

## Supplemental Data Tables and Figures

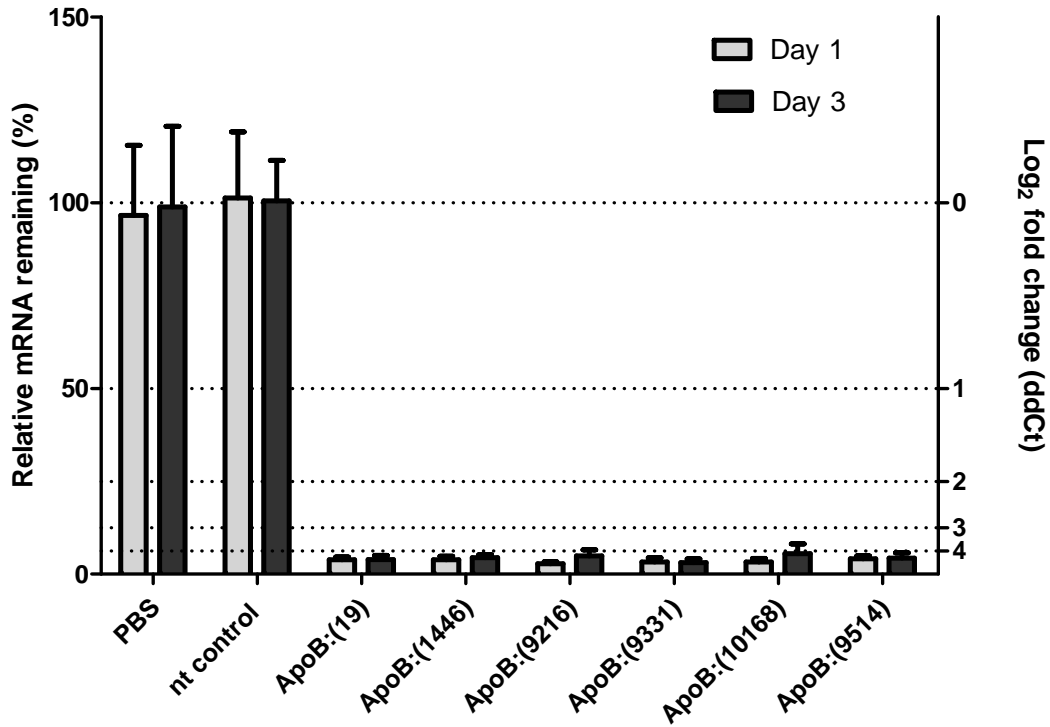
**Supplemental Table 1.** Changes in liver ApoB mRNA knockdown and serum lipid levels in *Ldlr<sup>+/-</sup> CETP<sup>+/-</sup>* mice at day 3 following a single 3 mg/kg dose of OCD-ApoB:(10168). Reduction in serum lipid profiles (including HDL) correlates with ApoB mRNA knockdown.

	<b>mRNA</b>	<b>TC</b>		<b>HDL</b>		<b>non-HDL</b>	
<b>ApoB siRNA dose</b>	<b>% Expression</b>	<b>% change</b>	<b>p-value</b>	<b>% change</b>	<b>p- value</b>	<b>% change</b>	<b>p-value</b>
<b>3.0 mg/kg</b>	5.5	-68.8	<0.0001	-56.0	0.0002	-81.7	<0.0001
<b>1.0 mg/kg</b>	7.4	-65.4	<0.0001	-52.4	0.0004	-78.5	<0.0001
<b>0.3 mg/kg</b>	13.9	-57.0	<0.0001	-34.5	0.0069	-79.7	<0.0001
<b>0.1 mg/kg</b>	42.9	-30.6	0.0002	-17.7	0.0946	-43.4	0.0002

**Supplemental Table 2.** Biological Pathways significantly enriched in liver upon ApoB KD.

<b>Similar Set</b>	<b>Expectation</b>	<b>Collection</b>
sterol metabolic process	3.87 E-17	GO Biological Process
sterol biosynthetic process	1.12 E-16	GO Biological Process
alcohol metabolic process	1.94 E-14	GO Biological Process
cholesterol metabolic process	2.87 E-14	GO Biological Process
Lipid synthesis	3.34 E-14	SwissProt Keywords
lipid metabolic process	1.54 E-12	GO Biological Process
small molecule metabolic process	1.14 E-11	GO Biological Process
steroid metabolic process	2.87 E-11	GO Biological Process
lipid biosynthetic process	1.18 E-09	GO Biological Process
steroid biosynthetic process	2.71 E-09	GO Biological Process

**Supplemental Figure 1.** *In vivo* efficacy of LNP201-ApoB siRNAs at day 1 and 3 post dosing in BALB/c mice. Animals were dosed i.v. with a single 3 mg/kg dose of ApoB siRNA-LNPs non-targeting control siRNA-LNP or PBS (vehicle) control. ApoB liver mRNA knockdown is over 90% for all siRNAs tested at day 1 and 3 post dosing.



**Supplemental Figure 2.** Increasing concentrations of LNP201-ApoB siRNA exhibit greater reductions of serum LDL on day 1 and day 7 post-treatment in individual *Ldlr<sup>+/-</sup> CETP<sup>+/-</sup>* mice. Mice were dosed i.v. with a single 0.3, 1.0, or 3.0 mg/kg dose of LNP201-ApoB:(10168) and their serum lipids determined at day 1 and 7 post siRNA dosing. Reductions in serum LDL levels are dose-dependent and very uniform among different animals.

