Supporting Information

Table S1. Atomic charges for LNA modified nucleotides calculated using the RESP methodology

A^L		G^L		T^L		$^{me}C^L$	
HO5'(end)	0.422147	HO5'(end)	0.422147	HO5'(end)	0.422147	HO5'(end)	0.422147
O5'(end)	−0.598876	O5'(end)	−0.598876	O5'(end)	−0.598876	O5'(end)	−0.598876
O5'(phos)	−0.487971	O5'(phos)	−0.487971	O5'(phos)	−0.487971	O5'(phos)	−0.487971
C5'	0.044409	C5'	0.044409	C5'	0.044409	C5'	0.044409
H5'	0.086419	H5'	0.086419	H5'	0.086419	H5'	0.086419
H5"	0.086419	H5"	0.086419	H5"	0.086419	H5"	0.086419
C4'	0.134159	C4'	0.134159	C4'	0.134159	C4'	0.134159
O4'	−0.358264	O4'	−0.358264	O4'	−0.358264	O4'	−0.358264
C3'	0.176766	C3'	0.176766	C3'	0.176766	C3'	0.176766
H3'	0.087216	H3'	0.087216	H3'	0.087216	H3'	0.087216
C2'	−0.001598	C2'	−0.001598	C2'	−0.001598	C2'	−0.001598
H2'	0.172345	H2'	0.172345	H2'	0.172345	H2'	0.172345
O2'	−0.408527	O2'	−0.408527	O2'	−0.408527	O2'	−0.408527
C6'	0.031728	C6'	0.031728	C6'	0.031728	C6'	0.031728
H6'	0.101307	H6'	0.101307	H6'	0.101307	H6'	0.101307
H6"	0.101307	H6"	0.101307	H6"	0.101307	H6"	0.101307
C1'	0.061466	C1'	0.042926	C1'	0.116683	C1'	−0.036224
H1'	0.192859	H1'	0.196431	H1'	0.164982	H1'	0.205448
N9	−0.056145	N9	−0.008209	N1	−0.010932	N1	−0.013980
C8	0.239929	C8	0.184193	C6	−0.244030	C6	−0.091445
H8	0.133321	H8	0.148513	H6	0.234347	H6	0.197296
N7	−0.613469	N7	−0.579078	C5	0.009683	C5	−0.110394
C5	0.062103	C5	0.160686	C5M	−0.231073	C5M	−0.189527
C6	0.693767	C6	0.506796	H5MA	0.079861	H5MA	0.064901
N6	−0.909935	O6	−0.543120	H5MB	0.079861	H5MB	0.064901
HN6A	0.413210	N1	−0.562456	H5MC	0.079861	H5MC	0.064901
HN6B	0.413210	H1	0.355198	C4	0.538615	C4	0.623580
N1	−0.786430	C2	0.860981	O4	−0.549159	N4	−0.841687
C2	0.641843	N2	−1.012507	N3	−0.412963	HN4A	0.392515
H2	0.047139	HN2A	0.442144	H3	0.332614	HN4B	0.392515
N3	−0.767107	HN2B	0.442144	C2	0.498251	N3	−0.720029
C4	0.345916	N3	−0.707355	O2	−0.574924	C2	0.732490
O3'(end)	−0.602327	C4	0.184391	O3'(end)	−0.602327	O2	−0.623582
HO3'(end)	0.413692	O3'(end)	−0.602327	HO3'(end)	0.413692	O3'(end)	−0.602327
O3'(phos)	−0.500143	HO3'(end)	0.413692	O3'(phos)	−0.500143	HO3'(end)	0.413692
P	1.203092	O3'(phos)	−0.500143	P	1.203092	O3'(phos)	−0.500143
O1P	−0.790172	P	1.203092	O1P	−0.790172	P	1.203092
O2P	−0.790172	O1P	−0.790172	O2P	−0.790172	O1P	−0.790172
		O2P	−0.790172			O2P	−0.790172

Table S2. A selection of chemical shifts (in ppm) for the (**^{me}CTGATATG ^{me}C**)^{L}: r(GCAUAUCAG) hybrid. Values are given at 25 °C relative to DSS.

	H6/H8	H1'	H2'	H3'	H4'	H5'	H5"
^{me}C^{L}1	7.61	5.44	5.12	4.47		3.93	3.93
T^{L}2	7.56	5.59	5.21	4.77		4.26	4.26
G^{L}3	7.42	5.75	4.97	4.79		4.25	4.25
A^{L}4	7.17	5.80	4.92	4.51		4.19	4.19
T^{L}5	6.77	5.29	4.96	4.51		4.14	4.14
A^{L}6	7.65	5.94	4.98	4.62		4.21	4.21
T^{L}7	6.79	5.26	4.96	4.53		4.16	4.16
G^{L}8	7.25	5.81	4.89	4.62		4.16	4.19
^{me}C^{L}9	6.94	5.46	4.31	4.02		4.08	4.11
G10	8.01	5.73	4.81	4.47	4.30	3.87	3.99
C11	7.73	5.64	4.68	4.61	4.50	4.15	
A12	8.12	6.05	4.63	4.65	4.58	4.19	4.50
U13	7.49	5.55	4.46	4.55	4.50	4.13	
A14	8.18	6.08	4.57	4.65	4.56	4.19	4.50
U15	7.47	5.53	4.35	4.40	4.46	4.09	4.56
C16	7.75	5.56	4.38	4.56	4.45	4.10	4.41
A17	8.01	5.92	4.49	4.74	4.47	4.15	4.57
G18	7.28	5.76	4.00	4.19	4.24	4.03	4.45

	H6'	H6"	H5/H2/CH_3	H1/H3	H4/<u>H4</u>
^{me}C^{L}1	4.09	4.09	1.95		6.82/8.50
T^{L}2	4.14	4.01	1.67	13.16	
G^{L}3	4.15	4.10		11.72	
A^{L}4	4.14	4.09	7.60		
T^{L}5	4.07	4.01	1.37	13.33	
A^{L}6	4.16	4.11	7.02		
T^{L}7	4.07	4.01	1.33	13.40	
G^{L}8	4.11	4.07		12.71	
^{me}C^{L}9	3.96	3.91	1.45		6.60/8.79
G10				–	
C11			5.34		6.86/8.53
A12			7.37		
U13			5.02	13.25	
A14			7.30		
U15			4.85	13.75	
C16			5.57		6.82/8.06
A17			7.15		
G18				–	

Table S3. A selection of chemical shifts (in ppm) for the (**^{me}CTGATATG^{me}C**)^{L}: d(GCATATCAG) hybrid. Values are given at 25 °C relative to DSS.

	H6/H8	H1'	H2'	H2"	H3'	H4'	H5'
^{me}C^{L}1	7.53	5.36	5.17		4.41		4.07
T^{L}2	7.55	5.52	5.30		4.72		4.25
G^{L}3	7.43	5.75	5.07		4.75		4.26
A^{L}4	7.24	5.77	5.00		4.50		4.19
T^{L}5	6.78	5.20	5.08		4.49		4.14
A^{L}6	7.68	5.92	5.04		4.62		4.21
T^{L}7	6.80	5.19	5.05		4.50		4.15
G^{L}8	7.28	5.79	4.92		4.63		4.17
^{me}C^{L}9	6.99	5.43	4.29		4.04		4.12
G10	8.06	6.12	2.86	2.83	4.73	4.26	3.88
C11	7.59	6.08	2.58	2.69	4.86	4.35	4.22
A12	8.14	6.34	2.71	2.94	4.87	4.45	4.29
T13	7.35	6.01	2.42	2.67	4.90	4.30	4.23
A14	8.03	6.31	2.58	2.86	4.85	4.44	4.28
T15	7.29	6.05	2.27	2.64	4.84	4.28	4.18
C16	7.48	5.95	2.20	2.56	4.84	4.22	4.16
A17	8.09	6.18	2.63	2.86	5.01	4.42	4.22
G18	7.50	6.11	2.28	2.34	4.61	4.22	4.16

	H5"	H6'	H6"	H5/H2/CH_3	H1/H3	H4/<u>H4</u>
^{me}C^{L}1	4.05	3.91	3.91	1.89		–
T^{L}2	4.25	3.99	4.11	1.64	13.52	
G^{L}3	4.26	4.09	4.14		11.82	
A^{L}4	4.19	4.10	4.14	7.68		
T^{L}5	4.14	4.01	4.05	1.42	13.40	
A^{L}6	4.21	4.14	4.14	7.01		
T^{L}7	4.15	4.01	4.05	1.36	13.50	
G^{L}8	4.17	4.07	4.09		12.82	
^{me}C^{L}9	4.12	3.92	3.92	1.47		–
G10	3.93				–	
C11	4.30			5.39		7.03/8.60
A12	4.29			7.48		
T13	4.34			1.21	13.27	
A14	4.25			7.36		
T15	4.21			1.02	13.56	
C16	4.29			5.44		6.80/8.11
A17	4.14			7.29		
G18	4.22				–	

Table S4. Minor groove width (in Å) in the LNA:RNA hybrid. For comparison, the minor groove widths of the unmodified DNA:RNA and the LNA3:RNA hybrids are included [a]

	LNA:RNA	DNA:RNA	LNA3:RNA
$P_4 – P_{18}$	10.0	8.9	9.8
$P_5 – P_{17}$	9.7	9.7	10.0
$P_6 – P_{16}$	9.8	7.8	9.9
$P_7 – P_{15}$	10.2	7.6	9.5
$P_8 – P_{14}$	10.3	7.9	9.3
$P_9 – P_{13}$	10.0	10.5	9.2
average	10.0	8.7	9.6

[a] The minor groove width is defined as the shortest interstrand phosphorous distance minus 5.8 Å which is the van der Waals radius for a phosphate group.

Table S5. Backbone torsion angles and sugar puckers (in degrees) in the LNA:RNA hybrid

	α	β	γ	δ	ϵ	ζ	χ	P	ϕ_{max}
$^{me}C^{L}$1			55/184	62	−172	−66	−164	20	60
T^{L}2	−72	178	58	68	−163	−59	−163	10	59
G^{L}3	−73	178	60	66	−166	−62	−165	13	61
A^{L}4	−70	177	64	66	−164	−60	−166	16	59
T^{L}5	−73	179	59	66	−162	−60	−160	11	59
A^{L}6	−73	181	59	66	−159	−61	−164	14	60
T^{L}7	−72	175	62	68	−164	−60	−162	10	60
G^{L}8	−73	178	61	66	−168	−61	−167	14	60
$^{me}C^{L}$9	−72	183	56	66			−164	10	61
G10			54	83	−157	−64	−164	7	43
C11	−68/141[a]	184	64/188[a]	77	−163	−73	−161	11	41
A12	−74/156[a]	179	64/183[a]	83	−162	−69	−164	10	36
U13	−87/122[a]	177	69/197[a]	81	−165	−69	−157	14	37
A14	−82	183	60	78	−156	−64	−165	16	39
U15	−81	184	65	76	−164	−68	−164	18	41
C16	−77	179	61	77	−164	−69	−158	14	40
A17	−78	181	59	76	−156	−65	−165	20	39
G18	−76	180	51	76			−156	27	39

[a] These torsion angles values are correlated. For C11, A12 and U13, 8, 17 and 19 structures, respectively, were found in gauche, gauche− conformations.