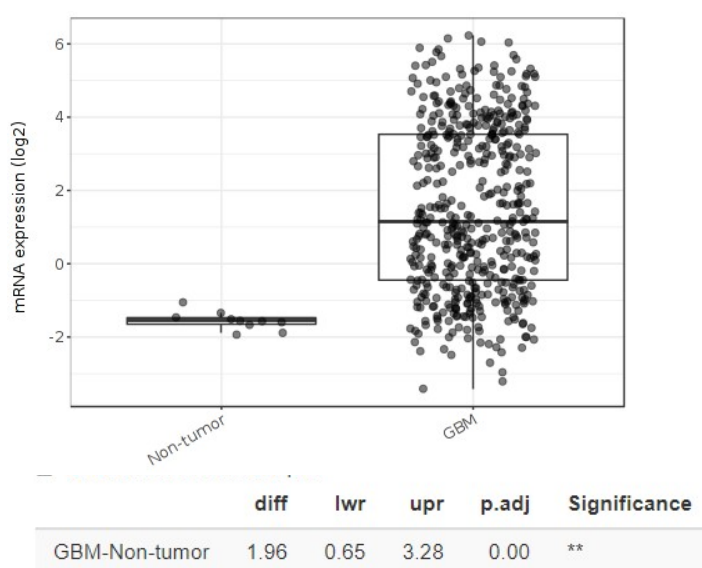


## SUPPLEMENTARY

### Title: Nanoparticle's shape is the game-changer for blood-brain barrier crossing and delivering through tunneling nanotubes among glioblastoma cells

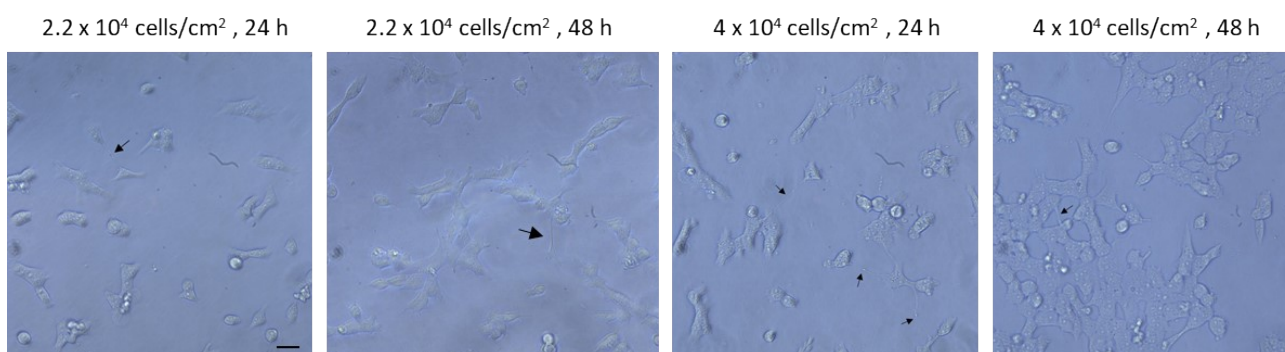
Giulia Sierra <sup>a\*§</sup>, Ines Saenz-de-Santa-Maria <sup>b§</sup>, Antonio Renda <sup>a</sup>, Marcus Koch <sup>c</sup>, Patrizia Sommi <sup>d</sup>,  
Umberto Anselmi-Tamburini <sup>e</sup>, Mario Mauri <sup>a</sup>, Alessia D'Aloia <sup>f</sup>, Michela Ceriani <sup>f</sup>, Domenico  
Salerno <sup>a</sup>, Francesco Mantegazza <sup>a</sup>, Chiara Zurzolo <sup>b‡</sup>, Francesca Re <sup>a‡</sup>

#### Supplementary S1



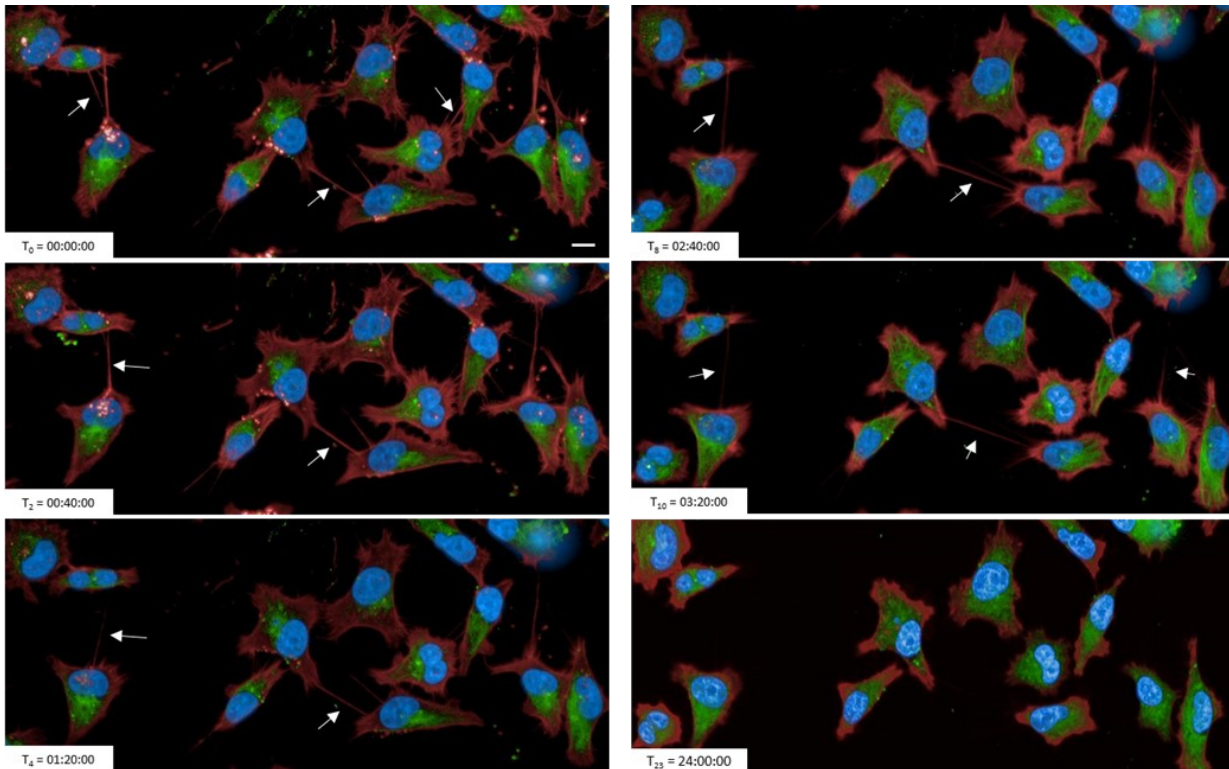
S1. mRNA expression level of EGFR in non-tumour and patient-derived GBM cells. Source: GlioVis.  
\*\*,  $p < 0.001$  calculated by Tukey's test.

#### Supplementary S2



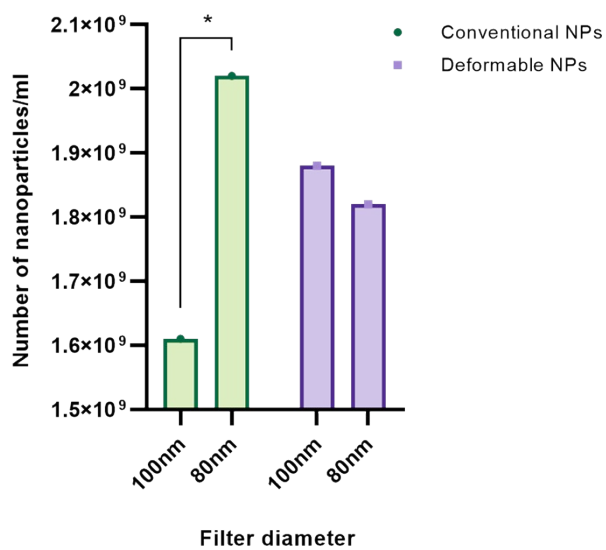
S2. Pictures obtained by optical microscopy of Gli36 $\Delta$ EGFR-2 cells. On the top of images: cell density, time growth. Scale bar in the image corresponds to 50  $\mu$ m.

### Supplementary S3



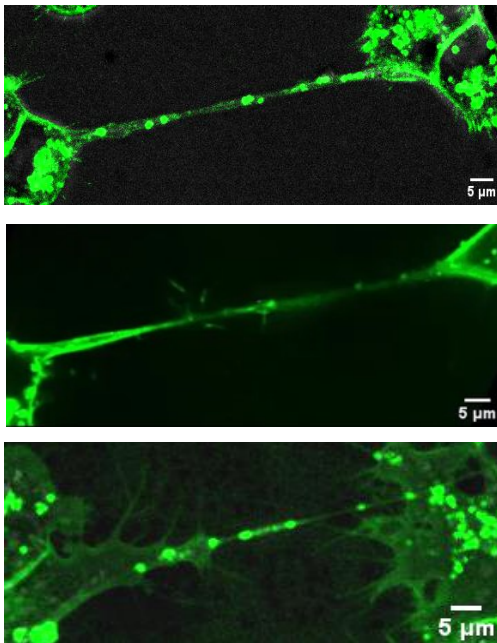
S3. TNTs dynamicity observed in live over-time up to 24 h by the Operetta CLS High Content Analysis System confocal microscope. Scale bar in the image corresponds to 50  $\mu\text{m}$ .

### Supplementary S4



S4. The penetration ability of deNPs under external forces, into polycarbonate films with pore sizes of 100 and then 80 nm size, under an applied extrusion force was evaluated by measuring the number of NPs/mL through Nanosight.

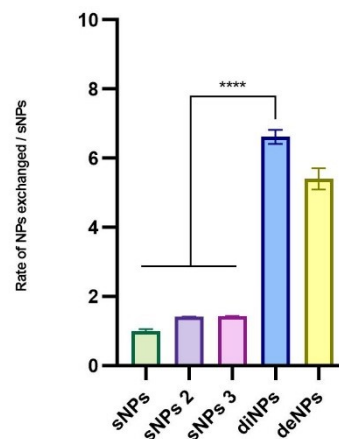
Supplementary S5



S5. Representative pictures obtained from videos of Gli36ΔEGFR-2 cells incubated with fluorescently-labelled nanoparticles.

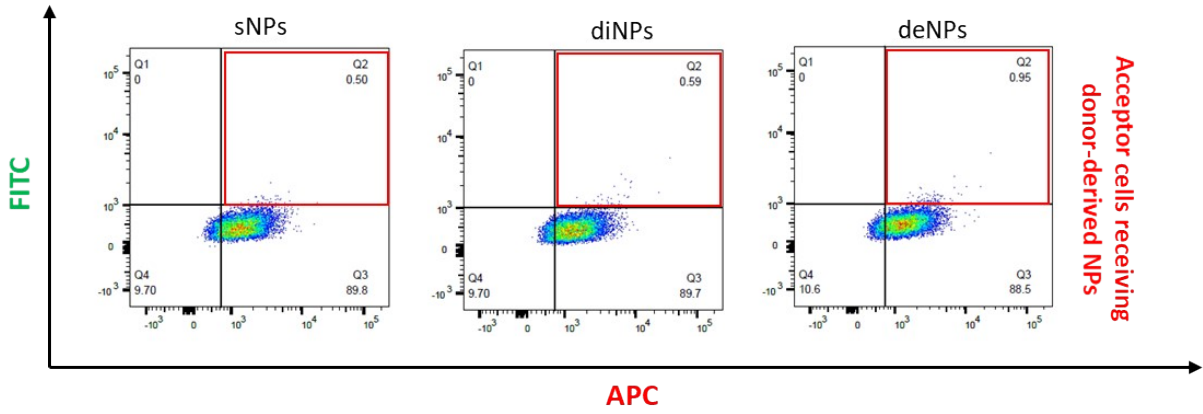
Supplementary S6

NPs	Diameter	PDI
sNP 2	109.5 ± 1.5	0.115 ± 0.02
sNP 3	115.5 ± 1.1	0.122 ± 0.02



S6. Characterization of sNPs 2, sNPs 3 and the rate of NPs exchange *via* TNTs by FACS. Each value obtained for sNPs 2, sNPs 3 (spherical NPs with different composition) and for diNPs, deNPs was normalized with sNPs used as a control. Even in this case, diNPs showed the highest transfer efficiency.

Supplementary S7



S7. NPs exchange by FACS when the two cell populations were separated by 1  $\mu\text{m}$  filter but shared the same medium.