Carbon nanotube-based targeting systems for cytoplasmic delivery

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The translocation of nanomaterials or complex delivery systems into the cytosol is a main challenge in nanobiotechnology.[1] Current nanodevices offer limited solutions to the problem of the cytoplasmic delivery of active compounds. The biggest challenges are i) specific cell recognition, ii) protection of the cargo from the hostile lysosomal chemical conditions, iii) nonlethal endolysosomal (E-L) escape, iv) the carriage of different particles or chemicals into the cytosol, and finally, v) clearance of the delivery vectors to avoid long-term cytotoxicity. To date, there is only partial understanding of how to control the intracellular fate of the carrier systems after endocytosis.

After receptor-mediated endocytosis, most delivery vectors are trapped in the endo-lysosomal vesicles,[2–4] where the hostile enzymatic and chemical conditions destroy the nanomaterials and/or inactivate the therapies,[5,6] or alternatively, undergoing exocytosis. We have explored a novel surface particle coating made of adsorbed carbon nanotubes (CNTs) that provides coated materials with new properties that reproduce the viral cell invasive mechanisms, namely: receptor mediated endocytosis, endo-lysosomal escape and cytosolic particle release preserving intact cell viability.

This fully biocompatible[7,8] novel biomimetic coating design will enable the **intracytoplasmic delivery** of many different nanomaterials thus, opening the door to a wide array of chemical and physical processes within the cytosolic or nuclear domains, and supporting the generation of new developments in the biotechnological, pharmaceutical and biomedical industries.

References

[1] H. K. Shete, R. H. Prabhu, V. B. Patravale, *J. Nanosci. Nanotechnol.* **2014**, *14*, 460–74.

[2] L. Lacerda, J. Russier, G. Pastorin, M. A. Herrero, E. Venturelli, H. Dumortier, K. T. Al-Jamal, M. Prato, K. Kostarelos, A. Bianco, *Biomaterials* **2012**, *33*, 3334–3343.

[3] K. Maruyama, H. Haniu, N. Saito, Y. Matsuda, T. Tsukahara, S. Kobayashi, M. Tanaka, K. Aoki, S. Takanashi, M. Okamoto, et al., *Biomed Res. Int.* **2015**, *2015*, 793186.

[4] P. N. Yaron, B. D. Holt, P. A. Short, M. Lösche, M. F. Islam, K. N. Dahl, *J. Nanobiotechnology* **2011**, *9*, 45.

[5] J. M. Kinchen, K. S. Ravichandran, *Nat. Rev. Mol. Cell Biol.* **2008**, *9*, 781–95.

[6] J. B. Lloyd, *Biochem. J.* **1986**, *237*, 271–2.

[7] N. Iturrioz-Rodríguez, E. González-Domínguez, E. González-Lavado, L. Marín-Caba, B. Vaz, M. Pérez-Lorenzo, M. A. Correa-Duarte, M. Fanarraga, *Angew. Chemie - Int. Ed.* **2017**, DOI 10.1002/anie.201707769.

[8] E. González-Domínguez, N. Iturrioz, E. Padín-González, J. C. Villegas, L. García-Hevia, M. Pérez-Lorenzo, W. J. Parak, M. A. Correa-Duarte, M. L. Fanarraga, *Int. J. Nanomedicine* **2017**, *12*, 6317–6328.

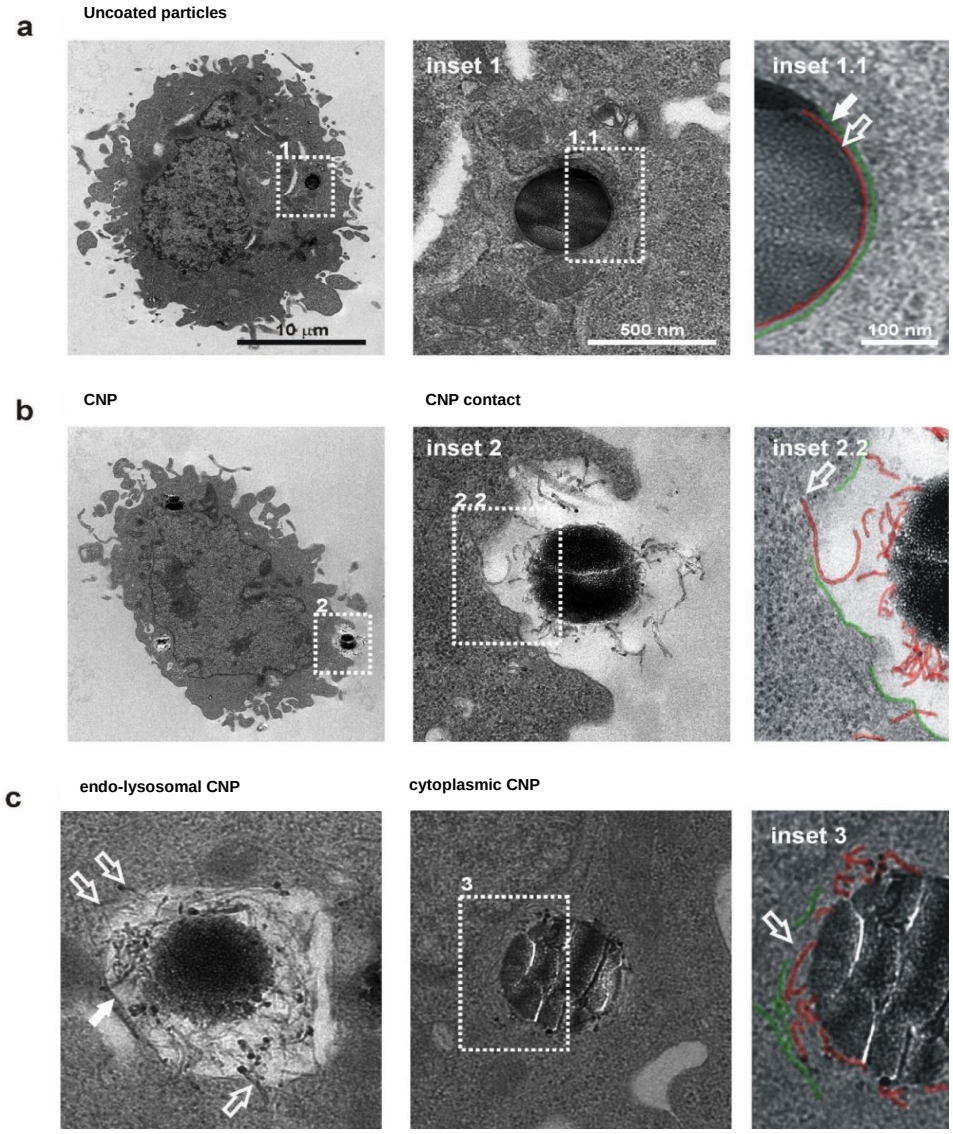

Figure 1: (a) TEM images of the cytoplasm of cells containing an uncoated particle. The endosomal membrane (pseudo-coloured in green) is clearly visible (solid arrow). (b) Section of a CNT-coated particle (CNP) contacting the surface of the HeLa cell. (Insets 2, 2.2) Some CNTs of the CNP coating (pseudo-coloured in red) are already penetrating into the cell cytoplasm (empty arrows). (c) Endo-lysosomal and cytoplasmic CNPs, Cytoplasmic CNTs and the membrane of the endosome are indicated with empty and solid arrows respectively. (Inset 3). More info in Refs. 7,8