## **Supplementary Materials**

**Title:** RNAi-mediated silencing of SOD1 profoundly extends survival and functional outcomes in ALS mice

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Supplemental Figure 1: SOD1 123 silences both human and non-human primate mRNA in vitro. (A, B) 7-point dose-response curves for SOD1 123 and SOD1\_NHP in (A) LLC-MK2 cells (NHP-derived) or (**B**) HeLa cells (human-derived) (n = 3, mean  $\pm$  SD). HeLa and LLC MK2 cells were treated with siRNAs at concentrations shown for 72 h (Passive uptake). mRNA levels were measured using QuantiGene, (n=3, mean  $\pm$  SD), UNT (untreated), NTC (non-targeting control). (C) Sequence of the human-targeting siRNA guide (red) against the NHP target mRNA (blue). Mismatch shown in bold. (D) Sequence of the NHP-targeting guide strand (red) against the human target mRNA (blue). Mismatch shown in bold. IC<sub>50</sub> values are shown above the graph. IC<sub>50</sub> values were calculated using the nonlinear least squares method (GraphPad Prism).



Supplemental Figure 2: Chemical optimization of SOD1\_123 reveals multiple potent configurations. (A) Schematic of siRNA patterns (top), and chemical modifications (bottom). (B)

HeLa cells treated by passive uptake with SOD1\_123 in four distinct patterns. The left panel shows diagram of the guide strands. (C) 7-point dose-reponse curves for siRNAs in B. (D) HeLa cells treated (by passive uptake) with SOD1\_123 (E) 7-point dose-response curves for siRNAs described in D. (F) HeLa cells treated (by passive uptake) with the modification patterns shown (G) 7-point dose-response curves for siRNAs described in F. (H) HeLa cells treated (by passive uptake) with four SOD1\_123 siRNAs in the Methyl-rich pattern, (I) 7-point dose-response curves for siRNAs described in F. (J) As in H but in the Balanced pattern. (K) Dose-dependent analysis of siRNAs described in H but in the Balanced pattern. Top dose 1.5  $\mu$ M, SOD1 mRNA evaluated at 72 hours, QuantiGene, (n=3, mean  $\pm$  SD). NTC (nontargeting control siRNA), UNT (untreated). The target site and IC<sub>50</sub> values are shown in the graphs. IC<sub>50</sub> values were calculated using the nonlinear least squares method (GraphPad Prism).



Supplemental Figure 3: Astrogliosis in the cortex but not lumbar spinal cord of di-siRNA treated G93A mice versus untreated G93A mice. (A, B) GFAP-stained sagittal section of brain (A) and transverse lumbar spinal cord (B) images with rectangles indicate the regions of interest (ROIs) used for quantification. (C) Representative images of layer V of primary motor cortex

and anterior horn. Scale bar=100  $\mu$ m. (**D**, **E**) Quantification of GFAP signal in layer V of primary motor cortex (**D**) and anterior horn of lumbar spinal cord (**E**). Data in the bar graphs are shown as mean ±SEM n=2 per group. One-way ANOVA with post hoc Holm-Šídák test.



Supplemental Figure 4: Di-siRNA treatment activates cortical microglia and attenuates microgliosis in the anterior horn. (A) Representative images and insets of Iba-1 stained microglia in Motor cortex. Scale bar=100  $\mu$ m Scale bar=15  $\mu$ m (inset). (B) Representative images and insets of Iba-1 stained microglia in anterior horn. Scale bar=100  $\mu$ m, scale bar in inset=15  $\mu$ m. (C) Quantification of Iba-1 stained microglia in layer V of primary motor cortex and (D) anterior horn of lumbar spinal cord. Data in the bar graphs are shown as mean ±SEM n=2 per group. One-way ANOVA with post hoc Holm-Šídák test.

Expe	riment	Antisense Strand (5'-3')	Sense Strand (5'-3')
Origi	nal SOD1 In Vitro Screen		
	siRNA Name		
	SOD1 796	P(m1)#(f1)#(mA)(fA)(mC)(f1)(mG)(fA)(mG)(f1)(m1)(f1)(m1)#(fA)#(m1)#(fA)#(mA)#(fA)#(mA)#(fC)	(f4)#(m1)#(f4)(m4)(f4)(m4)(fC)(m1)(fC)(m4)(fG)(m1)(f1)#(m4)#(f4)-TegChol
	5001_750		
	SOD1_788		(iG)#(iiG)#(iA)(iiG)(iA)(iiG)(iG)(iiG)(iiG)(iiG)(iA)(iiG)(iA)(iiG)(iA)#(iiA)#(iA)*regolio
-	30D1_393		[16]#(III6]#(III6)(IIC)(III6)(IC)(IIIA)(III6)(IC)(IIIA)(III0)(IA)#(IIIA)#(IIIA)#(IIA)=18gClibi
_	SOD1_205	P(mU)#(tU)#(mU)(tC)(mC)(tU)(mU)(tC)(mU)(tG)(mC)(tU)(mC)#(tG)#(mA)#(tA)#(mA)#(tU)#(mU)#(tG)	{tU}#(mC)#(tG)(mA)(tG)(mC)(tA)(mG)(tA)(mA)(tG)(mG)(tA)#(mA)#(tA)-TegChol
	SOD1_926	P(mU)#(tU)#(mU)(tA)(mA)(tU)(mA)(tG)(mC)(tC)(mU)(tC)(mA)#(tU)#(mA)#(tA)#(mU)#(tA)#(mA)#(tG)	(fU)#(mA)#(fU)(mG)(fA)(mG)(fG)(mC)(fU)(mA)(fU)(mU)(fA)#(mA)#(fA)-TegChol
	SOD1_406	P(mU)#(fU)#(mU)(fU)(mG)(fU)(mC)(fA)(mG)(fC)(mA)(fG)(mU)#(fC)#(mA)#(fC)#(mA)#(fU)#(mU)#(fG)	(fU)#(mG)#(fA)(mC)(fU)(mG)(fC)(mU)(fG)(mA)(fC)(mA)(fA)#(mA)#(fA)-TegChol
	SOD1_754	P(mU)#(fU)#(mA)(fA)(mA)(fU)(mC)(fA)(mG)(fU)(mU)(fU)(mC)#(fU)#(mC)#(fA)#(mC)#(fU)#(mA)#(fC)	(fG)#(mA)#(fG)(mA)(fA)(mA)(fC)(mU)(fG)(mA)(fU)(mU)(fU)#(mA)#(fA)-TegChol
	SOD1_888	P(mU)#(fU)#(mC)(fA)(mC)(fA)(mG)(fG)(mC)(fU)(mU)(fG)(mA)#(fA)#(mU)#(fG)#(mA)#(fC)#(mA)#(fA)	(fA)#(mU)#(fU)(mC)(fA)(mA)(fG)(mC)(fC)(mU)(fG)(mU)(fG)#(mA)#(fA)-TegChol
	SOD1 915	P(mU)#(fA)#(mU)(fA)(mA)(fU)(mA)(fA)(mG)(fU)(mG)(fC)(mC)#(fA)#(mU)#(fA)#(mC)#(fA)#(mG)#(fG)	(fA)#(mU)#(fG)(mG)(fC)(mA)(fC)(mU)(fU)(mA)(fU)(mU)(fA)#(mU)#(fA)-TegChol
-	SOD1 221	$P(m_1) = H(f_1) = H(m_2) (f_1) (m_2) (f_2) (m_1) (f_2) (m_2) (f_1) = H(m_1) (f_1) = H(m_2) (f_1) (m_1) (f_1) (m_1) (f_2) (m_2) (f_2) (m_2) (f_1) (m_2) (f_2) (m_2) (m_2) (f_2) (m_2) (m_$	(f1)#(m4)#(f4)(m1)(f6)(m6)(f4)(m6)(f6)(m1)(f6)(m1)(f6)#(m4)#(f4)-TegChol
	SOD1_222		(61)#(m1)#(fG)(m1)/(61)/(m1)/(6C)(m1)/(6C)(m4)(61)/(m1)/(6C)#(m4)#(f4) TegChol
-	30D1_8/9		[10]#(110]#(12)(110)(10)(110)(110)(110)(110)(110)(1
	SOD1_681	P(mU)#(tG)#(mU)(tG)(mU)(tU)(mU)(tA)(mA)(tU)(mG)(tU)(mU)#(tU)#(mA)#(tU)#(mC)#(tA)#(mG)#(tG)	(fU)#(mA)#(fA)(mA)(fC)(mA)(fU)(mU)(fA)(mA)(fA)(mC)(fA)#(mC)#(fA)-TegChol
	SOD1_744	P(mU)#(fU)#(mC)(fU)(mC)(fA)(mC)(fU)(mA)(fC)(mA)(fG)(mG)#(fU)#(mA)#(fC)#(mU)#(fU)#(mU)#(fA)	(fU)#(mA)#(fC)(mC)(fU)(mG)(fU)(mA)(fG)(mU)(fG)(mA)(fG)#(mA)#(fA)-TegChol
	SOD1_466	P(mU)#(fG)#(mC)(fA)(mA)(fU)(mG)(fG)(mU)(fC)(mU)(fC)(mC)#(fU)#(mG)#(fA)#(mG)#(fA)#(mG)#(fA)#(mG)#(fU)	(fC)#(mA)#(fG)(mG)(fA)(mG)(fA)(mC)(fC)(mA)(fU)(mU)(fG)#(mC)#(fA)-TegChol
	SOD1_893	P(mU)#(fU)#(mU)(fU)(mA)(fU)(mU)(fC)(mA)(fC)(mA)(fG)(mG)#(fC)#(mU)#(fU)#(mG)#(fA)#(mA)#(fU)	(fA)#(mG)#(fC)(mC)(fU)(mG)(fU)(mG)(fA)(mA)(fU)(mA)(fA)#(mA)#(fA)-TegChol
	SOD1 892	P(mU)#(fU)#(mU)(fA)(mU)(fU)(mC)(fA)(mC)(fA)(mG)(fG)(mC)#(fU)#(mU)#(fG)#(mA)#(fA)#(mU)#(fG)	(fA)#(mA)#(fG)(mC)(fC)(mU)(fG)(mU)(fG)(mA)(fA)(mU)(fA)#(mA)#(fA)-TegChol
	SOD1 821	P(m1)#fA)#(m1)(fA)(mC)(fA)(mG)(fG)(m1)(fC)(mA)(f1)(m1)#(fG)#(mA)#fA)#(mA)#(fC)#(mA)#(fG)	(fU)#(mC)#(fA)(mA)(fU)(mG)(fA)(mC)(fC)(mU)(fG)(mU)(fA)#(mU)#(fA)-TegChol
	SOD1 798	$P(m) \Psi(f1) \Psi(m) \Psi(f1) mA (fA) mC (f1) mC (fA) mC (f1) m1  \Psi(f1) \Psi(m1) \Psi(fA) mA  \Psi(fA)  \muA   \Psi(fA)  \Psi(fA)  mA  \Psi(fA)  \Psi$	(fA)#(mA)#(fA)(mA)(fC)(m11)(fC)(mA)(fG)(m11)(f11)(mA)(fA)#(mA)#(fA).TogChol
	5001_758		
	SOD1_657	P(m0)#(r0)#(m0)(r0)(m0)(r0)(mA)(r0)(mA)(r0)(m0)(r0)(mA)#(r0)#(m0)#(rA)#(m0)#(r0)#(mA)#(r0)	[TG]#(mC)#(TU)(mA)(TG)(mC)(TU)(mG)(TU)(mA)(TG)(mA)(TA)#(mA)#(TA)-TegChol
	SOD1_768	P(mU)#(tC)#(mU)(tU)(mC)(tC)(mA)(tA)(mG)(tU)(mG)(tA)(mU)#(tC)#(mA)#(tU)#(mA)#(tA)#(mA)#(tU)	(fU)#(mG)#(fA)(mU)(fC)(mA)(fC)(mU)(fU)(mG)(fG)(mA)(fA)#(mG)#(fA)-TegChol
	SOD1_750	P(mU)#(fU)#(mC)(fA)(mG)(fU)(mU)(fU)(mC)(fU)(mC)#(fU)#(mA)#(fC)#(mA)#(fG)#(mG)#(fU)	(fU)#(mA)#(fG)(mU)(fG)(mA)(fG)(mA)(fA)(mA)(fC)(mU)(fG)#(mA)#(fA)-TegChol
	SOD1_524	P(mU)#(fU)#(mU)(fC)(mC)(fA)(mC)(fC)(mU)(fU)(mU)(fG)(mC)#(fC)#(mC)#(fA)#(mA)#(fG)#(mU)#(fC)	(fG)#(mG)#(fG)(mC)(fA)(mA)(fA)(mG)(fG)(mU)(fG)(mG)(fA)#(mA)#(fA)-TegChol
	SOD1 252	P(mU)#(fU)#(mC)(fA)(mG)(fU)(mC)(fA)(mG)(fU)(mC)(fC)(mU)#(fU)#(mU)#(fA)#(mA)#(fU)#(mG)#(fC)	(fA)#(mA)#(fA)(mG)(fG)(mA)(fC)(mU)(fG)(mA)(fC)(mU)(fG)#(mA)#(fA)-TegChol
	SOD1 693	P(mL)#(fL)#(mL)/fL)(mA)/fA)(mG)(fA)(mL)/(fL)(mA)/fC)(mA)#(fG)#(mL)#(fG)#(mL)#(fL)#(mL)#(fL)#(mL)#(fA)	(fA)#(mC)#(fU)(mG)(fU)(mA)(fA)(mU)(fC)(mU)(fU)(mA)(fA)#(mA)#(fA)-TegChol
	SOD1-525		(fG)#(mA)#(fA)(mA)(fL1)(mG)(fA)(mA)(fG)(mA)(fG)(mA)(fG)#(mL1)#(fA).TogChol
	5001-555		
_	SUD1_123	P(mU)#(TC)#(mG)(mA)(mA)(TA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)(mU)(mG)#(TC)#(mC)#(mC)#(mC)#(mU)#(mU)(mU)(mU)(mC)(mA)(mU)(mU)(mU)(mC)(mA)(mU)(mU)(mU)(mU)(mU)(mU)(mU)(mU)(mU)(mU	(mc)#(ma)#(mu)(mc)(ta)(tu)(tu)(tu)(ma)(ta)(mu)(mu)(mu)(mu)#(ma)#(ma)-regunoi
_	SOD1_249	P(mU)#(fG)#(mA)(mG)(mG)(tA)(mC)(mC)(mC)(mG)(mC)(mA)(mC)#(fU)#(mG)#(fG)#(mU)#(mA)#(mC)#(fA)	(mC)#(mA)#(mG)(mU)(fG)(fC)(fA)(mG)(fG)(mU)(mC)(mU)#(mC)#(mA)-TegChol
	SOD1_263	P(mU)#(fU)#(mA)(mG)(mA)(fG)(mG)(mA)(mU)(mU)(mA)(mA)(mA)#(fG)#(mU)#(fG)#(mA)#(mG)#(mG)#(fA)	(mA)#(mC)#(mU)(mU)(fU)(fA)(fA)(mU)(fC)(mC)(mU)(mC)(mU)#(mA)#(mA)-TegChol
	SOD1_345	P(mU)#(fC)#(mC)(mA)(mC)(fA)(mC)(mA)(mU)(mC)(mU)(mU)#(fU)#(mG)#(fU)#(mC)#(mA)#(mG)#(fC)	(mC)#(mA)#(mA)(mA)(fG)(fA)(fU)(mG)(fG)(mU)(mG)(mU)(mG)#(mG)#(mA)-TegChol
	SOD1_368	P(mU)#(fA)#(mG)(mA)(mA)(fU)(mC)(mU)(mC)(mA)(mA)(mU)#(fA)#(mG)#(fA)#(mC)#(mA)#(mC)#(fA)	(mC)#(mU)#(mA)(mU)(fU)(fG)(fA)(mA)(fG)(mA)(mU)(mU)(mC)#(mU)#(mA)-TegChol
	SOD1_384	P(mU)#(fC)#(mU)(mG)(mA)(fG)(mA)(mG)(mU)(mG)(mA)(mG)(mA)#(fU)#(mC)#(fA)#(mC)#(mA)#(mG)#(fA)	(mG)#(mA)#(mU)(mC)(fU)(fC)(fA)(mC)(fU)(mC)(mU)(mC)(mA)#(mG)#(mA)-TegChol
	SOD1 457	P(mU)#(fU)#(mC)(mA)(mU)(fU)(mU)(mC)(mC)(mC)(mC)(mU)#(fU)#(mU)#(fG)#(mC)#(mC)#(mC)#(fA)	(mA)#(mA)#(mA)(mG)(fG)(fU)(fG)(mG)(fA)(mA)(mA)(mU)(mG)#(mA)#(mA)-TegChol
	SOD1 516	P(m1) # f(C) # (mG)(mA)(m1)(f(C)(mC)(mA)(mA)(m1)(m1)(mA) # f(C) # (mA) # (f(C) # (mA) # (mC) # (mA) # (mA	(m1))#(m6)#(m1)(m4)(f4)(f1)(f1)(m6)(f6)(m6)(m4)(m1)(m6)#(m6)#(m4).TegChol
	5001_572		(mC)#(m2)#(m1)/mC)(#1)/#C)(#1)/mC)(m2)(m2)(m2)(m2)/mC)/mC)/mC)/#(m2)#(m2)#(m2)#(m2)
-	5001_575	r(inc)#(ic)#(inc)(inc)(inc)(inc)(inc)(inc)(inc)(inc)	(inc)m(inc)m(inc)(inc)(inc)(inc)(inc)(inc)(inc)(inc)
-	5001_594	r(mu)#(tA)#(mG)(mA)(tU)(mA)(mC)(mA)(mU)(mU)(mU)(mC)#(tU)#(mA)#(tC)#(mA)#(mG)#(mC)#(fU)	(mu)#(mA)#(mG)(mA)(tA)(tA)(tU)(mG)(tU)(mA)(mU)(mC)(mC)#(mU)#(mA)-TegChol
	SOD1_614	P(mU)#(fU)#(mA)(mC)(mA)(fG)(mU)(mG)(mU)(mU)(mA)(mA)#(fU)#(mG)#(fU)#(mU)#(mU)#(mA)#(fU)	(mC)#(mA)#(mU)(mU)(fA)(fA)(fA)(mC)(fA)(mC)(mU)(mG)(mU)#(mA)#(mA)-TegChol
	SOD1_627	P(mU)#(fA)#(mC)(mA)(mC)(fU)(mU)(mU)(mU)(mA)(mA)(mG)(mA)#(fU)#(mU)#(fA)#(mC)#(mA)#(mG)#(fU)	(mA)#(mA)#(mU)(mC)(fU)(fU)(fA)(mA)(fA)(mA)(mG)(mU)(mG)#(mU)#(mA)-TegChol
1	SOD1_636	P(mU)#(fC)#(mA)(mC)(mA)(fC)(mA)(mA)(mU)(mA)(mC)(mA)#(fC)#(mU)#(fU)#(mU)#(mU)#(mA)#(fA)	(mA)#(mG)#(mU)(mG)(fU)(fA)(fA)(mU)(fU)(mG)(mU)(mG)(mU)#(mG)#(mA)-TegChol
	SOD1 681	P(mU)#(fA)#(mA)(mU)(mC)(fA)(mG)(mU)(mU)(mU)(mC)(mU)(mC)#(fA)#(mC)#(fU)#(mA)#(mC)#(mA)#(fG)	(mG)#(mU)#(mG)(mA)(fG)(fA)(fA)(mA)(fC)(mU)(mG)(mA)(mU)#(mU)#(mA)-TegChol
-	SOD1 682	P(m1)!#(fA)#(mA)(mA)(m1)(fC)(mA)(mG)(m1)(m1)(mC)(m1)!#(fC)#(mA)!#(fC)#(m1)!#(mA)!#(mC)!#(fA))	(m1))#(m6)#(m4)(m6)(f4)(f4)(m6)(m1)(m6)(m4)(m11)#(m11)#(m4)-TeeChol
-	SOD1_002		(mC)#(mC)(mC)(mC)(mC)(mC)(mC)(mC)(mC)(mC)(mC)
	3001_701		
	SOD1_/10	P(mU)#(tA)#(mA)(mA)(mC)(tU)(mA)(mU)(mA)(mC)(mA)(mA)(mA)#(tU)#(mC)#(tU)#(mU)#(mC)#(mC)#(tA)	(mG)#(mA)#(mU)(mU)(fU)(fG)(fU)(mA)(fU)(mA)(mG)(mU)(mU)#(mU)#(mA)-TegChol
	SOD1_724	P(mU)#(fA)#(mA)(mC)(mU)(fG)(mA)(mG)(mU)(mU)(mU)(mU)(mA)#(fU)#(mA)#(fA)#(mA)#(mA)#(mC)#(fU)	(mU)#(mA)#(mU)(mA)(fA)(fA)(fA)(mC)(fU)(mC)(mA)(mG)(mU)#(mU)#(mA)-TegChol
	SOD1_752	P(mU)#(fA)#(mA)(mA)(mU)(fA)(mC)(mA)(mG)(mG)(mU)(mC)(mA)#(fU)#(mU)#(fG)#(mA)#(mA)#(mA)#(fC)	(mA)#(mA)#(mU)(mG)(fA)(fC)(fC)(mU)(fG)(mU)(mA)(mU)(mU)#(mU)#(mA)-TegChol
	SOD1_769	P(mU)#(fG)#(mU)(mG)(mA)(fU)(mU)(mA)(mA)(mG)(mU)(mC)#(fU)#(mG)#(fG)#(mC)#(mA)#(mA)#(fA)	(mC)#(mA)#(mG)(mA)(fC)(fU)(fU)(mA)(fA)(mA)(mU)(mC)(mA)#(mC)#(mA)-TegChol
	SOD1 790	P(mU)#(fU)#(mG)(mA)(mC)(fA)(mG)(mU)(mU)(mU)(mA)#(fU)#(mA)#(fC)#(mC)#(mC)#(mA)#(fU)	(mU)#(mA)#(mU)(mU)(fA)(fA)(fA)(mC)(fU)(mU)(mG)(mU)(mC)#(mA)#(mA)-TegChol
	SOD1 797	P(mU)#(fG)#(mA)(mA)(mA)(fU)(mU)(mC)(mU)(mG)(mA)(mC)(mA)#(fA)#(mG)#(fU)#(mU)#(mU)#(mA)#(fA)	(mC)#(mU)#(mU)(mG)(fU)(fC)(fA)(mG)(fA)(mA)(mU)(mU)(mU)#(mC)#(mA)-TeeChol
	SOD1 813	P(m1)#(fA)#(mG)(mG)(mC)(f1))(m1)(mG)(mA)(m1)(mG)(mA)#(fC)#(mA)#(fA)#(mA)#(mG)#(mA)#(fA)	(m1))#(m6)#(m1)(m6)(f4)(f1)(f1)(m6)(f4)(m4)(m6)(m6)(m6)(m6)#(m1))#(m4)-Teg6bol
-	5001_815		(mo)#(mo)#(mo)(mo)(mo)(mo)(mo)(mo)(mo)(mo)(mo)(mo)
_	SUD1_848	P(mU)#(rC)#(mC)(mU)(mC)(rA)(mU)(mA)(mU)(mA)(mA)(mG)#(rU)#(mG)#(rC)#(mC)#(mC)#(mA)#(mU)#(rA)	(mc)#(mA)#(mc)(m0)(t0)(tA)(t0)(m0)(tA)(m0)(mG)(mA)(mG)#(mG)#(mA)-Tegcnol
SOD	1_123 Walk		
	SOD1_112	P(mU)#(fA)#(mU)(fG)(fC)(fC)(mC)(fU)(mG)(fC)(mA)(fC)(mU)(fG)#(mG)#(fG)#(mC)#(mC)#(mG)#(fU)#(mU)	(mC)#(mC)#(mC)(fA)(mG)(fU)(mG)(fC)(mA)(fG)(mG)(mG)(mC)(fA)#(mU)#(mA)-TegChol
	SOD1_113	P(mU)#(fG)#(mA)(fU)(fG)(fC)(mC)(fC)(mU)(fG)(mC)(fA)(mC)(fU)#(mG)#(fG)#(mG)#(mC)#(mC)#(fG)#(mU)	(mC)#(mC)#(mA)(fG)(mU)(fG)(mC)(fA)(mG)(fG)(mG)(mC)(mA)(fU)#(mC)#(mA)-TegChol
	SOD1_114	P(mU)#(fU)#(mG)(fA)(fU)(fG)(mC)(fC)(mC)(fU)(mG)(fC)(mA)(fC)#(mU)#(fG)#(mG)#(mG)#(mC)#(fC)#(mU)	(mC)#(mA)#(mG)(fU)(mG)(fC)(mA)(fG)(mG)(fG)(mC)(mA)(mU)(fC)#(mA)#(mA)-TegChol
	SOD1 115	P(mU)#(fA)#(mU)(fG)(fA)(fU)(mG)(fC)(mC)(fC)(mU)(fG)(mC)(fA)#(mC)#(fU)#(mG)#(mG)#(mG)#(fC)#(mU)	(mA)#(mG)#(mU)(fG)(mC)(fA)(mG)(fG)(mG)(fC)(mA)(mU)(mC)(fA)#(mU)#(mA)-TegChol
	SOD1 116	P(m1)#(fG)#(mA)(f1)(fG)(fA)(m1)(fG)(mC)(fC)(mC)(f1)(mG)(fC)#(mA)#(fC)#(m1)#(mG)#(mG)#(fG)#(m1))	(mG)#(mLI)#(mG)(fC)(mA)(fG)(mG)(fG)(mC)(fA)(mLI)(mC)(mA)(fLI)#(mC)#(mA)-TegChol
	SOD1 117		(m1))#(m6)#(m6)/f6)/m6)/f6)/m6)/f1)/(m6)/m1)/f6)#(m6)#(m6)#(m6)
	SOD1_119		(mC)#(mC)#(mC)/iC)/iC)/mC)/iC)/mC)/iC)/iC)/mC)/iC)/iC)/mC)/iC)/iC)/mC)/iC)/iC)/mC)/iC)/iC)/iC)/iC)/iC)/iC)/iC)/iC)/iC)/i
-	30D1_118		[IIIG]#(IIIC)#(IIIA)[IIG](IIIG)[IIIG](IIIC)(IIA)(IIIC)(IIIA)[IIIC)(IIIC)(IIIA)#(IIIA)#(IIIA)-Tegciloi
	SOD1_119	P(mU)#(tA)#(mU)(tU)(tG)(tA)(mU)(tG)(mA)(tU)(mG)(tC)(mC)(tC)#(mU)#(tG)#(mC)#(mA)#(mC)#(tU)#(mU)	(mC)#(mA)#(mG)(fG)(mG)(fC)(mA)(fU)(mC)(fA)(mU)(mC)(mA)(fA)#(mU)#(mA)-TegChol
	SOD1_120	P(mU)#(fA)#(mA)(fU)(fG)(mA)(fU)(mG)(fA)(mU)(fG)(mC)(fC)#(mC)#(fU)#(mG)#(mC)#(mA)#(fC)#(mU)	(mA)#(mG)#(mG)(fG)(mC)(fA)(mU)(fC)(mA)(fU)(mC)(mA)(fU)#(mU)#(mA)-TegChol
	SOD1_121	P(mU)#(fA)#(mA)(fA)(fU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)(mG)(fC)#(mC)#(fC)#(mU)#(mG)#(mC)#(fA)#(mU)	(mG)#(mG)#(mG)(fC)(mA)(fU)(mC)(fA)(mU)(fC)(mA)(mA)(mU)(fU)#(mU)#(mA)-TegChol
	SOD1 122	P(mU)#(fG)#(mA)(fA)(fA)(fU)(mU)(fG)(mA)(fU)(mG)(fA)(mU)(fG)#(mC)#(fC)#(mC)#(mG)#(mG)#(fC)#(mU)	(mG)#(mG)#(mC)(fA)(mU)(fC)(mA)(fU)(mC)(fA)(mA)(mU)(mU)(fU)#(mC)#(mA)-TegChol
	SOD1 123	P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(fG)#(mU)	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TeeChol
	SOD1 124	P(m1)#(f1)#(mC)(fG)(fA)(fA)(mA)(f1)(m1)(fG)(mA)(f1)(mG)(fA)#(m1)#(fG)#(mC)#(mC)#(mC)#(f1)(#(m1))	(mC)#(mA)#(mI)/(fC)(mA)(fI)/(mC)(fA)(mA)(fI)/(mI)/(mC)(fG)#(mA)#(mA)-TegChol
-	SOD1_125		(m6)#(m1)#(m6)(f6)(m1)(f6)(m6)(f6)(m6)(f6)(m6)(f6)#(m6)(f6)#(m6)(f6)#(m6)(f6)
-	SOD1_123		(mA)#(mC)(mA)(mC)(mA)(mC)(mC)(mC)(mC)(mC)(mC)(mC)(mA)#(mA)=TegCnoi
	SOD1_126	P(m0)#(rG)#(mC)(rO)(rC)(rG)(mA)(rA)(rA)(rO)(rG)(mA)(rO)#(mG)#(rA)#(mO)#(mG)#(mC)#(rC)#(mO)	[mu]#(mc)#(mA)(tu)(mc)(tA)(mA)(tu)(mu)(tu)(mc)(mG)(mA)(tG)#(mc)#(mA)-regchoi
	SOD1_127	P(mU)#(tU)#(mG)(tC)(tU)(tC)(mG)(tA)(mA)(tA)(mU)(tU)(mG)(tA)#(mU)#(tG)#(mA)#(mU)#(mG)#(tC)#(mU)	(mC)#(mA)#(mU)(fC)(mA)(fA)(mU)(fU)(mU)(fC)(mG)(mA)(mG)(fC)#(mA)#(mA)-TegChol
	SOD1_128	P(mU)#(fC)#(mU)(fG)(fC)(fU)(mC)(fG)(mA)(fA)(mA)(fU)(mU)(fG)#(mA)#(fU)#(mG)#(mA)#(mU)#(fG)#(mU)	(mA)#(mU)#(mC)(fA)(mA)(fU)(mU)(fU)(mC)(fG)(mA)(mG)(mC)(fA)#(mG)#(mA)-TegChol
	SOD1_129	P(mU)#(fU)#(mC)(fG)(fC)(mU)(fC)(mG)(fA)(mA)(fA)(mU)(fU)#(mG)#(fA)#(mU)#(mG)#(mA)#(fU)#(mU)	(mU)#(mC)#(mA)(fA)(mU)(fU)(mU)(fC)(mG)(fA)(mG)(mC)(mA)(fG)#(mA)#(mA)-TegChol
	SOD1 130	P(mU)#(fU)#(mU)(fC)(fU)(fG)(mC)(fU)(mC)(fG)(mA)(fA)(mA)(fU)#(mU)#(fG)#(mA)#(mU)#(mG)#(fA)#(mU)	(mC)#(mA)#(mA)(fU)(mU)(fU)(mC)(fG)(mA)(fG)(mC)(mA)(mG)(fA)#(mA)#(mA)-TegChol
	SOD1 131	P(mU)#(fC)#(mU)(fU)(fC)(fU)(mG)(fC)(mU)(fC)(mG)(fA)(mA)(fA)#(mU)#(fU)#(mG)#(mA)#(mU)#(fG)#(m1)	(mA)#(mA)#(mU)(fU)(mU)(fC)(mG)(fA)(mG)(fC)(mA)(mG)(mA)(fA)#(mG)#(mA)-TeeChol
	SOD1 132	$P(m_1)$ ##fC/#(m_1)(f1)(f1)(f1)(m_1)(fG)(m_1)(fG)(m_1)(fG)(m_1)(f_1)(m_1)(f_1))#(m_1)#(m_1)(m_1)(m_1)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1)(f_1)(m_1)(f_2)(m_1	(mA)#(m1))#(m1)(f1)(mC)(fG)(mA)(fG)(mC)(fA)(mG)(mA)(mA)(fG)#(mG)#(mA)-TeaChol
-	SOD1_132		(m1)#(m0)#(m0)#(0)(m0)(0)(m0)(0)(m0)(m0)(m0)(m0)(m0)#(m0)#
	5001_133		
-	5001_134	r(iiio)#(iio)#(iio)(iii)(iii)(iii)(iii)(i	(inc)#(inc)#(inc)(inc)(inc)(inc)(inc)(inc)(inc)(inc)
	SOD1_135	P(m0)#(r0)#(m0)(r0)(r0)(r0)(r0)(r0)(r0)(r0)(r0)(r0)(r	{mu}#(mu)#(mu)(tA)(mu)(tu)(mA)(tu)(mA)(tA)(mu)(mu)(mA)(tA)#(mA)#(mA)- i egunoi
Tofe	sen comparison		
	Tofersen	(eC)#(eA)(eG)#(eG)(eA)#(dT)#(dA)#(dC)#(dA)#(dT)#(dT)#(dT)#(dC)#(dA)#(eC)(eA)#(eG)(eC)#(eT)	
1			
Non-	Human Primate (NHP) Targeting		
	SOD1 NHP (position 47)	P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mU)(mG)(mA)(mU)(mG)(mG)(fU)#(mG)#(fC)#(mC)#(mC)#(mL))#(fG)#(mL)	(mG)#(mC)#(mA)(mC)(mC)(fA)(fU)(fC)(mA)(fA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TeeChol
	Human SOD1 123	P(mL)#(fC)#(mG)(mA)(mA)(fA)(mL))(mL))(mG)(mA)(mL)(mG)(mA)(fL)#(mG)#(fC)#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(m	(mG)#(mC)#(mA)(mL)(mC)(fA)(fL)(fC)(mA)(fA)(mL)(mL)(mL)(mC)#(mG)#(mA).TegChol
		, , , , , , , , , , , , , , , , , , ,	
Ch	aisel Ontimization Strendment		
cnen	Alternating 20/15	D(m1))#(6()#(mC)(65)(m5)(65)(m1))(61)(mC)(65)(m1)(6C)(m5)(65)(0, m2)(65)(0, m2)(65)(0, m2)(65)(0, m2)(65)	(6C)#(m.6.)#(61)/(m.C)(66.)/m11)(6C)/(m.6.)(66.)/m11)(61)/(m11)(6C)/(m11)(6C)/(m.6.) 765.
-	Atternating 20/15	r(iiio)#(iiio)/(TA)(mA)(TA)(mU)(TU)(mG)(TA)(mU)(TG)(mA)#(tU)#(mG)#(tC)#(mC)#(tC)#(mU)#(tG)	[icj#(iiiA)#(ioj(mc)(tA)(mo)(tc)(mA)(tA)(mo)(t0)(m0)(tC)#(mG)#(mA)-legChol
_	Balanced 20/15	P(mU)#(tC)#(mG)(tA)(tA)(tA)(mU)(tU)(mG)(tA)(mU)(tG)(mA)#(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)	(mc)#(mA)#(tU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol
	Methyl-high 20/15	P(mU)#(fC)#(mG)(mA)(mA)(mA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)#(fU)#(mG)#(mC)#(mC)#(mU)#(fG)	(mC)#(mA)#(mU)(mC)(mA)(mU)(mC)(mA)(mA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TegChol
L	Methyl-rich 20/15	P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)#(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)	(mC)#(mA)#(mU)(mC)(fA)(fU)(fC)(mA)(fA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TegChol
	Alternating 21/16 Final(mU)	P(mU)#(fC)#(mG)(fA)(mA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(fC)#(mU)#(fG)#(mU)	(mG)#(fC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(fU)(mU)(fC)#(mG)#(mA)-TegChol
	Balanced 21/16 Final (mU)	P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(fG)#(mU)	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TeeChol
	Methyl-high 21/16 Final (mII)	P(mU)#(fC)#(mG)(mA)(mA)(mA)(mU)(mU)(mG)(mA)(mL)(mG)(mA)(fL))#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(m	(mG)#(mC)#(mA)(mU)(mC)(mA)(mU)(mC)(mA)(mA)(mA)(mU)(mU)(mU)(mC)#(mG)#(mA).TearChol
-	Methylarich 21/16 Final (mt)	P(m1)#(fC)#(m6)(m4)(f4)(m1)(m1)(m6)(m4)(m1)(m6)(m4)(f1)(m6)(m4)(f1)(m6)(m6)(m6)(m6)(m6)(m6)(m6)(m6)(m6)(m6	(mG)#(mC)#(mA)(m1)(mC)(fA)(f1)(fC)(mA)(fA)(m1)(m1)(m1)(mC)#(mG)#(mA) TooCbal
H-	Palaneed 21/16 5-11C	1	(
	Balanced 21/16 FullComp	r(mu)#(tc)#(mG)(tA)(tA)(tA)(tA)(mU)(tU)(mG)(tA)(mU)(tG)(mA)(tU)#(mG)#(tC)#(mC)#(mC)#(mU)#(fG)#(mC)	[mG)#(mC)#(mA)(tU)(mC)(tA)(mU)(tC)(mA)(tA)(mU)(mU)(mU)(tC)#(mG)#(mA)-TegChol
	Methyl-rich 21/16 FullComp	P(mU)#(tC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mC)	(mG)#(mC)#(mA)(mU)(mC)(fA)(fU)(fC)(mA)(fA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TegChol
	Balanced 20/15 mm18-20	P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)#(fU)#(mG)#(fC)#(mC)#(mU)#(mC)#(fA)	(mC)#(mA)#(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol
L	Methyl-rich 20/15 mm18-20	P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(mU)(mG)(mA)#(fU)#(mG)#(fC)#(mC)#(mU)#(mC)#(fA)	(mC)#(mA)#(mU)(mC)(fA)(fU)(fC)(mA)(fA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TegChol
	Balanced 21/16 mm18-21	P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mC)#(fA)#(m1)	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TeeChol
-	Methyl-rich 21/16 mm18-21	P(mU)#(f()#(mG)(mA)(mA)(mA)(mU)(mG)(mA)(mU)(mG)(mA)(f(1)#(mG)#(f()#(mC)#(m1)#(mG)#(m0)	(mG)#(mC)#(mA)(mU)(mC)(fA)(fU)(fC)(mA)(fA)(mU)(mU)(mU)(mC)#(mG)#(mA).TogCool
-	Mothyl rich 21/16 Final (m11)	D(m(1)#(fC)#(mG)(mA)(mA)(mA)(m(1)(m(1)(mG)(mA)(m(1)(mG)(mA)(1))) = O(m(1)(m(1)(m(1)(m(1)(m(1)(m(1)(m(1)(m(1	(mc)#(mc)#(ma)/m1)/mc)/fa)/f1)/fc)/ma)/fa)/mc)/mc)/mc)/mc)#(mc)#(mc)#(mc)/m1)/mc)/fa)/f1)/f2)/f2)/f2)/f2)/f2)/f2)/f2)/f2)/f2)/f2
⊢	Mathud sigh 24 /46 ft 1 / (mU)	rtinoj#ncj#niojminoj(inAj(inAj(inOj(inOj(inOj(inOj(inOj(inO)(mO)(mO)(mO)(TO)#(mO)#(TO)#(mO)#(TO)#(mO)#(TO)#(mO)	(Inc)#(Inc)#(Inc)#(Inc)(Inc)(Inc)(Inc)(Inc)(Inc)(Inc)(Inc)
1	inaethylarich 71/16 tinal (fll)	r(mu)#(ru)#(mG)(mA)(rA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mG)#(fU)	[mu]#(mu]#(mA)[mu](mu](tA)[tu](tC)[mA](tA)(mU)(mU)(mU)(mC)#(mG)#(mA)-TegChol
-	incertify new 21/10 million (10)		[[mG]#[mC]#[mA][mU][mC][fA][fU][fC][mA][fA][mU][mU][mU][mC]#[mG]#[mA]-TegChol
	Methyl-rich 21/16 mm20-21	P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU)	
	Methyl-rich 21/16 mm20-21 Balanced 21/16 Final (mU)	P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU)	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol
	Methyl-rich 21/16 mm20-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU)	P(mU)#(C]#(mG)(mA)((mA)(fA)(mU)(mU)(mG)(mA)((mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU)#(fU)#(mU)#(fC)#(mG)#(fA)(mU))#(fO)#(mU)#(fC)#(mC)#(fA)(mU)= P(mU)#(fC)#(mG)(fA)(fA)(A)(fU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(mC)#(fU)= P(mU)#(fC)#(mG)(fA)(fA)(A)(U)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(mC)#(fU)=	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol (mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol
	Methyl-rich 21/16 mm20-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 mm20-21	P(mU)#{(fQ#(mG){mA}{mA}){fA}(mU){mU}{mG}(mA){mU}{mG}(mA){fU}#{mG}#{fC}#{mQ}#{mQ}#{mU}#{fU} P{(mU)#{(fQ#(mG){A}{mQ}){fA}{mU}{mU}}{fG}{mU}{mU}{mU}{mU}{mU}{mU}{mU}{mU}{mU}{mU	[mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(fC)#(mG)#(mA)-TegChol [mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol [mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(mU)(fC)#(mG)#(mA)-TegChol
	Methyl-rich 21/16 mm20-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 mm20-21	PImUJH(CB#(mG)(MA)(MA)(MA)(MU)(mG)(MA)(MU)(MG)(MA)(U)#(mG)#(CB#(mG)#(mU)#(MU)#(U)#(MU)#(U)#(MU)#(MU)#(MU)#(MU)	(mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol (mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(f(fH)(mG)#(mA)-TegChol (mG)#(mC)#(mA)(fU)(mC)(fA)(mU)(fC)(mA)(fA)(mU)(mU)(mU)(fC)#(mG)#(mA)-TegChol
	Methyl-rich 21/16 mm2(0-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 mm20-21	P(mu)#(f0#(mc)(mA)(mA)(fA)(mu)(mu)(mc)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mu)#(f0#(mc)(fA)(A)(A)(mU)(U)(mc)(fA)(A)(U)(G)(mA)(fU)(mG)#(fC)#(mC)#(mC)#(mU)#(fM)(U) P(mU)#(fC)#(mC)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(A)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(FA)(FA)(FC)(FA)(FC)(FA)(FC)#(FC)#(mG)#(fC)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(mG)#(fC)#(fC)#(fC)#(fC)#(fC)#(fC)#(fC)#(fC	[mG]#(mC]#(mA){(U)(mC){(fA)(mU){(fG}(mA){(fA)(mU)(mU){(fG}(mG)#(mA)-TegChol (mG)#(mC)#(mA){(fU)(mC){(fA}(mU){(fG}(mA){(fA)(mU)(mU)}(mU){(G}(mG)#(mA)-TegChol (mG)#(mC)#(mA){(U)(mC){(fA}(mU){(fG}(mA){(fA}(mU)(mU)(mU)(G)#(mA)-TegChol
In viv	Methy-rich 21/16 mm2(-021 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 final (fU) Balanced 21/16 mm20-21	P(mU)#(fC#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mG)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(fG)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fB)(mU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fC)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fC)(mA)(fG)(mA)(fC)#(mG)#(fC)#(mC)#(mU)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fC)(mA)(fC)(mA)(fC)#(mG)#(fC)#(mC)#(mU)#(fC) P(mU)#(fC)#(mG)(fA)(fA)(fA)(fA)(mU)(fC)(mA)(fC)(mA)(fA)(mA)(fA)(mA)(fA)(mU)#(fA)(mC)#(fA)(mA)(fA)(mU)#(fA)(mA)(fA	[ImSiFIncDFfmA][U]ImC[[A]ImU][C][mA][[A]ImU][mU][ImU][C]F[ImSiFInA]-TegDol [ImSiFIncDFfmA][U]ImC[[A]ImU][C][(mA][[A]ImU][U][U][U][U][U][ImU][ImU][ImU][ImU]
In viv	Methy-Indi 21/36 mm20-21 Balanced 21/16 Final (MU) Balanced 21/16 Final (MU) Balanced 21/16 Final (FU) Balanced 21/16 mm20-21 o Experiments SOD1_123 Di-valent Original	P(mU)#(fC)#(mC)(mA)(mA)(fA)(mU)(mC)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU) #(mU)#(fC)#(mC)(fA)(A)(A)(mU)(U)(mC)(fA)(MU)(G)(mA)(U)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU) #(mU)#(fC)#(mG)(fA)(A)(A)(MU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mU)#(MU)#(MU)#(FU) #(mU)#(fC)#(mG)(fA)(A)(MU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(MU)#(FU) #(mU)#(fC)#(mG)(fA)(fA)(A)(MU)(fU)(mG)(fA)(MU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(G)#(MU) #(mU)#(fC)#(mG)(fA)(A)(MU)(fU)(mG)(fA)(MU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(A)(MU)(fG)(mA)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(MU)(fU)(mG)(fA)(MU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU))#(fG)#(MU) #(mU)#(fC)#(mG)(fA)(MU)(fG)(mA)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(MU)(fG)(mA)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(MU)(fG)(mA)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(mU)(fG)(mA)(fG)(mA)(fG)#(mC)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(mU)(fG)(mA)(fG)(mA)(fG)#(mC)#(fC)#(mC)#(mC)#(mC)#(fG)#(mU)#(fG)#(mU) #(mC)#(fC)#(mG)(fA)(mU)(fG)(mA)(fG)#(mC)#(fC)#(mC)#(mC)#(mC)#(mC)#(mU)#(fG)#(mU) #(mU)#(fC)#(mG)(fA)(mU)(fG)(mA)(fG)#(mA)(fG)#(mC)#(fC)#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(mC)#(m	[mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][C]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC]#[mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC][mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC][mG]#[mA]-TegChol [mG]#[mC]#[mA][fU][mC][fA][mU][fC][mA][fA][mU][mU][mU][fC][mG]#[mA]-TegChol [mA][fA][mA]
In viv	Methyl-rich 21/16 mm20-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 Final (fU) Balanced 21/16 mm20-21 o Experiments SOD1_123 Di-valent Original SOD1_123 Di-valent Original	P(mU)#(fC)#(mC)(mA)(mA)(fA)(mU)(mC)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(HU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(UU)(U()(mG)(fA)(UU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU) P(mU)#(fC)#(mC)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fU) P(mU)#(fC)#(mG)(fA)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(fA)(fA)(mU)(fU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(fA)(fA)(mU)(mG)(fA)(mU)(fG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(fA)(mA)(fA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(mA)(fA)(mU)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(mD)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mG)(mA)(mA)(fA)(mU)(mG)(mA)(mD)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mC)(mA)(mA)(fA)(mU)(mG)(mA)(mU)(mG)(mA)(fU)#(mG)#(fC)#(mC)#(mC)#(mU)#(fG)#(mU) P(mU)#(fC)#(mC)(mA)(mA)(mA)(mA)(mA)(mA)(mA)(mA)(mA)(fC)#(mC)#(mA)(mA)(mA)(mA)(mA)(mA)(mA)(mA)(mA)(mA)	(mG)#(mC)#(mA){(fU)(mC){(fA)(mU){(fC}(mA){(fA)(mU)(mU){(fC)#(mA)+TegChol           (mG)#(mC)#(mA){(fU)(mC){(fA}(mU){(fC)(mA){(fA}(mU)(mU){(fC)})           (mG)#(mC)#(mA){(fU)(mC){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(FC})#(mA)+TegChol           (mG)#(mC)#(mA){(fU)(mC){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(FC})#(mA)+TegChol           (mG)#(mC)#(mA){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(FC})#(mC)#(mA)+TegChol           (mG)#(mC)#(mA){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(mU){(mC})#(mC)#(mA)+TegChol           (mG)#(mC)#(mA){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(mC})#(mC)#(mA)+TegChol           (mG)#(mC)#(mA){(fC}(mA){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(mC})#(mC)#(mA)+TegChol           (mG)#(mC)#(mA){(fU)(mC){(fC}(mA){(fA}(mU){(mU){(mU){(mC)}#(mC)#(mA)+TegChol           (mG)#(mC)#(mA){(fU)(mC){(fC}(mA){(fA}(mU){(mU){(mU){(mC)}#(mC)#(mA)+TegChol           (mG)#(mA){(fU)(mC){(fA}(mU){(fC}(mA){(fA}(mU){(mU){(mU){(mC)}#(mC)#(mA)+TegChol
In viv	Methy-Incl. 21/16 mm.20-21 Balanced 21/16 Final (mU) Balanced 21/16 Final (mU) Balanced 21/16 Final (fU) Balanced 21/16 final (fU) so Experiments SOD1_123 Methyl Rich SOD1_123 Methyl Rich SOD1_123 exNA	P(mU)#(10#(mG)(mA)(mA)(14)(mU)(mG)(mA)(mU)(mG)(mA)(10)#(mG)#(10)#(mG)#(10)#(mU)#(mU)#(10) P(mU)#(10)#(mG)(14)(A)(14)(mU)(10)(mG)(14)(MU)(16)(mA)(10)#(mG)#(10)#(mG)#(10)#(mU)#(mU)#(10) P(mU)#(10)#(mG)#(A)(1A)(mU)(10)(mG)(A)(mU)(16)(mA)(10)#(mG)#(10)#(mG)#(10)#(mU)#(10) P(mU)#(10)#(mG)#(A)(A)(A)(mU)(10)(mG)(A)(mU)(16)(mA)(10)#(mG)#(10)#(mG)#(10)#(mU)#(10) P(mU)#(10)#(10)#(10)(A)(A)(MU)(10)(mG)(A)(MU)(16)(mA)(10)#(mG)#(10)#(mG)#(10)#(mU)#(16)#(10) P(mU)#(10)#(10)#(10)(A)(A)(MU)(10)(MC)(10)(10)(MG)(10)#(mG)#(10)#(mG)#(10)#(mU)#(16)#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(mG)(A)(10)#(mG)#(10)#(mG)#(10)#(mU)#(16)#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(MC)(10)(MG)(10)#(mG)#(10)#(mG)#(10)#(16)#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(MC)(10)(MG)#(10)#(10)#(10)#(10)#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(MC)(10)#(mG)#(10)#(10)#(10)#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(MC)(10)#(10)#(10)#(10)#(10)#(10))#(10) P(mU)#(10)#(10)#(10)(A)(A)(A)(MU)(10)(MC)(10)#(10)#(10)#(10)#(10)#(10)#(10))#(10)) P(mU)#(10)#(10)#(10)(A)(A)(A)(A)(A)(A)(A)(A)(A)(A)(A)(A)(A)	[Ims]#Imc]#(ma){[U](mc]{[A](mu){[C](mA](A](mu)[mu](mU](C][#Ims]#[ma]-TegChol           [Ims]#Imc]#(ma){[U](mc]{[A](mu){[C](mA](A](mu)[mu](mU](mU](C][#Ims]#[mA]-TegChol           [Ims]#Imc]#(mA){[U](mc]{[A](mU](C](mA)[A](A](mU)[mU](mU](mU](mU](mA)-TegChol           [Ims]#Imc]#(mA){[U](mc](A](mU)[(mA)[A](A](mU)[mU](mU](mU](mU](mA)-TegChol           [Ims]#Imc]#(mA){[U](mc](A](mU)[(mA)[A](A](mU)[mU](mU](mU](mU](mA)-TegChol           [Ims]#Imc]#(mA){[U](mc](A](mA)[(A](mA)[A](mU)[mU](mU](mU](mU](mA)-TegChol           [Ims]#Imc]#(mA){[U](mC](A](mA)[(A](mA)[(A](mU)[mU](mU](mU](mU](mU](mU](mU)(mU)(mA)-TeGChol           [Ims]#Imc]#(mA){[U](mC](A](A](U)([C](mA)[(A)(mU)(mU)(mU)(mU)(mU)(mU](mU)(mU)(mA)-TeGChol           [Ims]#Imc]#(mA){[U](mC](A](U)(U](mA)(AA)(TeGL(mA)-TEGChol           [Ims]#(mC]#(mA){[U](mC](A](TU)([C](mA)(AA)(TEGL(mA)-TEGChol           [Ims]#(mC]#(mA){[U](mC](A](TU)([C](mA)(AA)(TEGL(mA)-TEGChol           [Ims]#(mC]#(mA){[U](mC](A](TU)([C](mA)(AA)(TEGL(mA)-TEGChol           [Ims]#(mC]#(mA){[U](mC](A](TU)([C](TEGL(TEG)#(mA)-TEGChol           [Ims]#(mC]#(mA){[U](mC](AA)(TEGL(TEGL(TEGL(TEGL(TEGL(TEGL(TEGL(TEGL

## Supplemental Table 1: siRNA sequences used for *in vitro* and *in vivo* studies