

Table S2A:

CD4:CD3 T cell ratio

|              |                     |      |         |          |          |          |          |          |          |          |          |    |    |    |
|--------------|---------------------|------|---------|----------|----------|----------|----------|----------|----------|----------|----------|----|----|----|
|              | Treatment week      | 0    | -1      | -2       | 1        | 3        | 5        | 2        | 4        | 6        | 11       | 15 | 17 | 19 |
|              | Week post infection | 1    | 4       | 5        | 7        | 9        | 11       | 13       | 15       | 17       | 22       | 26 | 28 | 30 |
| Non-infected | J411                | 72.7 | 73.4    | 59.9     | 64.9     | 75.4     | 77.8     | 71.7     | 70.2     | 59.9     | 78.3     |    |    |    |
|              | J412                | 69.5 | 65.4    | 60.2     | 61.4     | 57.6     | 54.3     | 55.1     | 56.5     | 54.1     | 58.4     |    |    |    |
|              | average             | 71.1 | 69.4    | 60.05    | 63.15    | 66.5     | 66.05    | 63.4     | 63.35    | 57       | 68.35    |    |    |    |
|              |                     | 1    | 0.97609 | 0.844585 | 0.888186 | 0.935302 | 0.928973 | 0.891702 | 0.890999 | 0.801688 | 0.961322 |    |    |    |

|             |         |          |           |           |          |           |           |           |           |          |          |           |           |           |
|-------------|---------|----------|-----------|-----------|----------|-----------|-----------|-----------|-----------|----------|----------|-----------|-----------|-----------|
| Non-treated | J377    | 56.2     | 54.9      | 50.2      | 46.6     | 45.1      | 35.7      | 33.7      | 30.3      | 31.3     | 28.6     |           |           |           |
|             | J378    | 62.3     | 67.6      | 54.8      | 67.2     | 58.8      | 55.2      | 49.4      | 57.8      | 50.3     | 43       | 47.6      | 43.7      | 45.7      |
|             | J379    | 47.3     | 50.1      | 42.2      | 44.5     | 41.2      | 44.3      | 41.8      | 38.4      | 32.7     | 35.9     | 59.8      | 40.2      | 25        |
|             | J380    | 56.6     | 59.6      | 62.6      | 55.7     | 46.9      | 37.5      | 40.2      | 40.1      | 43.2     | 25.2     | 25.7      | 28.7      | 24.6      |
|             | J381    | 71.7     | 63        | 67        | 54.8     | 52.1      | 15.5      | 25.8      | 22.3      | 16.9     | 12.4     | N/A       | N/A       | N/A       |
|             | J389    | 64.3     | 43.9      | 54.9      | 52.8     | 48.5      | 47.3      | 41.4      | 40.9      | 42.1     |          |           |           |           |
|             | J390    | 71.2     | 67.8      | 62.3      | 67.7     | 56.4      | 51.2      | 47.8      | 43.1      | 40       |          |           |           |           |
|             | average | 61.37143 | 58.128571 | 56.285714 | 55.61429 | 49.857143 | 40.957143 | 40.014286 | 38.985714 | 36.64286 | 29.02    | 44.366667 | 37.533333 | 31.766667 |
|             |         | 1        | 0.9471601 | 0.9171322 | 0.906192 | 0.8123836 | 0.667365  | 0.6520019 | 0.6352421 | 0.597067 | 0.472859 | 0.7229205 | 0.6115767 | 0.5176133 |

|                          |         |       |           |           |          |           |           |           |           |          |  |  |  |
|--------------------------|---------|-------|-----------|-----------|----------|-----------|-----------|-----------|-----------|----------|--|--|--|
| Naked siRNAs (cocktails) | J431    | 67.2  | 68        | 64.4      | *        | 58.3      | 37.5      | 40        | 37.5      | 34.4     |  |  |  |
|                          | J432    | 52    | 47.7      | 44.1      | 47.8     | 40.9      | 39.1      | 43.3      | 41.8      | 40.1     |  |  |  |
|                          | J433    | 73.9  | 80        | 63.1      | 64.6     | 67.4      | 62.5      | 64.1      | 55.2      | 43.8     |  |  |  |
|                          | J434    | 67.8  | 66.7      | 64        | 58.1     | 58.3      | 40        | 45.5      | 42.1      | 38.7     |  |  |  |
|                          | J435    | 55.4  | 49.7      | 60.7      | 74.8     | 64.5      | 53.1      | 50.6      | 51.1      | 65.8     |  |  |  |
|                          | average | 63.26 | 62.42     | 59.26     | 61.325   | 57.88     | 46.44     | 48.7      | 45.54     | 44.56    |  |  |  |
|                          |         | 1     | 0.9867215 | 0.9367689 | 0.969412 | 0.9149542 | 0.7341132 | 0.7698388 | 0.7198862 | 0.704395 |  |  |  |

|                                       |         |       |           |           |          |           |          |           |           |          |          |           |           |           |
|---------------------------------------|---------|-------|-----------|-----------|----------|-----------|----------|-----------|-----------|----------|----------|-----------|-----------|-----------|
| A-1-stick-cocktailed siRNA conjugates | J472    | 64.4  | 64.3      | 50.2      | 38.5     | 46.7      | 30.7     | 31.4      | 49.4      | 47.6     | 35       | 41.7      | 35.9      | 46.6      |
|                                       | J473    | 45.3  | 58.8      | 45.4      | 50.7     | 45        | 40.6     | 42.3      | 64.6      | 60.4     | 62.5     | 51.2      | 65.6      | 26.6      |
|                                       | J474    | 50.7  | 43.5      | 42.3      | 45.8     | 42.3      | 46.2     | 38.5      | 52.1      | 53.3     | 46.7     |           |           |           |
|                                       | J475    | 61.8  | 50.8      | 45.5      | 42.4     | 38.6      | 32       | 28.7      | 42.4      | 54.5     | 51.8     | 47        | 25        | 0         |
|                                       | J481    | 71.2  | 62.5      | 64.3      | 65.8     | 60.1      | 55.6     | 60.2      | 60.2      | 64.5     | 81.9     | 53.4      | 50        | N/A       |
|                                       | J482    | 70.6  | 67        | 61.9      | 69.4     | 66.9      | 58.3     | 62.4      | 64.9      | 58.6     | 58.3     |           |           |           |
|                                       | J483    | 80.9  | 82.1      | 63.4      | 66.6     | 67.4      | 65.3     | 64.8      | 66.2      | 61.5     | 50       |           |           |           |
|                                       | J484    | 72.3  | 70.3      | 65.7      | 68.5     | 63.2      | 65.5     | 60.9      | 68.7      | 61.9     | 55.9     |           |           |           |
|                                       | average | 64.65 | 62.4125   | 54.8375   | 55.9625  | 53.775    | 49.275   | 48.65     | 58.5625   | 57.7875  | 55.2625  | 48.325    | 44.125    | 24.4      |
|                                       |         | 1     | 0.9653906 | 0.8482212 | 0.865623 | 0.8317865 | 0.762181 | 0.7525135 | 0.9058391 | 0.893852 | 0.854795 | 0.7474865 | 0.6825213 | 0.3774169 |

\*Sample not collected due to health of mice

# Table S2B:

## CD3+CD4+/CD3+CD4- Ratios

| <b>Comparison</b>       |    |                                            | <b>p-value</b> |
|-------------------------|----|--------------------------------------------|----------------|
| Uninfected Control      | vs | Naked cocktailed DsiRNA                    | P = 0.2179     |
| Uninfected Control      | vs | Non-Treated                                | P = 0.1403     |
| Uninfected Control      | vs | Aptamer-stick-cocktailed DsiRNA conjugates | P = 0.3162     |
| Naked cocktailed DsiRNA | vs | Non-Treated                                | P = 0.1203     |
| Naked cocktailed DsiRNA | vs | Aptamer-stick-cocktailed DsiRNA conjugates | P = 0.4050     |
| Non-Treated             | vs | Aptamer-stick-cocktailed DsiRNA conjugates | P = 0.0162     |

Overall p-value = 0.0348