



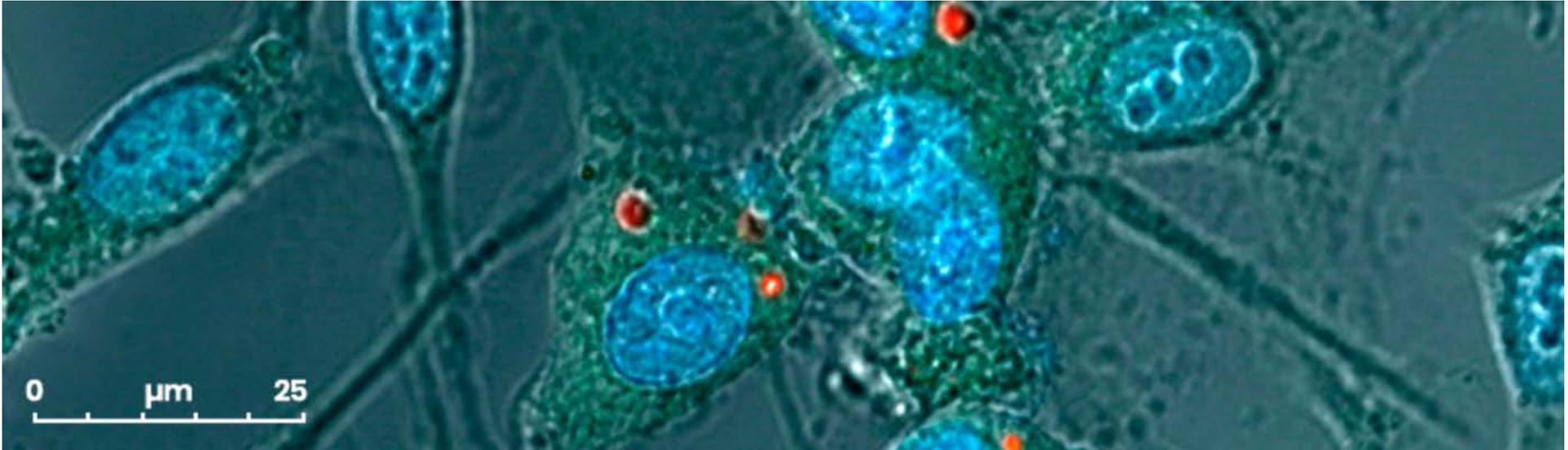
**Stefano Leporatti, PhD**

## ***Nanocarriers for Nanomedicine***

**Team & collaborators:** Francesca Persano (Uni-Salento & CNR Nanotec), Dr. Nemanly Hanafy (now Lecturer @Kafrelsheikh University, Egypt), Dr. Mariafrancesca Cascione and Valeria De Matteis (Uni-Salento, Lecce), Prof. Alessandro Parodi (Sechenov University, Moscow, Russia), Prof. Luciana Dini (Uni-Sapienza, Roma). Dr. Elisa Panzerini (DiSteBA, Uni-Salento, Lecce) Prof. Gianluigi Giannelli (IRCSS De Bellis, Castellana Grotte, Bari), Prof. A-M. Safer (Kuwait University, Kuwait), Prof. Rawil Fakhrullin (Kazan University, Kazan, Russia), Prof. Yuri M. Lvov (Ruston University, Ruston, USA), Prof. Michele Maffia (DiSteBA, Uni-Salento, Lecce).



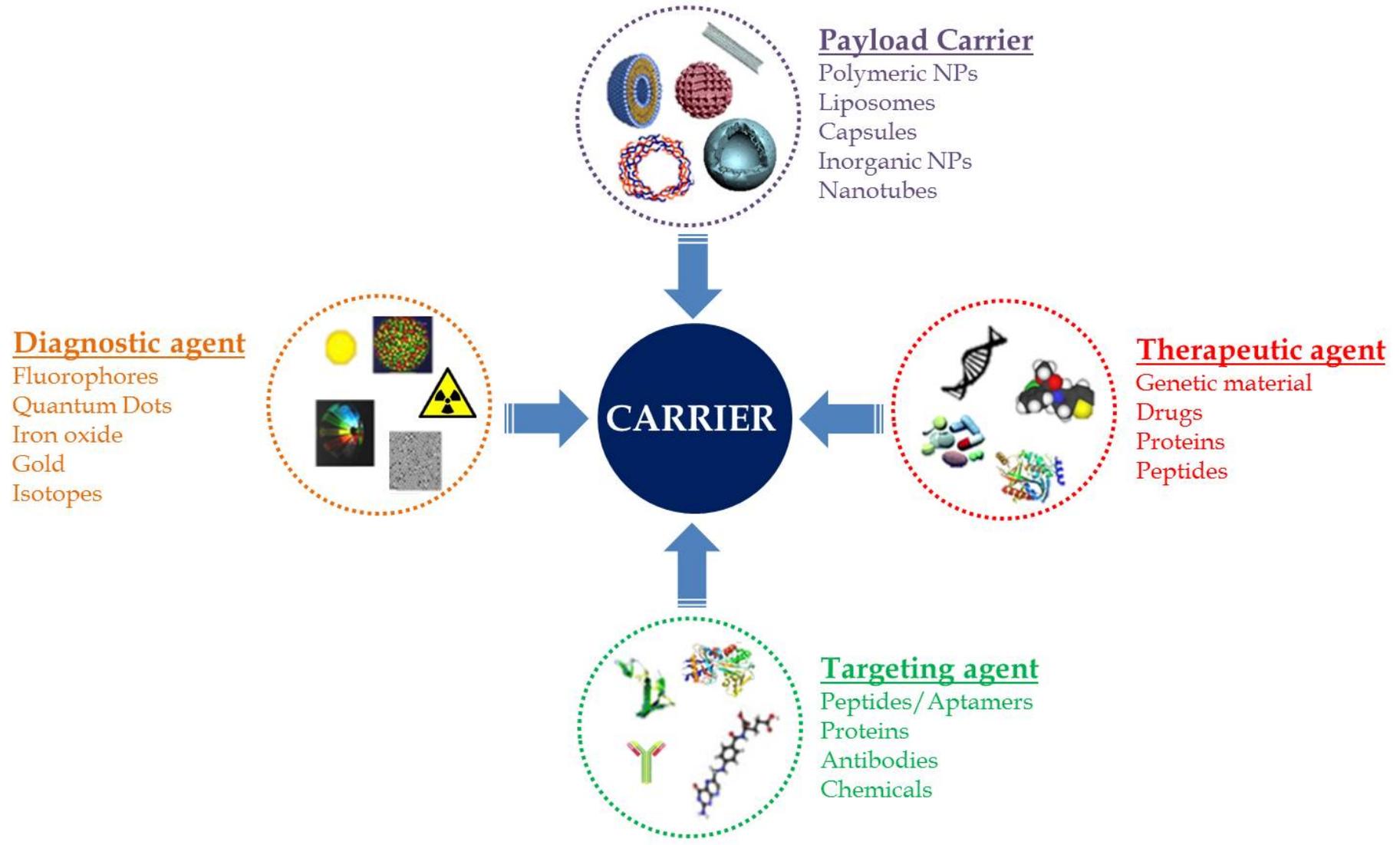
# Biomolecular Delivery



<http://www.nanotec.cnr.it/en/nano-biotechnology>

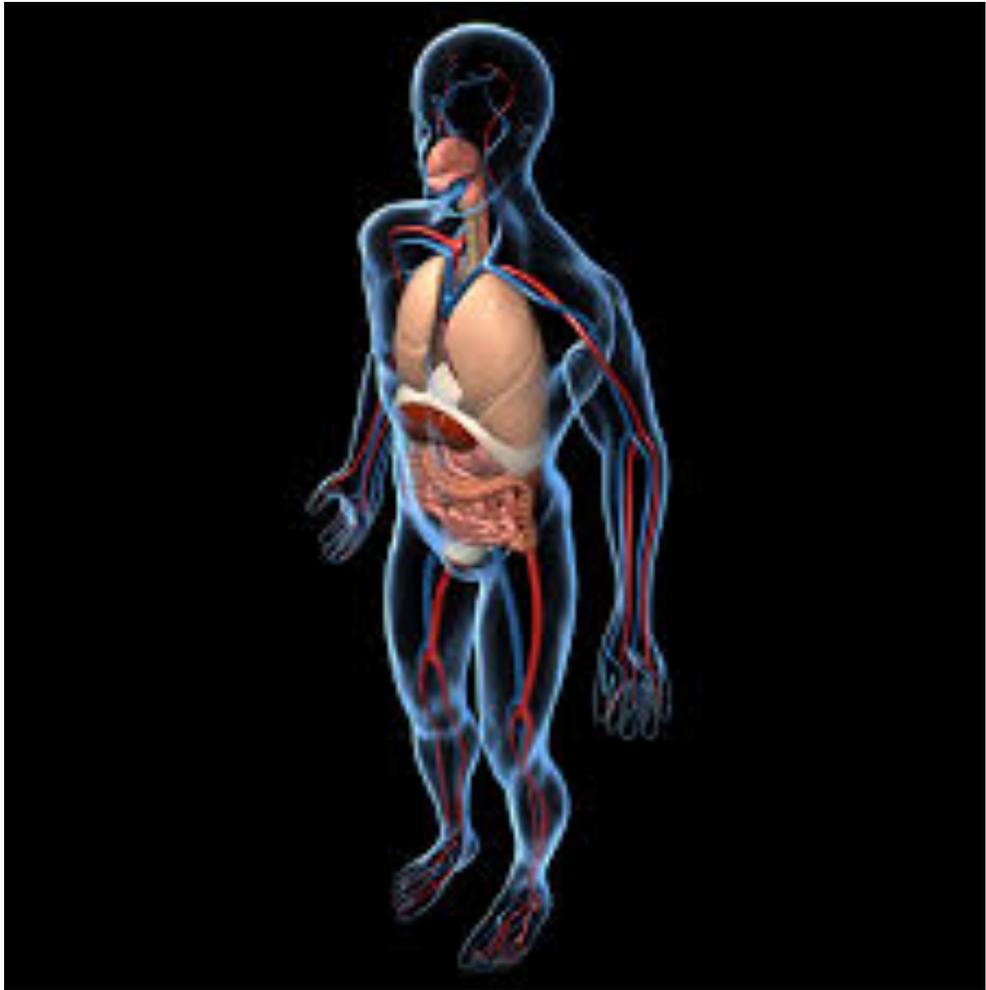
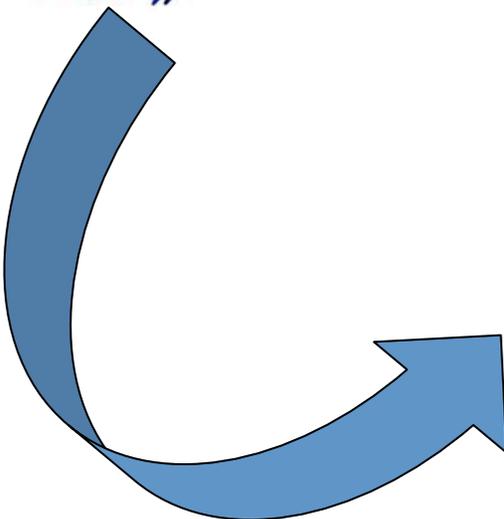
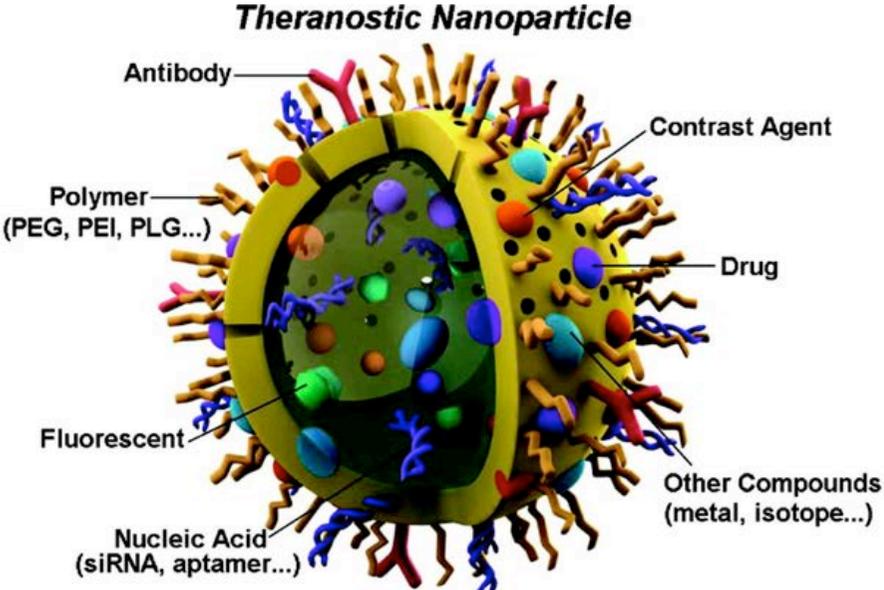
Incorporation of bioactive molecules into nanocarrier often offers several advantages for therapeutic purposes: it facilitates the delivery of insoluble drugs, ensures protection from enzymatic degradation, prolongs the halftime in the bloodstream and controls the release kinetics. The characteristics of a nanocarrier (size, composition, surface chemistry, response to intra- and extracellular stimuli) could be tuned for each specific application.

# Nanocarrier Design



Credits: Bionanotechnology @ CNR Nanotec

# Nanomedicine



# Outline

**Layer-by-Layer Polyelectrolyte NanoCarriers  
(Nano and Micro-capsules, Nanocolloids,  
LbL-coated Iron Oxide Nanoparticles)**

**Inorganic Nanoparticles (Halloysite NanoTubes  
(HNTs), Calcium Carbonate Nanorods, Silica  
Nanoparticles)**

**Hybrid Nanoparticles (Nanomicelles, Chitosan  
Nanoparticles, Lipid Protein Nanoparticles)**

# The Future of Layer-by-Layer Assembly: A Tribute to ACS Nano Associate Editor Helmuth Möhwald

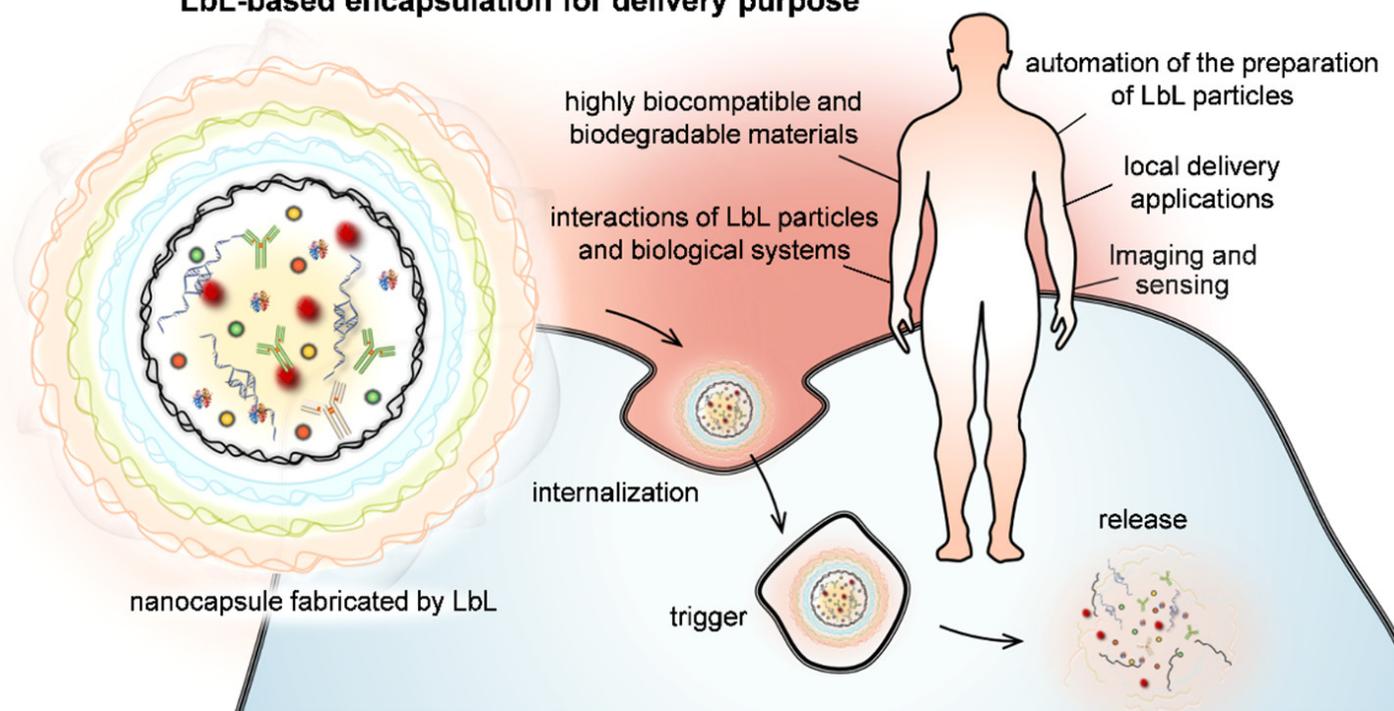
Shuang Zhao,<sup>†</sup> Frank Caruso,<sup>‡,⊗</sup> Lars Dähne,<sup>§</sup> Gero Decher,<sup>||,⊥</sup> Bruno G. De Geest,<sup>#</sup> Jinchen Fan,<sup>¶</sup> Neus Feliu,<sup>‡</sup> Yury Gogotsi,<sup>§</sup> Paula T. Hammond,<sup>□</sup> Mark C. Hersam,<sup>■</sup> Ali Khademhosseini,<sup>○</sup> Nicholas Kotov,<sup>‡</sup> Stefano Loporatti,<sup>△</sup> Yan Li,<sup>▲</sup> Fred Lisdat,<sup>▽</sup> Luis M. Liz-Marzán,<sup>▼,○</sup> Sergio Moya,<sup>▽,⊙</sup> Paul Mulvaney,<sup>●</sup> Andrey L. Rogach,<sup>††</sup> Sathi Roy,<sup>†</sup> Dmitry G. Shchukin,<sup>‡‡</sup> Andre G. Skirtach,<sup>§§</sup> Molly M. Stevens,<sup>¶¶</sup> Gleb B. Sukhorukov,<sup>⊥,⊥</sup> Paul S. Weiss,<sup>○,¶¶</sup> Zhao Yue,<sup>β</sup> Dingcheng Zhu,<sup>†</sup> and Wolfgang J. Parak<sup>\*,†,‡,▽</sup>

<sup>†</sup>Fachbereich Physik, CHvN, Universität Hamburg, 22607 Hamburg, Germany



Professor Dr. Dr. h.c. Helmuth Möhwald (19.01.1946 - 27.3.2018)

## LbL-based encapsulation for delivery purpose



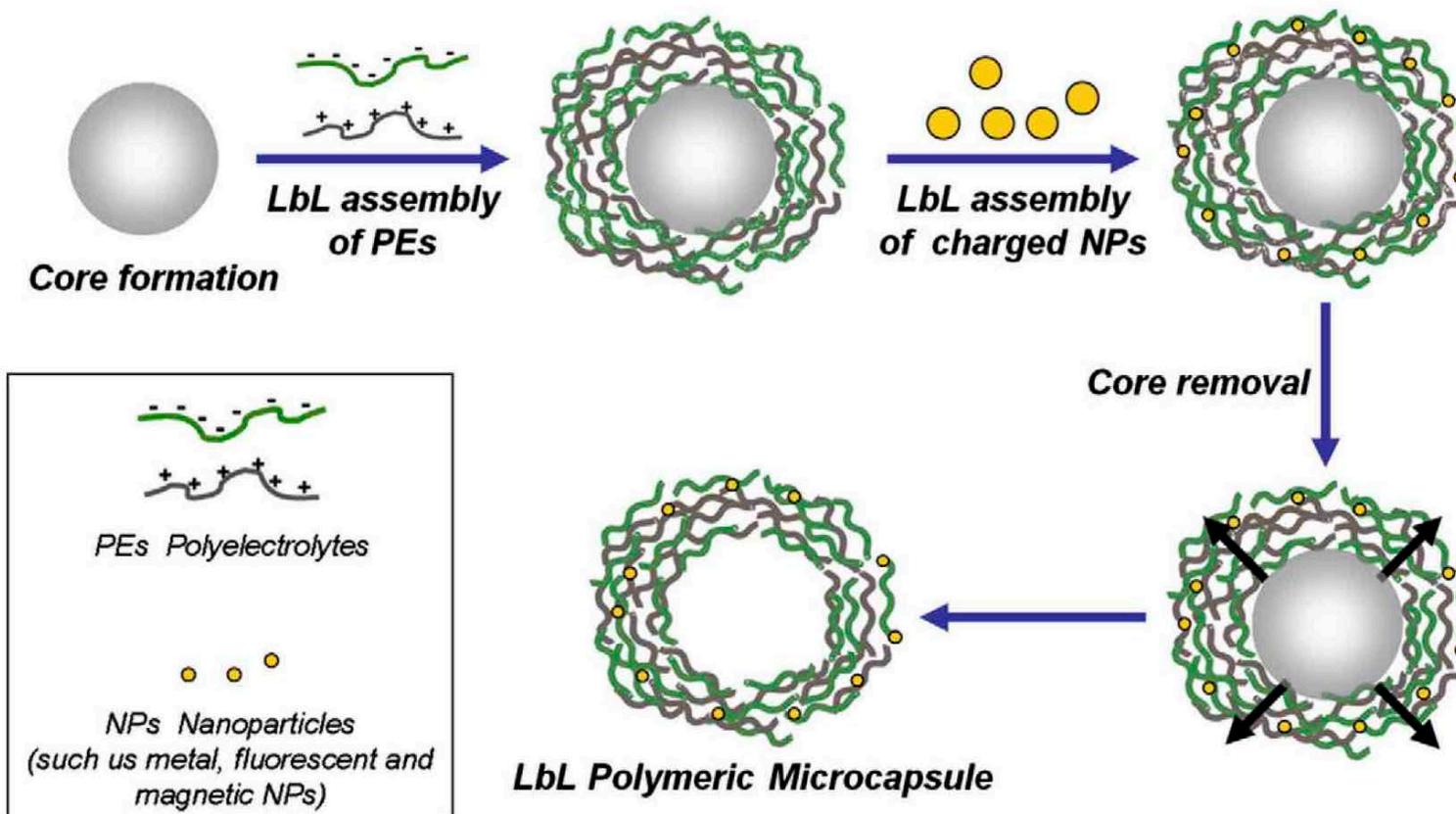
Layer-by-layer (LbL) assembly can be used to fabricate encapsulation platforms for nanodelivery

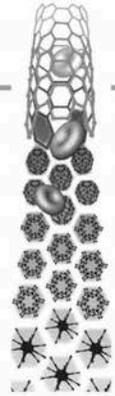


## Biological applications of LbL multilayer capsules: From drug delivery to sensing



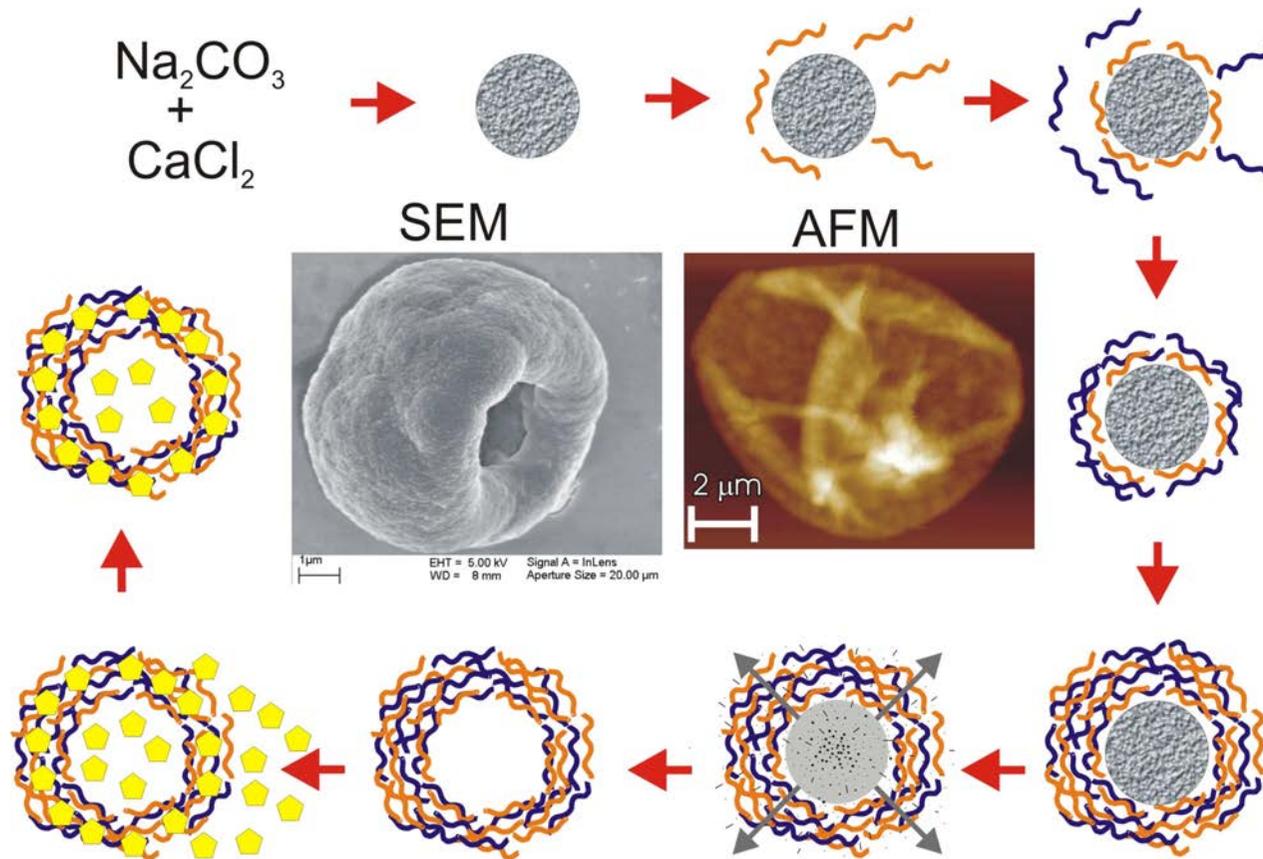
Loretta Laureana del Mercato <sup>a</sup>, Marzia Maria Ferraro <sup>a</sup>, Francesca Baldassarre <sup>a</sup>, Serena Mancarella <sup>a</sup>,  
Valentina Greco <sup>a</sup>, Ross Rinaldi <sup>a,b</sup>, Stefano Leporatti <sup>a,\*</sup>





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# Imatinib-loaded polyelectrolyte microcapsules for sustained targeting of BCR-ABL<sup>+</sup> leukemia stem cells



Ilaria E Palamà<sup>1\*</sup>,  
Stefano Loporatti<sup>1\*</sup>,  
Emanuela de Luca<sup>2</sup>,  
Nicola Di Renzo<sup>2</sup>,  
Michele Maffia<sup>2</sup>, Carlo  
Gambacorti-Passerini<sup>3</sup>,  
Ross Rinaldi<sup>1</sup>, Giuseppe  
Gigli<sup>1</sup>, Roberto Cingolani<sup>1</sup>  
& Addolorata  
ML Coluccia<sup>1,2†</sup>

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Milano-Bicocca, Italy

\*Authors contributed equally



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8 (2012) 891–899

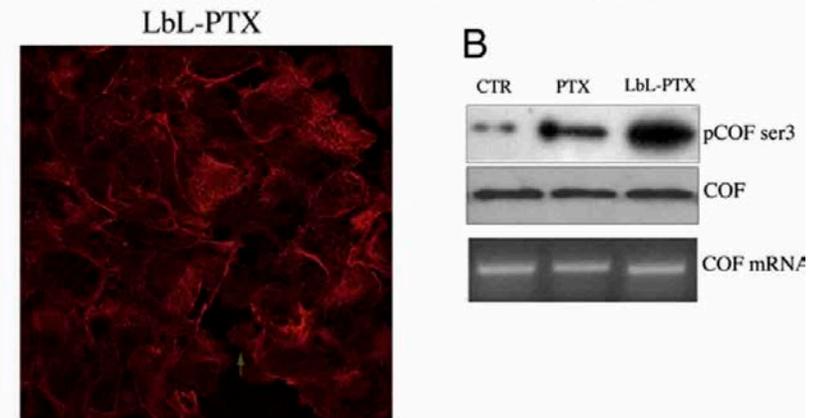
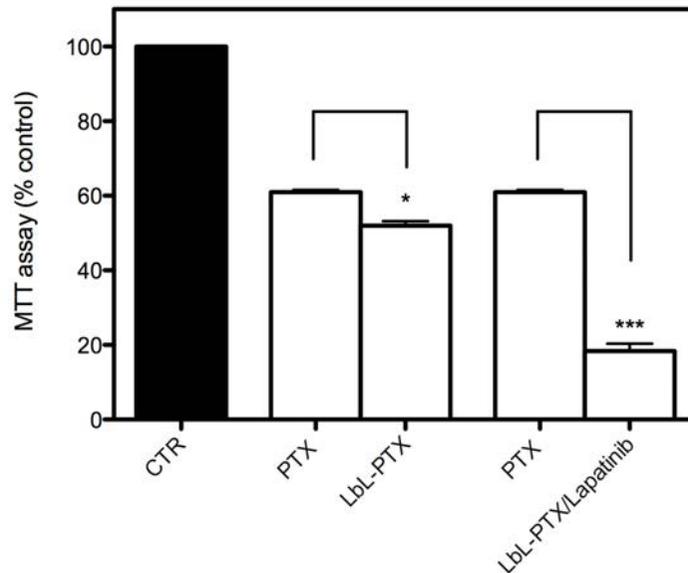
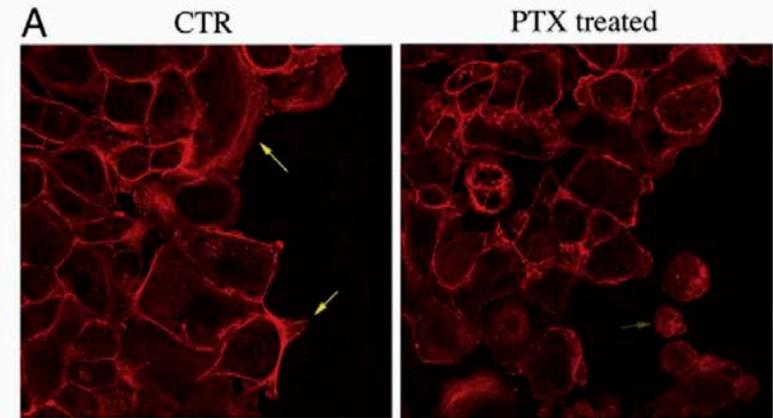
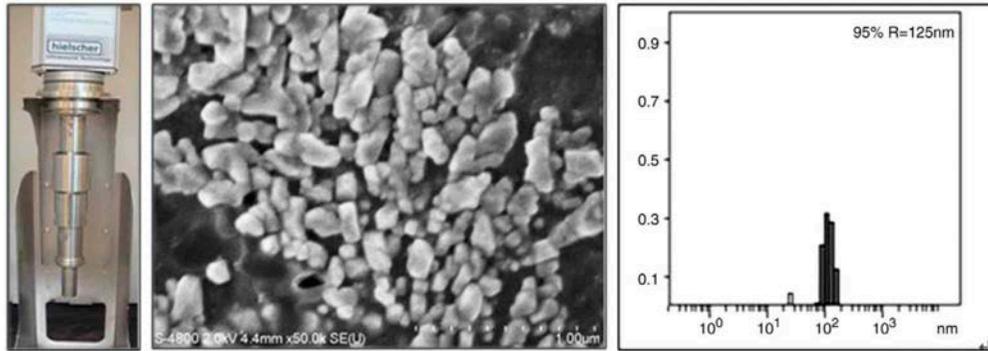


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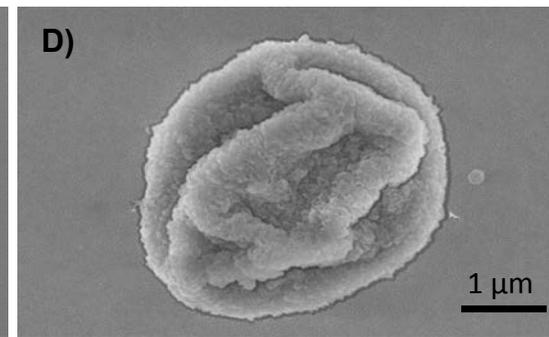
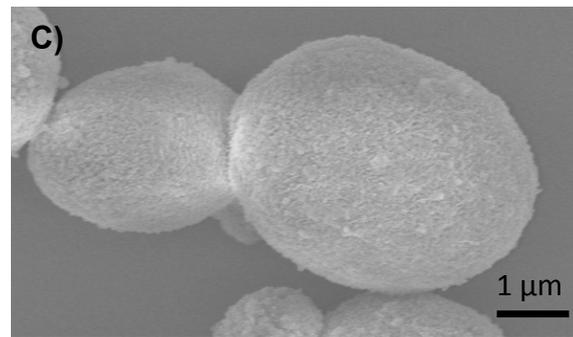
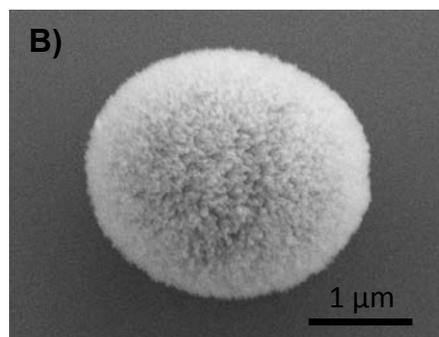
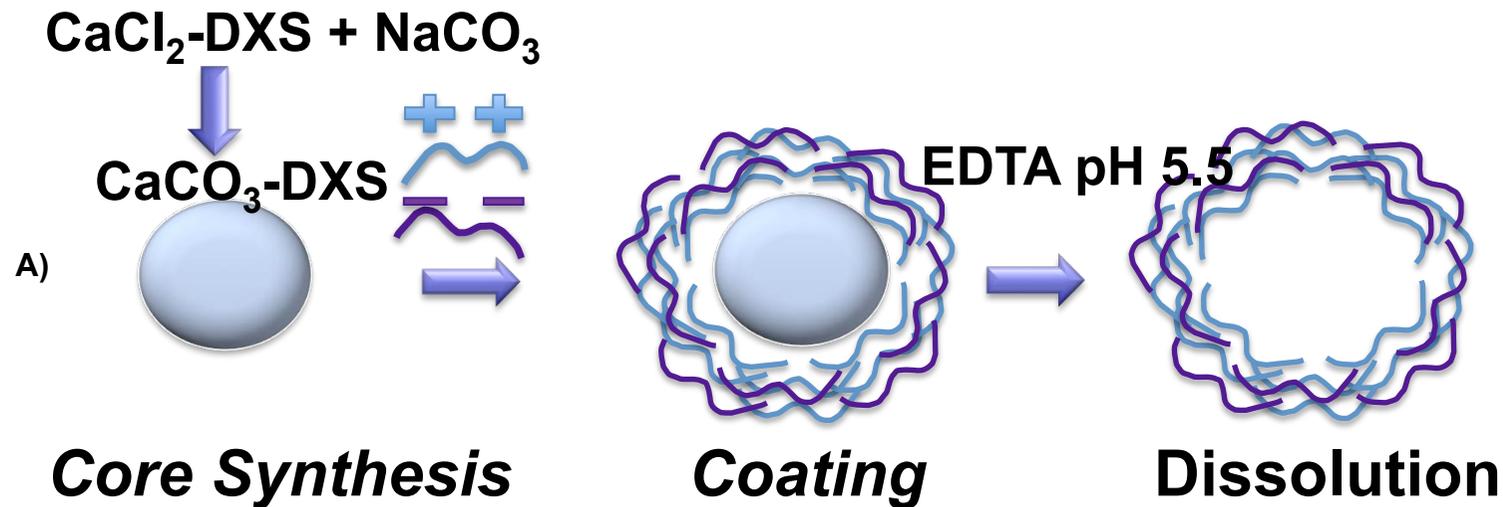
# Lapatinib/Paclitaxel polyelectrolyte nanocapsules for overcoming multidrug resistance in ovarian cancer

Daniele Vergara, PhD<sup>a,b</sup>, Claudia Bellomo, MS<sup>c</sup>, Xingcai Zhang, MS<sup>d</sup>, Viviana Vergaro, MS<sup>c</sup>, Andrea Tinelli, MD<sup>e</sup>, Vito Lorusso, MD<sup>f</sup>, Ross Rinaldi, PhD<sup>g</sup>, Yuri M. Lvov, PhD<sup>d</sup>, Stefano Leporatti, PhD<sup>c,\*</sup>, Michele Maffia, PhD<sup>a,b</sup>



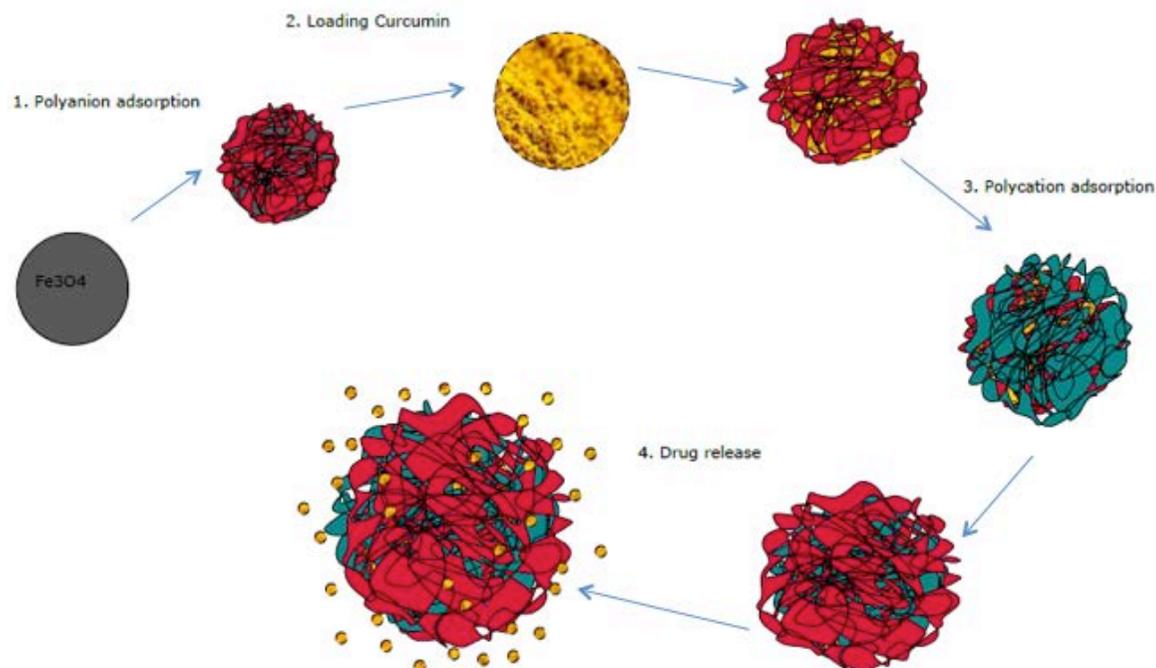
# Polyelectrolyte Capsules as Carriers for Growth Factor Inhibitor Delivery to Hepatocellular Carcinoma

Francesca Baldassarre, Viviana Vergaro, Flavia Scarlino, Flavia De Santis, Giovanna Lucarelli, Antonio della Torre, Giuseppe Ciccarella, Ross Rinaldi, Gianluigi Giannelli, Stefano Leporatti\*

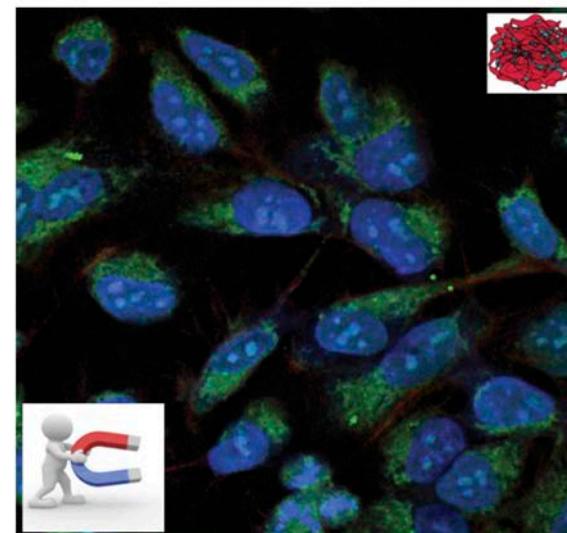


# Polymer-Coated Magnetic Nanoparticles for Curcumin Delivery to Cancer Cells

Serena Mancarella, Valentina Greco, Francesca Baldassarre, Daniele Vergara, Michele Maffia, Stefano Leporatti\*



Macromolecular  
Bioscience



Macromol. Biosci. 2015, 15, 1365–1374

Polymer-Coated Magnetic Nanoparticles  
for Curcumin Delivery to Cancer Cells  
Serena Mancarella, Valentina Greco,  
Francesca Baldassarre, Daniele Vergara,  
Michele Maffia, Stefano Leporatti\*

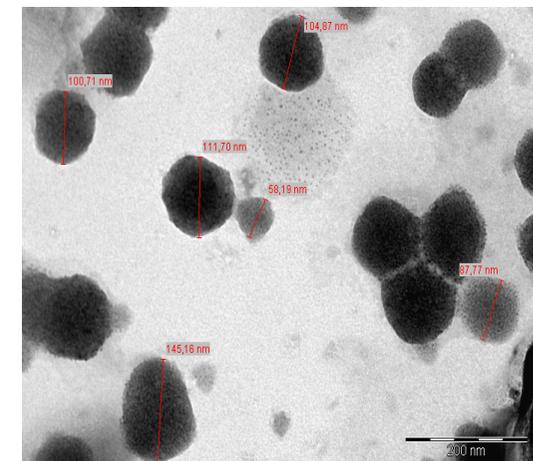
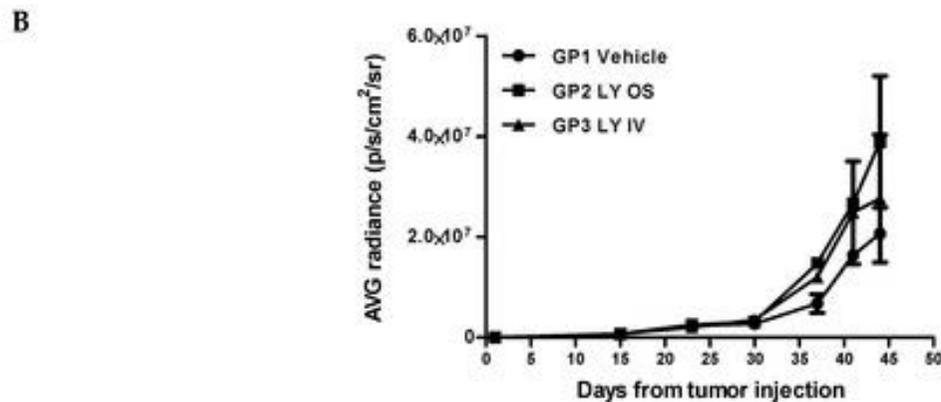
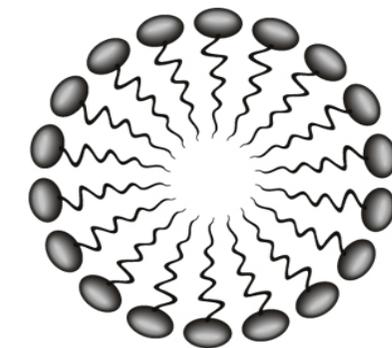
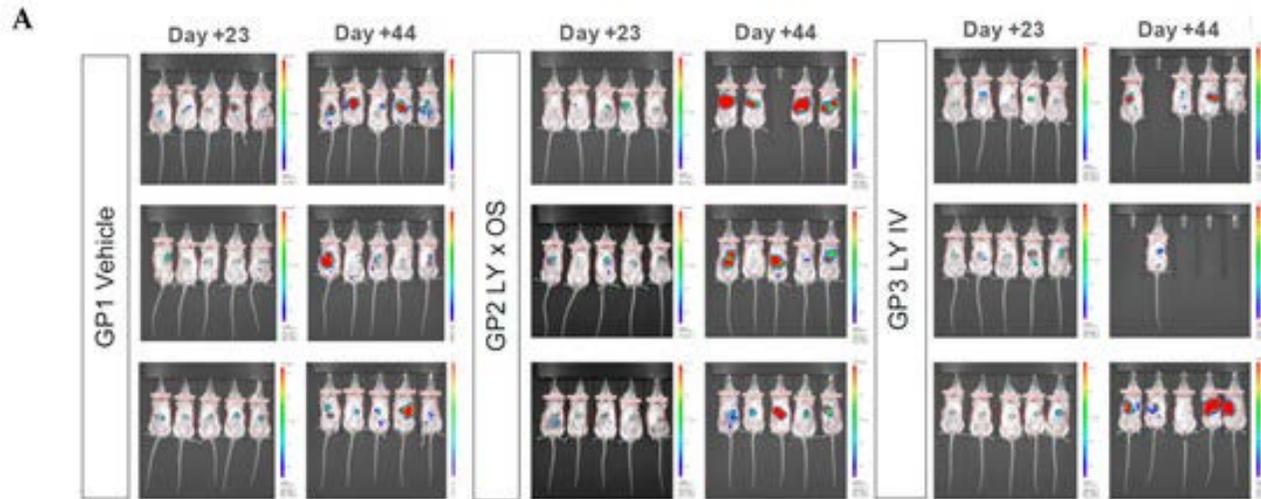
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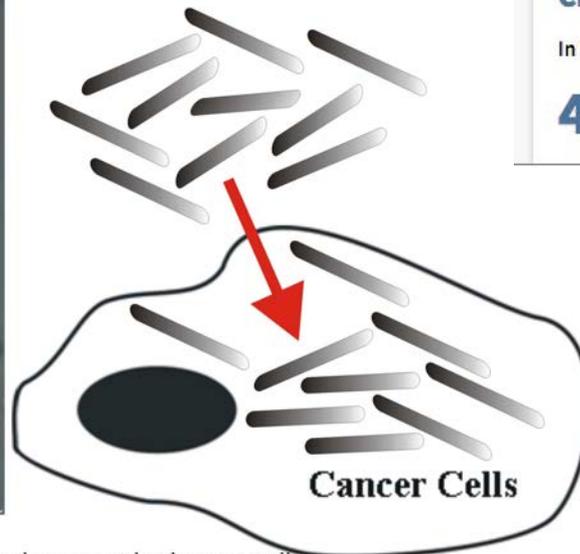
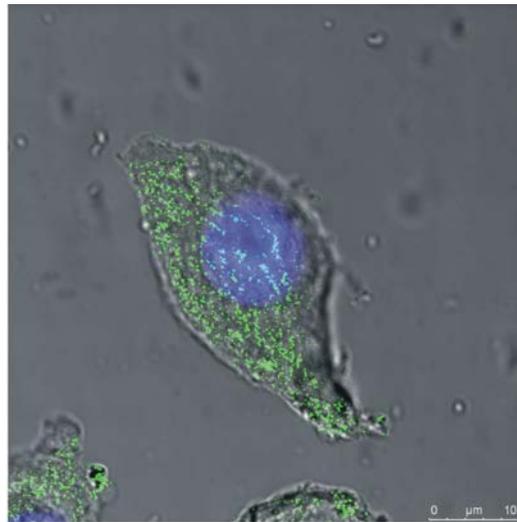
# Validation of Hepatocellular Carcinoma Experimental Models for TGF- $\beta$ Promoting Tumor Progression

Serena Mancarella <sup>1</sup> , Silke Krol <sup>1,\*</sup>, Alberto Crovace <sup>1</sup>, Stefano Leporatti <sup>2</sup> , Francesco Dituri <sup>1</sup>, Martina Frusciante <sup>1</sup> and Gianluigi Giannelli <sup>1,\*</sup>



# Cytocompatibility and Uptake of Halloysite Clay Nanotubes

Viviana Vergaro,<sup>†</sup> Elshad Abdullayev,<sup>‡</sup> Yuri M. Lvov,<sup>‡</sup> Andre Zeitoun,<sup>§</sup> Roberto Cingolani,<sup>†</sup> Ross Rinaldi,<sup>†</sup> and Stefano Leporatti<sup>\*,†</sup>

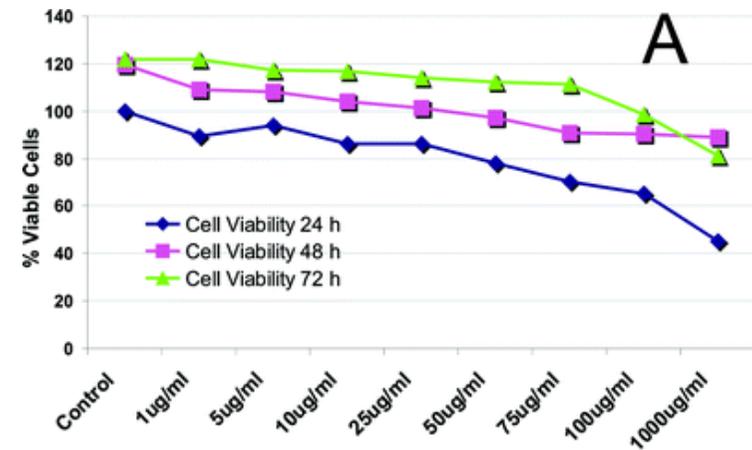


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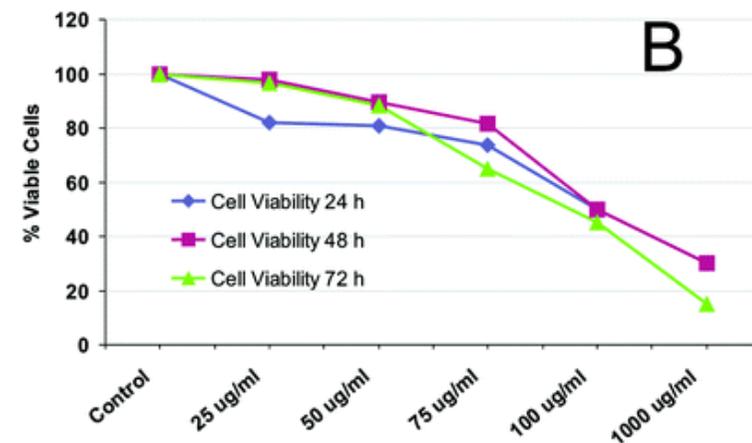
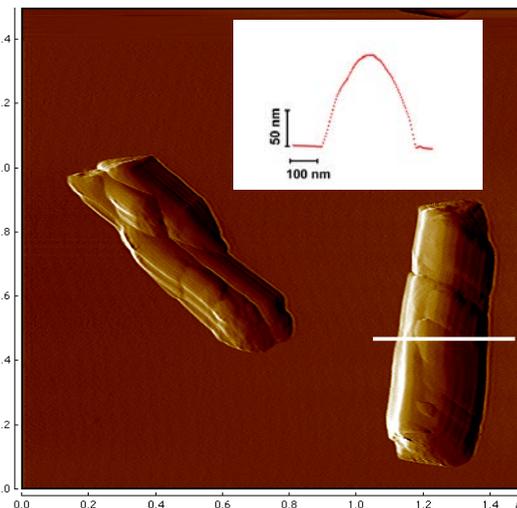
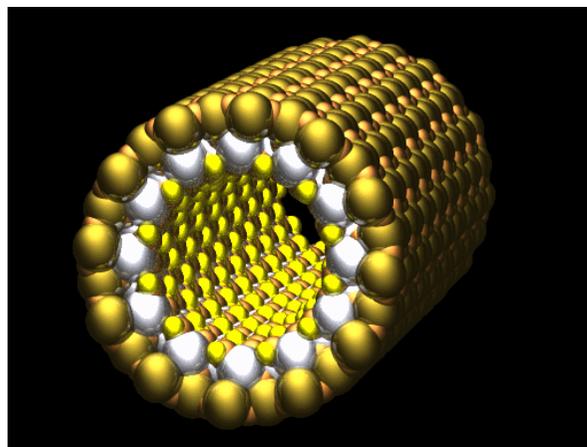
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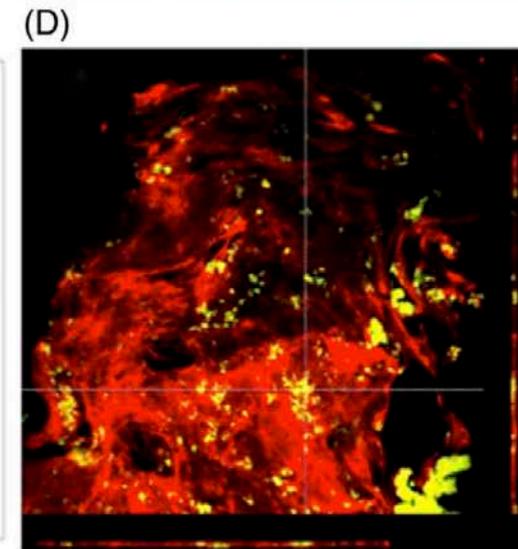
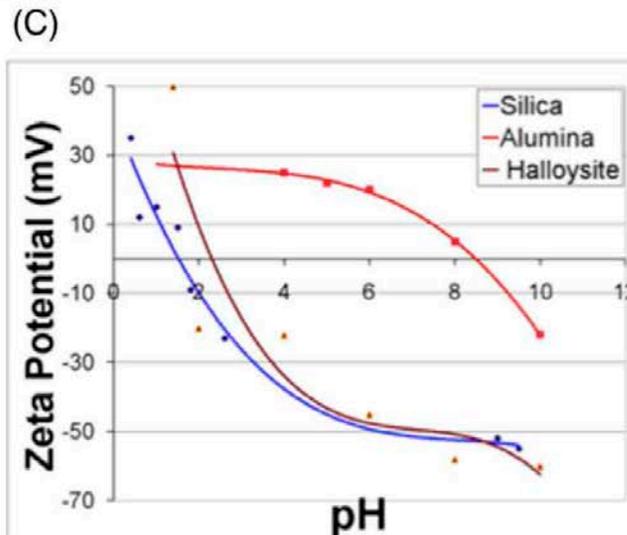
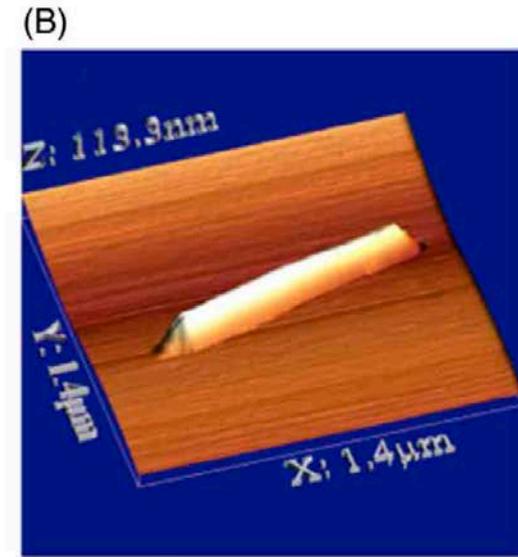
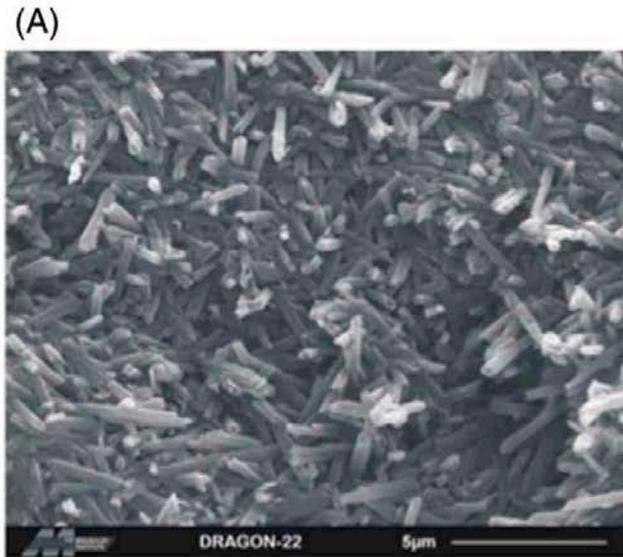


Halloysite clay nanotubes show high cytocompatibility after they are taken up by cancer cells. Fluorescence and optical overlaid confocal image shows halloysite nanotubes internalized inside a cancer cell (nucleus appears blue for Hoechst staining whereas tubes appear green due to FITC labeling through LbL coating)



# Halloysite clay nanotubes as nano-bazookas for drug delivery

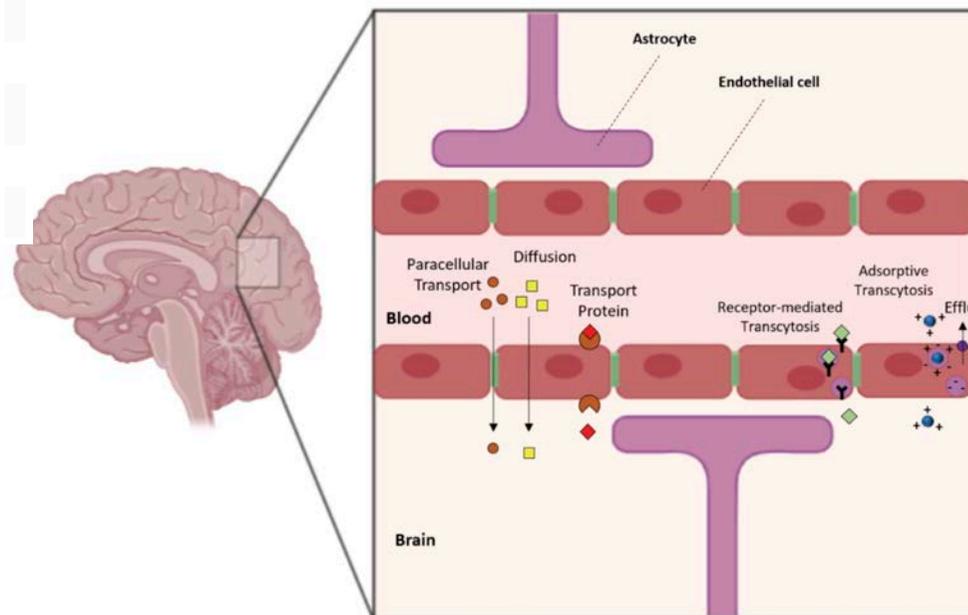
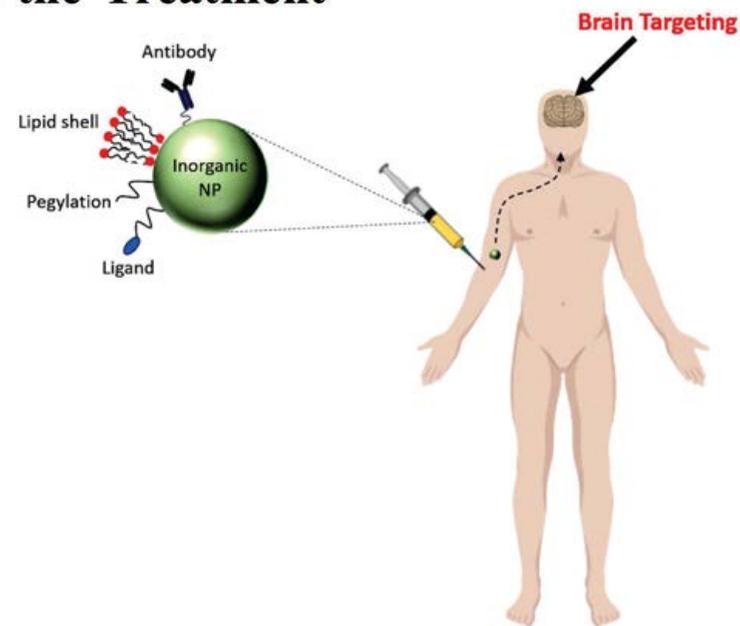
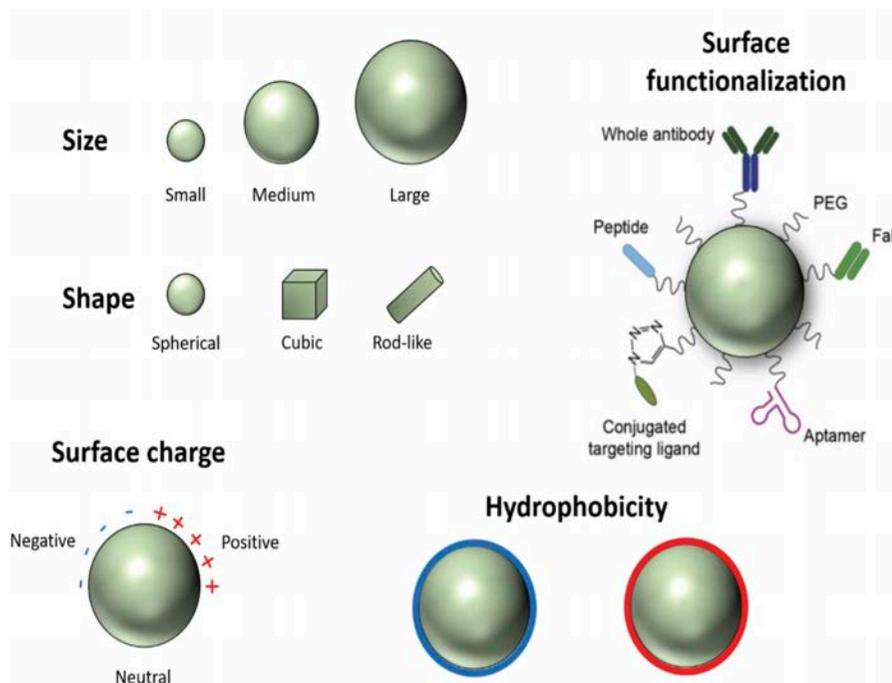
Stefano Leporatti\*



REVIEW ARTICLE

# Current Overview of Inorganic Nanoparticles for the Treatment of Central Nervous System (CNS) Diseases

Francesca Persano<sup>1,2</sup> and Stefano Leporatti<sup>2,\*</sup>



Volume 9  
Number 12  
28 March 2021  
Pages 2749–2938

# Journal of Materials Chemistry B

Materials for biology and medicine

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ISSN 2050-750X

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**REVIEW ARTICLE**

Stefano Leporatti, Rawil Fakhrollin *et al.*  
Recent advances in the design of inorganic and nano-clay  
particles for the treatment of brain disorders

Indexed in  
Medline!

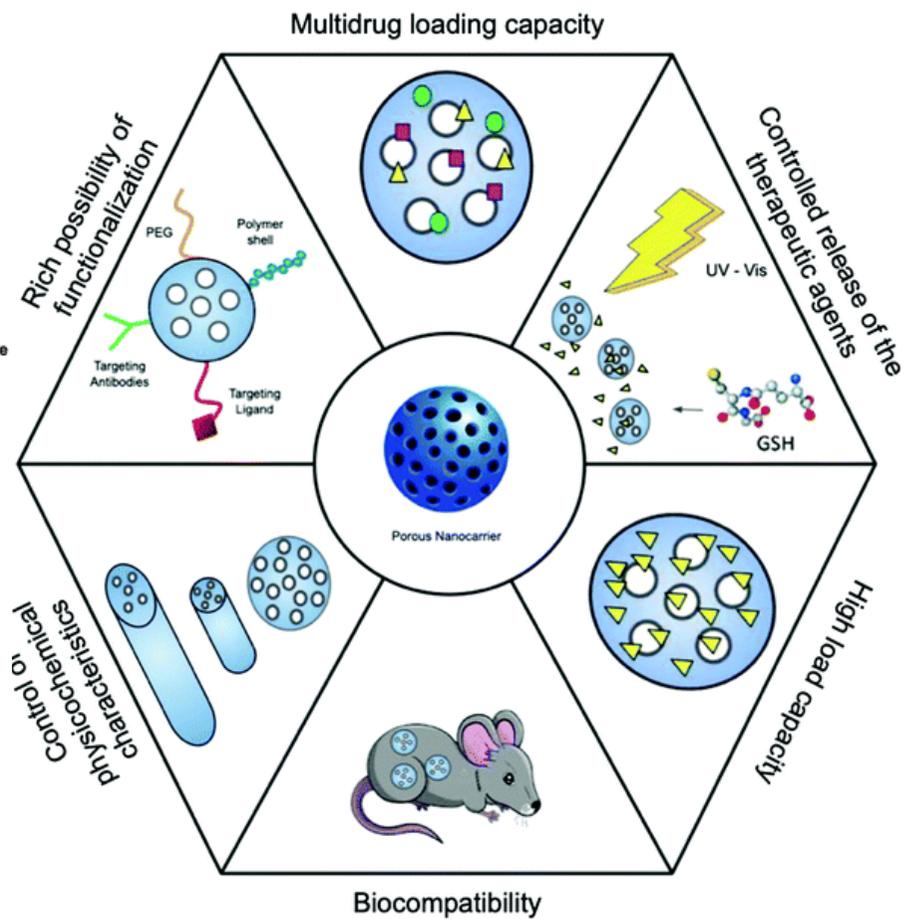
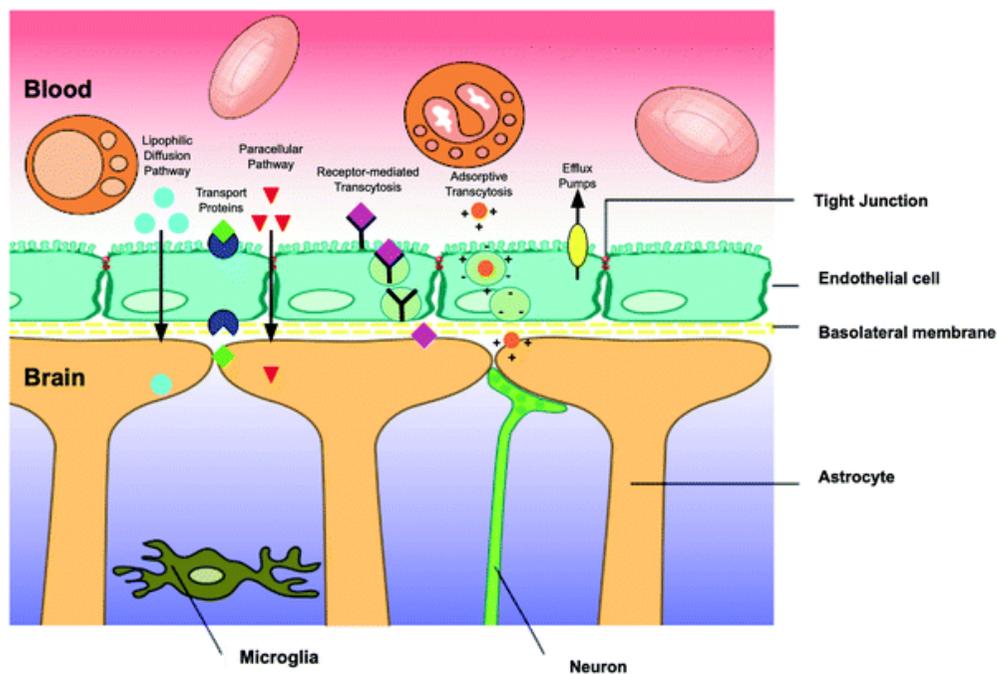
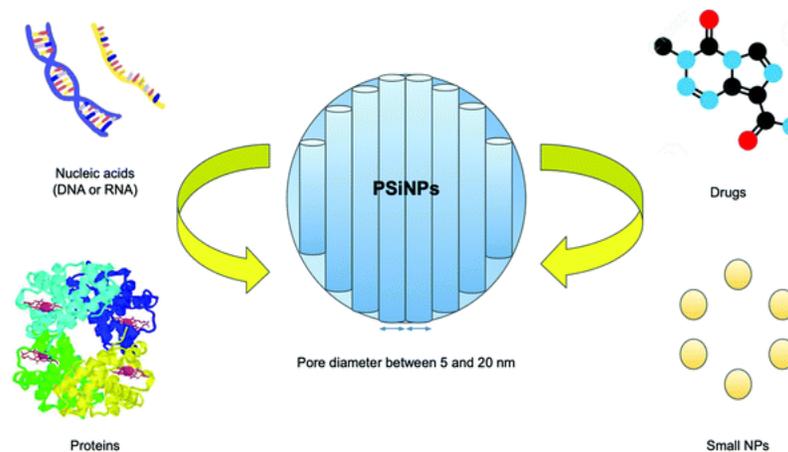




Cite this: *J. Mater. Chem. B*, 2021, 9, 2756

## Recent advances in the design of inorganic and nano-clay particles for the treatment of brain disorders

Francesca Persano,<sup>†ab</sup> Svetlana Batasheva,<sup>†c</sup> Gölnur Fakhru'llina,<sup>†c</sup> Giuseppe Gigli,<sup>†ab</sup> Stefano Loporatti,<sup>†\*b</sup> and Rawil Fakhru'llin,<sup>†\*c</sup>





# The New Frontiers in Neurodegenerative Diseases Treatment: Liposomal-Based Strategies



Mariafrancesca Cascione<sup>1\*</sup>, Valeria De Matteis<sup>1</sup>, Stefano Leporatti<sup>2\*</sup> and Rosaria Rinaldi<sup>1</sup>

<sup>1</sup> Department of Mathematics and Physics "Ennio De Giorgi," University of Salento, Lecce, Italy, <sup>2</sup> National Research Council Nanotec Institute of Nanotechnology, Lecce, Italy

Conventional  
Liposomes

Ethosome

Drug crystallized  
in aqueous fluid

Solid lipid(s)

Ethanol

Homing peptide

Solid Lipid  
Nanoparticle

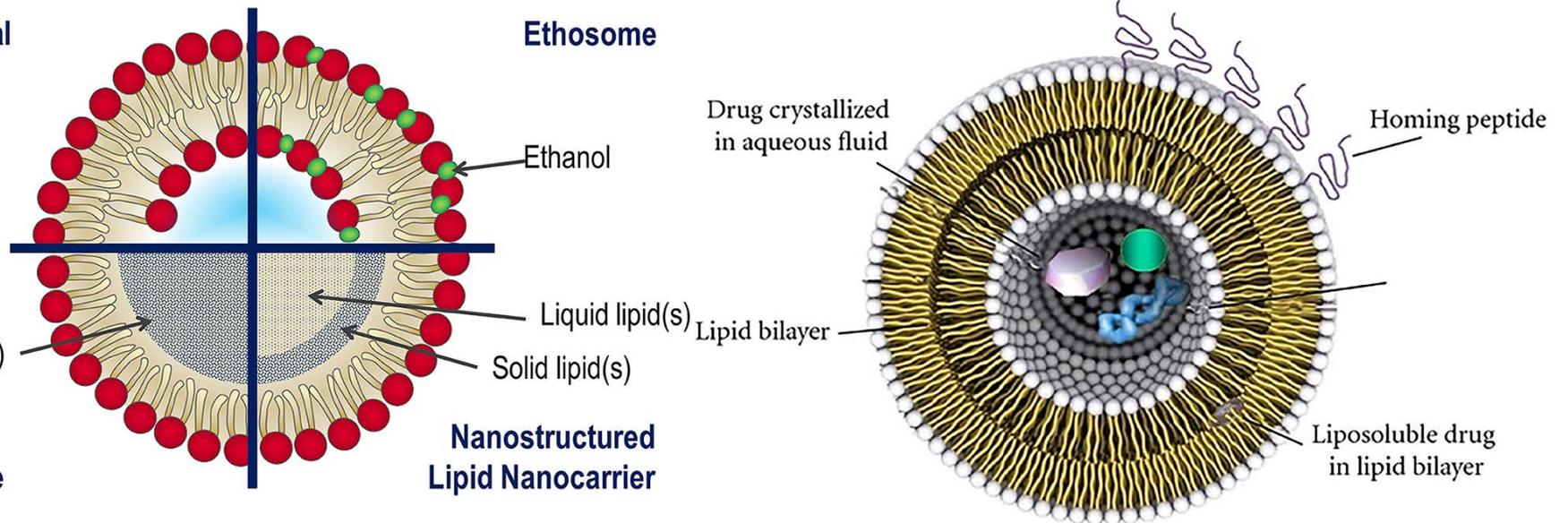
Liquid lipid(s)

Lipid bilayer

Solid lipid(s)

Nanostructured  
Lipid Nanocarrier

Liposoluble drug  
in lipid bilayer



# Solid Lipid Nanoparticles for mRNA Vaccines against COVID-19

## BNT162b2 \$\$

### BioNTech/Pfizer 🇩🇪

**Encapsulated mRNA Vaccine**

mRNA encoding for the Spike protein is protected in a lipid nanoparticles (like soap bubbles). Once absorbed, the cell expresses the Spike protein resulting in an immune response.

**Efficacy:** 95% (US/UK strain)  
--% (B.1.351 "SA" strain)

**Dosing:** 0.3mL - 2 doses - 21 days apart

**Storage:** -70°C - 6 months  
+2-8°C - 5 days

@LaPipette.labs  
Last updated on 14/02/21

## mRNA-1273 \$\$\$

### Moderna 🇺🇸

**Encapsulated mRNA Vaccine**

mRNA encoding for the Spike protein is protected in a lipid nanoparticles (like soap bubbles). Once absorbed, the cell expresses the Spike protein resulting in an immune response.

**Efficacy:** 94.1% (US/UK strain)  
--% (B.1.351 "SA" strain)

**Dosing:** 0.5mL - 2 doses - 28 days apart

**Storage:** -20°C - 6 months  
+2-8°C - 30 days

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IN FOCUS

A Comprehensive Review of the Global Efforts on COVID-19 Vaccine Development

Cite This: <https://doi.org/10.1021/acscentsci.1c00120>

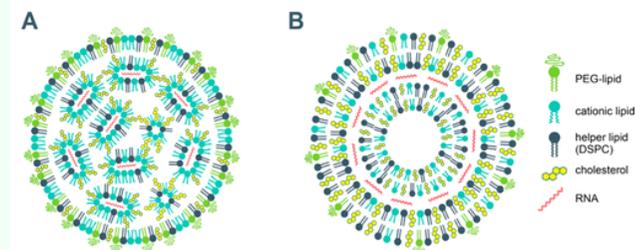
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Article Recommendations

Yingzhu Li,<sup>\*</sup> Rumiana Tenchov,<sup>\*</sup> Jeffrey Smoot, Cynthia Liu, Steven Watkins and Qiongqiong Zhou<sup>\*</sup>



Suggested structures of lipid nanoparticle vaccine carriers: mRNA organized in inverse lipid micelles inside the nanoparticle (A); mRNA intercalated between the lipid bilayers (B)

Credits: Lapipette.Labs

Review

# Micelles Structure Development as a Strategy to Improve Smart Cancer Therapy

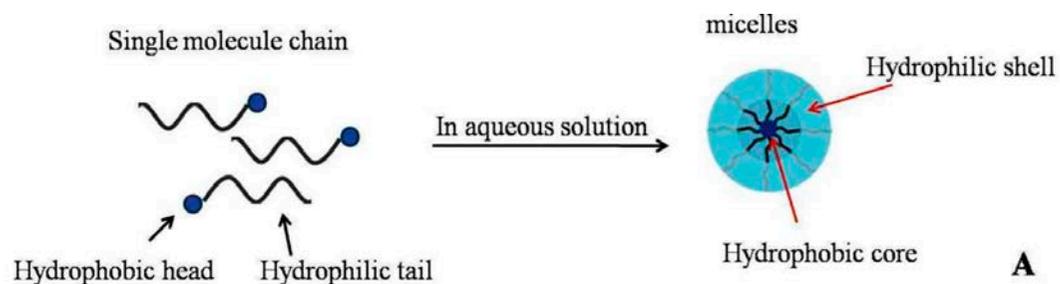
Nemany A. N. Hanafy <sup>1,2</sup> , Maged El-Kemary <sup>2</sup> and Stefano Loporatti <sup>3,\*</sup> 

<sup>1</sup> Sohag Cancer Center, Sohag 82511, Egypt; nemany.hanafy@nanotec.cnr.it

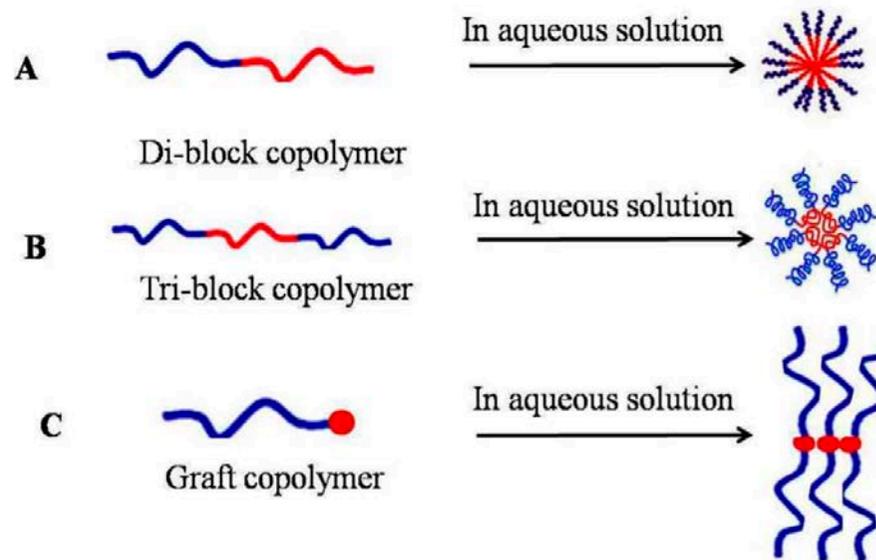
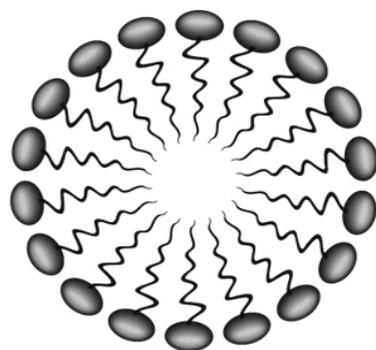
<sup>2</sup> Institute of Nanoscience and Nanotechnology, Kafrelsheikh University, Kafrelsheikh 33516, Egypt; elkemary@sci.kfs.edu.eg

<sup>3</sup> CNR NANOTEC-Istituto di Nanotecnologia, 73100 Lecce, Italy

\* Correspondence: stefano.leporatti@nanotec.cnr.it; Tel.: +39-083-231-9829



Scheme 1. Assembled micelles structure.

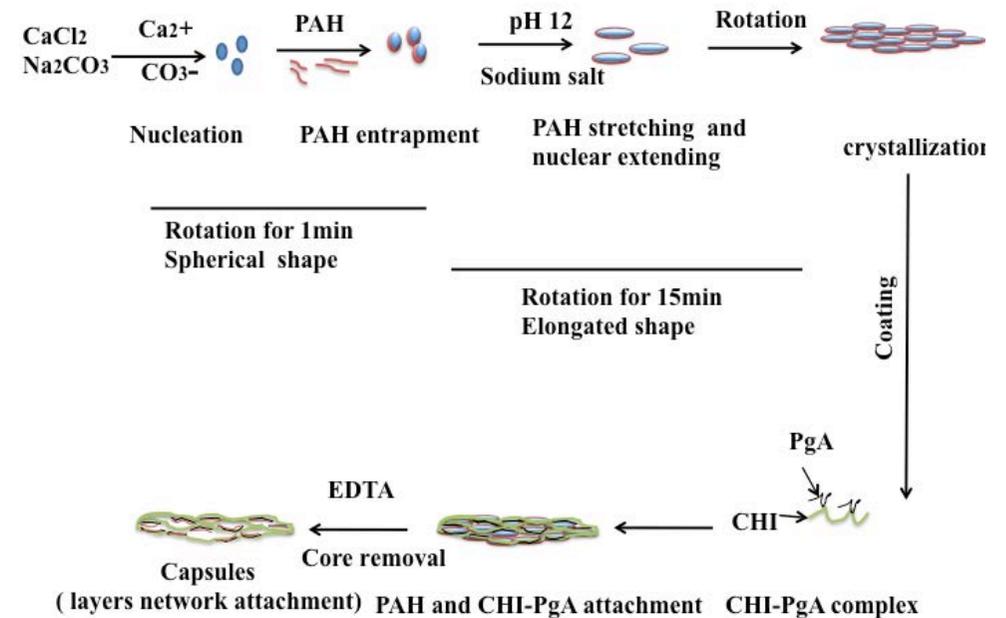
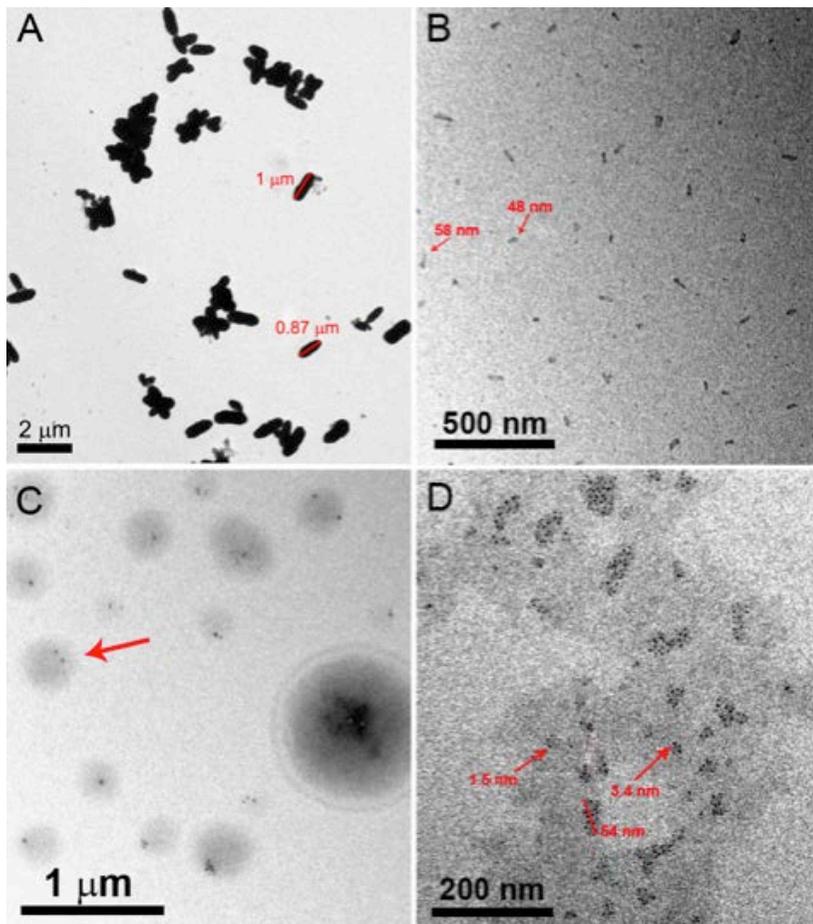


Scheme 2. Polymer micelle structures.



## CaCO<sub>3</sub> Rods as Chitosan-Polygalacturonic Acid Carriers for Bromopyruvic Acid Delivery

Nemany A. N. Hanafy<sup>1,2</sup>, Maria Luisa De Giorgi<sup>2</sup>, Concetta Nobile<sup>1</sup>, Mariafrancesca Cascione<sup>2</sup>, Ross Rinaldi<sup>2</sup>, and Stefano Leporatti<sup>1,\*</sup>



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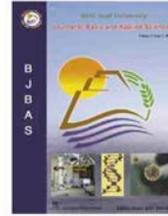


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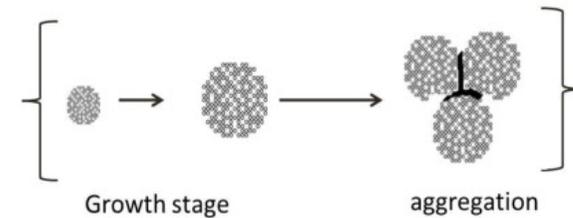
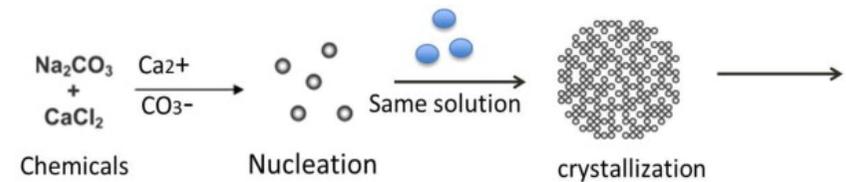
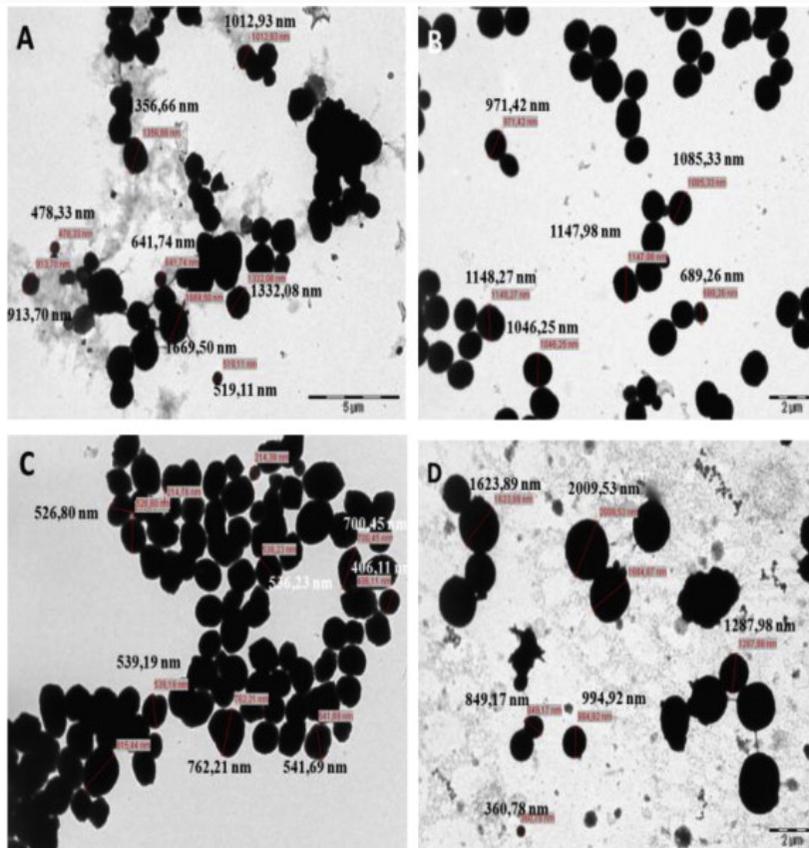
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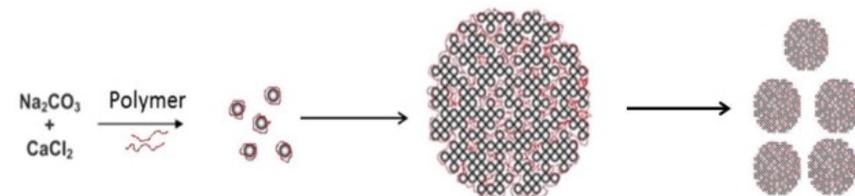
Full Length Article

# Control of colloidal CaCO<sub>3</sub> suspension by using biodegradable polymers during fabrication

Nemany Abdelhamid Nemany Hanafy <sup>a,b</sup>, Maria Luisa De Giorgi <sup>b</sup>, Concetta Nobile <sup>a</sup>, Ross Rinaldi <sup>a</sup>, Stefano Loporatti <sup>a,\*</sup>



Scheme A

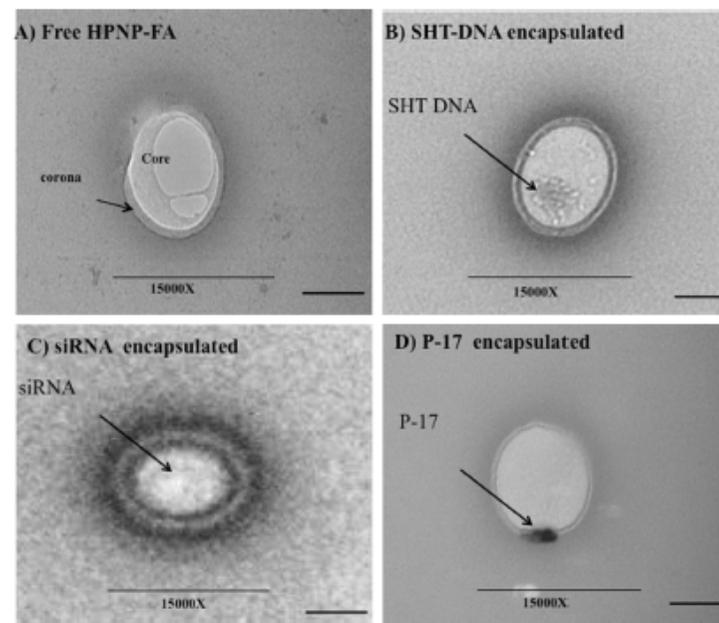
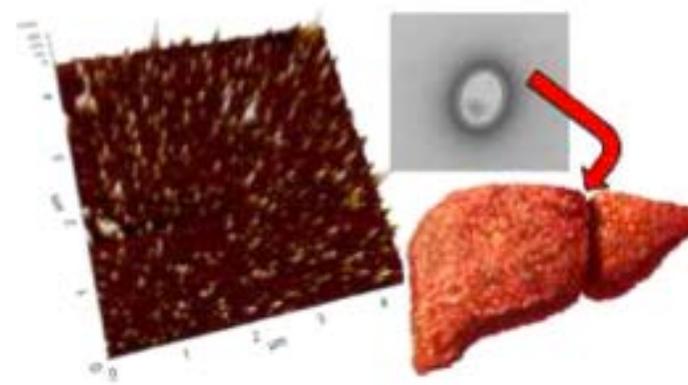
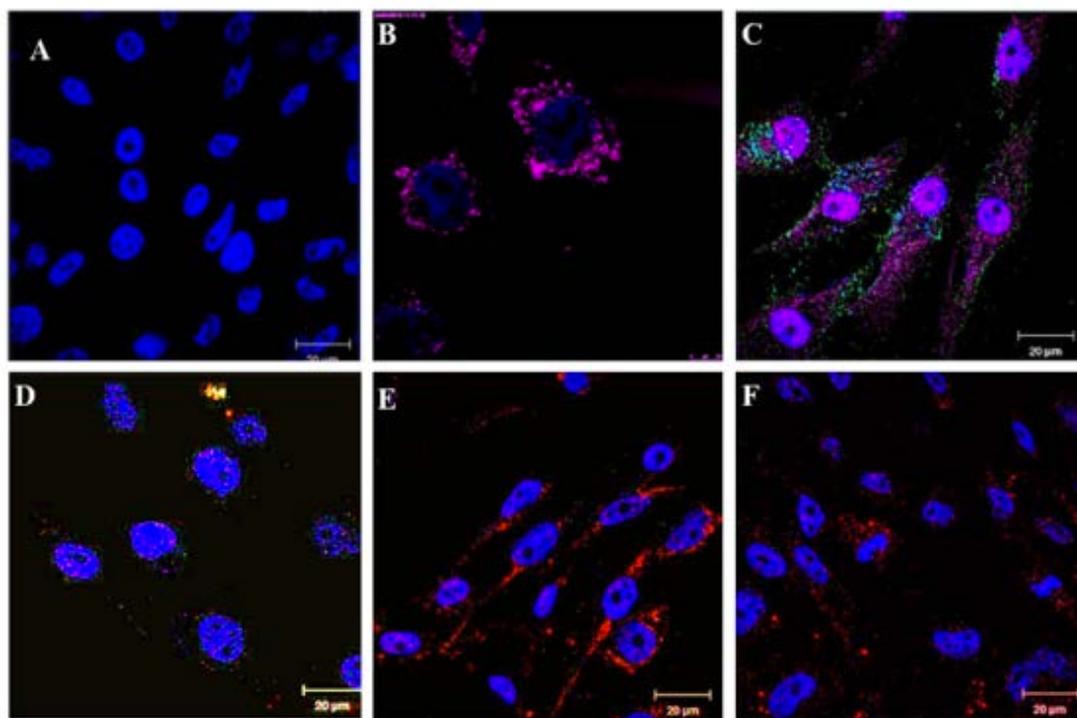


Scheme B

## Hybrid polymeric-protein nano-carriers (HPPNC) for targeted delivery of TGF $\beta$ inhibitors to hepatocellular carcinoma cells

Nemany A. N. Hanafy<sup>1,2</sup> · Alessandra Quarta<sup>1</sup> · Riccardo Di Corato<sup>3</sup> · Luciana Dini<sup>4</sup> · Concetta Nobile<sup>1</sup> · Vittorianna Tasco<sup>1</sup> · Sonia Carallo<sup>1</sup> · Mariafrancesca Cascione<sup>2</sup> · Andrea Malfettone<sup>5</sup> · Jitka Soukupova<sup>5</sup> · Rosaria Rinaldi<sup>2</sup> · Isabel Fabregat<sup>5</sup> · Stefano Leporatti<sup>1</sup>

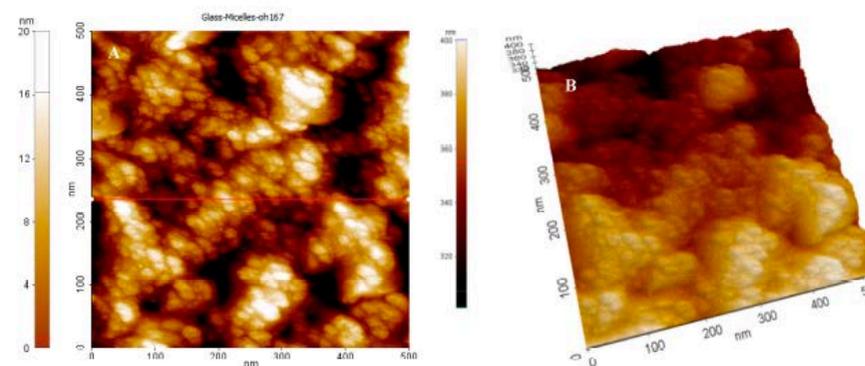
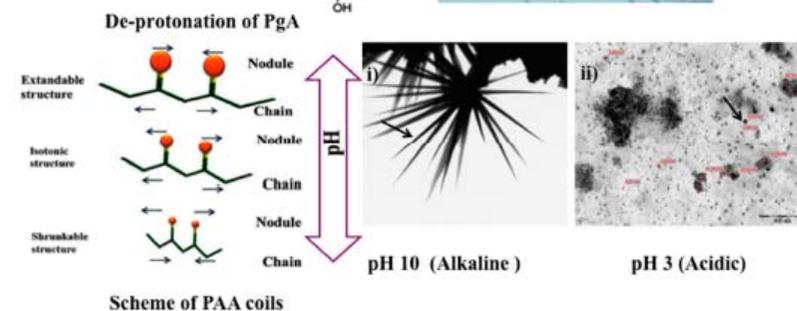
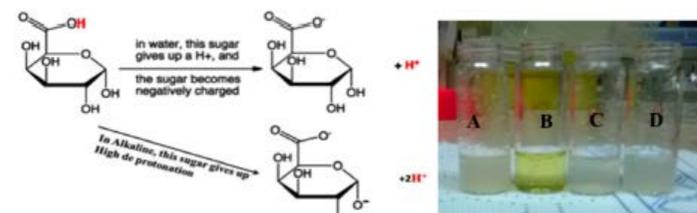
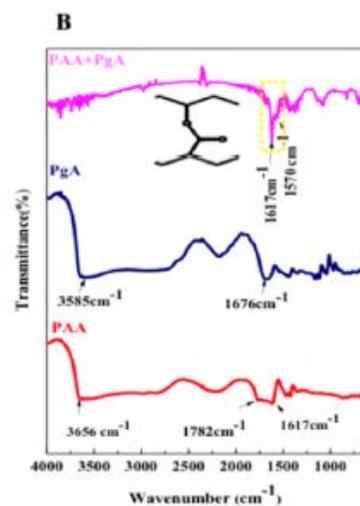
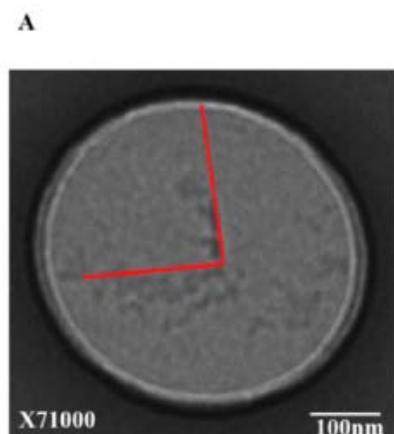
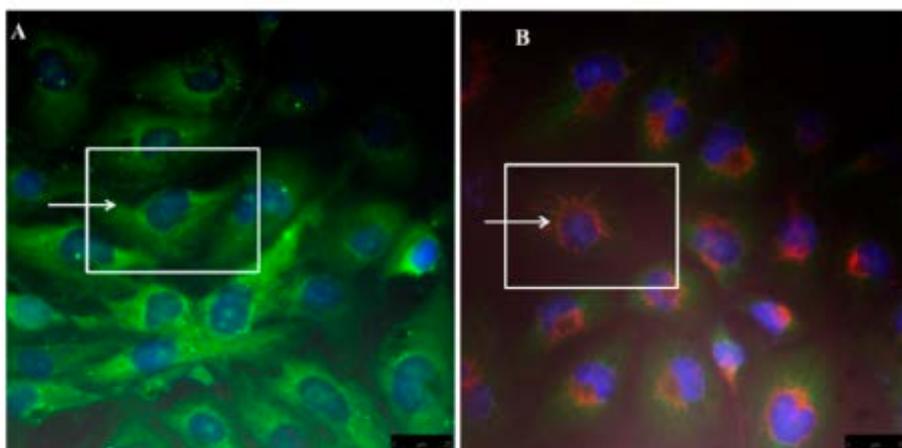
**Graphical Abstract** A novel fabrication of Hybrid Polymeric-Protein Nano-Carriers (HPPNC) for delivering TGF  $\beta$ 1 inhibitors to HCC cells has been developed. SHT-DNA, siRNA and P-17 have been successfully encapsulated. TGF  $\beta$ 1 inhibitors-loaded HPPNC were efficiently uptaken by HLF cells.



Article

# Polymeric Nano-Micelles as Novel Cargo-Carriers for LY2157299 Liver Cancer Cells Delivery

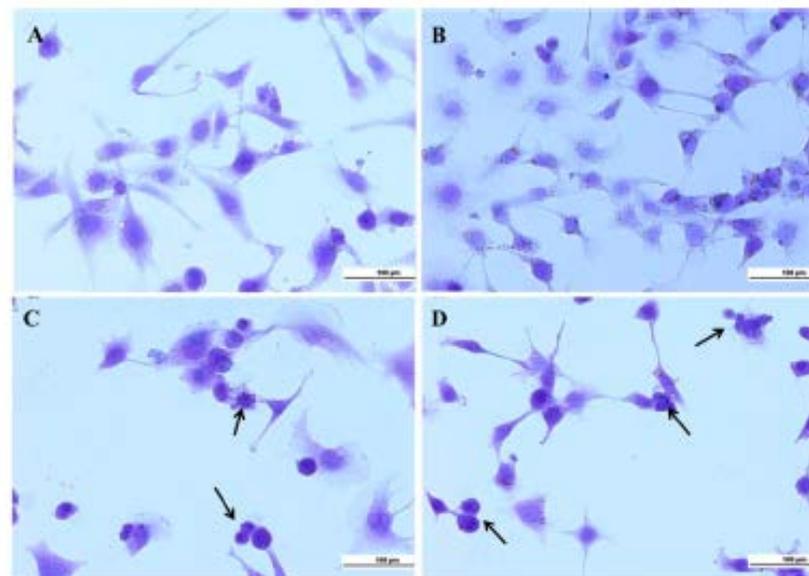
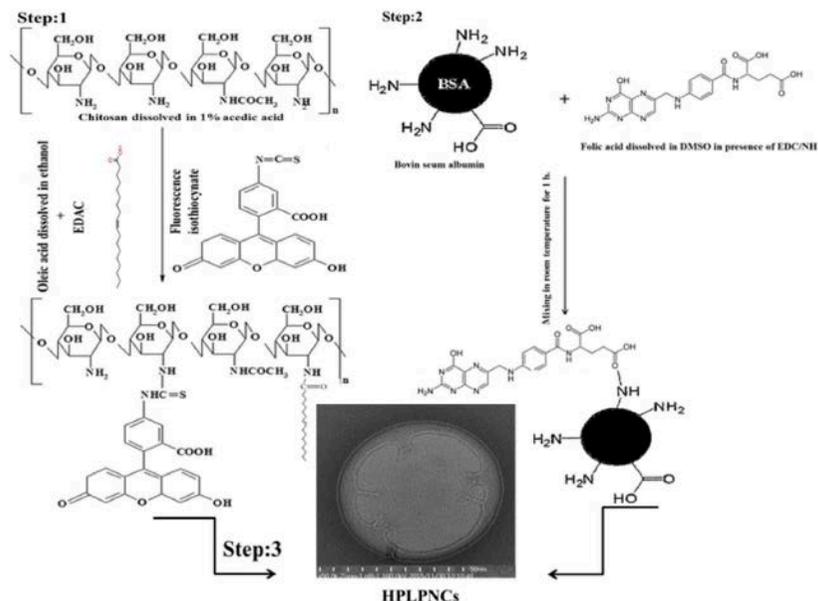
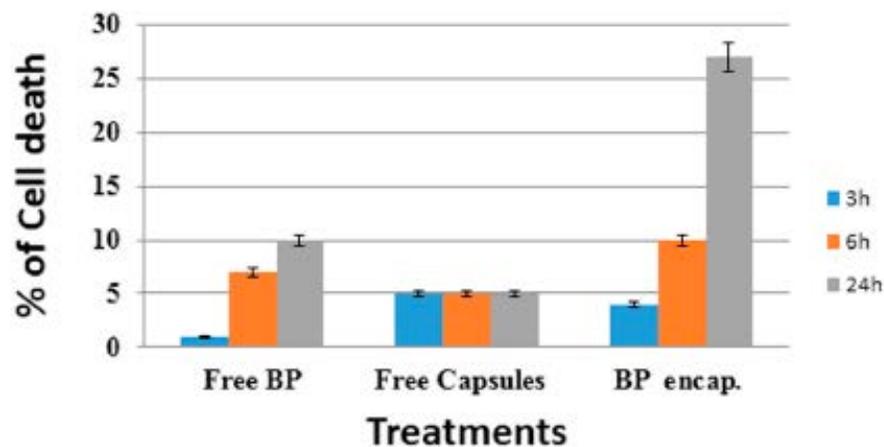
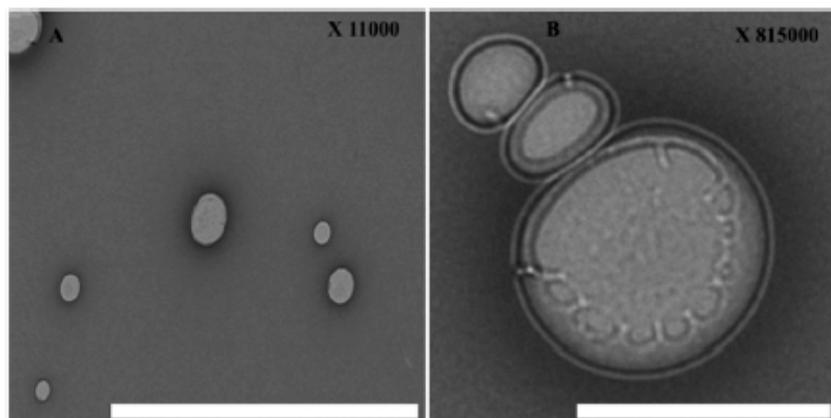
Nemany Abdelhamid Nemany Hanafy <sup>1,2,†</sup>, Alessandra Quarta <sup>1</sup>, Marzia Maria Ferraro <sup>3</sup>, Luciana Dini <sup>3</sup>, Concetta Nobile <sup>1</sup>, Maria Luisa De Giorgi <sup>2</sup>, Sonia Carallo <sup>1</sup>, Cinzia Citti <sup>1,3</sup>, Antonio Gaballo <sup>1</sup>, Giuseppe Cannazza <sup>4</sup>, Rosaria Rinaldi <sup>2</sup>, Gianluigi Giannelli <sup>5</sup> and Stefano Leporatti <sup>1,\*</sup>



Communication

# Inhibition of Glycolysis by Using a Micro/Nano-Lipid Bromopyruvic Chitosan Carrier as a Promising Tool to Improve Treatment of Hepatocellular Carcinoma

Nemany A. Hanafy <sup>1,2,†,‡</sup> , Luciana Dini <sup>3</sup>, Cinzia Citti <sup>1,3</sup>, Giuseppe Cannazza <sup>3,4</sup> and Stefano Leporatti <sup>1,\*</sup> 



*Nanomaterials* 2018, 8, 34; doi:10.3390/nano8010034

# Conjugation Of EGCG And Chitosan NPs As A Novel Nano-Drug Delivery System

This article was published in the following Dove Press journal:  
International Journal of Nanomedicine

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Stefano Loporatti<sup>2</sup>  
Jacquilion Jose<sup>3</sup>  
Mahmoud S Soliman<sup>4</sup>

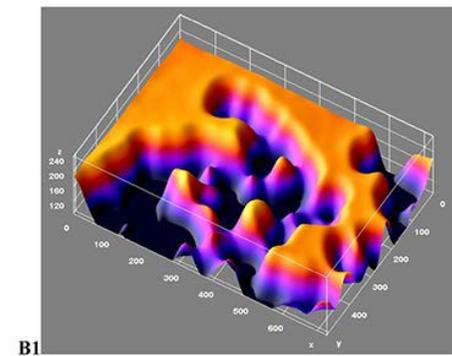
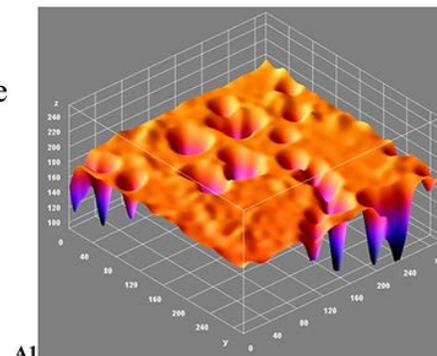
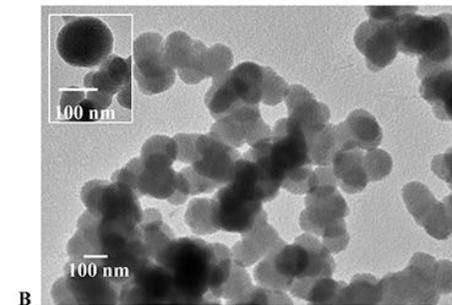
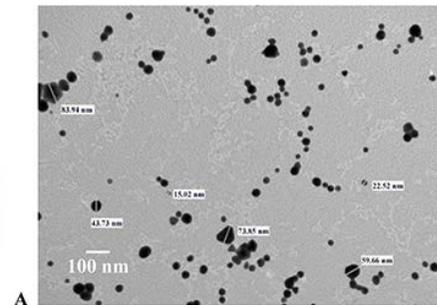
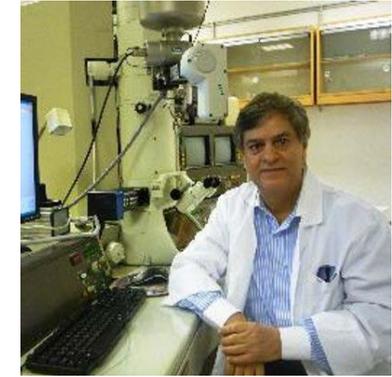
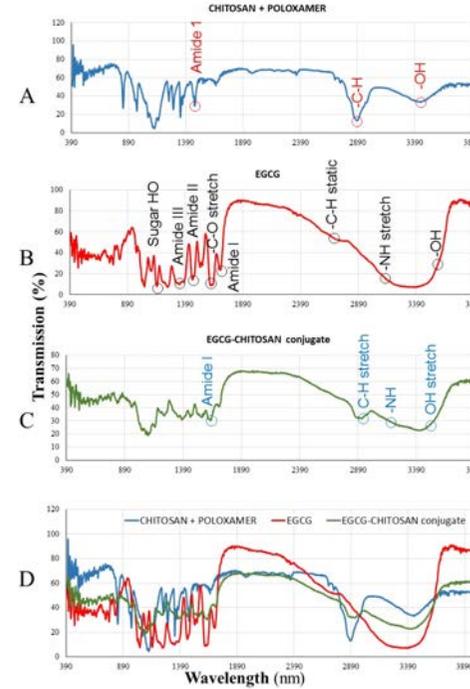
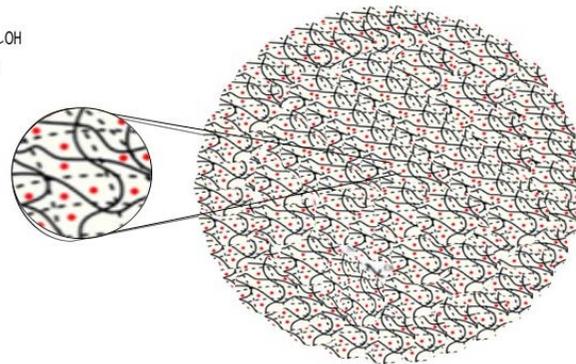
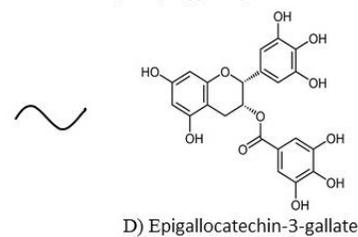
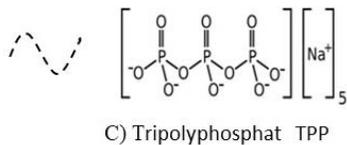
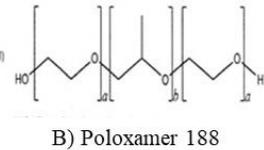
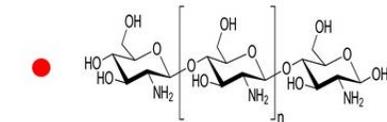
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**Purpose:** Chitosan nanoparticles (CS NPs) have been used as a good vehicle for nano-drug delivery due to their good physicochemical properties. Epigallocatechin-3-gallate (EGCG), one of the major active ingredients of green tea, is a natural antioxidant that helps in reducing and preventing cell damage and fighting cancer, plus providing other benefits. The aim of this study is to optimise the preparation parameters in terms of the physical characteristics and stability in CS/EGCG NPs conjugation.

**Results:** The conjugation of CS/EGCGNPs was obtained by means of Poloxamer 188. The average CS/EGCG NPs complex was of size 117.8±38.71nm with a surface charge of +67.8 ±4.38mV and isoelectric point at pH 7.61.

**Conclusion:** In conclusion, NPs produced were stable at 4°C with nanometric size, good polydispersity, good loading and efficiency, envisaging to be a possible candidate for nano-therapeutic delivery system against hepatic fibrosis.

**Keywords:** chitosan, EGCG, conjugation, nano-drug delivery





## TOPICAL REVIEW

# Lipid-polymer hybrid nanoparticles in cancer therapy: current overview and future directions

### OPEN ACCESS

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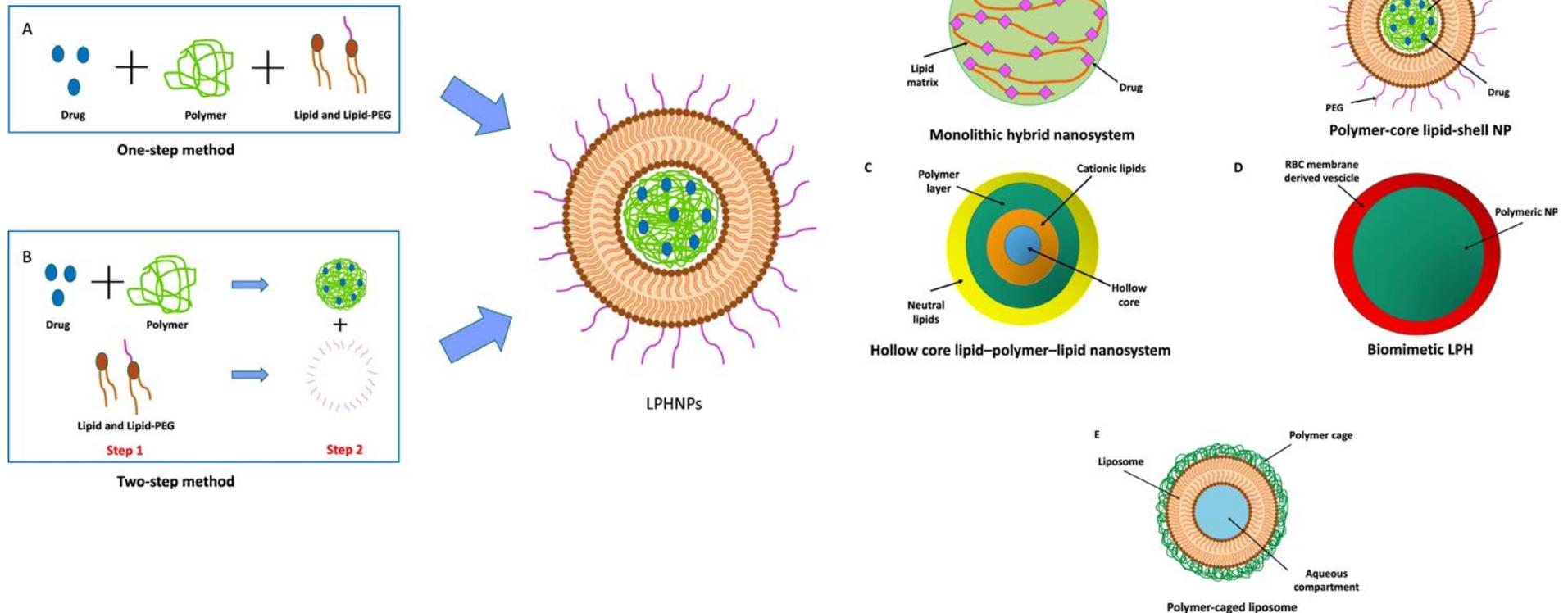
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**Keywords:** hybrid nanosystem, lipid-polymer hybrid nanoparticle, lipid shell, polymeric core, nanomedicine, cancer, drug delivery



# Conclusions and Prospectives

- **Layer-by-Layer Polyelectrolyte Nano-Carriers are efficient nano-delivery tools to vehicle drugs to Cancer Cells**
- **Inorganic Nanoparticles are smart delivery systems that can be multi-fuctionalised to target tumoral and brain diseases**
- **Hybrid Nanocarriers are biocompatible weapons against neoplastic diseases**
- **Personalised Medicine through Nano-theranostic particles can be envisaged**
- **Nano-vaccines are already available against pandemic outbreaks**

# Team Work



**Prof. Gianluigi Giannelli**



**Prof. Isabel Fabregat**

**Nemany Hanafy**



**Serena Mancarella**

**Mariafrancesca Cascione**



**Dr. Maria Luisa De Giorgi**



**Dr. Concetta Nobile**



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**Dr. Antonio Gaballo**



**Prof. Rosaria RINALDI**



**Dr Luigi Carbone and Betty Perrone**



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***Thank You for Your attention !!!***

