

Supplemental Table 1. siRNA sequences (A). The first column in the table indicates the passenger strand from 5' to 3' end and the second column is the guide strand from 3' to 5' end. Abbreviations for the modifications are as follows: d (deoxy), flu (2' fluoro), ome (2'-O-methyl), ribo (ribose), iB (inverted abasic nucleotide). siRNA screen (B).

Supplemental Table 2. Gene expression changes at day 14 for control PBS, control siRNA, ApoB and Mtp siRNA treatments. Genes within the triglyceride synthesis (SREBP1c) pathway are highlighted (brown).

Supplemental Table 1

| A | Passenger Strand | Guide Strand |
|----------------------|---|---|
| control siRNA | iB;fluU;fluC;fluU;fluU;fluU;fluU;dA;dA;fluC;fluU;fluC;fluU;fluC;fluU;fluU;fluC;dA;dG;dG;dT;dT;iBSup | fluC;fluC;fluU;omeG;omeA;omeA;omeG;omeA;omeG;omeA;omeG;fluU;omeA;omeA;omeA;rA;rG;rA;omeU;omeUSup |
| Dgat2 | aba;fluC;fluU;dG;fluU;dA;dA;dA;fluU;fluU;fluU;dG;dG;dA;dA;dG;fluC;dG;fluU;fluC;dT;dT;iBSup | rG;rA;rC;omeG;fluC;fluU;fluU;fluC;fluC;omeA;omeA;omeA;fluU;fluU;fluU;omeA;fluC;omeA;omeG;omeU;omeUSup |
| Mtp | [[B]][dG][dA][fluU][dA][fluU][dG][fluC][fluU][dA][fluU][dG][dA][fluC][dG][fluU][dG][fluC][fluC][fluU]dTdT[iB] | rA;rG;rG;fluC;omeA;fluC;omeG;fluU;fluC;omeA;fluU;omeA;omeG;fluC;omeA;fluU;omeA;fluU;fluC;omeU;omeUSup |
| ApoB | iB;fluU;fluC;dA;fluU;fluC;dA;fluC;dA;fluC;fluU;dG;dA;dA;fluU;dA;fluC;fluC;dA;dA;dT;dT;iBSup | rU;rU;rG;omeG;fluU;omeA;fluU;fluU;fluC;omeA;omeG;fluU;omeG;fluU;omeG;omeA;fluU;omeG;omeA;omeU;omeUSup |

| B | siRNA | % Expression | EC50 (pM) |
|----------|--------------|---------------------|------------------|
| | Dgat2 | 25 | 20 |
| | Mtp | 7 | 2 |
| | ApoB | 6 | 99 |

| Gene | PBS | | Cntrl | | ApoB | | Mtp | |
|-----------------|--------------|---------|--------------|---------|--------------|---------|--------------|---------|
| | Ave Fold Reg | p-value | Ave Fold Reg | p-value | Ave Fold Reg | p-value | Ave Fold Reg | p-value |
| Aacs | -2.08 | 0.447 | -0.08 | N/A | -2.6 | 0.003 | -2.6 | 0.005 |
| Acaca | -0.87 | 0.419 | -0.1 | N/A | -2.08 | 0.003 | -2.79 | 0.004 |
| Acacb | -1.94 | 0.66 | 0.11 | N/A | -4.81 | 0.001 | -4.68 | 0.002 |
| Acat2 | -2.11 | 0.149 | 0.12 | N/A | -2.14 | 0.015 | -2.49 | 0.005 |
| Acly | -1.55 | 0.948 | -0.11 | N/A | -1.75 | 0.063 | -2.66 | 0.015 |
| Acscf2 | -0.95 | 0.527 | 0.12 | N/A | 0.5 | 0.793 | -1.35 | 0.111 |
| Acs1 | -3.36 | 0.082 | -0.02 | N/A | -1.26 | 0.258 | -1.44 | 0.097 |
| Acs3 | -1.47 | 0.274 | -0.29 | N/A | -1.85 | 0.055 | -2.67 | 0.017 |
| Acs4 | -1.36 | 0.344 | -0.28 | N/A | -2.02 | 0.033 | -1.7 | 0.083 |
| Acs5 | -1.37 | 0.30 | -0.30 | N/A | -2.24 | 0.01 | -2.57 | 0.00 |
| Acscs2 | -2.63 | 0.19 | 0.21 | N/A | -3.49 | 0.00 | -4.53 | 0.00 |
| ActB | 0.01 | 1.00 | 0.14 | N/A | 1.00 | 1.00 | 1.00 | 1.00 |
| Adi1 | -2.97 | 0.06 | -0.55 | N/A | -1.78 | 0.14 | -1.88 | 0.03 |
| Agpat1 | -0.75 | 0.54 | 0.27 | N/A | -1.27 | 0.42 | -1.22 | 0.22 |
| Agpat2 | -1.26 | 0.36 | -0.35 | N/A | -1.67 | 0.04 | -1.81 | 0.02 |
| Agpat3 | -1.39 | 0.24 | -0.31 | N/A | -1.67 | 0.06 | -1.71 | 0.06 |
| Agpat4 | -0.34 | 0.93 | 0.06 | N/A | 0.10 | 0.90 | -0.78 | 0.42 |
| Agpat5 | -0.23 | 0.81 | -0.07 | N/A | -1.05 | 0.29 | -0.84 | 0.29 |
| Agpat6 | -0.68 | 0.55 | 0.06 | N/A | -0.80 | 0.34 | -1.37 | 0.17 |
| Agpat9 | -1.75 | 0.22 | -0.35 | N/A | -1.11 | 0.28 | -1.84 | 0.06 |
| Angptl4 | 0.37 | 0.81 | 0.11 | N/A | -0.21 | 0.97 | 0.90 | 0.21 |
| ApoA1 | -1.96 | 0.08 | -0.39 | N/A | -1.93 | 0.02 | -1.60 | 0.07 |
| ApoB | -1.08 | 0.25 | -0.35 | N/A | -8.27 | 0.00 | -1.23 | 0.13 |
| ApoC3 | -1.00 | 0.29 | -0.36 | N/A | -1.00 | 0.38 | -1.06 | 0.29 |
| ApoE | -1.11 | 0.17 | -0.36 | N/A | -1.08 | 0.23 | -1.01 | 0.30 |
| Baat | -0.53 | 0.56 | -0.14 | N/A | -0.72 | 0.28 | -1.11 | 0.16 |
| Cds1 | -1.29 | 0.24 | -0.26 | N/A | -1.86 | 0.07 | -2.14 | 0.04 |
| Chpt1 | -1.41 | 0.27 | -0.61 | N/A | -1.45 | 0.14 | -1.81 | 0.03 |
| Cyb5r3 | -1.99 | 0.13 | -0.38 | N/A | -1.91 | 0.01 | -1.99 | 0.00 |
| Cyp27a1 | -1.50 | 0.18 | -0.05 | N/A | -1.77 | 0.06 | -1.57 | 0.11 |
| Cyp39a1 | -1.72 | 0.24 | -0.26 | N/A | -3.00 | 0.00 | -2.77 | 0.02 |
| Cyp46a1 | -2.14 | 0.25 | 0.34 | N/A | -1.27 | 0.14 | -2.30 | 0.01 |
| Cyp51a1 | -0.95 | 0.47 | 0.15 | N/A | -2.31 | 0.00 | -2.13 | 0.00 |
| Cyp7a1 | -0.49 | 0.64 | -0.13 | N/A | -0.57 | 0.53 | -2.23 | 0.10 |
| Cyp7b1 | 0.77 | 0.60 | 0.19 | N/A | 1.19 | 0.42 | 1.80 | 0.26 |
| Cyp8b1 | -1.29 | 0.25 | 0.40 | N/A | -2.47 | 0.00 | -3.05 | 0.03 |
| Dgat1 | -1.37 | 0.35 | -0.12 | N/A | -1.57 | 0.04 | -1.81 | 0.01 |
| Dgat2 | -0.72 | 0.50 | 0.15 | N/A | -0.18 | 0.84 | -1.45 | 0.06 |
| Dhcr24 | -0.16 | 0.85 | 0.14 | N/A | -1.90 | 0.00 | -2.27 | 0.01 |
| Dhcr7 | -1.05 | 0.34 | 0.14 | N/A | -1.80 | 0.00 | -2.24 | 0.00 |
| Elovl1 | -0.01 | 0.95 | -0.14 | N/A | -0.80 | 0.08 | -0.61 | 0.27 |
| Elovl2 | -0.72 | 0.59 | -0.42 | N/A | -3.55 | 0.00 | -2.99 | 0.00 |
| Elovl3 | -1.94 | 0.09 | -0.29 | N/A | -3.80 | 0.00 | -1.19 | 0.53 |
| Elovl4 | 3.37 | 0.07 | -0.23 | N/A | 1.79 | 0.23 | 1.93 | 0.16 |
| Elovl5 | -1.97 | 0.23 | -0.13 | N/A | -5.22 | 0.00 | -5.67 | 0.00 |
| Elovl6 | -2.13 | 0.53 | -0.14 | N/A | -3.19 | 0.00 | -4.00 | 0.00 |
| Fads1 | -1.48 | 0.47 | 0.14 | N/A | -3.49 | 0.00 | -3.37 | 0.00 |
| Fads2 | -1.63 | 0.40 | 0.38 | N/A | -3.72 | 0.00 | -3.66 | 0.00 |
| Fads3 | -0.05 | 0.95 | 0.14 | N/A | -0.50 | 0.73 | -0.47 | 0.76 |
| Fasn | -1.54 | 0.39 | 0.08 | N/A | -2.45 | 0.00 | -7.43 | 0.00 |
| Fdft1 | 2.23 | 0.20 | -0.36 | N/A | -0.62 | 0.55 | -0.54 | 0.68 |
| Fdps | -0.01 | 0.81 | -0.15 | N/A | -2.87 | 0.00 | -3.33 | 0.01 |
| Gpat | -0.91 | 0.65 | 0.03 | N/A | -1.09 | 0.35 | -3.89 | 0.04 |
| Gpr65 | -0.21 | 0.64 | 0.14 | N/A | -0.52 | 0.60 | -0.53 | 0.65 |
| Haa0 | -0.16 | 0.85 | -0.12 | N/A | -0.90 | 0.27 | -1.03 | 0.09 |
| Hmgcr | -0.93 | 0.64 | -0.43 | N/A | -1.47 | 0.00 | -2.17 | 0.00 |
| Hmgcs1 | -1.05 | 0.25 | 0.15 | N/A | -2.06 | 0.00 | -2.25 | 0.01 |
| Hsd17b6 | -1.15 | 0.51 | 0.19 | N/A | -0.11 | 0.98 | -2.22 | 0.15 |
| Hsd3b7 | 0.55 | 0.72 | -0.28 | N/A | -0.51 | 0.78 | -0.59 | 0.63 |
| Idi1 | -1.30 | 0.22 | -0.14 | N/A | -2.52 | 0.00 | -2.72 | 0.01 |
| Lcat | 0.00 | 0.94 | -0.13 | N/A | -1.19 | 0.28 | -0.87 | 0.43 |
| Ldlr | -0.81 | 0.46 | -0.14 | N/A | -1.42 | 0.02 | -2.02 | 0.00 |
| Lpcat4 (Agpat7) | -0.04 | 0.88 | 0.14 | N/A | -0.22 | 0.72 | -0.31 | 0.45 |
| Lrp8 | 0.67 | 0.47 | 0.37 | N/A | 0.24 | 0.82 | 0.83 | 0.38 |
| Lycat (Agpat8) | -1.03 | 0.27 | -0.13 | N/A | -0.58 | 0.32 | -0.89 | 0.05 |

| | | | | | | | | |
|---------|--------------|-------------|--------------|-----|--------------|-------------|--------------|-------------|
| Mogat1 | -0.92 | 0.48 | 0.11 | N/A | 0.51 | 0.71 | -3.03 | 0.08 |
| Mogat2 | -0.57 | 0.60 | -0.15 | N/A | 1.19 | 0.30 | -2.17 | 0.08 |
| Mtp | -0.64 | 0.63 | -0.15 | N/A | -1.59 | 0.00 | -6.86 | 0.00 |
| Mvd | -0.06 | 0.93 | 0.13 | N/A | -1.81 | 0.09 | -2.58 | 0.30 |
| Mvk | 0.68 | 0.58 | 0.14 | N/A | 0.51 | 0.39 | -0.21 | 0.71 |
| Pcsk9 | -0.08 | 1.00 | 0.13 | N/A | -1.59 | 0.01 | -2.46 | 0.01 |
| Pcyt2 | -0.80 | 0.37 | 0.14 | N/A | -1.63 | 0.00 | -1.69 | 0.00 |
| Pmvk | -1.63 | 0.15 | 0.38 | N/A | -3.21 | 0.00 | -3.27 | 0.01 |
| Ppap2a | -74.81 | 0.00 | -0.13 | N/A | -50.58 | 0.27 | -26.10 | 0.61 |
| Ppap2b | 0.33 | 0.78 | 0.14 | N/A | -0.93 | 0.21 | -1.70 | 0.00 |
| Ppap2c | -0.17 | 0.87 | -0.13 | N/A | -0.88 | 0.39 | -0.34 | 0.39 |
| Ppara | -0.65 | 0.64 | 0.14 | N/A | -0.73 | 0.21 | -1.33 | 0.04 |
| Ppard | -0.54 | 0.56 | -0.36 | N/A | -2.16 | 0.02 | -0.52 | 0.81 |
| Pparg | -0.37 | 0.93 | -0.13 | N/A | -2.00 | 0.00 | -1.21 | 0.04 |
| Ppia | -0.29 | 0.85 | -0.14 | N/A | -0.92 | 0.28 | -0.59 | 0.41 |
| Scap | 0.09 | 0.90 | -0.12 | N/A | -1.04 | 0.06 | -0.66 | 0.19 |
| Scarb1 | 0.27 | 0.87 | -0.11 | N/A | -0.87 | 0.49 | -0.46 | 0.87 |
| Scd1 | -1.47 | 0.18 | 0.14 | N/A | -4.92 | 0.00 | -5.56 | 0.00 |
| Scd2 | 0.21 | 0.79 | 0.14 | N/A | 0.48 | 0.67 | -0.03 | 0.78 |
| Sgpl1 | 0.49 | 0.79 | -0.14 | N/A | -1.09 | 0.09 | -1.18 | 0.05 |
| Sgpp1 | 0.06 | 0.98 | 0.42 | N/A | -0.98 | 0.13 | -1.07 | 0.08 |
| Slc27a5 | -0.36 | 0.83 | 0.17 | N/A | -0.57 | 0.57 | -0.96 | 0.34 |
| Soat1 | 0.22 | 0.77 | -0.15 | N/A | -0.51 | 0.53 | -0.15 | 0.93 |
| Soat2 | -0.39 | 0.60 | 0.15 | N/A | -0.55 | 0.39 | -1.76 | 0.00 |
| Sptlc1 | 0.06 | 0.95 | -0.14 | N/A | -1.35 | 0.04 | -1.42 | 0.01 |
| Srebf2 | -0.24 | 0.61 | 0.42 | N/A | -0.71 | 0.07 | -1.13 | 0.02 |
| Stard3 | 0.29 | 0.75 | 0.14 | N/A | -0.83 | 0.41 | -0.26 | 0.52 |
| Tm7sf2 | -0.95 | 0.47 | 0.14 | N/A | -2.55 | 0.00 | -3.10 | 0.00 |
| Vldlr | -23.98 | 0.43 | -0.18 | N/A | -0.96 | 0.81 | -1.97 | 0.20 |
| Xpnpep3 | 0.08 | 0.98 | 0.14 | N/A | 0.74 | 0.82 | -0.22 | 0.68 |