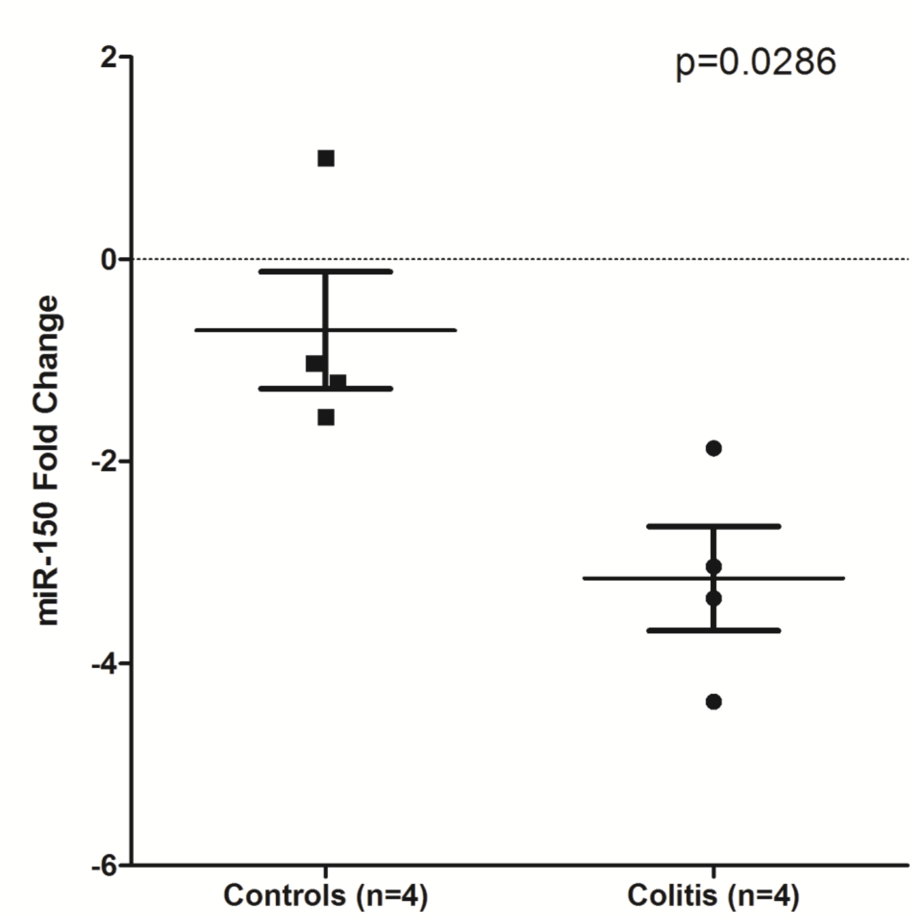
Supplemental Table 1. Schematic representation of CD69 3’ UTR depicting predicted miRNA binding sites. Alignment of CD69 mRNA sequence with specific miRNAs: top strand- CD69 mRNA; bottom strand-miRNA.

<table>
<tr><th>miRNA ID</th><th>GenBank Access No</th><th>Site Conservation</th><th>Binding site position</th><th>Target Site sequence</th><th>Prediction algorithm</th></tr>
<tr><td>miR-15a</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>65-71</td><td>5' ...AUCUGUGUCAAUGGAUGCUGCUC...
| || || ||
3' AAGUUUUGUACUUAACGACGAC</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-15b</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>65-71</td><td>5' ...AUCUGUGUCAAUGGAUGCUGCUC...
| | || |||
3' ACAUUUGGUACUACACGACGAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-20a</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>284-291</td><td>5' ...AUGAAACCUUUGGAUGCACUUUA...
| ||| || |
3' AUGGACGUGAUAUUCGUGAAAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-20b</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>284-291</td><td>5' ...AUGAAACCUUUGGAUGCACUUUA...
| || | || |
3' GAUGGACGUGAUACUCGUGAAAC</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-106b</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>284-291</td><td>5' ...AUGAAACCUUUGGAUGCACUUUA...
| | ||| | |
3' UAGACGUGACAGUCGUGAAAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-21</td><td>NM_001781</td><td>Human/Chimp/Macaque</td><td>953-959</td><td>5' ...GUGUUCAGUACAAUUAUAAGCUG...
| || | | | || || | |
3' AGUUGUAGUCAGAC------UAUUCGAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-301a</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse</td><td>384-391</td><td>5' ...GAGCGCUUCAUGCCUUUGCACUA...
| | || || |
3' CGAAACUGUUAUGAUAACGUGAC</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-181a</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Mouse/Rat</td><td>423-430</td><td>5' ...GUUGGUACUAGAUACUGAAUGUA...
| | || | ||
3' UGAGUGGCUGUCGCAACUUACAA</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-92a
(site 1)</td><td>NM_001781</td><td>Human/Chimp/Macaque</td><td>761-768</td><td>5' ...AAAGUGUUGGAAAAUGUGCAAUA...
| | | ||| |
3' UGUCCGGCCCUGUUCACGUUAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-92a
(site 2)</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Rat</td><td>872-879</td><td>5' ...AAUCAAUUCUAUUAUGUGCAAUA...
| | ||| ||
3' UGUCCGGCCCUGUUCACGUUAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-92a
(site 3)</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Rat</td><td>909-916</td><td>5' ...UUAAAAUAUUUUUAUGUGCAAUA...
| | | ||| |
3' UGUCCGGCCCUGUUCACGUUAU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-142-5p
(Proximal site)</td><td>NM_001781</td><td>Human/Chimp/Macaque/ Orangutan/Mouse/Rat</td><td>281-288</td><td>5' ...GCAACCUUUGGAUGCACUUUAUA...
|| | | | | |
3' UCAUCACGAAAGAUGAAAUAC</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-142-5p
(distal site)</td><td>NM_001781</td><td>Human/Chimp/Macaque</td><td>666-672</td><td>5' ...UACAUAUUUCUUUGC-CUUUAUAA...
| | || | | | | ||
3' UCAUCACGAAAGAUGAAAUAC</td><td>TargetScan (Lewis et al. 2005)</td></tr>
</table>

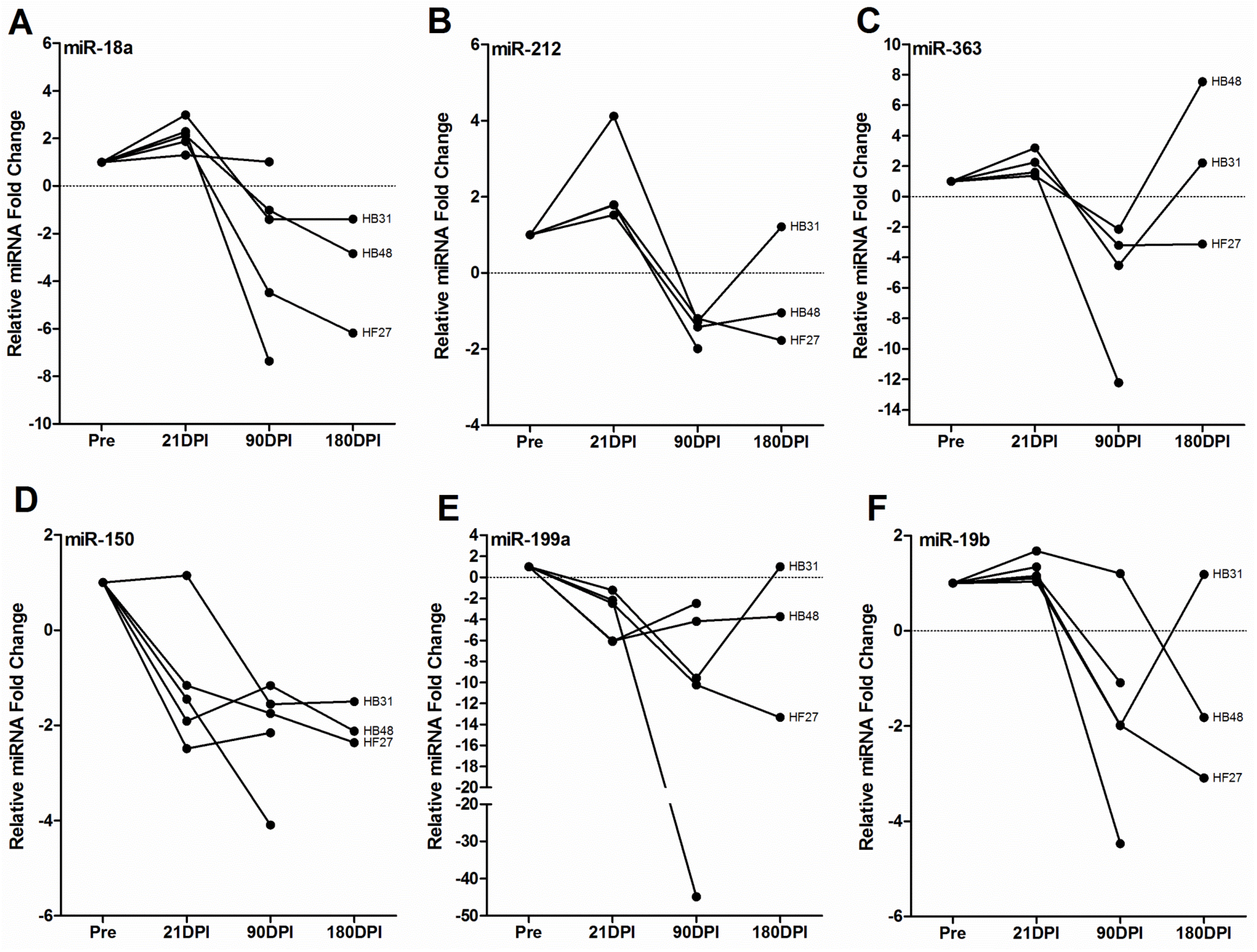
Supplemental Table 2. Schematic representation of IRAK1 3’ UTR depicting predicted miRNA binding sites. Alignment of IRAK1 mRNA sequence with specific miRNAs: top strand- IRAK1 mRNA; bottom strand-miRNA.

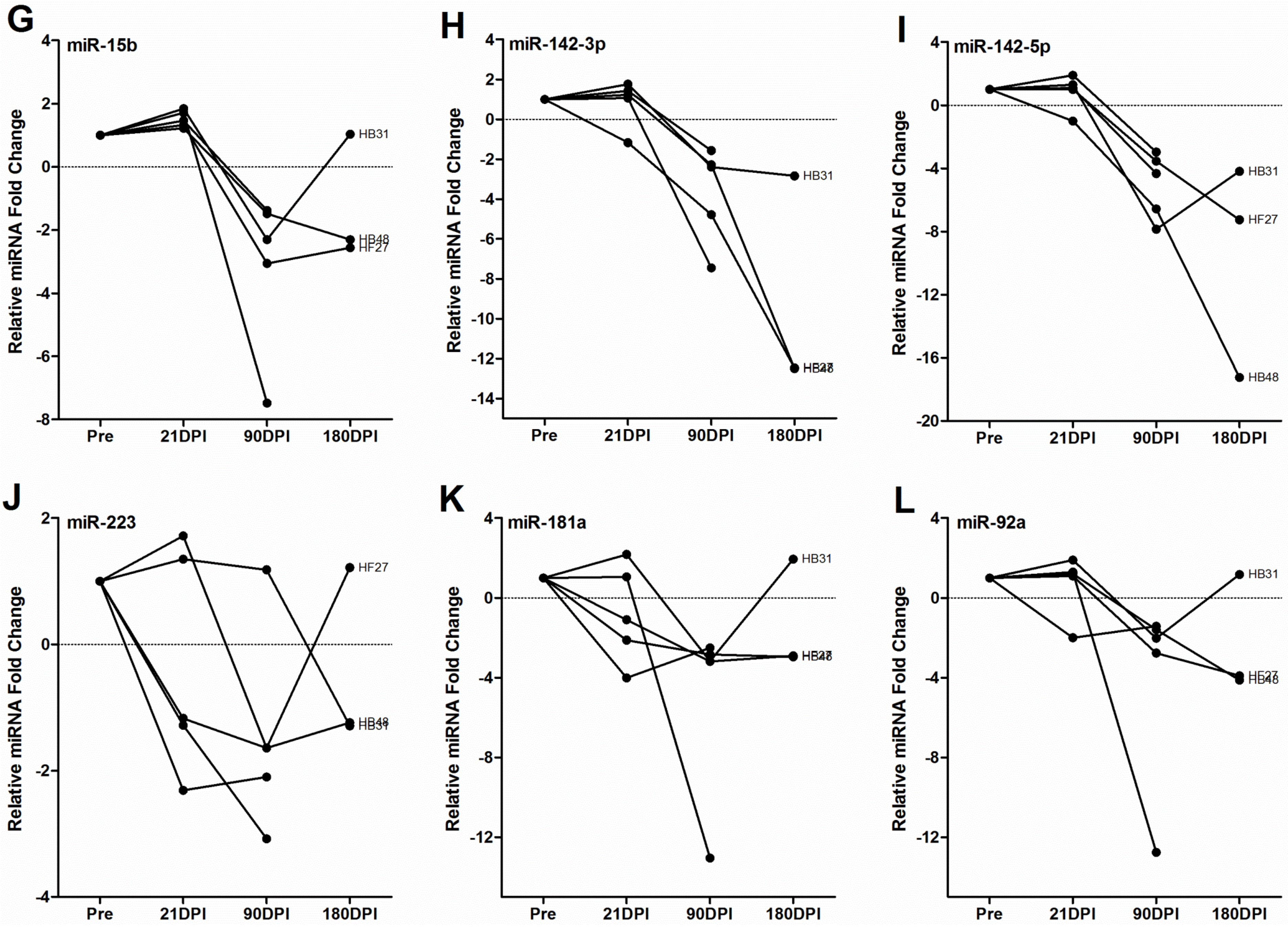
<table>
<tr><th>miRNA ID</th><th>GenBank Access Number</th><th>Site Conservation</th><th>Binding sites on 3’ UTR</th><th>Target Site sequence</th><th>Prediction algorithm</th></tr>
<tr><td>miR-150
(site 1)</td><td>NM_001025242</td><td>Human/Chimp/Macaque/</td><td>247-253</td><td>5' ...GGAGGCUGGCGCAUGUUGGGAGG...
| | | | | | | |
3' GUGACCAUGUUCCCAACCCUCU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-150
(site 2)</td><td>NM_001025242</td><td>Human/Chimp/Macaque/</td><td>505-511</td><td>5' ...UGUAAUCCCAGCACUUUGGGAGG...
| | | | | | | |
3' GUGACCAUGUUCCCAACCCUCU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-150
(site 3)</td><td>NM_001025242</td><td>Human/Chimp/Macaque/</td><td>664-671</td><td>5' ...UGUGGUCCCAGCUACUUGGGAGG...
| | | | | | | |
3' GUGACCAUGUUCCCAACCCUCU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-150
(site 4)</td><td>NM_001025242</td><td>Human/Chimp/Macaque/</td><td>1088-1094</td><td>5' ...GAGGAUCAUUUAUGCUUGGGAGA...
| | | | | | | |
3' GUGACCAUGUUCCCAACCCUCU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
<tr><td>miR-142-3p</td><td>NM_001025242</td><td>Human/Chimp/Macaque/
Orangutan/Mouse/Rat</td><td>1257-1264</td><td>5' ...GCUCAGCCGUGAGUCACACUACA...
| | | | | | | |
3' AGGUAUUUCAUCCUUUGUGAUGU</td><td>TargetScan (Lewis et al. 2005)</td></tr>
</table>

Supplemental Figure 1. Similar to SIV-infected macaques, miR-150 expression is significantly downregulated in colonic LPL of SIV-uninfected macaques with diarrhea and colitis suggesting that its downregulation is due to immune activation and not a consequence of $CD4^+$ T cell depletion as these animals have moderate to severe colitis and do not have $CD4^+$ T cell depletion. Data was normalized to snoU6. The error bars represent standard error of mean fold change within each group.

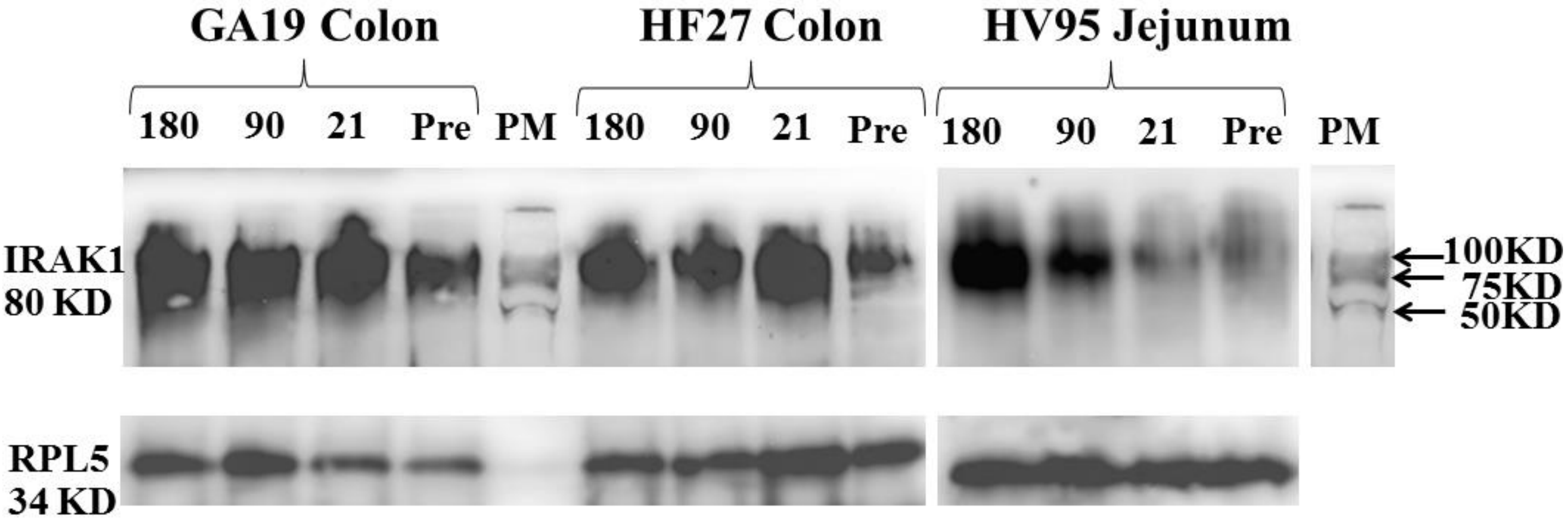


Supplemental Figure 2. Longitudinal expression of 12 miRNAs that showed statistically significant differential expression at 21 (miR-18a, -212, -363, -150 and -199a-5p) and 90 or180DPI (miR-15b, -19b, -92a, -142-3p, -142-5p, -150, -181a, -199a-5p and -223) based on TLDA profiling.




G
miR-15b
4
2
0
-2
-4
-6
-8
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HB31
HB48
HF27
H
miR-142-3p
4
2
0
-2
-4
-6
-8
-10
-12
-14
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HB31
HB48
HF27
I
miR-142-5p
4
0
-4
-8
-12
-16
-20
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HB31
HF27
HB48
J
miR-223
2
0
-2
-4
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HF27
HB48
HB31
K
miR-181a
4
0
-4
-8
-12
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HB31
HF27
HB48
L
miR-92a
4
0
-4
-8
-12
Relative miRNA Fold Change
Pre
21DPI
90DPI
180DPI
HB31
HF27
HB48

Supplemental Figure 3. Immunoprecipitation/western blotting revealed increased IRAK1 protein expression in colon and jejunum longitudinally as disease progressed. IRAK1 and ribosomal protein L5 (RPL5) were immunoprecipitated from colon and jejunal mucosal samples, run on SDS-PAGE, and thereafter, the membranes probed with appropriate antibodies. Notice the increased IRAK1 protein expression in colon (GA19 and HF27) at 21, 90 and 180 days post SIV (DPI) compared to the preinfection (Pre) time point. In the jejunum (HV95), significant increases in IRAK1 protein expression was observed at the 90 and 180DPI time points compared to the 21 and preinfection time point. The lane containing the precision plus protein™ dual color standard (BIO-RAD, Hercules, CA) (PM) has been moved to the right to show the actual sizes of the marker/reference bands.



REFRENCES

1. **Lewis BP, Burge CB, Bartel DP.** 2005. Conserved seed pairing, often flanked by adenosines, indicates that thousands of human genes are microRNA targets. Cell **120:**15–20. http://dx.doi.org/10.1016/j.cell.2004.12.035.