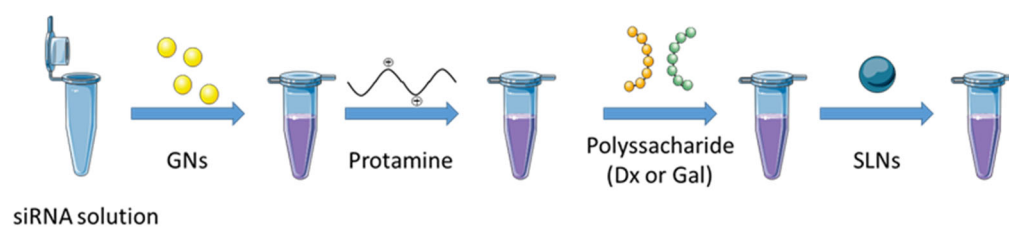


## Supplementary material



**Figure S1.** Preparation of siRNA-based vectors.

**Table S1.** Composition of siRNA-based vectors.

Vector	Type of SLN	Dx:P:siRNA (w:w:w ratio)	Gal:P:siRNA (w:w:w ratio)	Size of GN (nm)
DX-P2-GN5-HT	HT	1:2:1		5
DX-P3-GN5-HT	HT	1:3:1		5
Gal-P2-GN5-HT	HT		0.1:2:1	5
Gal-P3-GN5-HT	HT		0.1:3:1	5
DX-P2-GN5-HD	HD	1:2:1		5
DX-P3-GN5-HD	HD	1:3:1		5
Gal-P2-GN5-HD	HD		0.1:2:1	5
Gal-P3-GN5-HD	HD		0.1:3:1	5
DX-P3-ET	ET	1:3:1		-
DX-P2-GN5-ET	ET	1:2:1		5
DX-P3-GN5-ET	ET	1:3:1		5
DX-P2-GN1.8-ET	ET	1:2:1		1.8
DX-P3-GN1.8-ET	ET	1:3:1	0.1:3:1	1.8
3Gal-P3-ET	ET		0.1:3:1	-
Gal-P2-GN5-ET	ET		0.1:2:1	5
Gal-P3-GN5-ET	ET		0.1:3:1	5
Gal-P2-GN1.8-ET	ET		0.1:2:1	1.8
Gal-P3-GN1.8-ET	ET		0.1:3:1	1.8
DX-P3-ED	ED	1:3:1		-
DX-P2-GN5-ED	ED	1:2:1		5
DX-P3-GN5-ED	ED	1:3:1		5
DX-P2-GN1.8-ED	ED	1:2:1		1.8
DX-P3-GN1.8-ED	ED	1:3:1		1.8
Gal-P3-ED	ED		0.1:3:1	-
Gal-P2-GN5-ED	ED		0.1:2:1	5
Gal-P3-GN5-ED	ED		0.1:3:1	5
Gal-P2-GN1.8-ED	ED		0.1:2:1	1.8

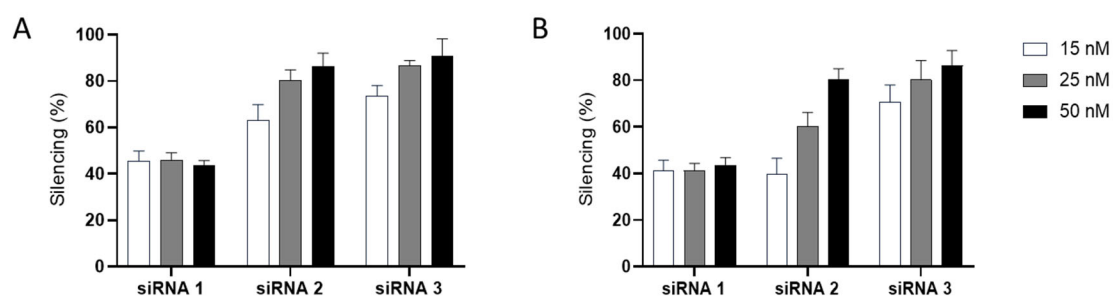
Gal-P3-GN1.8-ED	ED		0.1:3:1	1.8
-----------------	----	--	---------	-----

HT: HT-based vectors. HD: HD-based vectors. ET: ET-based vectors. ED: ED-based vectors. DX: dextran. Gal: galactomannan. P: protamine. GN5: gold nanoparticles of 5 nm diameter. GN1.8: gold nanoparticles of 1.8 nm diameter. PDI: polydispersity index. SLNs were added in a weight ratio of 5 referred to siRNA. GN of 5 nm were added in a volume of 5  $\mu$ L while 1  $\mu$ L of 1.8 nm GN were used. Data are expressed as mean  $\pm$  standard deviation;  $n=3$ .

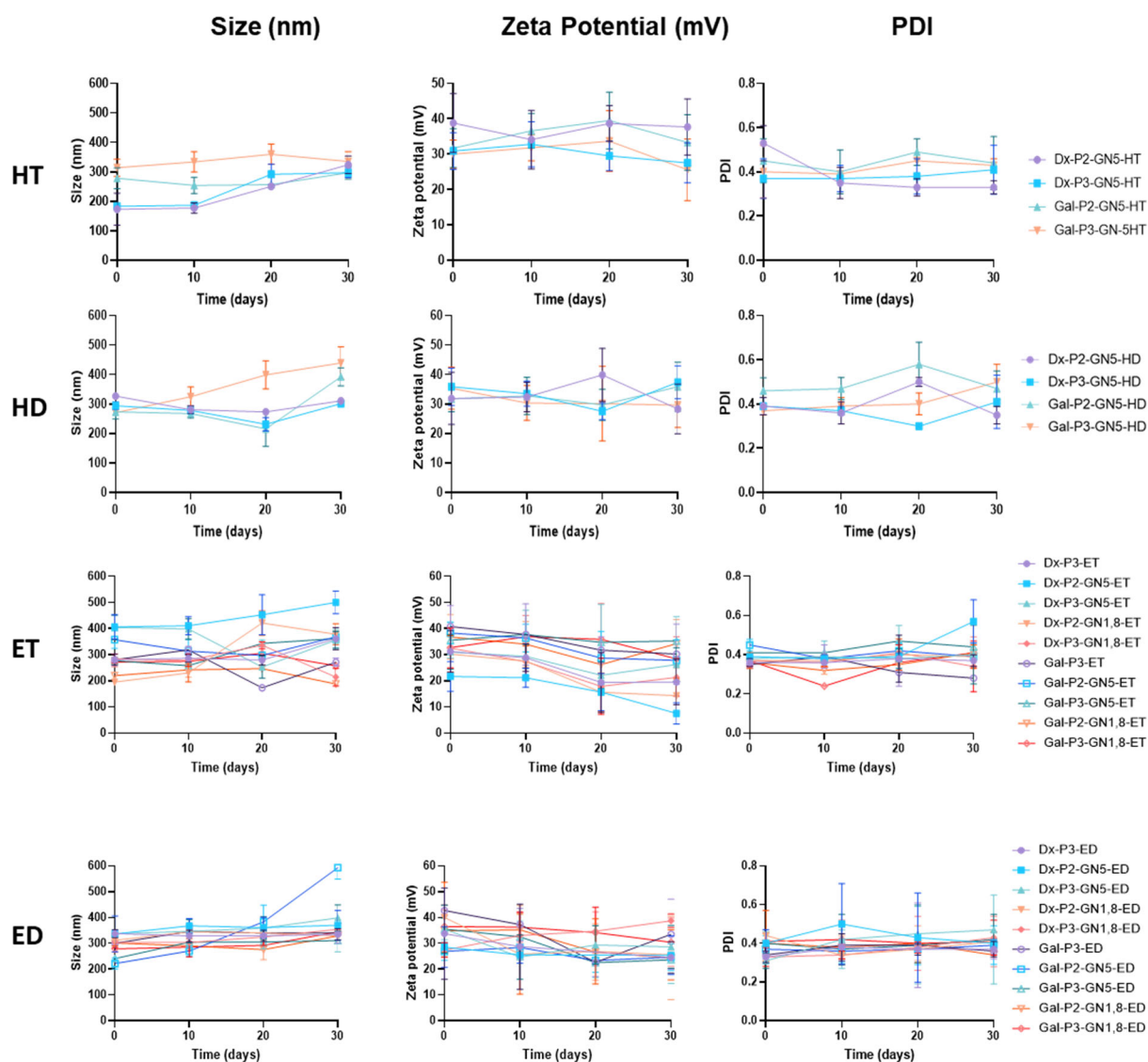
**Table S2.** Physical characterization of SLNs-based vectors.

SLN-based vector	Vector	Size Z-average (d.nm)	PDI	$\zeta$ -Potential (mV)
HT	DX-P2-GN5-HT	173.3 $\pm$ 55.2	0.35 $\pm$ 0.08	38.8 $\pm$ 8.3
	DX-P3-GN5-HT	237.2 $\pm$ 14.8	0.44 $\pm$ 0.05	30.9 $\pm$ 5.2
	Gal-P2-GN5-HT	278.0 $\pm$ 85.0	0.40 $\pm$ 0.09	31.7 $\pm$ 10.5
	Gal-P3-GN5-HT	314.3 $\pm$ 28.9	0.40 $\pm$ 0.08	30.0 $\pm$ 4.0
HD	DX-P2-GN5-HD	326.8 $\pm$ 8.1	0.39 $\pm$ 0.04	31.9 $\pm$ 8.8
	DX-P3-GN5-HD	294.3 $\pm$ 12.8	0.39 $\pm$ 0.01	35.9 $\pm$ 6.3
	Gal-P2-GN5-HD	273.0 $\pm$ 24.6	0.46 $\pm$ 0.06	31.7 $\pm$ 7.3
	Gal-P3-GN5-HD	270.9 $\pm$ 9.9	0.37 $\pm$ 0.02	35.4 $\pm$ 8.2
ET	DX-P3-ET	280.4 $\pm$ 7.3	0.36 $\pm$ 0.02	31.2 $\pm$ 7.9
	DX-P2-GN5-ET	406.2 $\pm$ 21.7	0.39 $\pm$ 0.01	31.7 $\pm$ 5.7
	DX-P3-GN5-ET	263.3 $\pm$ 26.6	0.38 $\pm$ 0.01	31.0 $\pm$ 6.6
	DX-P2-GN1.8-ET	195.2 $\pm$ 6.5	0.35 $\pm$ 0.05	30.2 $\pm$ 7.1
	DX-P3-GN1.8-ET	284.3 $\pm$ 18.3	0.36 $\pm$ 0.01	32.5 $\pm$ 7.6
	Gal-P3-ET	280.6 $\pm$ 7.5	0.36 $\pm$ 0.02	40.8 $\pm$ 8.0
	Gal-P2-GN5-ET	381.9 $\pm$ 43.9	0.45 $\pm$ 0.03	38.3 $\pm$ 6.2
	Gal-P3-GN5-ET	276.5 $\pm$ 13.7	0.37 $\pm$ 0.04	35.5 $\pm$ 6.8
	Gal-P2-GN1.8-ET	219.7 $\pm$ 9.7	0.34 $\pm$ 0.09	36.8 $\pm$ 8.5
	Gal-P3-GN1.8-ET	274.1 $\pm$ 8.6	0.39 $\pm$ 0.04	32.7 $\pm$ 7.8
ED	DX-P3-ED	337.5 $\pm$ 15.3	0.33 $\pm$ 0.03	33.8 $\pm$ 7.7
	DX-P2-GN5-ED	336.8 $\pm$ 69.7	0.40 $\pm$ 0.07	28.5 $\pm$ 7.9
	DX-P3-GN5-ED	336.5 $\pm$ 7.9	0.31 $\pm$ 0.04	35.5 $\pm$ 9.3
	DX-P2-GN1.8-ED	311.7 $\pm$ 22.2	0.44 $\pm$ 0.03	34.0 $\pm$ 7.6
	DX-P3-GN1.8-ED	304.1 $\pm$ 21.6	0.33 $\pm$ 0.05	32.6 $\pm$ 8.4
	Gal-P3-ED	300.3 $\pm$ 7.9	0.34 $\pm$ 0.02	32.7 $\pm$ 10.1
	Gal-P2-GN5-ED	221.5 $\pm$ 21.5	0.37 $\pm$ 0.09	33.9 $\pm$ 9.5
	Gal-P3-GN5-ED	240.9 $\pm$ 10.0	0.40 $\pm$ 0.06	35.4 $\pm$ 8.1
	Gal-P2-GN1.8-ED	301.1 $\pm$ 8.6	0.40 $\pm$ 0.05	34.9 $\pm$ 10.0
	Gal-P3-GN1.8-ED	278.9 $\pm$ 13.4	0.41 $\pm$ 0.05	36.5 $\pm$ 6.4

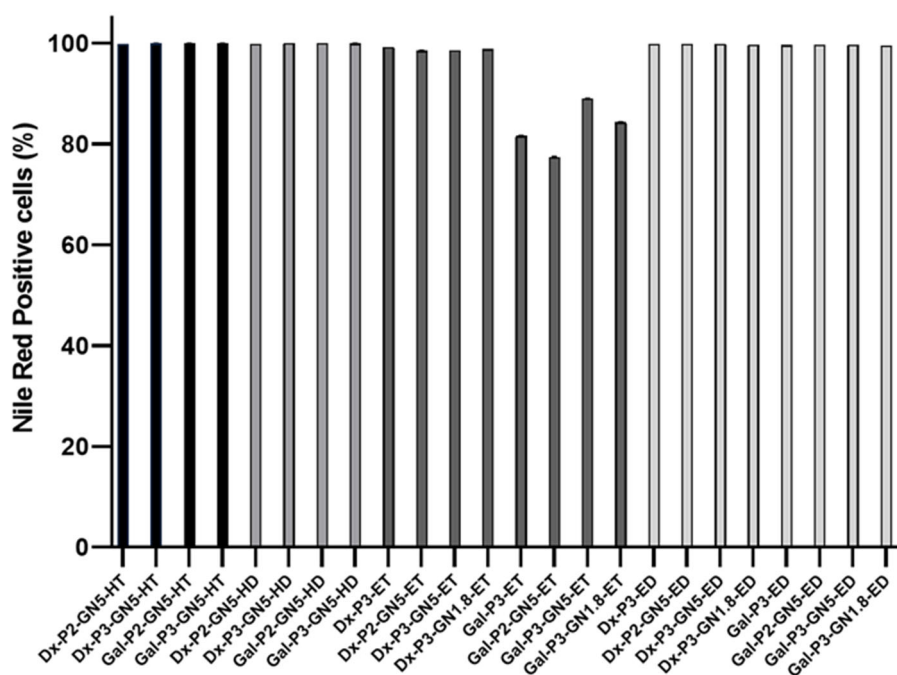
HT: HT-based vectors. HD: HD-based vectors. ET: ET-based vectors. ED: ED-based vectors. DX: dextran. Gal: galactomannan. P: protamine. GN5: gold nanoparticles of 5 nm diameter. GN1.8: gold nanoparticles of 1.8 nm diameter. PDI: polydispersity index. Data are expressed as mean  $\pm$  standard deviation;  $n=3$ .



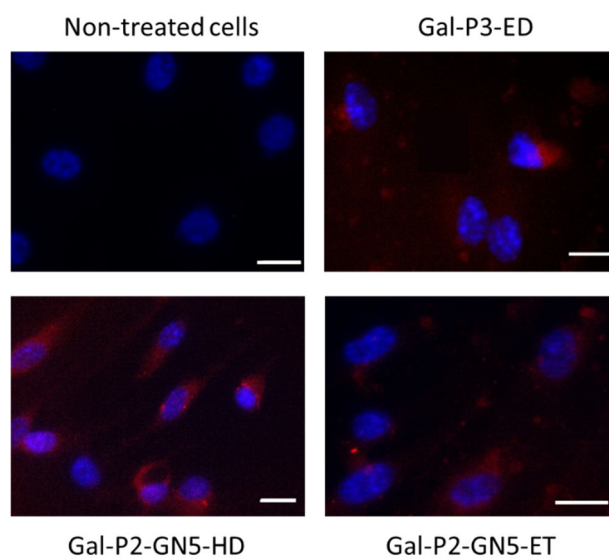
**Figure S2.** Study of the silencing capacity of different siRNA at 15, 25 and 50 nM. **(A)** Silencing effect of siRNAs 1, 2 and 3 formulated in Dx-P2-GN5-HT. **(B)** Silencing effect of siRNAs 1, 2 and 3 formulated with DharmaFECT®. Data are expressed as mean  $\pm$  standard deviation; n=3.



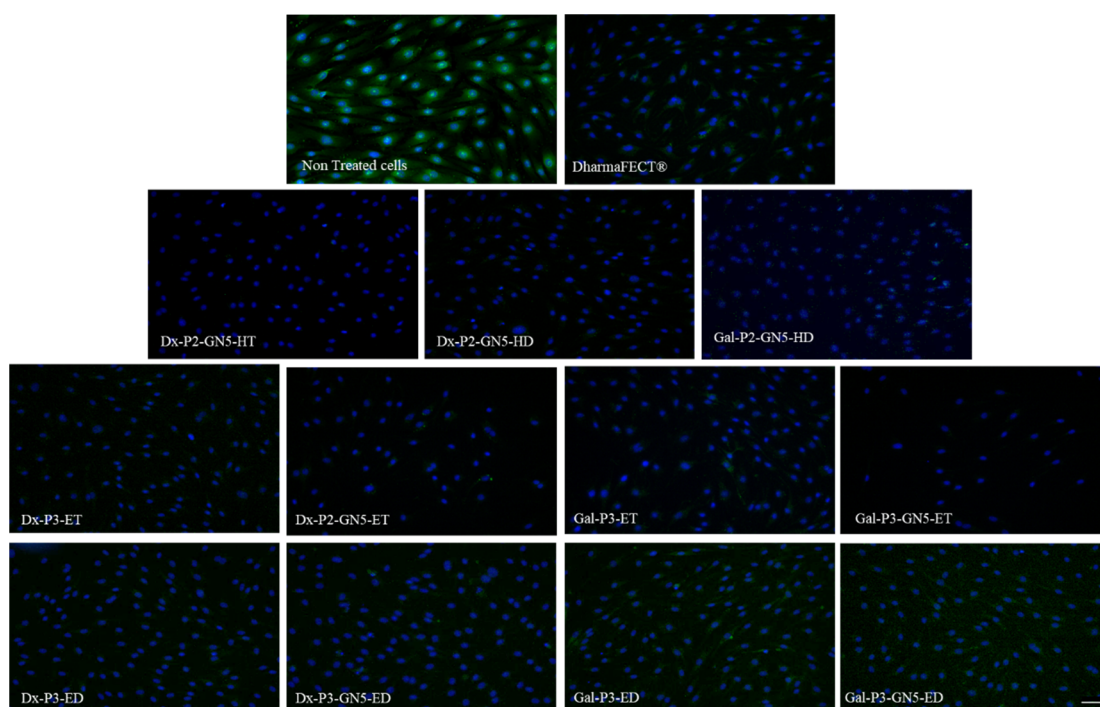
**Figure S3.** Size,  $\zeta$ -Potential and polydispersity index of siRNA-based vectors formulated with different SLNs at time zero, ten, twenty and thirty days. **(HT)** HT- Vectors. **(HD)** HD-Vectors. **(ET)** ET-Vectors. **(ED)** ED-Vectors. Data are expressed as mean  $\pm$  standard deviation; n=3.



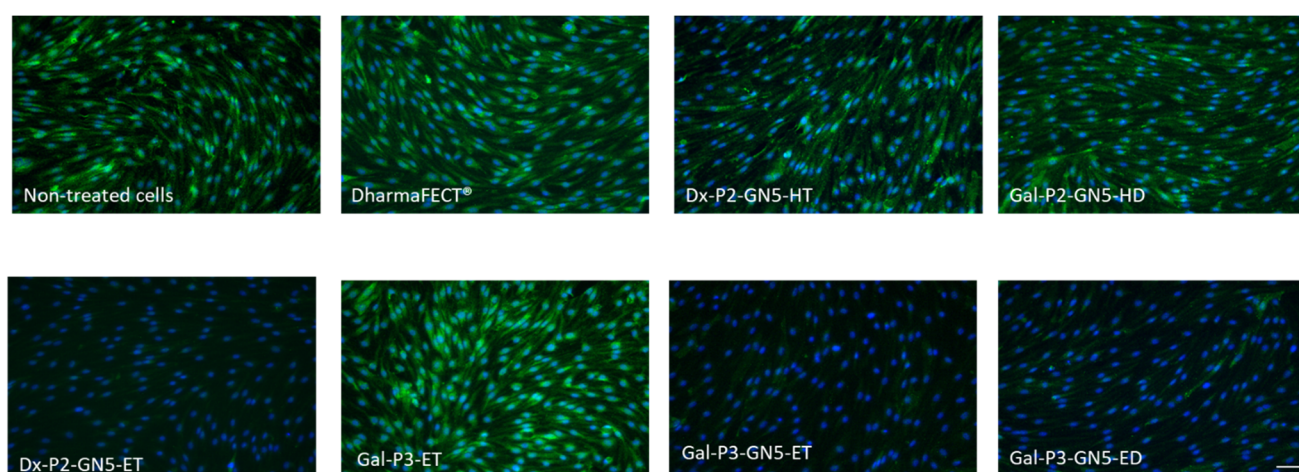
**Figure S4.** Cellular uptake of vectors using Nile-Red labelled SLNs in IMFE-1 cells 2 hours after transfection measured by flow cytometry. Data are expressed as mean  $\pm$  standard deviation; n=3.



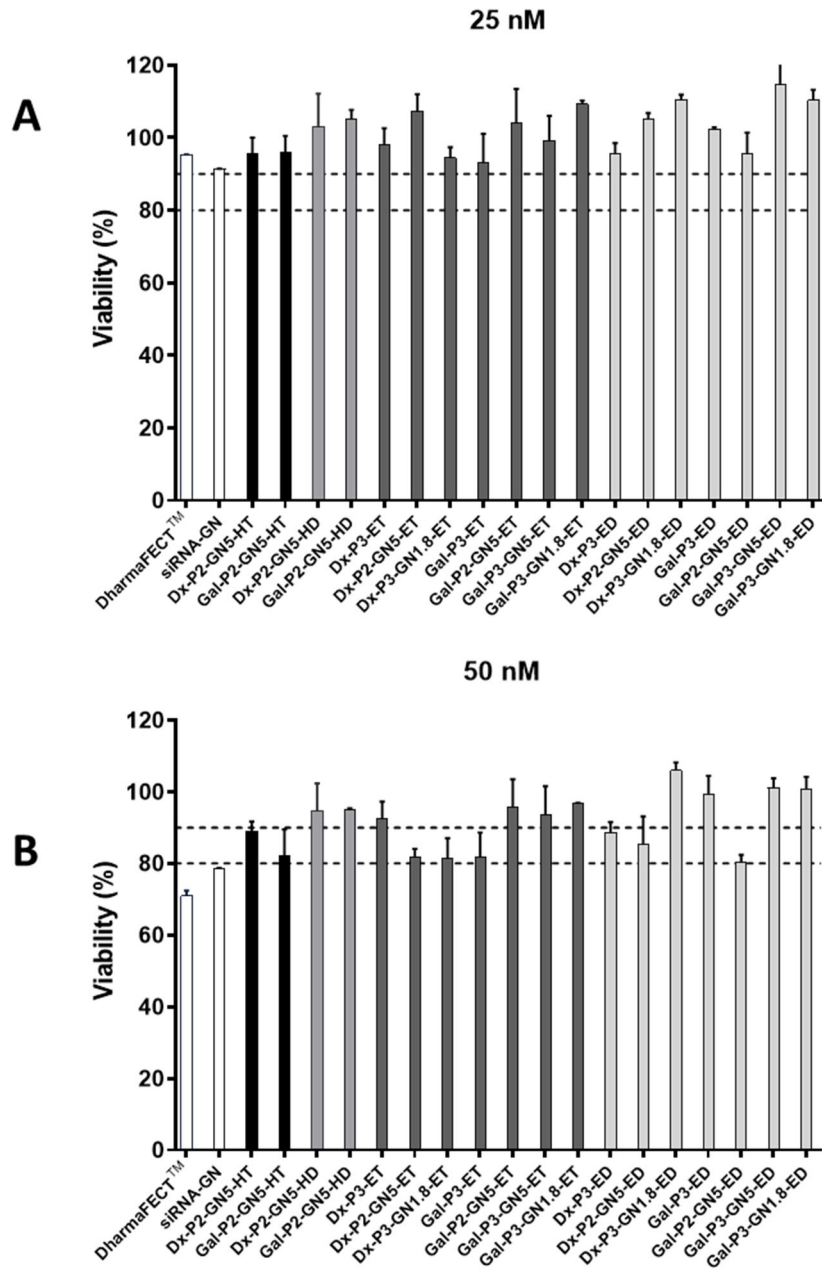
**Figure S5.** Cellular uptake of vectors using Nile-Red labelled SLNs in IMFE-1 cells 2 hours after transfection obtained by fluorescent microscopy. Scale bar = 15  $\mu$ m.



**Figure S6.** Immunocytochemistry study of Gb3S expression in IMFE-1 cells 7 days after treatment with different siRNA-based vectors. Scale bar: 100  $\mu$ m.



**Figure S7.** Immunocytochemistry study of Gb3S expression in IMFE-1 cells 15 days after treatment with different siRNA-based vectors. Scale bar: 100  $\mu$ m.



**Figure S8.** Viability in IMFE-1 cells two hours after the addition of siRNA-based vectors analyzed by MTT assay. Data are expressed as mean  $\pm$  standard deviation;  $n=3$ . **(A)** Viability in IMFE-1 after the addition of vectors a dose 25 nM. **(B)** Viability in IMFE-1 cells after the addition of vectors of vector at a dose 50 nM. Lines represent 80% and 90%.