Supplemental Table 4. Schematic representation of CXCL12β (Transcript variant 1) 3' UTR depicting predicted miRNA binding sites. Alignment of CXCL12 mRNA sequence with specific miRNAs: top strand- CXCL12 mRNA; bottom strand-miRNA.

| miRNA<br>ID               | GenBank Access<br>Number    | Site Conservation                       | Binding sites<br>on 3' UTR | Target Site sequence   | Prediction algorithm             |
|---------------------------|-----------------------------|---|----------------------------|--|----------------------------------|
| miR-141<br>(prox site)    | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 51-58                      | 5' GCCCAGCUCUGAAACCAGUGUUA<br>        <br>3' GGUAGAAAUGGUCUGUCACAAU                | TargetScan (38), miRanda<br>(44) |
| miR-141<br>(distal site)  | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 2940-2947                  | 5'GAGCAGUGAAUGAUUCAGUGUUA<br>         <br>3' GGUAGAAAUGGUCUGUCACAAU                | TargetScan (38), miRanda<br>(44) |
| miR-200a<br>(prox site)   | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 51-58                      | 5'GCCCAGCUCUGAAACCAGUGUUA<br>        <br>3' UGUAGCAAUGGUCUGUCACAAU                 | TargetScan (38), miRanda<br>(44) |
| miR-200a<br>(distal site) | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 2940-2947                  | 5'GAGCAGUGAAUGAUUCAGUGUUA<br>        <br>3' UGUAGCAAUGGUCUGUCACAAU                 | TargetScan (38), miRanda<br>(44) |
| miR-23a<br>(prox site)    | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 2948-2954                  | 5'AAUGAUUCAGUGUUAAAUGUGAU<br>           <br>3' CCUUUAGGGACCGUUACACUA               | TargetScan (38), miRanda<br>(44) |
| miR-23a<br>(idstal site)  | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Orangutan/Mouse | 2997-3004                  | 5'UUGCAUCUCCCAGAUAAUGUGAA<br>               <br>3' CCUUUAGGGACCGUUACACUA           | TargetScan (38), miRanda<br>(44) |
| miR-152<br>(prox site)    | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Mouse/Rat       | 876-882                    | 5'CAAUGUCUUGAUGCAUGCACUGU<br>           <br>3' GGUUCAAGACAGUACGUGACU               | TargetScan (38), miRanda<br>(44) |
| miR-152<br>(idstal site)  | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque                     | 2495-2501                  | 5'UCCCCCUCUGUCCAGGCACUGAG<br>                         <br>3' GGUUCAAGACAGUACGUGACU | TargetScan (38), miRanda<br>(44) |
| miR-539<br>(prox site)    | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque/<br>Rat             | 1331-1337                  | 5'CCCUUCCCACAGGACAUUUCUCU<br>              <br>3' UGUGUGGUUCCUAUUAAAGAGG           | TargetScan (38), miRanda<br>(44) |
| miR-539<br>(idstal site)  | NM_000609<br>mRNA Variant 2 | Human/Chimp/Macaque                     | 2071-2077                  | 5'AAAGGAAUCAUUUCUAUUUCUCC<br>        <br>3' UGUGUGGUUCCUAUUAAAGAGG                 | TargetScan (38), miRanda<br>(44) |

Supplemental Table 5. Schematic representation of CXCL12α (Transcript variant 1) 3' UTR depicting predicted miRNA binding sites. Alignment of CXCL12 mRNA sequence with specific miRNAs: top strand- CXCL12mRNA; bottom strand-miRNA.

| miRNA<br>ID              | GenBank<br>Access Number    | Site Conservation                           | Binding sites<br>on 3' UTR | Target Site sequence   | Prediction algorithm             |
|--------------------------|-----------------------------|---|----------------------------|--|----------------------------------|
| miR-23a<br>(prox site)   | NM_199168<br>mRNA Variant 1 | Human/Chimp/Macaque/<br>Orangutan/Mouse     | 1387-1393                  | 5' UAUAUAUGAUAUAUAAAUGUGAU<br>        <br>3' CCUUUAGGGACCGUUACACUA           | TargetScan (38), miRanda<br>(44) |
| miR-23a<br>(distal site) | NM_199168<br>mRNA Variant 1 | Human/Chimp/Macaque/<br>Orangutan/Mouse     | 1452-1458                  | 5'ACUAAAAUUGUAUCAAAUGUGAC<br>          <br>3' CCUUUAGGGACCGUUACACUA          | TargetScan (38), miRanda<br>(44) |
| miR-301a                 | NM_199168<br>mRNA Variant 1 | Human/Chimp/Macaque/<br>Orangutan/Mouse/Rat | 1466-1472                  | 5'AAAUGUGACAUUAUAUGCACUAG<br>                 <br>3' CGAAACUGUUAUGAUAACGUGAC | TargetScan (38), miRanda<br>(44) |
| miR-362-3p               | NM_199168<br>mRNA Variant 1 | Human/Chimp/Macaque                         | 111-117                    | 5'UAACCAUGAGGACCAGGUGUGUG<br>             <br>3' ACUUAGGAACUUAUCCACACAA      | TargetScan (38), miRanda<br>(44) |

Supplemental Table 6. Schematic representation of CXCL12∆ (Transcript variant 4) 3' UTR depicting predicted miRNA binding sites. Alignment of CXCL12 mRNA sequence with specific miRNAs: top strand- CXCL12mRNA; bottom strand-miRNA.

| miRNA<br>ID              | GenBank Access<br>Number       | Site Conservation                           | Binding sites on<br>3' UTR | Target Site sequence  | Prediction algorithm             |
|--------------------------|--------------------------------|---|----------------------------|---|----------------------------------|
| miR-23a<br>(prox site)   | NM_001178034<br>mRNA Variant   | Human/Chimp/Macaque/<br>Orangutan/Mouse     | 503-509                    | 5'UAUAUAUGAUAUAUAAAUGUGAU<br>        <br>3' CCUUUAGGGACCGUUACACUA             | TargetScan (38), miRanda<br>(44) |
| miR-23a<br>(idstal site) | NM_001178034<br>mRNA Variant   | Human/Chimp/Macaque/<br>Orangutan/Mouse     | 568-574                    | 5'ACUAAAAUUGUAUCAAAUGUGAC<br>          <br>3' CCUUUAGGGACCGUUACACUA           | TargetScan (38), miRanda<br>(44) |
| miR-301a                 | NM_001178034<br>mRNA Variant 4 | Human/Chimp/Macaque/<br>Orangutan/Mouse/Rat | 582-588                    | 5'AAAUGUGACAUUAUAUGCACUAG<br>                  <br>3' CGAAACUGUUAUGAUAACGUGAC | TargetScan (38), miRanda<br>(44) |

Supplemental Table 7. Schematic representation of CXCL12 targeting miRNAs that showed incremental increase in THC only, VEH/SIV and THC/SIV macaques at 60 days post SIV infection. 3' UTR depicting predicted miRNA binding sites. Alignment of CXCL12 mRNA sequence with specific miRNAs: top strand- CXCL12 mRNA; bottom strand-miRNA.

| miRNA<br>ID              | GenBank Access<br>Number                   | Site Conservation                           | Binding sites<br>on 3' UTR | Target Site sequence   | Prediction<br>algorithm          |
|--------------------------|--|---|----------------------------|--|----------------------------------|
| miR-101                  | NM_000609<br>mRNA Variant 2<br>CXCL-12β    | Human/Chimp/Macaque/<br>Orangutan/Mouse     | 2959-2965                  | 5'GUUAAAUGUGAUGAAUACUGUAU<br>        <br>3' AAGUCAAUAGUGUCAUGACAU      | TargetScan (38), miRanda<br>(44) |
| miR-29b<br>(prox site)   | NM_000609<br>mRNA Variant 2<br>CXCL-12β    | Human/Chimp/Macaque/<br>Orangutan/Rat       | 2321-2327                  | 5'UGUCCCUCCGGGACCUGGUGCUG<br>          <br>3' AUUGGCUAAAGUCUACCACGAU   | TargetScan (38), miRanda<br>(44) |
| miR-29b<br>(distal site) | NM_000609<br>mRNA Variant 2<br>CXCL-12β    | Human/Chimp/Macaque                         | 2732-2738                  | 5'UGAUCGCCUUUCCCA-GGUGCUAC<br>           <br>3' AUUGGCUAAAGUCUACCACGAU | TargetScan (38), miRanda<br>(44) |
| miR-130a                 | NM_199168<br>mRNA Variant 1<br>CXCL-12α    | Human/Chimp/Macaque/<br>Orangutan/Mouse/Rat | 1466-1472                  | 5'AAAUGUGACAUUAUAUGCACUAG<br>        <br>3' UACGGGAAAAUUGUAACGUGAC     | TargetScan (38), miRanda<br>(44) |
| miR-101                  | NM_199168<br>mRNA Variant 1<br>CXCL-12α    | Human/Chimp/Macaque/<br>Orangutan/Rat       | 1510-1516                  | 5'AUGGUAUAAACGUCCUACUGUAU<br>       <br>3' AAGUCAAUAGUGUCAUGACAU       | TargetScan (38), miRanda<br>(44) |
| miR-130a                 | NM_001178034<br>mRNA Variant 4<br>CXCL-12∆ | Human/Chimp/Macaque/<br>Orangutan/Mouse/Rat | 582-588                    | 5'AAAUGUGACAUUAUAUGCACUAG<br>         <br>3' UACGGGAAAAUUGUAACGUGAC    | TargetScan (38), miRanda<br>(44) |
| miR-101                  | NM_001178034<br>mRNA Variant 4<br>CXCL-12∆ | Human/Chimp/Macaque/<br>Orangutan/Rat       | 626-632                    | 5'AUGGUAUAAACGUCCUACUGUAU<br>        <br>3' AAGUCAAUAGUGUCAUGACAU      | TargetScan (38), miRanda<br>(44) |



Supplemental Figure 1. Percentage of CD4+ (**A**) and CD8+ (**B**) T cells among duodenal lamina propria leukocytes (LPLs) isolated at 14, 30 and 60 days post SIV infection (DPI). The cells were first gated on singlets followed by lymphocytes, CD3 and then on CD3<sup>+</sup>CD4<sup>+/-</sup>CD8<sup>+/-</sup> and CD3<sup>+</sup>CD4<sup>+/-</sup>CD8<sup>+</sup> T- cell subsets.



Supplemental Figure 2. qRT-PCR demonstrated no difference in duodenal proinflammatory cytokine (TNF- $\alpha$ , IL-1 $\beta$ , MCP-1, CXCL11, IFN- $\gamma$ ) mRNA expression between VEH/SIV (n=4) and THC/SIV (n=4) macaques at 60 days post SIV infection.



Supplemental Figure 3. miR-99b localized to duodenal epithelium and lamina prorpria cells of both uninfected control macaques (**A-B**). Note the markedly weak miR-99b signal intensity compared to the VEH/SIV (Figure 4**A-B**) and THC/SIV (Figure 4**D-E**) macaques.



Supplemental Figure 4. Lipopolysaccharide-binding protein (LBP) was measured in plasma as a marker of microbial translocation. The plasma LBP concentrations (ng/ml plasma) did not differ statistically between VEH/SIV and THC/SIV groups at necropsy (60 days post SIV). Data were analyzed using non-parametric kruskal wallis test using the Prism v5 software (GraphPad software). The error bars represent standard error of mean LBP levels within each group.