTRL	0.0026667	−0.034255	0.0395888	0.8840
48h	24h	0.0016667	−0.035255	0.0385888	0.9273

Power Details

Test TIME
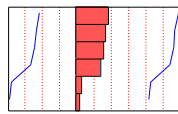
Power

α	σ	δ	Number	Power
0.0500	0.038452	0.007609	36	0.1341

Oneway Analysis of H3 By TIME PCR=Tf/Tr
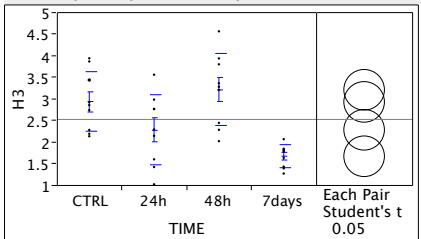
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	2.92289	0.688267	0.22942	2.3938	3.4519
24h	9	2.27722	0.821222	0.27374	1.6460	2.9085
48h	9	3.20344	0.835733	0.27858	2.5610	3.8458
7days	9	1.66478	0.258868	0.08629	1.4658	1.8638

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	215.000	23.8889	1.754
24h	9	147.000	16.3333	−0.694
48h	9	236.000	26.2222	2.521
7days	9	68.000	7.5556	−3.580

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
17.2823	3	0.0006*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
48h	7days	1.538667	0.874520	2.202813	<.0001*
CTRL	7days	1.258111	0.593965	1.922257	0.0005*
48h	24h	0.926222	0.262076	1.590369	0.0078*
CTRL	24h	0.645667	−0.018480	1.309813	0.0563
24h	7days	0.612444	−0.051702	1.276591	0.0695
48h	CTRL	0.280556	−0.383591	0.944702	0.3959
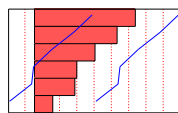
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.691661	0.595762	36	0.9901

Fig 1 panel B stat: Oneway   Page 11 of 12

Fit Y by X Group

Oneway Analysis of H3K9m3 By TIME PCR=Tf/Tr
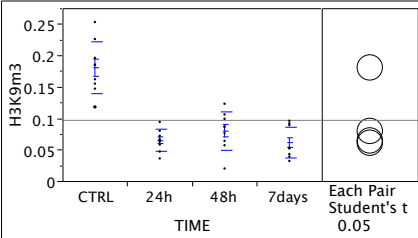
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.180778	0.041273	0.01376	0.14905	0.21250
24h	9	0.064667	0.017081	0.00569	0.05154	0.07780
48h	9	0.079778	0.030355	0.01012	0.05644	0.10311
7days	9	0.061000	0.024566	0.00819	0.04212	0.07988

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	287.000	31.8889	4.385
24h	9	118.000	13.1111	−1.754
48h	9	159.000	17.6667	−0.256
7days	9	102.000	11.3333	−2.339

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
21.1183	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p–Value	
CTRL	7days	0.1197778	0.091292	0.1482631	<.0001*	
CTRL	24h	0.1161111	0.087626	0.1445964	<.0001*	
CTRL	48h	0.1010000	0.072515	0.1294853	<.0001*	
48h	7days	0.0187778	−0.009708	0.0472631	0.1888	
48h	24h	0.0151111	−0.013374	0.0435964	0.2880	
24h	7days	0.0036667	−0.024819	0.0321519	0.7949	

Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.029665	0.049132	36	1.0000
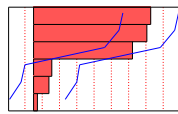
Oneway Analysis of H3K9m2 By TIME PCR=Tf/Tr
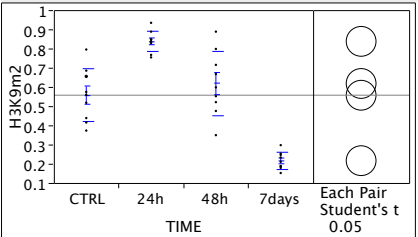
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.556889	0.138124	0.04604	0.45072	0.66306
24h	9	0.837444	0.054850	0.01828	0.79528	0.87961
48h	9	0.618111	0.167364	0.05579	0.48946	0.74676
7days	9	0.216222	0.045047	0.01502	0.18160	0.25085

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	159.000	17.6667	−0.256
24h	9	276.500	30.7222	4.001
48h	9	185.500	20.6111	0.676
7days	9	45.000	5.0000	−4.421

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
27.3103	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p–Value	
24h	7days	0.6212222	0.511607	0.7308374	<.0001*	
48h	7days	0.4018889	0.292274	0.5115041	<.0001*	
CTRL	7days	0.3406667	0.231051	0.4502818	<.0001*	
24h	CTRL	0.2805556	0.170940	0.3901707	<.0001*	
24h	48h	0.2193333	0.109718	0.3289485	0.0003*	
48h	CTRL	0.0612222	−0.048393	0.1708374	0.2637	
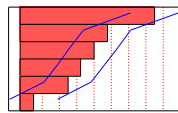
Power Details

Test TIME

Power

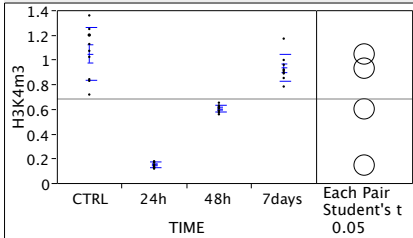| α	σ	δ	Number	Power
0.0500	0.114156	0.222774	36	1.0000

Statistical Table 1.

Statistical analysis of data presented in Figure 1, panel B

Fit Y by X Group

Oneway Analysis of H3K4m3 By TIME PCR=Tf/Tr

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.04556	0.214169	0.07139	0.88093	1.2102
24h	9	0.14567	0.022130	0.00738	0.12866	0.1627
48h	9	0.60133	0.029576	0.00986	0.57860	0.6241
7days	9	0.93056	0.108550	0.03618	0.84712	1.0140

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	260.000	28.8889	3.398
24h	9	45.000	5.0000	-4.421
48h	9	126.000	14.0000	-1.461
7days	9	235.000	26.1111	2.484

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
29.8669	3	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
CTRL 24h	0.8998889	0.783255	1.016523	<.0001*	
7days 24h	0.7848889	0.668255	0.901523	<.0001*	
48h 24h	0.4556667	0.339033	0.572301	<.0001*	
CTRL 48h	0.4442222	0.327588	0.560856	<.0001*	
7days 48h	0.3292222	0.212588	0.445856	<.0001*	
CTRL 7days	0.1150000	-0.001634	0.231634	0.0531	

Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.121466	0.349323	36	1.0000
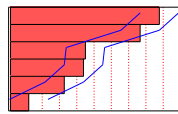
Oneway Analysis of H3K4m2 By TIME PCR=Tf/Tr
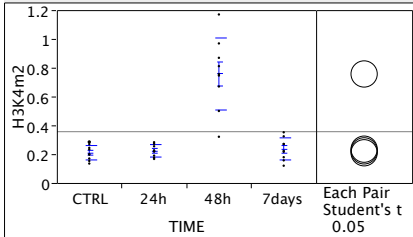
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.209778	0.052002	0.01733	0.16981	0.24975
24h	9	0.223111	0.041205	0.01374	0.19144	0.25478
48h	9	0.756889	0.248699	0.08290	0.56572	0.94806
7days	9	0.234778	0.076684	0.02556	0.17583	0.29372

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	112.500	12.5000	-1.955
24h	9	130.000	14.4444	-1.315
48h	9	286.000	31.7778	4.348
7days	9	137.500	15.2778	-1.041

#### 1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
19.3914	3	0.0002*

Means Comparisons

Comparisons for each pair using Student's t

Level – Level	Difference	Lower CL	Upper CL	p-Value	
48h CTRL	0.5471111	0.418165	0.6760576	<.0001*	
48h 24h	0.5337778	0.404831	0.6627242	<.0001*	
48h 7days	0.5221111	0.393165	0.6510576	<.0001*	
7days CTRL	0.0250000	-0.103946	0.1539465	0.6955	
24h CTRL	0.0133333	-0.115613	0.1422798	0.8345	
7days 24h	0.0116667	-0.117280	0.1406131	0.8549	
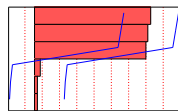
Power Details

Test TIME

Power

α	σ	δ	Number	Power
0.0500	0.134289	0.231542	36	1.0000

Statistical Table 1.

Statistical analysis of data presented in Figure 1, panel B

Fig 1 panel C stat: Oneway by Treat   **Page 1 of 5**

Fit Y by X Group

Oneway Analysis of ctrl Ig By Treat
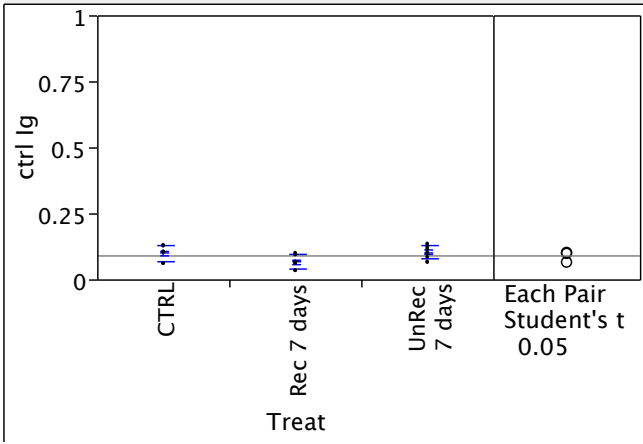
Statistical Table 2.
Statistical analysis of data
presented in Figure 1, panel C

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.098333	0.029707	0.00990	0.07550	0.12117
Rec 7 days	9	0.065222	0.026971	0.00899	0.04449	0.08595
UnRec 7 days	9	0.102000	0.025690	0.00856	0.08225	0.12175

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	145.000	16.1111	0.952
Rec 7 days	9	74.000	8.2222	−2.651
UnRec 7 days	9	159.000	17.6667	1.673

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
7.3397	2	0.0255*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
UnRec 7 days	Rec 7 days	0.0367778	0.010015	0.0635404	0.0091*
CTRL	Rec 7 days	0.0331111	0.006348	0.0598738	0.0174*
UnRec 7 days	CTRL	0.0036667	−0.023096	0.0304293	0.7798
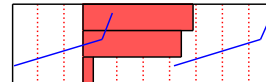
Power Details

Test Treat

Power

α	σ	δ	Number	Power
0.0500	0.027507	0.016541	27	0.7503

Median Test (Number of Points Above Median)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	6.000	0.666667	1.336
Rec 7 days	9	1.000	0.111111	−2.673
UnRec 7 days	9	6.000	0.666667	1.336

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
7.1429	2	0.0281*
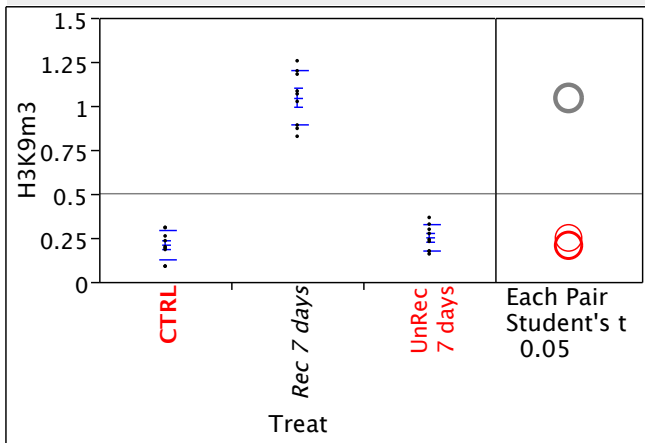
27

Fig 1 panel C stat: Oneway by Treat   **Page 2 of 5**

Fit Y by X Group

Oneway Analysis of H3K9m3 By Treat

Statistical Table 2.
Statistical analysis of data
presented in Figure 1, panel C

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.20767	0.081270	0.02709	0.14520	0.2701
Rec 7 days	9	1.04467	0.154143	0.05138	0.92618	1.1632
UnRec 7 days	9	0.24978	0.072955	0.02432	0.19370	0.3059

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean–Mean0)/Std0
CTRL	9	77.000	8.5556	−2.495
Rec 7 days	9	207.000	23.0000	4.140
UnRec 7 days	9	94.000	10.4444	−1.620

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
17.6120	2	0.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec 7 days	CTRL	0.8370000	0.730885	0.9431152	<.0001*	
Rec 7 days	UnRec 7 days	0.7948889	0.688774	0.9010041	<.0001*	
UnRec 7 days	CTRL	0.0421111	−0.064004	0.1482263	0.4208	
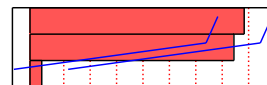
Power Details

Test Treat

Power

α	σ	δ	Number	Power
0.0500	0.109068	0.385024	27	1.0000

Median Test (Number of Points Above Median)

Level	Count	Score Sum	Score Mean	(Mean–Mean0)/Std0
CTRL	9	2.000	0.22222	−1.871
Rec 7 days	9	9.000	1.00000	3.742
UnRec 7 days	9	2.000	0.22222	−1.871

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.0000	2	0.0009*

Fig 1 panel C stat: Oneway by Treat   **Page 3 of 5**

Fit Y by X Group

Oneway Analysis of H3K9m2 By Treat
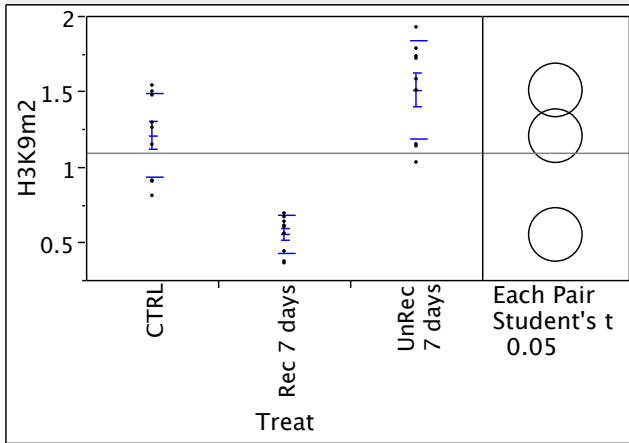
Statistical Table 2.
Statistical analysis of data
presented in Figure 1, panel C

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.20556	0.278589	0.09286	0.9914	1.4197
Rec 7 days	9	0.55111	0.125812	0.04194	0.4544	0.6478
UnRec 7 days	9	1.50889	0.325120	0.10837	1.2590	1.7588

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	144.000	16.0000	0.900
Rec 7 days	9	45.000	5.0000	−4.140
UnRec 7 days	9	189.000	21.0000	3.215

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
19.1429	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
UnRec 7 days	Rec 7 days	0.9577778	0.7071065	1.208449	<.0001*	
CTRL	Rec 7 days	0.6544444	0.4037732	0.905116	<.0001*	
UnRec 7 days	CTRL	0.3033333	0.0526621	0.554005	0.0198*	
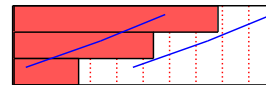
Power Details

Test Treat

Power

α	σ	δ	Number	Power
0.0500	0.257645	0.399673	27	1.0000

Median Test (Number of Points Above Median)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	6.000	0.666667	1.336
Rec 7 days	9	0.000	0.000000	−3.474
UnRec 7 days	9	7.000	0.777778	2.138

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
12.2857	2	0.0021*

Fig 1 panel C stat: Oneway by Treat   **Page 4 of 5**
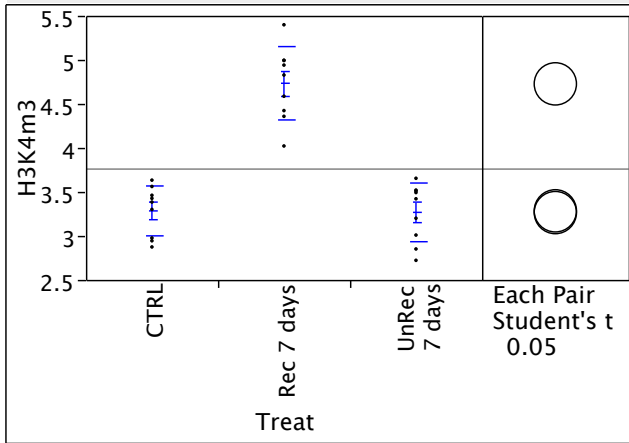
Fit Y by X Group

Oneway Analysis of H3K4m3 By Treat

Statistical Table 2.
Statistical analysis of data
presented in Figure 1, panel C

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	3.28433	0.282587	0.09420	3.0671	3.5015
Rec 7 days	9	4.72667	0.417515	0.13917	4.4057	5.0476
UnRec 7 days	9	3.26433	0.333211	0.11107	3.0082	3.5205

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	85.000	9.4444	-2.083
Rec 7 days	9	207.000	23.0000	4.140
UnRec 7 days	9	86.000	9.5556	-2.032

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
17.3580	2	0.0002*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec 7 days	UnRec 7 days	1.462333	1.12287	1.801794	<.0001*	
Rec 7 days	CTRL	1.442333	1.10287	1.781794	<.0001*	
CTRL	UnRec 7 days	0.020000	-0.31946	0.359460	0.9042	
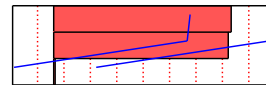
Power Details

Test Treat

Power

α	σ	δ	Number	Power
0.0500	0.348905	0.684685	27	1.0000

Median Test (Number of Points Above Median)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	2.000	0.22222	-1.871
Rec 7 days	9	9.000	1.00000	3.742
UnRec 7 days	9	2.000	0.22222	-1.871

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.0000	2	0.0009*

Fig 1 panel C stat: Oneway by Treat　　　　　　　　　　　　　　　　**Page 5 of 5**

Fit Y by X Group

Oneway Analysis of H3K4m2 By Treat

Statistical Table 2.
Statistical analysis of data
presented in Figure 1, panel C

Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.88278	0.169354	0.05645	0.7526	1.0130
Rec 7 days	9	1.80189	0.425075	0.14169	1.4751	2.1286
UnRec 7 days	9	1.41167	0.248539	0.08285	1.2206	1.6027

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	46.000	5.1111	−4.089
Rec 7 days	9	190.000	21.1111	3.266
UnRec 7 days	9	142.000	15.7778	0.797

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.9630	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value
Rec 7 days	CTRL	0.9191111	0.6266154	1.211607	<.0001*
UnRec 7 days	CTRL	0.5288889	0.2363932	0.821385	0.0010*
Rec 7 days	UnRec 7 days	0.3902222	0.0977265	0.682718	0.0111*
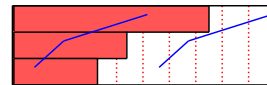
Power Details

Test Treat

Power

α	σ	δ	Number	Power
0.0500	0.300634	0.376646	27	0.9999

Median Test (Number of Points Above Median)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	0.000	0.000000	−3.474
Rec 7 days	9	8.000	0.888889	2.940
UnRec 7 days	9	5.000	0.555556	0.535

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.0000	2	0.0009*

Fit Y by X Group

Oneway Analysis of Ig CTRL By TREAT PCR=a/c

Statistical Table 3.
Statistical analysis of data
presented in Figure 2, panel B
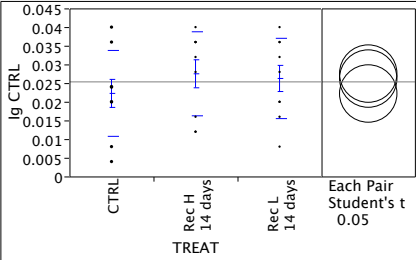
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.022222	0.011508	0.00384	0.01338	0.03107
Rec H 14 days	9	0.027556	0.011215	0.00374	0.01893	0.03618
Rec L 14 days	9	0.026222	0.010791	0.00360	0.01793	0.03452

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	109.000	12.1111	−0.856
Rec H 14 days	9	139.000	15.4444	0.649
Rec L 14 days	9	130.000	14.4444	0.182

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
0.8510	2	0.6534

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec H 14 days	CTRL	0.0053333	−0.005540	0.0162062	0.3215	
Rec L 14 days	CTRL	0.0040000	−0.006873	0.0148729	0.4551	
Rec H 14 days	Rec L 14 days	0.0013333	−0.009540	0.0122062	0.8024	
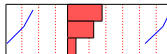
Oneway Analysis of H3K9m3 By TREAT PCR=a/c
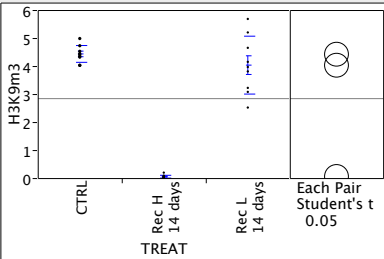
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	4.42367	0.30581	0.10194	4.1886	4.6587
Rec H 14 days	9	0.05756	0.05778	0.01926	0.0131	0.1020
Rec L 14 days	9	4.03044	1.02458	0.34153	3.2429	4.8180

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	180.000	20.0000	2.752
Rec H 14 days	9	45.000	5.0000	−4.140
Rec L 14 days	9	153.000	17.0000	1.363

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.0000	2	0.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
CTRL	Rec H 14 days	4.366111	3.76462	4.967603	<.0001*	
Rec L 14 days	Rec H 14 days	3.972889	3.37140	4.574381	<.0001*	
CTRL	Rec L 14 days	0.393222	−0.20827	0.994715	0.1898	
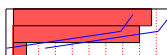
Oneway Analysis of H3K9m2 By TREAT PCR=a/c
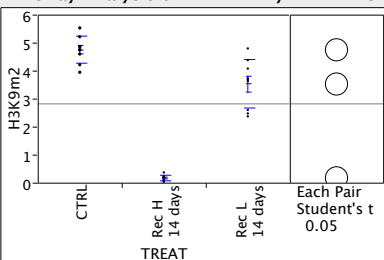
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	4.74556	0.475057	0.15835	4.3804	5.1107
Rec H 14 days	9	0.17433	0.103056	0.03435	0.0951	0.2535
Rec L 14 days	9	3.52411	0.867069	0.28902	2.8576	4.1906

Wilcoxon / Kruskal–Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	199.000	22.1111	3.729
Rec H 14 days	9	45.000	5.0000	−4.140
Rec L 14 days	9	134.000	14.8889	0.386

1–way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
21.0829	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
CTRL	Rec H 14 days	4.571222	4.012850	5.129594	<.0001*	
Rec L 14 days	Rec H 14 days	3.349778	2.791406	3.908150	<.0001*	
CTRL	Rec L 14 days	1.221444	0.663072	1.779817	0.0001*	
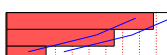
Fig 2 panel B stat: Oneway   **Page 2 of 5**

Fit Y by X Group

Oneway Analysis of H3K4m3 By TREAT PCR=a/c

Statistical Table 3.
Statistical analysis of data
presented in Figure 2, panel B
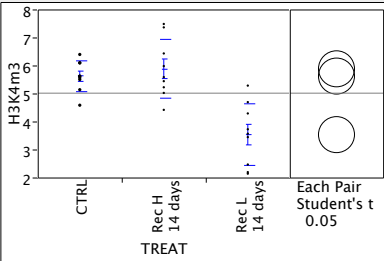
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	5.62322	0.54547	0.18182	5.2039	6.0425
Rec H 14 days	9	5.88267	1.04094	0.34698	5.0825	6.6828
Rec L 14 days	9	3.53300	1.11258	0.37086	2.6778	4.3882

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	162.000	18.0000	1.826
Rec H 14 days	9	164.000	18.2222	1.929
Rec L 14 days	9	52.000	5.7778	-3.780

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.4903	2	0.0007*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec H 14 days	Rec L 14 days	2.349667	1.44062	3.258710	<.0001*	
CTRL	Rec L 14 days	2.090222	1.18118	2.999265	<.0001*	
Rec H 14 days	CTRL	0.259444	-0.64960	1.168488	0.5613	
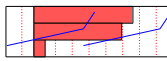
Oneway Analysis of H3K4m2 By TREAT PCR=a/c
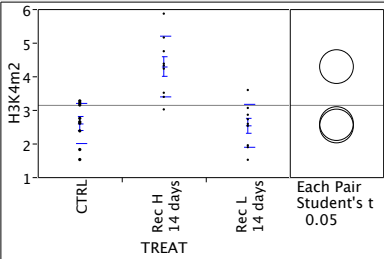
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	2.59444	0.607542	0.20251	2.1274	3.0614
Rec H 14 days	9	4.28989	0.900818	0.30027	3.5975	4.9823
Rec L 14 days	9	2.52267	0.644924	0.21497	2.0269	3.0184

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	93.000	10.3333	-1.672
Rec H 14 days	9	200.000	22.2222	3.780
Rec L 14 days	9	85.000	9.4444	-2.083

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.5432	2	0.0007*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec H 14 days	Rec L 14 days	1.767222	1.05747	2.476975	<.0001*	
Rec H 14 days	CTRL	1.695444	0.98569	2.405197	<.0001*	
CTRL	Rec L 14 days	0.071778	-0.63797	0.781531	0.8364	
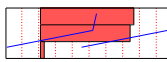
Fit Y by X Group

Oneway Analysis of Ig CTRL By TREAT PCR=p/q
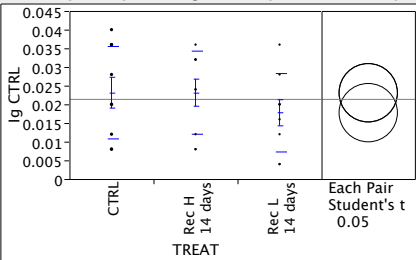
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.023111	0.012454	0.00415	0.01354	0.03268
Rec H 14 days	9	0.023111	0.011096	0.00370	0.01458	0.03164
Rec L 14 days	9	0.017778	0.010414	0.00347	0.00977	0.02578

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	137.500	15.2778	0.570
Rec H 14 days	9	137.500	15.2778	0.570
Rec L 14 days	9	103.000	11.4444	-1.166

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
1.4216	2	0.4913

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
CTRL	Rec L 14 days	0.0053333	-0.005712	0.0163789	0.3289	
Rec H 14 days	Rec L 14 days	0.0053333	-0.005712	0.0163789	0.3289	
Rec H 14 days	CTRL	0.0000000	-0.011046	0.0110456	1.0000	
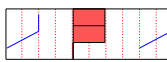
Fit Y by X Group

Oneway Analysis of H3K9m3 By TREAT PCR=p/q

Statistical Table 3.
Statistical analysis of data
presented in Figure 2, panel B
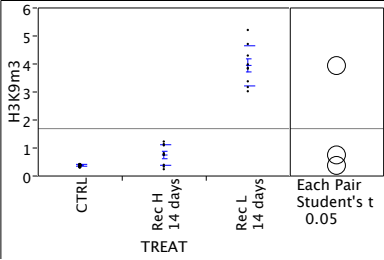
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.36167	0.033619	0.01121	0.3358	0.3875
Rec H 14 days	9	0.73711	0.363637	0.12121	0.4576	1.0166
Rec L 14 days	9	3.92733	0.716216	0.23874	3.3768	4.4779

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	64.000	7.1111	−3.163
Rec H 14 days	9	107.000	11.8889	−0.952
Rec L 14 days	9	207.000	23.0000	4.140

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.9877	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	CTRL	3.565667	3.11407	4.017260	<.0001*	
Rec L 14 days	Rec H 14 days	3.190222	2.73863	3.641816	<.0001*	
Rec H 14 days	CTRL	0.375444	−0.07615	0.827038	0.0991	
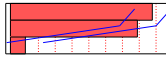
Oneway Analysis of H3K9m2 By TREAT PCR=p/q
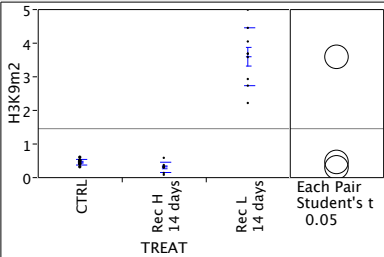
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.45378	0.084269	0.02809	0.3890	0.5186
Rec H 14 days	9	0.29278	0.142598	0.04753	0.1832	0.4024
Rec L 14 days	9	3.58133	0.865235	0.28841	2.9163	4.2464

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	116.000	12.8889	−0.489
Rec H 14 days	9	55.000	6.1111	−3.627
Rec L 14 days	9	207.000	23.0000	4.142

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
20.6511	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	Rec H 14 days	3.288556	2.79371	3.783403	<.0001*	
Rec L 14 days	CTRL	3.127556	2.63271	3.622403	<.0001*	
CTRL	Rec H 14 days	0.161000	−0.33385	0.655847	0.5083	
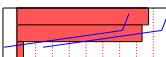
Oneway Analysis of H3K4m3 By TREAT PCR=p/q
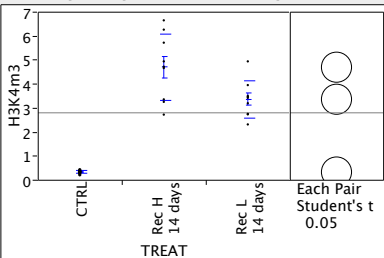
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.32333	0.06231	0.02077	0.2754	0.3712
Rec H 14 days	9	4.68933	1.37593	0.45864	3.6317	5.7470
Rec L 14 days	9	3.35467	0.77162	0.25721	2.7615	3.9478

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	45.000	5.0000	−4.140
Rec H 14 days	9	186.000	20.6667	3.060
Rec L 14 days	9	147.000	16.3333	1.054

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.6984	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec H 14 days	CTRL	4.366000	3.479177	5.252823	<.0001*	
Rec L 14 days	CTRL	3.031333	2.144510	3.918156	<.0001*	
Rec H 14 days	Rec L 14 days	1.334667	0.447844	2.221490	0.0048*	
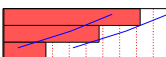
Fig 2 panel B stat: Oneway   Page 4 of 5

Fit Y by X Group

Oneway Analysis of H3K4m2 By TREAT PCR=p/q
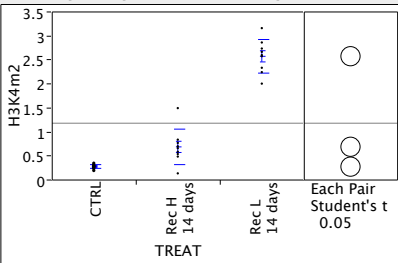
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.26878	0.044192	0.01473	0.2348	0.3027
Rec H 14 days	9	0.68311	0.363880	0.12129	0.4034	0.9628
Rec L 14 days	9	2.56911	0.345104	0.11503	2.3038	2.8344

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	54.000	6.0000	−3.678
Rec H 14 days	9	117.000	13.0000	−0.437
Rec L 14 days	9	207.000	23.0000	4.141

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
20.8635	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	− Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	CTRL	2.300333	2.017536	2.583131	<.0001*	
Rec L 14 days	Rec H 14 days	1.886000	1.603203	2.168797	<.0001*	
Rec H 14 days	CTRL	0.414333	0.131536	0.697131	0.0059*	
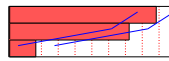
Fit Y by X Group

Oneway Analysis of Ig CTRL By TREAT PCR=r/h
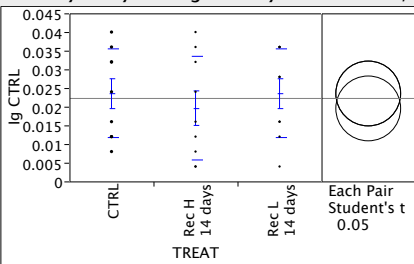
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.023556	0.011907	0.00397	0.01440	0.03271
Rec H 14 days	9	0.019556	0.013920	0.00464	0.00886	0.03026
Rec L 14 days	9	0.023556	0.011907	0.00397	0.01440	0.03271

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	133.000	14.7778	0.337
Rec H 14 days	9	110.500	12.2778	−0.778
Rec L 14 days	9	134.500	14.9444	0.415

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
0.6478	2	0.7233

Means Comparisons

Comparisons for each pair using Student's t

Level	− Level	Difference	Lower CL	Upper CL	p-Value	
CTRL	Rec H 14 days	0.0040000	−0.008272	0.0162725	0.5076	
Rec L 14 days	Rec H 14 days	0.0040000	−0.008272	0.0162725	0.5076	
CTRL	Rec L 14 days	3.469e-18	−0.012272	0.0122725	1.0000	
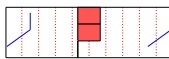
Oneway Analysis of H3K9m3 By TREAT PCR=r/h
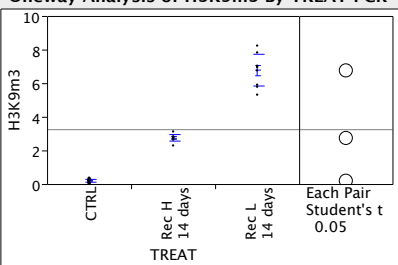
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.19867	0.105235	0.03508	0.1178	0.2796
Rec H 14 days	9	2.74400	0.216147	0.07205	2.5779	2.9101
Rec L 14 days	9	6.76411	0.952182	0.31739	6.0322	7.4960

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean-Mean0)/Std0
CTRL	9	45.000	5.0000	−4.140
Rec H 14 days	9	126.000	14.0000	0.000
Rec L 14 days	9	207.000	23.0000	4.140

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
23.1429	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	− Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	CTRL	6.565444	6.013799	7.117090	<.0001*	
Rec L 14 days	Rec H 14 days	4.020111	3.468466	4.571757	<.0001*	
Rec H 14 days	CTRL	2.545333	1.993688	3.096979	<.0001*	
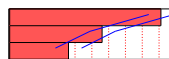
Statistical Table 3.
Statistical analysis of data
presented in Figure 2, panel B

Fit Y by X Group

Oneway Analysis of H3K9m2 By TREAT PCR=r/h
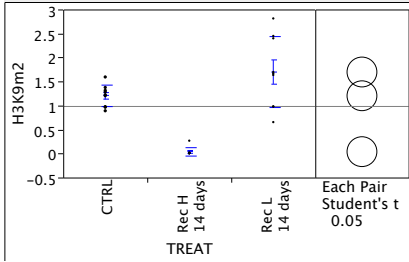
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	1.20378	0.226046	0.07535	1.030	1.3775
Rec H 14 days	9	0.03956	0.085766	0.02859	−0.026	0.1055
Rec L 14 days	9	1.69833	0.743538	0.24785	1.127	2.2699

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	147.000	16.3333	1.054
Rec H 14 days	9	45.000	5.0000	−4.140
Rec L 14 days	9	186.000	20.6667	3.060

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.6984	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	Rec H 14 days	1.658778	1.219591	2.097965	<.0001*	
CTRL	Rec H 14 days	1.164222	0.725035	1.603409	<.0001*	
Rec L 14 days	CTRL	0.494556	0.055369	0.933742	0.0289*	

Oneway Analysis of H3K4m3 By TREAT PCR=r/h
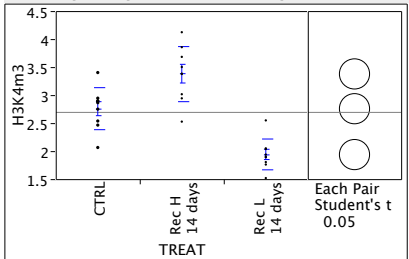
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	2.75789	0.373277	0.12443	2.4710	3.0448
Rec H 14 days	9	3.37889	0.491986	0.16400	3.0007	3.7571
Rec L 14 days	9	1.93900	0.279319	0.09311	1.7243	2.1537

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	135.000	15.0000	0.437
Rec H 14 days	9	194.000	21.5556	3.472
Rec L 14 days	9	49.000	5.4444	−3.935

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
18.7549	2	<.0001*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec H 14 days	Rec L 14 days	1.439889	1.059157	1.820621	<.0001*	
CTRL	Rec L 14 days	0.818889	0.438157	1.199621	0.0002*	
Rec H 14 days	CTRL	0.621000	0.240268	1.001732	0.0026*	

Oneway Analysis of H3K4m2 By TREAT PCR=r/h
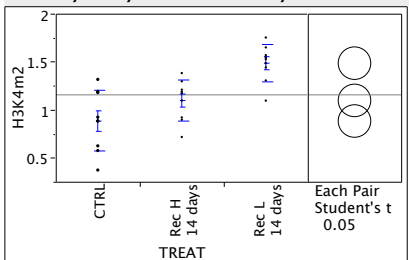
Means and Std Deviations

Level	Number	Mean	Std Dev	Std Err Mean	Lower 95%	Upper 95%
CTRL	9	0.88289	0.315166	0.10506	0.6406	1.1251
Rec H 14 days	9	1.09733	0.213400	0.07113	0.9333	1.2614
Rec L 14 days	9	1.48522	0.192653	0.06422	1.3371	1.6333

Wilcoxon / Kruskal-Wallis Tests (Rank Sums)

Level	Count	Score Sum	Score Mean	(Mean−Mean0)/Std0
CTRL	9	73.000	8.1111	−2.701
Rec H 14 days	9	109.000	12.1111	−0.849
Rec L 14 days	9	196.000	21.7778	3.575

1-way Test, ChiSquare Approximation

ChiSquare	DF	Prob>ChiSq
14.1101	2	0.0009*

Means Comparisons

Comparisons for each pair using Student's t

Level	– Level	Difference	Lower CL	Upper CL	p-Value	
Rec L 14 days	CTRL	0.6023333	0.362705	0.8419618	<.0001*	
Rec L 14 days	Rec H 14 days	0.3878889	0.148260	0.6275174	0.0027*	
Rec H 14 days	CTRL	0.2144444	−0.025184	0.4540729	0.0771	

Statistical Table 3.
Statistical analysis of data
presented in Figure 2, panel B

Fig 2 Panel C: Matched Pairs **Page 1 of 3**

Matched Pairs PCR=a/c, Ig=H3K9m2, Cell=Rec H

Difference: +AZA–Basal

+AZA	0.10156	t–Ratio	0.404291
Basal	0.091	DF	8
Mean Difference	0.01056	Prob > |t|	0.6966
Std Error	0.02611	Prob > t	0.3483
Upper95%	0.07076	Prob < t	0.6517
Lower95%	–0.0497		
N	9		
Correlation	0.77192		

Matched Pairs PCR=a/c, Ig=H3K9m2, Cell=Rec L

Difference: +AZA–Basal

+AZA	0.05256	t–Ratio	–11.7517
Basal	3.52233	DF	8
Mean Difference	–3.4698	Prob > |t|	<.0001*
Std Error	0.29526	Prob > t	1.0000
Upper95%	–2.7889	Prob < t	<.0001*
Lower95%	–4.1506		
N	9		
Correlation	0.62601		

Matched Pairs PCR=a/c, Ig=H3K9m3, Cell=Rec H

Difference: +AZA–Basal

+AZA	0.04856	t–Ratio	–1.39535
Basal	0.05856	DF	8
Mean Difference	–0.01	Prob > |t|	0.2004
Std Error	0.00717	Prob > t	0.8998
Upper95%	0.00653	Prob < t	0.1002
Lower95%	–0.0265		
N	9		
Correlation	0.99643		

Matched Pairs PCR=a/c, Ig=H3K9m3, Cell=Rec L

Difference: +AZA–Basal

+AZA	1.78922	t–Ratio	–9.29174
Basal	4.04567	DF	8
Mean Difference	–2.2564	Prob > |t|	<.0001*
Std Error	0.24284	Prob > t	1.0000
Upper95%	–1.6964	Prob < t	<.0001*
Lower95%	–2.8164		
N	9		
Correlation	0.80001		

Matched Pairs PCR=a/c, Ig=Ig-CTRL, Cell=Rec H

Difference: +AZA–Basal

+AZA	0.01056	t–Ratio	–0.05707
Basal	0.01067	DF	8
Mean Difference	–0.0001	Prob > |t|	0.9559
Std Error	0.00195	Prob > t	0.5221
Upper95%	0.00438	Prob < t	0.4779
Lower95%	–0.0046		
N	9		
Correlation	–0.4376		

Matched Pairs PCR=a/c, Ig=Ig-CTRL, Cell=Rec L

Difference: +AZA–Basal

+AZA	0.00911	t–Ratio	–0.09035
Basal	0.00922	DF	8
Mean Difference	–0.0001	Prob > |t|	0.9302
Std Error	0.00123	Prob > t	0.5349
Upper95%	0.00272	Prob < t	0.4651
Lower95%	–0.0029		
N	9		
Correlation	0.43208		

Matched Pairs PCR=p/q, Ig=H3K9m2, Cell=Rec H

Difference: +AZA–Basal

+AZA	0.29411	t–Ratio	0.682803
Basal	0.28167	DF	8
Mean Difference	0.01244	Prob > |t|	0.5140
Std Error	0.01823	Prob > t	0.2570
Upper95%	0.05447	Prob < t	0.7430
Lower95%	–0.0296		
N	9		
Correlation	0.98657		

Statistical Table 4.
Statistical analysis of data
presented in Figure 2, panel C

Fig 2 Panel C: Matched Pairs   **Page 2 of 3**

Matched Pairs PCR=p/q, Ig=H3K9m2, Cell=Rec L

Difference: +AZA−Basal

+AZA	0.34089	t–Ratio	−13.3869
Basal	3.59022	DF	8
Mean Difference	−3.2493	Prob > |t|	<.0001*
Std Error	0.24273	Prob > t	1.0000
Upper95%	−2.6896	Prob < t	<.0001*
Lower95%	−3.8091		
N	9		
Correlation	0.88252		

Matched Pairs PCR=p/q, Ig=H3K9m3, Cell=Rec H

Difference: +AZA−Basal

+AZA	0.91167	t–Ratio	8.654662
Basal	0.734	DF	8
Mean Difference	0.17767	Prob > |t|	<.0001*
Std Error	0.02053	Prob > t	<.0001*
Upper95%	0.22501	Prob < t	1.0000
Lower95%	0.13033		
N	9		
Correlation	0.99943		

Matched Pairs PCR=p/q, Ig=H3K9m3, Cell=Rec L

Difference: +AZA−Basal

+AZA	1.97689	t–Ratio	−12.3681
Basal	3.94711	DF	8
Mean Difference	−1.9702	Prob > |t|	<.0001*
Std Error	0.1593	Prob > t	1.0000
Upper95%	−1.6029	Prob < t	<.0001*
Lower95%	−2.3376		
N	9		
Correlation	0.86646		

Matched Pairs PCR=p/q, Ig=Ig−CTRL, Cell=Rec H

Difference: +AZA−Basal

+AZA	0.01211	t–Ratio	1.370315
Basal	0.01	DF	8
Mean Difference	0.00211	Prob > |t|	0.2078
Std Error	0.00154	Prob > t	0.1039
Upper95%	0.00566	Prob < t	0.8961
Lower95%	−0.0014		
N	9		
Correlation	−0.3947		

Matched Pairs PCR=p/q, Ig=Ig−CTRL, Cell=Rec L

Difference: +AZA−Basal

+AZA	0.01189	t–Ratio	0.862976
Basal	0.01011	DF	8
Mean Difference	0.00178	Prob > |t|	0.4133
Std Error	0.00206	Prob > t	0.2066
Upper95%	0.00653	Prob < t	0.7934
Lower95%	−0.003		
N	9		
Correlation	0.02634		

Matched Pairs PCR=r/h, Ig=H3K9m2, Cell=Rec H

Difference: +AZA−Basal

+AZA	0.05567	t–Ratio	1.533677
Basal	0.01778	DF	8
Mean Difference	0.03789	Prob > |t|	0.1637
Std Error	0.0247	Prob > t	0.0818
Upper95%	0.09486	Prob < t	0.9182
Lower95%	−0.0191		
N	9		
Correlation	0.7957		

Matched Pairs PCR=r/h, Ig=H3K9m2, Cell=Rec L

Difference: +AZA−Basal

+AZA	0.07433	t–Ratio	−8.56859
Basal	1.69844	DF	8
Mean Difference	−1.6241	Prob > |t|	<.0001*
Std Error	0.18954	Prob > t	1.0000
Upper95%	−1.187	Prob < t	<.0001*
Lower95%	−2.0612		
N	9		
Correlation	0.62913		

Statistical Table 4.
Statistical analysis of data
presented in Figure 2, panel C

Fig 2 Panel C: Matched Pairs   **Page 3 of 3**

Matched Pairs PCR=r/h, Ig=H3K9m3, Cell=Rec H

  Difference: +AZA–Basal

+AZA	2.18767	t–Ratio	–7.73435
Basal	2.78011	DF	8
Mean Difference	–0.5924	Prob > |t|	<.0001*
Std Error	0.0766	Prob > t	1.0000
Upper95%	–0.4158	Prob < t	<.0001*
Lower95%	–0.7691		
N	9		
Correlation	0.72727		

Matched Pairs PCR=r/h, Ig=H3K9m3, Cell=Rec L

  Difference: +AZA–Basal

+AZA	2.70956	t–Ratio	–26.3437
Basal	6.75311	DF	8
Mean Difference	–4.0436	Prob > |t|	<.0001*
Std Error	0.15349	Prob > t	1.0000
Upper95%	–3.6896	Prob < t	<.0001*
Lower95%	–4.3975		
N	9		
Correlation	0.85039		

Matched Pairs PCR=r/h, Ig=Ig-CTRL, Cell=Rec H

  Difference: +AZA–Basal

+AZA	0.01056	t–Ratio	–0.17933
Basal	0.011	DF	8
Mean Difference	–0.0004	Prob > |t|	0.8621
Std Error	0.00248	Prob > t	0.5689
Upper95%	0.00527	Prob < t	0.4311
Lower95%	–0.0062		
N	9		
Correlation	–0.4214		

Matched Pairs PCR=r/h, Ig=Ig-CTRL, Cell=Rec L

  Difference: +AZA–Basal

+AZA	0.01189	t–Ratio	0.8745
Basal	0.01011	DF	8
Mean Difference	0.00178	Prob > |t|	0.4073
Std Error	0.00203	Prob > t	0.2037
Upper95%	0.00647	Prob < t	0.7963
Lower95%	–0.0029		
N	9		
Correlation	–0.2743		