Electronic Supplementary Material (ESI) for Nanoscale.

SUPPORTING INFORMATION

S1.1 Isothermal Titration Calorimetry Experiment

Ligand (dendrimer) and Receptor (siRNA) parameters were given in term of: concentration, moles, mass. Moreover experimental operative parameters (Table S1) are reported in term of: injection volume, number of injections, volume for each injection, duration of the injection, injection spacing in time, and stirring speed.

Table S1. Experimental set up. For each tested dendrimer (DM, DP), one dilution and two binding experiment repetitions were performed. The Ligand (dendrimer) is released by the ITC syringe, whereas the Receptor (siRNA) is kept into the calorimetric cell. Both samples are dissolved in HEPES buffer. Ligand (dendrimer) and Receptor (siRNA) parameters are given in term of: concentration, moles, mass. Moreover experiment operative parameters are reported in term of: injection volume, number of injections, volume for each injection, duration of the injection, injection spacing in time, agitation (samples are put in rotative motion to increase the mixing).

			Dilution		***Repetition 1***		***Repetition 2***	
Ligand (syringe)	*experiment name*		*R0*	*R0*	*R1*	*R1*	*R2*	*R2*
	syringe solution		***DM***	***DP***	***DM***	***DP***	***DM***	***DP***
	syringe conc.	*mM*	0.35	0.35	0.35	0.35	0.35	0.35
	syringe moles	*µmol*	0.099	0.099	0.099	0.099	0.099	0.099
	syringe mass	*mg*	1.672	1.596	1.672	1.596	1.672	1.596
Receptor (cell)	*cell solution*		***HEPES***	***HEPES***	***siRNA***	***siRNA***	***siRNA***	***siRNA***
	cell conc.	*mM*	-	-	0.02	0.04	0.02	0.04
	cell moles	*µmol*	-	-	0.029	0.058	0.029	0.058
	cell mass	*mg*	-	-	0.491	0.982	0.491	0.982
Injection	*total injection volume*	*µL*	282	282	282	282	282	282
	number of injections	*#*	28	28	28	28	28	28
	vol. of each injection	*µL*	10	10	10	10	10	10
	injection duration	*s*	30	30	30	30	30	30
	injection spacing	*s*	400	400	400	400	400	300
	stirring speed	*rpm*	220	220	220	220	220	220
	Dendrimer/siRNA	*µmol/µmol*	-	-	3.427	1.714	3.427	1.714

S1.2 ITC Experiments, Injection Curves

In Figure S1 main results for ICT experiments in terms of injection curves are reported. Injection peaks are shown for dilution experiment (top panels, red curve) and two repetitions (R1, and R2 in Table S1) of binding experiments (bottom panels, black curves). Each peak represents a heat change associated with the injection of a small volume of sample into the ITC reaction cell (Figure S1, top panels). A successive amounts of the dendrimer is titrated into the ITC cell, the quantity of heat absorbed or released is in direct proportion to the amount of binding. As the system reaches saturation, the heat signal diminishes until only heats of dilution are observed. The area underneath each the injection peak (Figure S1) is equal to the total heat released for that injection.

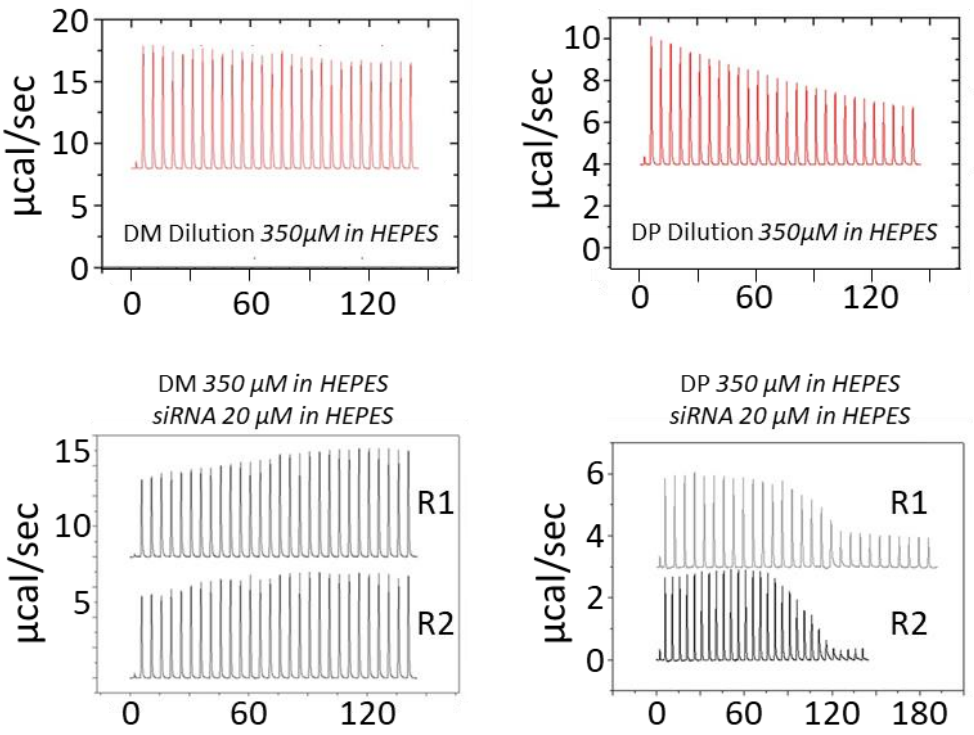


Figure S1. ITC injection curves for DM (left panels) and DP (right panel). Injections of DM solution are added to HEPES buffer (top panel, red curve) and siRNA solution in HEPES (bottom panel , black curves for 2 repetitions R1 and R2) in the ITC cell. The area underneath each injection peak is equal to the total heat released for that injection. When this integrated heat is plotted against the molar ratio of dendrimer added to siRNA in the cell, a complete binding isotherm for the interaction can be obtained. Dilution experiments (top panels, red curves) deal with the dilution of the dendrimer into the HEPES buffer. R1 and R2 are two repetitions of the binding experiment (bottom panels, black curves) dealing with a titration of the dendrimer in the siRNA solution contained in the calorimetric cell.

Interestingly, the injection peaks are roughly constant for each injection during dilution in case of DM (Figure S1, left top panel, red curve). This may let suppose that, for DM, there are no supramolecular phenomena such as dendrimer-dendrimer self-assembly.

Instead, the injection curves of DP (Figure S1, right top panel, red curve), shows that the heat peaks from dilution experiments are not constant throughout the injections. This may let suppose an dendrimer-dendrimer interaction tendency for DP the dendrimers.

When this integrated heat is plotted against the molar ratio of dendrimer added to siRNA in the cell, a complete binding isotherm for the interaction can be obtained (Figure S1, bottom panel). The heat released upon the dendrimer-siRNA interaction (ΔH) is monitored over time.

S1.3 Simulation Setup

Dendrimer building strategy

Stoichiometry and the knowledge about the physical and chemical properties of related atoms and bonds have been considered as starting point (Figure S2). All dendrimers are composed by connected residues: a central core, a repetitive branch unit and a terminal surface group. Dendrimer terminals were constituted of pyrrolidinium (DP), or morpholinium (DM).

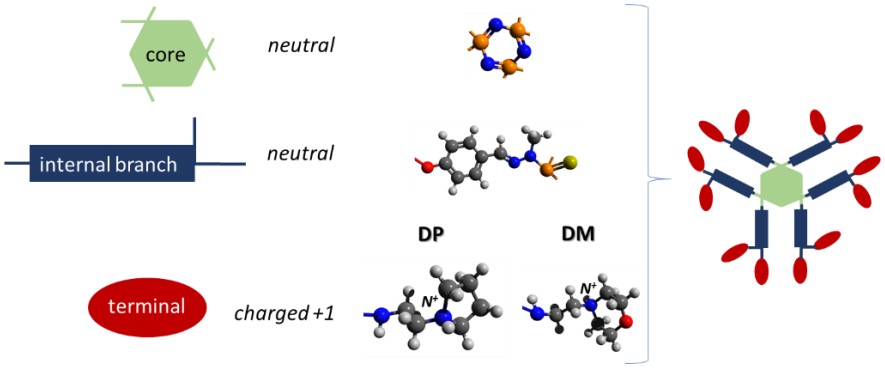
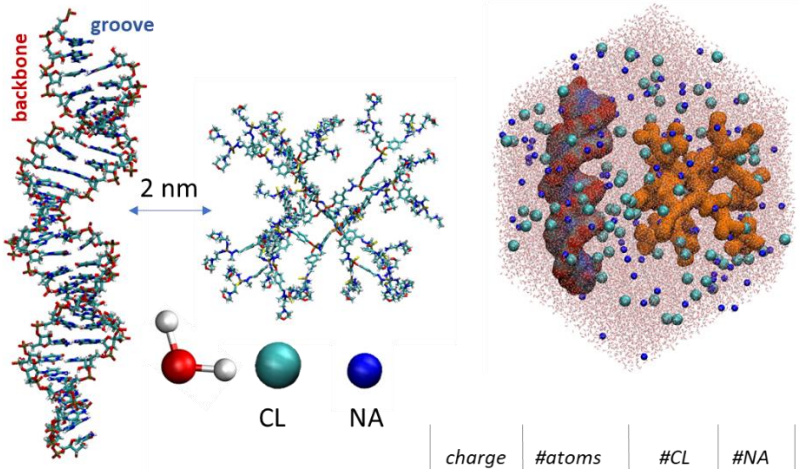


Figure S2. All-Atom Models for Generation 3 of DP and DM. Each dendrimer is built by assembling several repeating 3D building blocks. Internal branch is repeated n times where n is the dendrimer generation. DM and DP differ only in the terminals.

Dendrimer-siRNA complex in water and ions



	charge	#atoms	#CL	#NA
DM-siRNA	-2	81635	76	88
DP-siRNA	-2	81719	76	78

Figure S3. A view of the simulated dendrimer-siRNA complex in water and ions (right) built from single components (left). Information on charge, total number of atoms and number of added ions in the solution, are also provided.