

## Supplementary Table S1: Sequence Information

lower case letters denote RNA bases; UPPER CASE letters denote DNA bases

<u>Name</u>	<u>Sequence</u>
siR2A	5' cccaucgaguaccaugauauc 3' (sense) 3' agggguagcucaugguacuau 5' (antisense)
siR2B	5' ggagcgauuuagccaagaagu 3' (sense) 3' caccucgcuaaaucgguucuu 5' (antisense)
siR2C	5' ggcucaagaaacgaggacuga 3' (sense) 3' gaccgaguucuuugcuccuga 5' (antisense)
siCON1	5' uagcgacuaaacacaucaauu 3' (sense) 3' uuaucgcugauuuuguguaguu 5' (antisense)
GTI-2040	5' GGCTAAATCGCTCCACCAAG 3' *see note*
siGTI-2040	5' ggcuaaaucgcuccaccaaguu 3' (sense) 3' aaccgauuuagcgaggugguuc 5' (antisense)
siJBC2003	5' gaggcuaccuaggugaacgu 3' (sense) 3' uucuccgauggauaccacuug 5' (antisense)
siR2A-5	5' ucuuccccaucgaguaccaug 3' (sense) 3' guagaagggguagcucauggu 5' (antisense)
siR2A-4	5' cuuccccaucgaguaccauga 3' (sense) 3' uagaagggguagcucauggua 5' (antisense)
siR2A-3	5' uuccccaucgaguaccaugau 3' (sense) 3' agaagggguagcucaugguac 5' (antisense)
siR2A-2	5' uccccaucgaguaccaugaua 3' (sense) 3' gaagggguagcucaugguacu 5' (antisense)
siR2A-1	5' cccaucgaguaccaugauau 3' (sense) 3' aagggguagcucaugguacua 5' (antisense)
siR2A+1	5' ccaucgaguaccaugauaucu 3' (sense) 3' gggguagcucaugguacuaua 5' (antisense)
siR2A+2	5' caucgaguaccaugauaucug 3' (sense) 3' gggguagcucaugguacuauag 5' (antisense)
siR2A+3	5' aucgaguaccaugauaucugg 3' (sense) 3' gguagcucaugguacuauaga 5' (antisense)
siR2A+4	5' ucgaguaccaugauaucuggc 3' (sense) 3' guagcucaugguacuauagac 5' (antisense)
siR2A+5	5' cgaguaccaugauaucuggca 3' (sense) 3' uagcucaugguacuauagacc 5' (antisense)
siR2B-5	5' uugguggagcgauuuagccaa 3' (sense) 3' ugaaccaccucgcuaaaucgg 5' (antisense)
siR2B-4	5' ugguggagcgauuuagccaag 3' (sense) 3' gaaccaccucgcuaaaucggu 5' (antisense)
siR2B-3	5' gguggagcgauuuagccaaga 3' (sense) 3' aaccaccucgcuaaaucgguu 5' (antisense)
siR2B-2	5' guggagcgauuuagccaagaa 3' (sense) 3' accaccucgcuaaaucgguuc 5' (antisense)
siR2B-1	5' uggagcgauuuagccaagaag 3' (sense) 3' ccaccucgcuaaaucgguucu 5' (antisense)
siR2B+1	5' gagcgauuuagccaagaaguu 3' (sense) 3' accucgcuaaaucgguucuuc 5' (antisense)
siR2B+2	5' agcgauuuagccaagaaguuc 3' (sense)

	3' ccucgcuaaaucgguucuuca 5' (antisense)
siR2B+3	5' gcgauuuagccaagaaguuca 3' (sense) 3' cucgcuaaaucgguucuucuaa 5' (antisense)
siR2B+4	5' cgauuuagccaagaaguucag 3' (sense) 3' ucgcuaaaucgguucuucaag 5' (antisense)
siR2B+5	5' gauuuagccaagaaguucaga 3' (sense) 3' cgcuaaaucgguucuucaagu 5' (antisense)
siR2C-5	5' auucuggcucaagaaacgagg 3' (sense) 3' uauaagaccgaguucuuugcu 5' (antisense)
siR2C-4	5' uucuggcucaagaaacgagga 3' (sense) 3' auaagaccgaguucuuugcuc 5' (antisense)
siR2C-3	5' ucuggcucaagaaacgaggac 3' (sense) 3' uaagaccgaguucuuugcucc 5' (antisense)
siR2C-2	5' cuggcucaagaaacgaggacu 3' (sense) 3' aagaccgaguucuuugcuccu 5' (antisense)
siR2C-1	5' uggcucaagaaacgaggacug 3' (sense) 3' agaccgaguucuuugcuccug 5' (antisense)
siR2C+1	5' gcucaagaaacgaggacugau 3' (sense) 3' accgaguucuuugcuccugac 5' (antisense)
siR2C+2	5' cucaagaaacgaggacugaug 3' (sense) 3' ccgaguucuuugcuccugacu 5' (antisense)
siR2C+3	5' ucaagaaacgaggacugaugc 3' (sense) 3' cgaguucuuugcuccugacua 5' (antisense)
siR2C+4	5' caagaaacgaggacugaugcc 3' (sense) 3' gaguucuuugcuccugacuac 5' (antisense)
siR2B+6	5' auuuagccaagaaguucagau 3' (sense) 3' gcuaaaucgguucuucaaguc 5' (antisense)
siR2B+7	5' uuuagccaagaaguucagauu 3' (sense) 3' cuaaaucgguucuucaagucu 5' (antisense)
siR2B+8	5' uuagccaagaaguucagauua 3' (sense) 3' uaaaucgguucuucaagucua 5' (antisense)
siR2B+9	5' uagccaagaaguucagauuac 3' (sense) 3' aaaucgguucuucaagucuaa 5' (antisense)
siR2B+10	5' agccaagaaguucagauuaca 3' (sense) 3' aaucgguucuucaagucuaau 5' (antisense)
Luc105-21	5' gguuccuggaacaauugcuuu 3' (sense) 3' gaccaaggaccuuguaacga 5' (antisense)

\* For the GTI-2040 antisense oligodeoxyribonucleotide, all linkages are phosphorothioates. For all other molecules, all linkages are phosphodiester.

**Supplementary Table S2: Sequence Homology for siRNA Duplex Target Sites**

<b>siR2B+3</b>				
<u>Species</u>	<u>GenBank Accession #</u>	<u>Target Site Location</u>	<u>Target Sequence</u>	<u>Homology (to Human)</u>
Human (HeLa, HT-29, HepG2, Hep3B)	NM_001034	nt 635-653	5' gcgauuuagccaagaaguu 3'	
Mouse (Neuro2A)	NM_009104	nt 498-516	5' gcgauuuagccaagaaguu 3'	19/19 (100%)
Rat (McA-RH7777)	NM_001025740	nt 495-513	5' gcgauuuagccaagaaguu 3'	19/1 (100%)
Dog (BW.KOSA.P)	XM_540076	nt 486-504	5' gcg <u>g</u> uuuagccaagaaguu 3'	18/19 (94.7%)
Monkey (CMMT)	**	nt 40283-40301	5' gcgauuuagccaagaaguu 3'	19/19 (100%)

<b>siR2B+6</b>				
<u>Species</u>	<u>GenBank Accession #</u>	<u>Target Site Location</u>	<u>Target Sequence</u>	<u>Homology (to Human)</u>
Human (HeLa, HT-29, HepG2, Hep3B)	NM_001034	nt 638-656	5' auuuagccaagaaguucag 3'	
Mouse (Neuro2A)	NM_009104	nt 501-519	5' auuuagccaagaaguuca <u>a</u> 3'	18/19 (94.7%)
Rat (McA-RH7777)	NM_001025740	nt 498-516	5' auuuagccaagaaguuca <u>a</u> 3'	18/19 (94.7%)
Dog (BW.KOSA.P)	XM_540076	nt 489-507	5' <u>g</u> uuuagccaagaaguucag 3'	18/19 (94.7%)
Monkey (CMMT)	**	nt 40286-40304	5' auuuagccaagaaguucag 3'	19/19 (100%)

<b>siR2B+7</b>				
<u>Species</u>	<u>GenBank Accession #</u>	<u>Target Site Location</u>	<u>Target Sequence</u>	<u>Homology (to Human)</u>
Human (HeLa, HT-29, HepG2, Hep3B)	NM_001034	nt 639-657	5' uuuagccaagaaguucaga 3'	
Mouse (Neuro2A)	NM_009104	nt 502-520	5' uuuagccaagaaguuca <u>ag</u> 3'	17/19 (89.5%)
Rat (McA-RH7777)	NM_001025740	nt 499-517	5' uuuagccaagaaguuca <u>ag</u> 3'	17/19 (89.5%)
Dog (BW.KOSA.P)	XM_540076	nt 490-508	5' uuuagccaagaaguucaga 3'	19/19 (100%)
Monkey (CMMT)	**	nt 40287-40305	5' uuuagccaagaaguucaga 3'	19/19 (100%)

<b>siR2B+9</b>				
<u>Species</u>	<u>GenBank Accession #</u>	<u>Target Site Location</u>	<u>Target Sequence</u>	<u>Homology (to Human)</u>
Human (HeLa, HT-29, HepG2, Hep3B)	NM_001034	nt 641-659	5' uagccaagaaguucagauu 3'	

Mouse (Neuro2A)	NM_009104	nt 504-522	5' uagccaagaagu <u>ca</u> guu 3'	17/19 (89.5%)
Rat (McA-RH7777)	NM_001025740	nt 501-519	5' uagccaagaagu <u>ca</u> guc 3'	16/19 (84.2%)
Dog (BW.KOSA.P)	XM_540076	nt 492-510	5' uagccaagaaguucagauu 3'	19/19 (100%)
Monkey (CMMT)	**	nt 40289- 40307	5' uagccaagaaguucagauu 3'	19/19 (100%)

**Supplementary Table S2.** The homologies of target sites (within RRM2 mRNA) of the siR2B+3, siR2B+6, siR2B+7, and siR2B+9 duplexes were explored across various species. The mismatched bases (with respect to the human sequences) are identified by underline.

\*\* Sequence alignment was performed between hRRM2 mRNA and a rhesus sequence scaffold (10568:34896-42414) at <http://genome.ucsc.edu/>.