

Carbon nanotubes In Biomedicine

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What Next at LNF: scienze dei materiali INFN, Laboratori Nazionali di Frascati, 26-27 February 2015 Delivery and imaging of miRNAs by multifunctional carbon nanotubes and circulating miRNAs as innovative therapeutic and diagnostic tools for pediatric pulmonary hypertension



Lab. Microarrays

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Bambino Gesù Children's Hospital (2013)



Bambino Gesù Children's Hospital (2014)



GENE EXPRESSION - MICROARRAYS LABORATORY

RESEARCH TOPICS

BASIC RESEARCH

- Assessment of the expression of genes (mRNAs) in cells and tissues (normal and pathological)

- Assessment of the expression of non-coding RNAs and their role in gene regulation.
- Bioinformatics (Next Generation Sequencing, microRNAs and Microarrays Data)
- Non-viral drug delivery vectors (polymer and lipid systems)
- Nanotechnologies (superparamagnetic nanoparticles and multifunctional nanotubes)



TRANSLATIONAL RESEARCH

- The research is mainly focused on different pediatric diseases
- Biomarkers discovery and Validation (circulating microRNAs)

Carbon Nanotubes (CNTs)

Current applications (use of bulk nanotubes):

- As <u>composite fibers</u> embedded in polymers to improve the mechanical, thermal and electrical properties of the bulk product.

- As <u>tips</u> for atomic force microscope probes.

- As <u>scaffold for bone growth</u> in tissue engineering (Zanello LP et al., Bone cell proliferation on carbon nanotubes. Nano Lett. 2006;6(3):562-7).

In the biomedical field the use of CNTs is further limited by their **insolubility** in aqueous solutions, by their intrinsic **toxicity** and in some cases by safety regulations.

AIM: Develop novel non-toxic CNT-based vectors for nucleic acid delivery in human cells (i.e. endothelial cells).





Functionalization of CNTs



perfect globular structure, high functionality



Hyperbranched Polymer (Highly branched Polymer)

less perfect structure, high functionality

Functionalization of CNTs



Functionalization of CNTs





Two Hypotheses

Neutral/hydrophobic 'Somehow' charged Н H+ Н н A benzenium ion $C_6H_7^+$ (also called Wheland intermediate or σ -complex) - Ramesh, S. et al. J. Phys. Chem. B 2004, 108, 8794-8798. - Davis, V. A. et al. Macromolecules 2004, 37, 154-160. VVTLT VVILI polymer backbones charged amine groups (CH₂CH₂ chains) (protonated terminal

-NH₂ groups)

Supramolecular Chemistry Principle

Polar Solvents (WATER)



Apolar Solvents



Supramolecular Chemistry Principle



Supramolecular Chemistry Principle





The guiding principle that lead to complexation of polyamine polymers to CNTs are hydrophobic interactions

What about structure?

What about toxicity ?

What about biological effects?

PEI25-CNT



PAMAM-CNT



Dimension



Cytotoxicity of polymer-coated CNTs



Internalization of CNTs

CNTs both inside and outside cells.





Transfection efficiency of polymer-coated CNTs

On HUVEC cells

PEI25-CNT + Pre-miR (Cy3) (1mg/ml; 50nM Pre-miR)



PAMAM-CNT + Pre-miR (Cy3) (1mg/ml PAMAM; 50nM Pre-miR)







Looking forward





Looking forward



Multifunctional Drug Delivery Vector



Lu, Y. J et al. 2012. Colloids Surf. B Biointerfaces, 89, 1-9.

THANK YOU FOR YOUR ATTENTION

