

Carbon nanotubes display intrinsic anticancer properties

García-Hevia L, Valiente, R, González J, Villegas JC, **Fanarraga ML**.
Universidad de Cantabria, Santander, Spain
fanarrag@unican.es

Abstract

Carbon nanotubes (CNTs) have been proposed as the technological counterpart of nature's microtubules (MTs) [1]. MTs are 25 nm diameter protein polymer nanotubes that constitute the cellular cytoskeleton and are essential for cell proliferation and migration.

CNTs and MTs share various aspects of their architecture and properties [1]. They have similar dimensions, (ii) a similar tubular morphology that ensures structural efficiency, have analogous mechanical behaviors, and are exceptionally resilient [2,3]. Their similarities are quite likely to be responsible for their association *in vitro* [4] and *in vivo* [5]. There is, however, a big difference between these polymers that has critical implications in the *in vivo* system, while CNTs are very stable polymers, microtubules are highly dynamic structures that are continuously undergoing assembly/disassembly cycles in a process known as dynamic instability [6].

Functionalized CNTs are easily translocated intracellularly [5,7]. Inside cells they assemble mixed polymers with tubulin [5]. Due to the scaffolding effect of CNTs, MTs display an enhanced stability that is critical during cell division, triggering mitotic arrest and cell death [5,8]. Interestingly, CNTs behave as microtubule stabilizing cytotoxic agents interfering with microtubule dynamics, leading to anti-proliferative, anti-migratory and pro-apoptotic effects [9]. These findings support the idea that CNTs represent a ground-breaking type of synthetic microtubule-stabilizing agents that could play a pivotal role in future cancer treatments in combination to traditional antineoplastic drugs.

References

- [1] Pampaloni F, Florin EL. Microtubule Architecture: Inspiration for Novel Carbon Nanotube-Based Biomimetic Materials. *Trends Biotechnol* **26** (2008) 302.
- [2] Odde DJ, et al. Microtubule bending and breaking in living fibroblast cells. *J Cell Sci.* **112** (1999) 3283.
- [3] de Pablo PJ, et al. Deformation and collapse of microtubules on the nanometer scale. *Phys Rev Lett* **91** (2003) 98101.
- [4] Dinu CZ, et al. Tubulin Encapsulation of CNTs into Functional Hybrid Assemblies. *Small* **5** (2009) 310.
- [5] Rodriguez-Fernandez, et al. Multiwalled carbon nanotubes display microtubule biomimetic properties *in vivo*, enhancing microtubule assembly and stabilization. *ACS Nano* **6**, (2012) 6614.
- [6] Jordan MA, Wilson L. Microtubules as a Target for Anticancer Drugs. *Nat Rev Cancer* **4** (2004) 253.
- [7] Lacerda L, et al. Translocation Mechanisms of chemically functionalised carbon nanotubes across plasma membranes. *Biomaterials* **33** (2012) 3334.
- [8] Sargent L, et al. Single-Walled Carbon Nanotube-Induced Mitotic Disruption. *Mutat Res* **14** (2012) 28.
- [9] García-Hevia L, et al. Nanotube interactions with microtubules: implications for cancer medicine. *Nanomedicine (Lond)*. **9** (2014) 1581.

Figures:

Confocal microscopy image of a mitotic spindle of a dividing HeLa cell treated with MWCNT during 70 h displaying an abnormal microtubule/chromosomal organization. Microtubules are shown in the red channel immunostained with anti-tubulin antibody-Cy3. Chromosome miss-positioning is observed in the blue channel, Hoechst staining. Scale bar 2µm.

