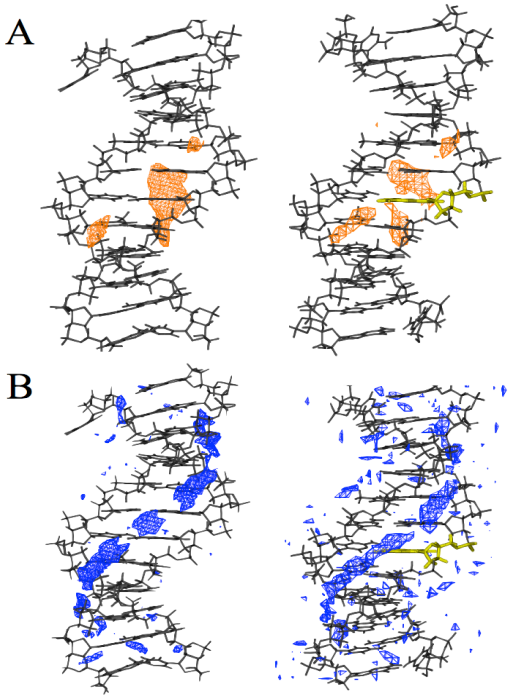

Figure S1. MIP profiles and solvation maps for duplex (left) and Se-duplex (right) molecules. (A) The probe molecule for MIP calculations was Na^+ and the depicted contour corresponds to -4.5 kcal/mol. (B) Solvation maps depicted with contours at 2.0 g/mL density. The 6-selenoguanine residue is depicted in yellow.

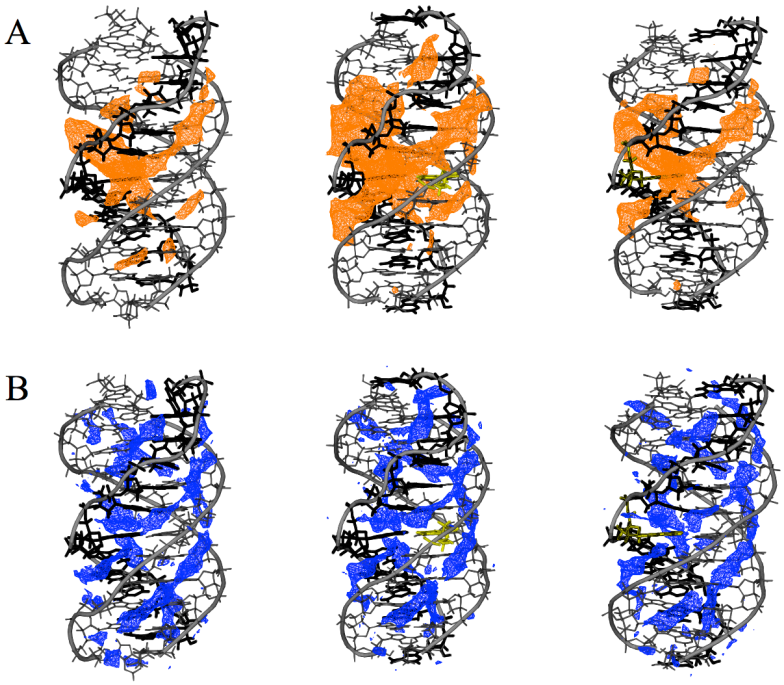

Figure S2. MIP profiles (A) and solvation maps (B) for canonical (left), WC-modified (center) and H-modified (right) triplexes. (A) The probe molecule for MIP calculations was Na^+ and the depicted contour corresponds to -6 kcal/mol. (B) Solvation maps depicted with contours at 2.0 g/mL density. The Hoogsteen strand is depicted in black while the 6-selenoguanine residue is depicted here in yellow.

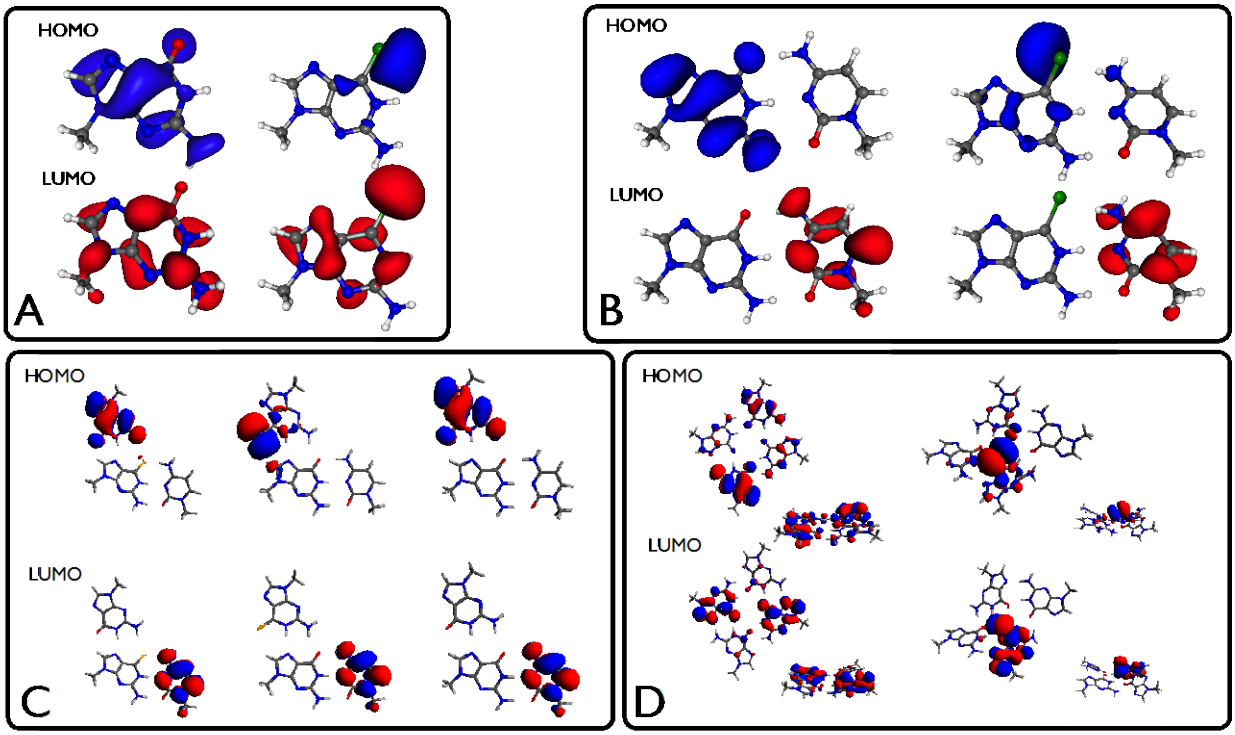

Figure S3. SVWN5/6-31++G(d,p) contour plot (isovalue at 0.02 au) of HOMO (blue) and LUMO (red) for monomers (A), H-bonded dimers (B; G·C dimer on the left and SeG·C dimer on the right), H-bonded triads (C; C·SeG#G triad on the left, C·G#SeG triad in the center and C·G#G on the right) and G-quartets (D; G4 on the left and G4 with one SeG on the right).

	MP2/6-31G(d,p)	MP2/cc-pVDZ	MP2/cc-pVTZ	MP2/cc-pVQZ	CCSD(T)/CBS
1H-2c6c-SeG	22.8	21.5	21.3	21.2	21.4
1H-2c6t-SeG	22.8	21.5	21.4	21.2	21.4
1H-2t6c-SeG	17.2	16.6	16.6	16.6	16.7
1H-2t6t-SeG	20.0	19.2	19.0	18.9	18.9
1H-SeG	0.0	0.0	0.0	0.0	0.0
3H-2c6c-SeG	20.3	19.8	19.9	19.9	19.9
3H-2c6t-SeG	20.3	19.5	19.3	19.1	19.2
3H-2t6c-SeG	23.7	22.6	22.9	22.9	23.1
3H-2t6t-SeG	27.8	26.7	26.4	26.2	26.3
3H-SeG	17.7	17.4	17.3	17.2	17.4
6c-SeG	-7.0	-7.6	-6.5	-6.2	-6.1
6t-SeG	-7.4	-8.3	-7.5	-7.3	-7.2

Table S1. Tautomerization free energies (kcal/mol) relative to the 1H-SeG tautomer at different levels of theory.

	μvac	Δμ
1H-2c6c-SeG	4.7	1.5
1H-2c6t-SeG	4.7	1.5
1H-2t6c-SeG	3.6	0.5
1H-2t6t-SeG	4.9	1.4
1H-SeG	9.1	3.2
3H-2c6c-SeG	6.3	2.1
3H-2c6t-SeG	7.4	2.7
3H-2t6c-SeG	8.8	3.2
3H-2t6t-SeG	9.8	3.7
3H-SeG	13.0	6.2
6c-SeG	4.0	1.2
6t-SeG	4.5	1.5

Table S2. Gas phase and difference between water-induced and gas phase dipole moments (in Debye) for the SeG tautomers. The values in gas phase and in water solution were determined at the MP2/cc-pVQZ and the B3LYP/cc-pVQZ levels of theory respectively.

	Rise		Roll		Twist	
	Duplex	Se-duplex	Duplex	Se-duplex	Duplex	Se-duplex
6-GX/CC	3.6 ± 0.4	3.6 ± 0.4	6.3 ± 5.4	5.0 ± 5.5	30.9 ± 5.2	32.3 ± 5.1
7-XA/TC	3.3 ± 0.3	3.3 ± 0.3	2.6 ± 5.5	0.7 ± 6.0	33.9 ± 5.2	32.7 ± 5.2
	Stretch		Buckle		Opening	
	Duplex	Se-duplex	Duplex	Se-duplex	Duplex	Se-duplex
6-GC	0.02 ± 0.1	0.02 ± 0.1	5.6 ± 9.8	4.2 ± 9.9	1.0 ± 3.2	1.2 ± 3.2
7-XC	0.03 ± 0.1	0.24 ± 0.1	-4.9 ± 12.4	-6.7 ± 12.1	1.6 ± 3.7	6.2 ± 3.8
8-AT	0.04 ± 0.1	0.04 ± 0.1	-1.4 ± 12.5	-6.0 ± 11.5	3.2 ± 5.9	3.3 ± 6.1

Table S3. Averaged values and standard errors of selected helical parameters calculated for duplex structures (X stands for G or SeG) and adjacent base pairs using the Curves+ program (see Methods).

WC	Rise			Roll			Twist		
	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex
6-CT/AX	3.4 ± 0.3	3.7 ± 0.4	3.4 ± 0.4	-0.7 ± 4.4	-1.2 ± 5.3	0.6 ± 4.7	28.0 ± 3.5	24.4 ± 3.2	25.2 ± 3.7
7-TC/XA	3.3 ± 0.3	3.4 ± 0.3	3.2 ± 0.3	-0.4 ± 5.0	-2.8 ± 5.2	-2.3 ± 5.6	33.9 ± 3.9	33.1 ± 4.1	32.6 ± 3.8
WC	Stretch			Buckle			Opening		
	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex
6-TA	0.04 ± 0.1	0.04 ± 0.2	0.04 ± 0.3	-5.5 ± 9.3	-1.7 ± 8.9	-9.0 ± 7.1	1.2 ± 5.7	4.2 ± 7.1	1.8 ± 10.3
7-CX	0.03 ± 0.1	0.31 ± 0.1	0.05 ± 0.1	2.9 ± 9.1	9.3 ± 9.0	0.6 ± 8.7	1.3 ± 3.1	7.8 ± 3.4	1.9 ± 3.2
8-TA	0.03 ± 0.1	0.07 ± 0.2	0.04 ± 0.2	0.2 ± 8.6	-1.3 ± 8.7	0.2 ± 9.8	5.6 ± 5.1	8.0 ± 5.9	6.7 ± 5.5

Table S4. Averaged values and standard errors of selected helical parameters for the WC duplex calculated for triplex structures (X stands for G or SeG) and adjacent base pairs using the Curves+ program (see Methods).

rH	Rise			Roll			Twist		
	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex
6-AX/XA	3.1 ± 0.2	3.1 ± 0.3	3.4 ± 0.4	-3.7 ± 6.1	-1.6 ± 6.4	-2.6 ± 7.3	27.9 ± 4.6	28.5 ± 5.0	22.8 ± 14.3
7-XA/AX	3.3 ± 0.3	3.3 ± 0.3	3.3 ± 0.3	13.1 ± 8.4	10.5 ± 8.6	11.3 ± 7.8	26.4 ± 3.5	27.4 ± 4.0	23.6 ± 3.2
rH	Stretch			Buckle			Opening		
	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex	triplex	WC-Se-triplex	rH-Se-triplex
6-AA	0.82 ± 0.3	1.00 ± 0.4	0.84 ± 2.8	-18.2 ± 9.6	-18.9 ± 12.9	-13.9 ± 12.5	-99.7 ± 4.9	-102.2 ± 5.3	-99.2 ± 28.6
7-XX	-0.89 ± 0.4	-0.79 ± 0.5	-1.21 ± 0.3	9.4 ± 11.0	7.0 ± 11.9	8.9 ± 13.8	-105.5 ± 5.3	-109.9 ± 5.8	-103.7 ± 7.0
8-AA	1.29 ± 0.4	1.19 ± 0.5	1.31 ± 0.4	-20.8 ± 9.3	-23.3 ± 10.3	-20.8 ± 10.9	-105.5 ± 6.2	-105.4 ± 7.5	-103.2 ± 5.7

Table S5. Averaged values and standard errors (in parenthesis) of selected helical parameters for the rH duplex calculated for triplex structures (X stands for G or SeG) and adjacent base pairs using the Curves+ program (see Methods).