



June 12-14, 2019, Bucharest, Romania



# Drug delivery systems and gene therapy non-viral vectors. Design and applications



Mariana PINTEALA  
pinteala@icmpp.ro

“Petru Poni” Institute of Macromolecular Chemistry

Centre of Advanced Research in Bionanoconjugates and Biopolymers



# **CONTENT:**

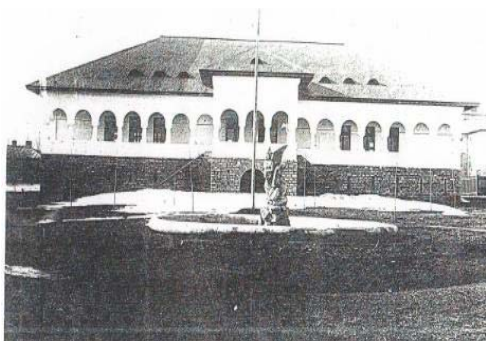
- **SHORT PRESENTATION OF ICMPP**
- **GENE DELIVERY**
  - **THE “PHILOSOPHY”...**
  - **THE “TOOLS”...**
  - **APPLICATION...**
- **DRUG DELIVERY SYSTEMS...**
- **THE PROMISE...**



**Romania on the Globe**



**“Petru Poni” Institute of  
Macromolecular Chemistry**  
<http://www.icmpp.ro/>



1949  
“Moldova”  
Building



1952 – 1956  
(1100 sq m)



1972 (10000 sq m)

*Founded* in 1949, as an institute of the Romanian Academy.

*Institute of Excellence of the Romanian Academy* .

*Ranked* in the first / second position among the 64 institutes / centres of the Romanian Academy

- The Institute for Scientific Information (ISI), Philadelphia, USA, lists the Institute among the **“main Romanian actors on the international scientific scene”**.

## Competences

- (a) Scientific competence, reflected in publications in **macromolecular and organic chemistry, biochemistry, physical chemistry, biology, physics and materials science**.
- (b) Technological competence dedicated to technology transfer and industrial implementation of the original research.





**Court of  
Moldavia  
(1434)**



**“Petru Poni” Institute  
of Macromolecular Chemistry**  
<http://www.icmpp.ro>

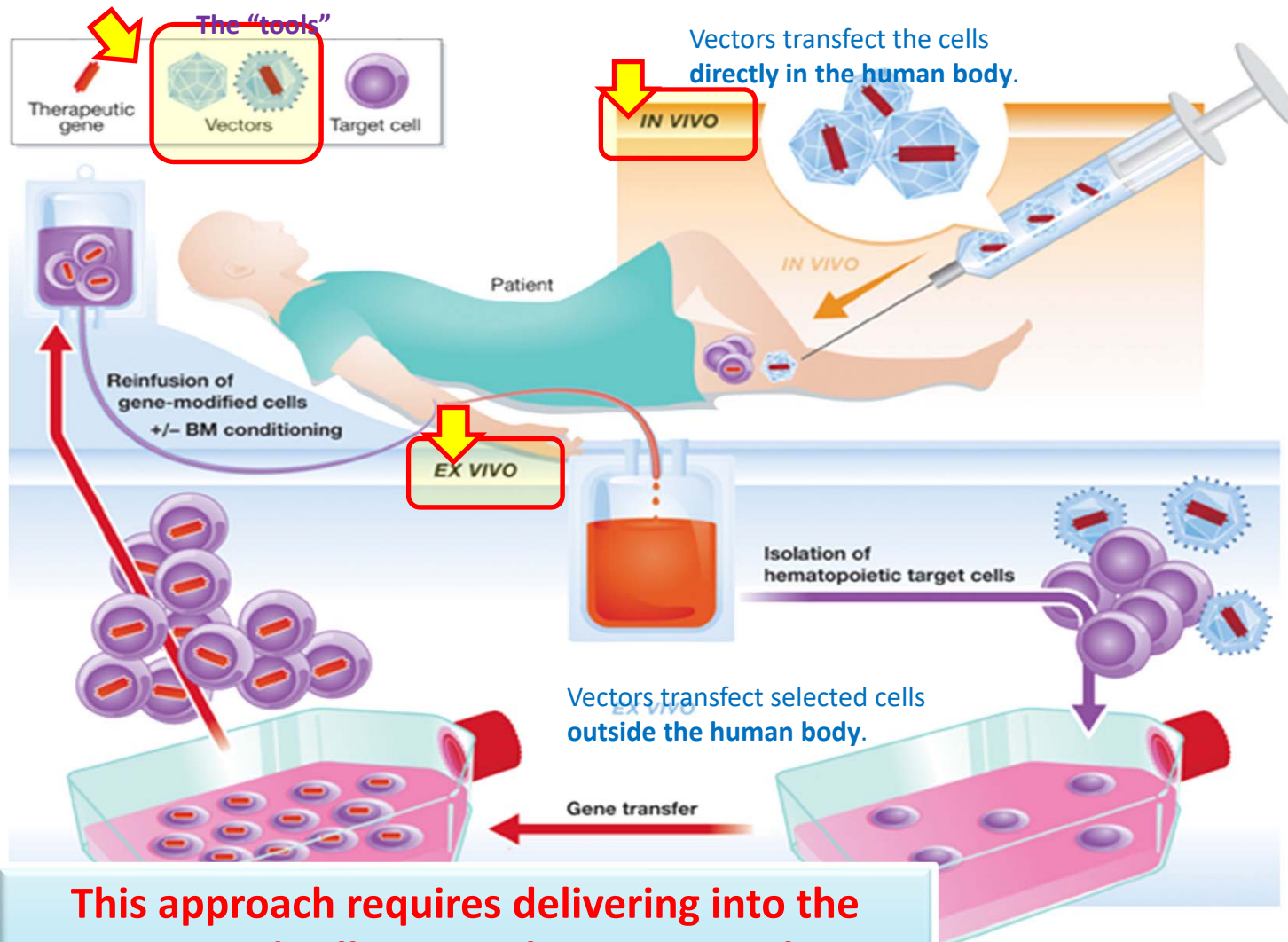


**Iasi University  
(1860)**



**Centre of Advanced Research in  
Bionanoconjugates and Biopolymers**  
<http://www.intelcentru.ro>

# Gene delivery: The “philosophy”...

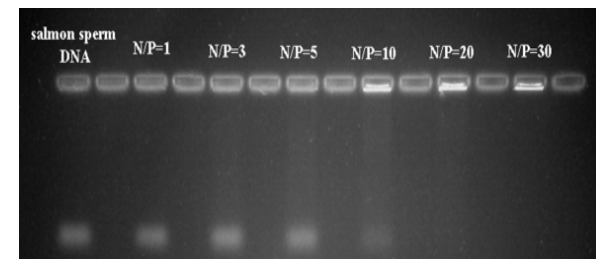
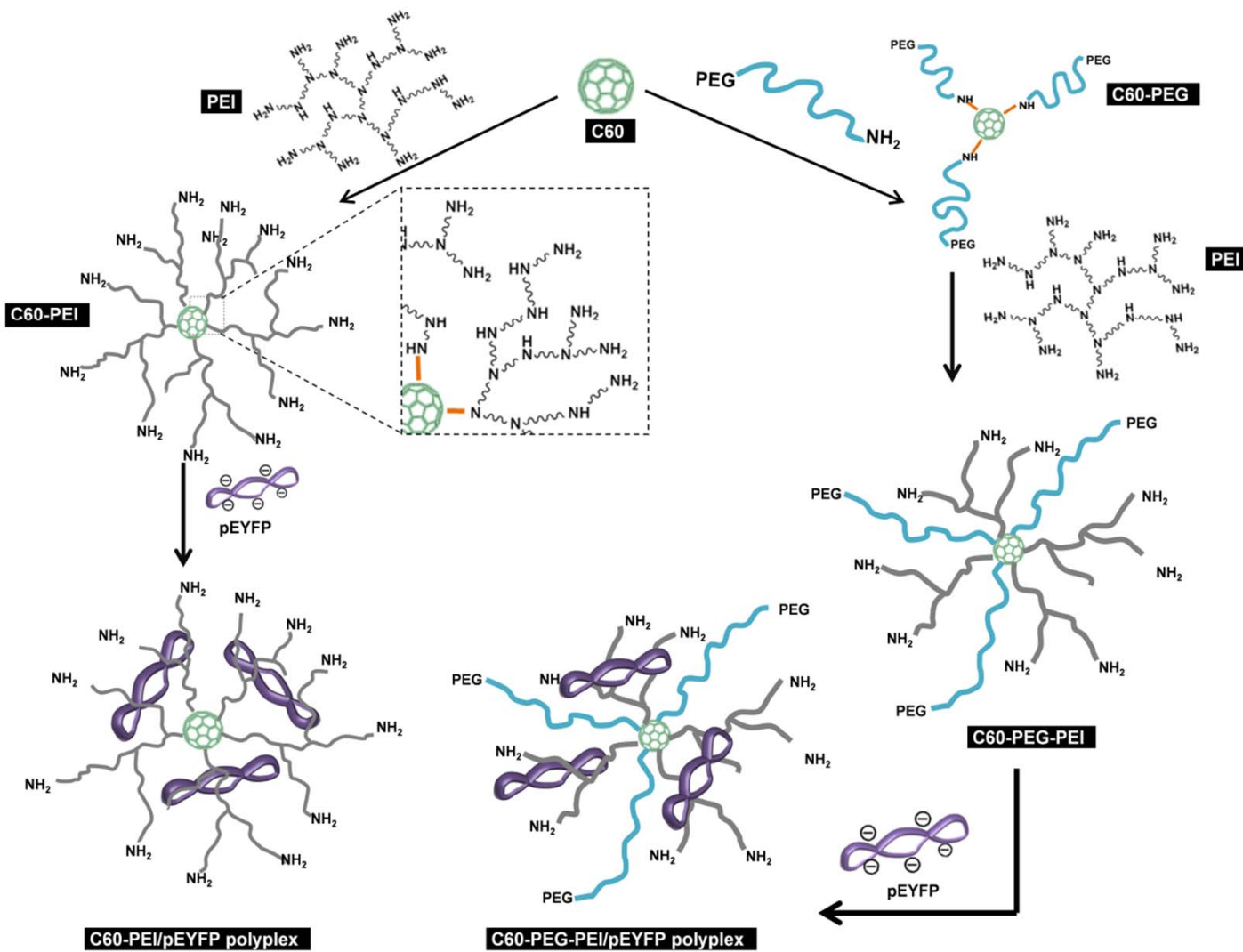


**This approach requires delivering into the targeted cells a complete gene, with thousands of nucleotides !**

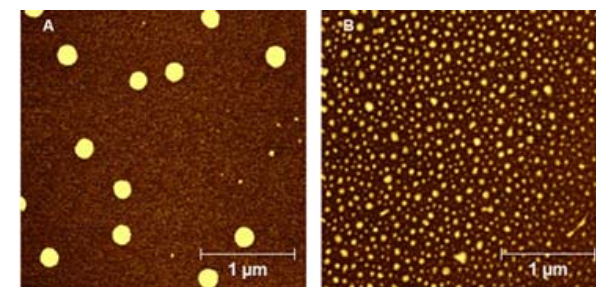
Kerstin B. Kaufmann et al.,  
EMBO Mol Med., 2013, 5, p.1642-1661.

# Gene delivery: The “tools”...

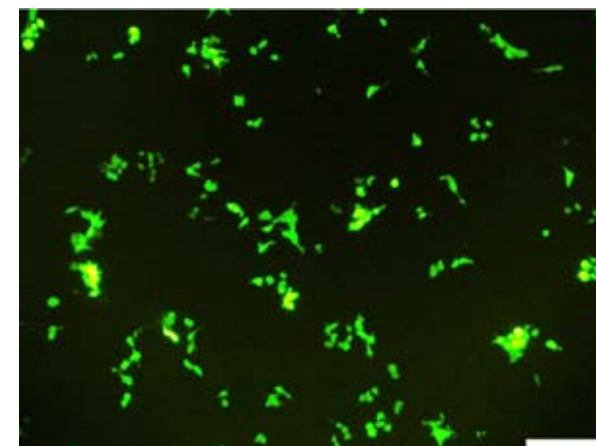
## C60 Fullerene-Polyethyleneimine



Gel retardation assay



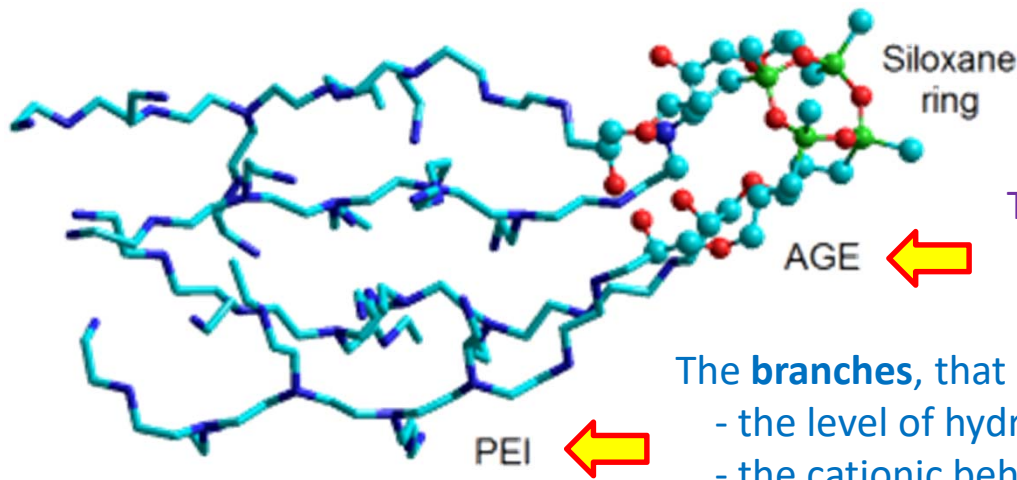
AFM



Transfection HEK 293T (reporter gene: pEYFP)

# Gene delivery: The “tools”...

## Cyclic siloxane -Polyethyleneimine



The **core**, which induces:

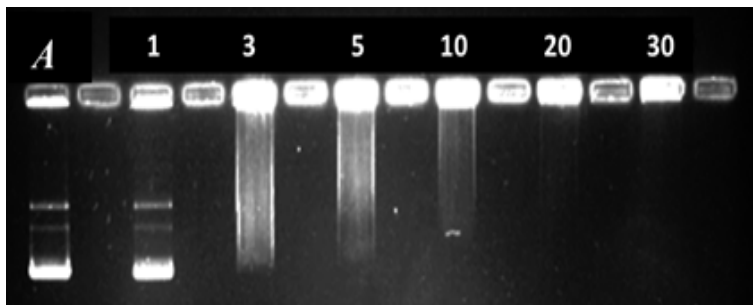
- the level of hydrophobicity;
- the biochemical inertia;
- the articulation flexibility.

The **spacer**, which ensures:

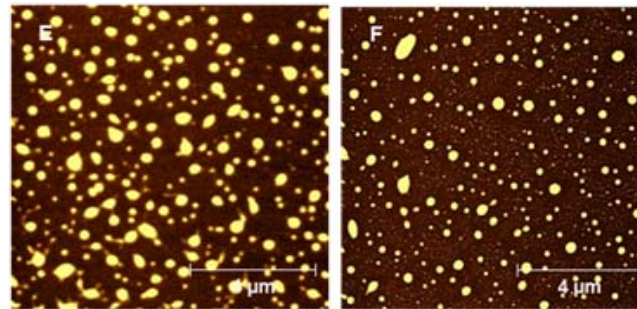
- the biochemical inert elongation;
- the enhancement of amphipathic behavior.

The **branches**, that confer:

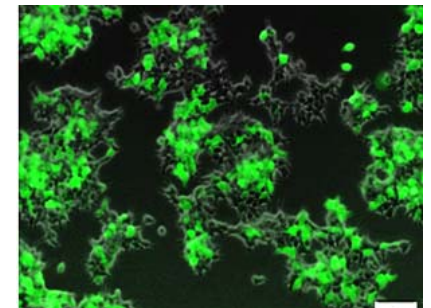
- the level of hydrophilicity;
- the cationic behavior;
- the affinity for (negatively charged) nucleic acids .



Gel retardation assay



AFM

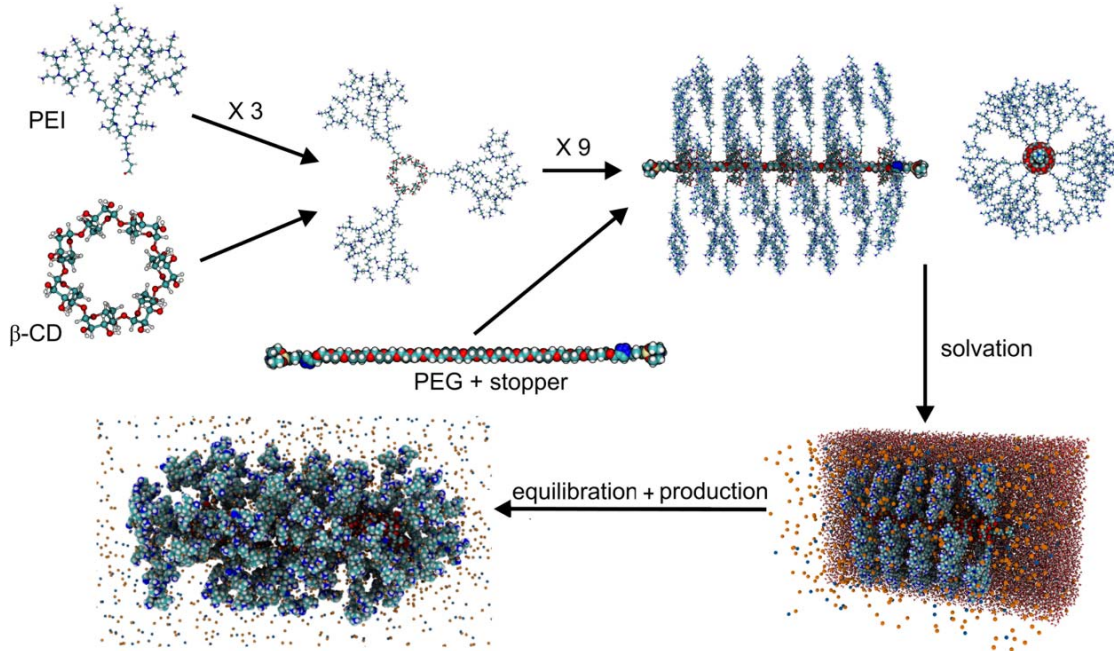


Transfection HEK 293T  
(reporter gene: pEYFP)

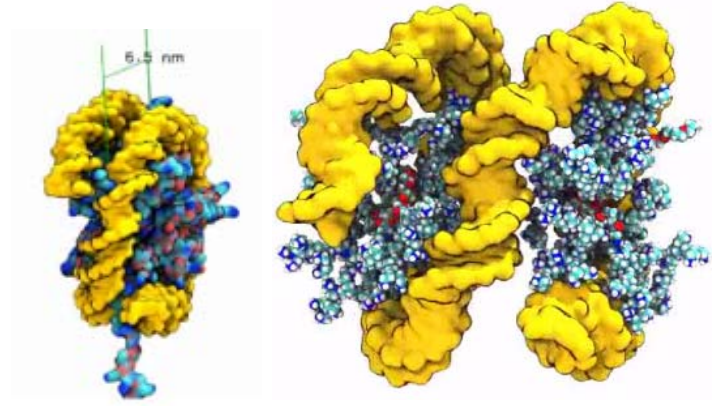


# Gene delivery: The “tools”...

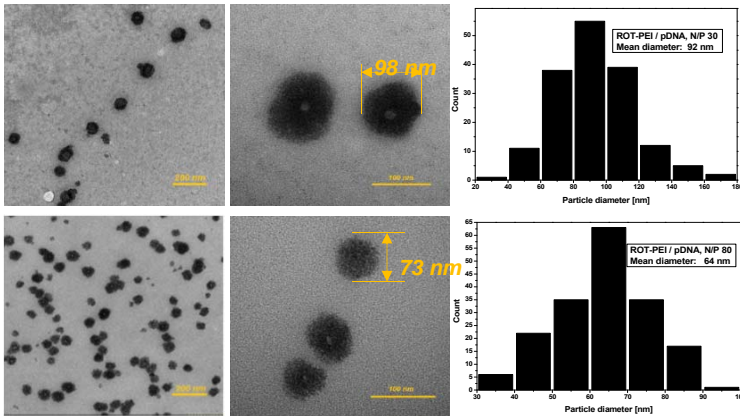
## Supramolecular structures



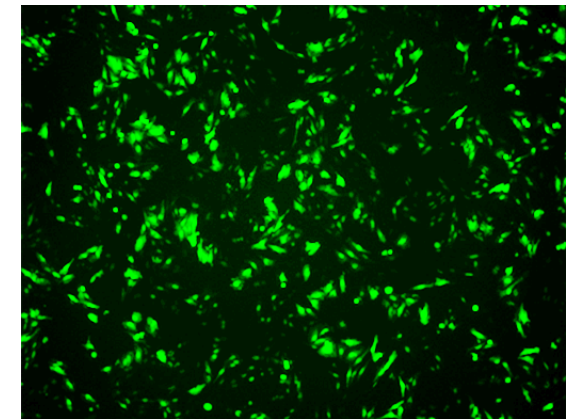
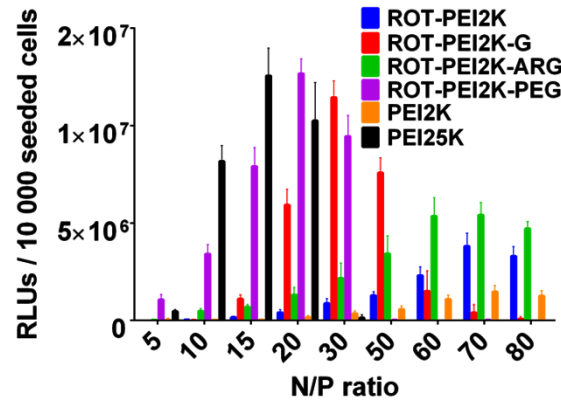
MD simulation in physiological environment  
(519 720 atoms) *Maestro/Desmond* (Schrödinger Inc.)  
simulation software



Luger, K.; Mäder, A. W.; Richmond, R. K.; Sargent, D. F.; Richmond, T. J. Crystal structure of the nucleosome core particle at 2.8 Å resolution. *Nature*. 1997, 389(6648), 251–260;  
Clima L *Organic & biomolecular chemistry*, 2015, 13(36), 9445–56.



TEM

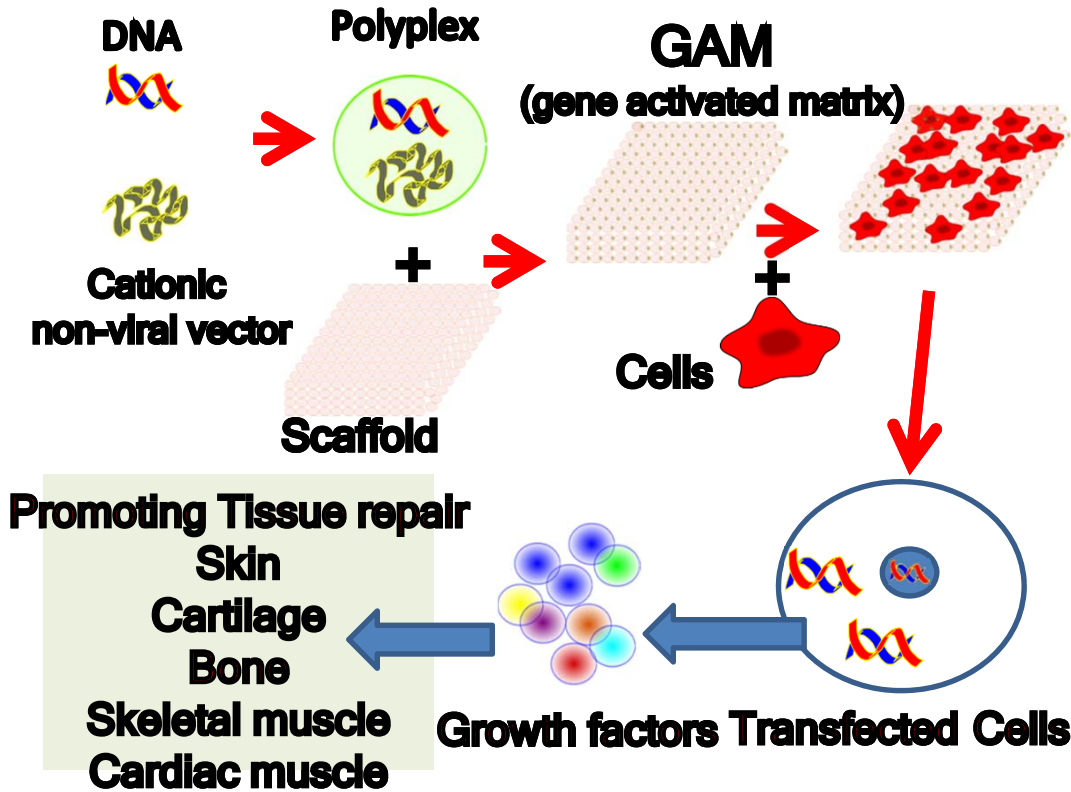


Transfection HEK 293T  
(reporter gene: pEYFP)

9

# Gene delivery: Application...

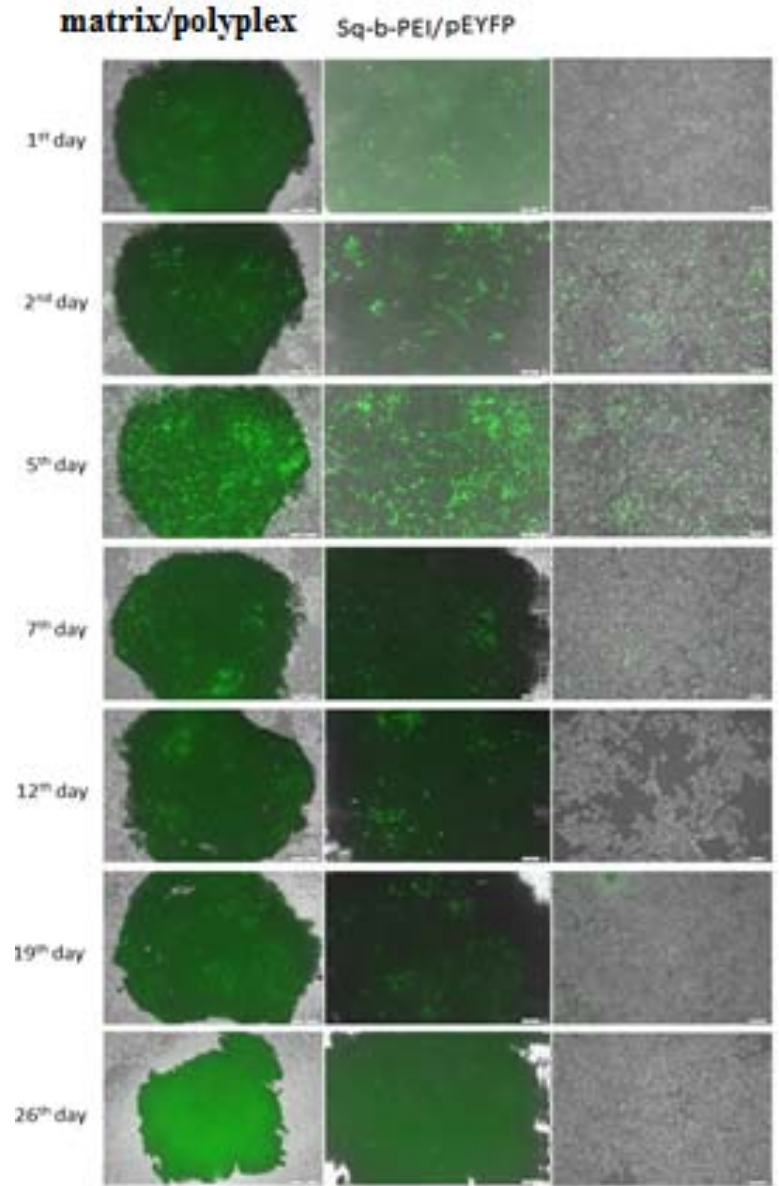
## Gene-activated Matrix (GAM)



**GAM:** Novel solution for the restoration of structure and function of damaged or dysfunctional tissues, combines gene therapy and tissue engineering .

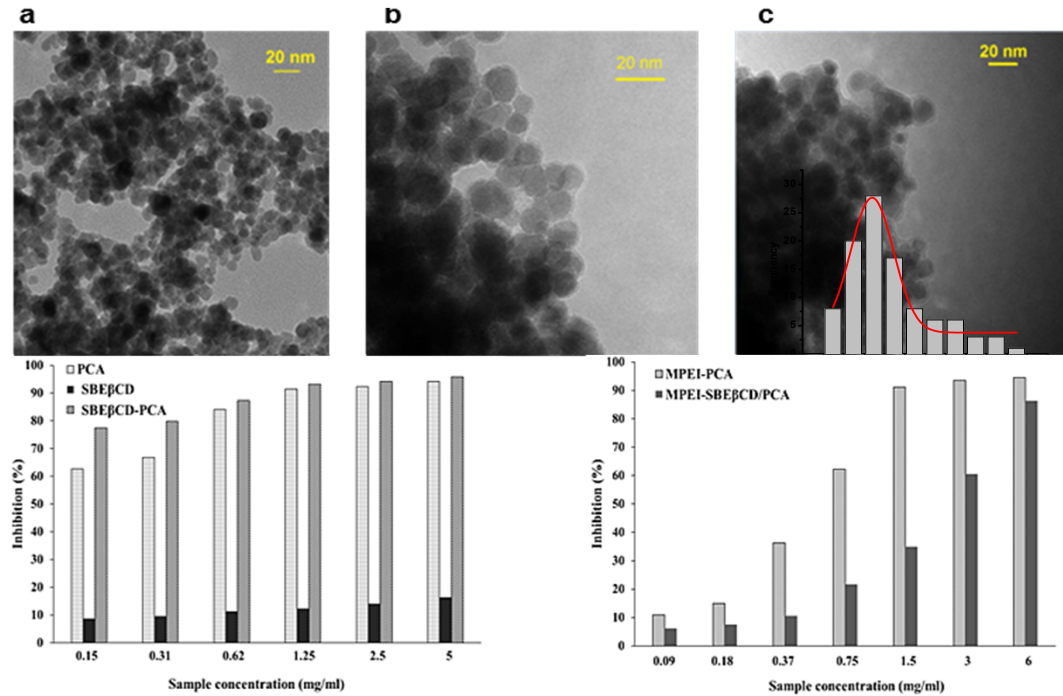
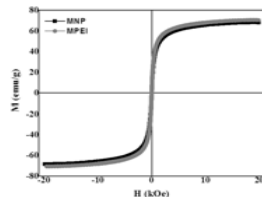
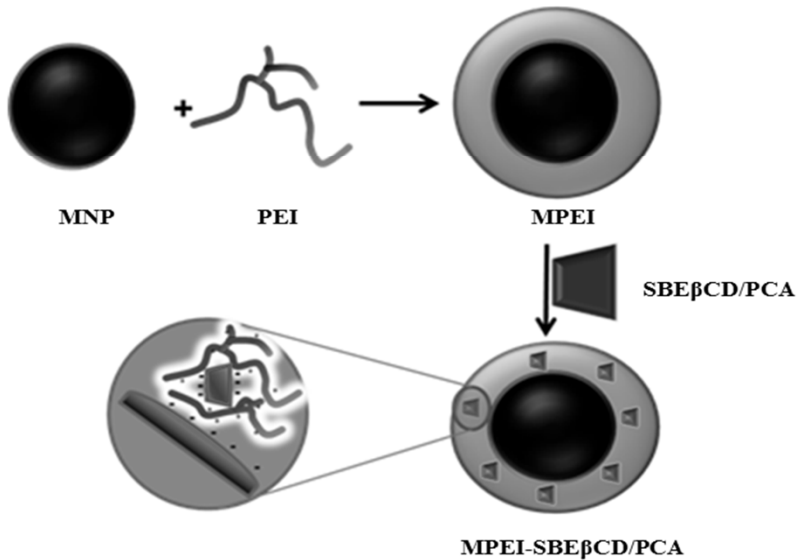
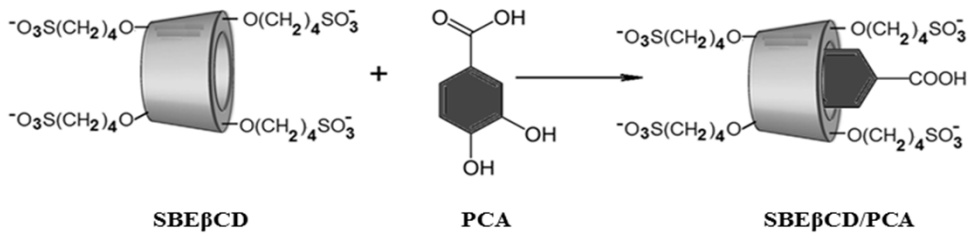
1<sup>st</sup> Jeffrey Bonadio, Nature Medicine (1999) - plasmid genes was physically entrapped in a polymer matrix sponge (canine bone model).  
 2<sup>nd</sup> Fergal J. O'Brien, Organogenesis, (2013) - combining scaffold with gene therapy approaches to further enhance the therapeutic potential of these constructs.

## Bone Repair

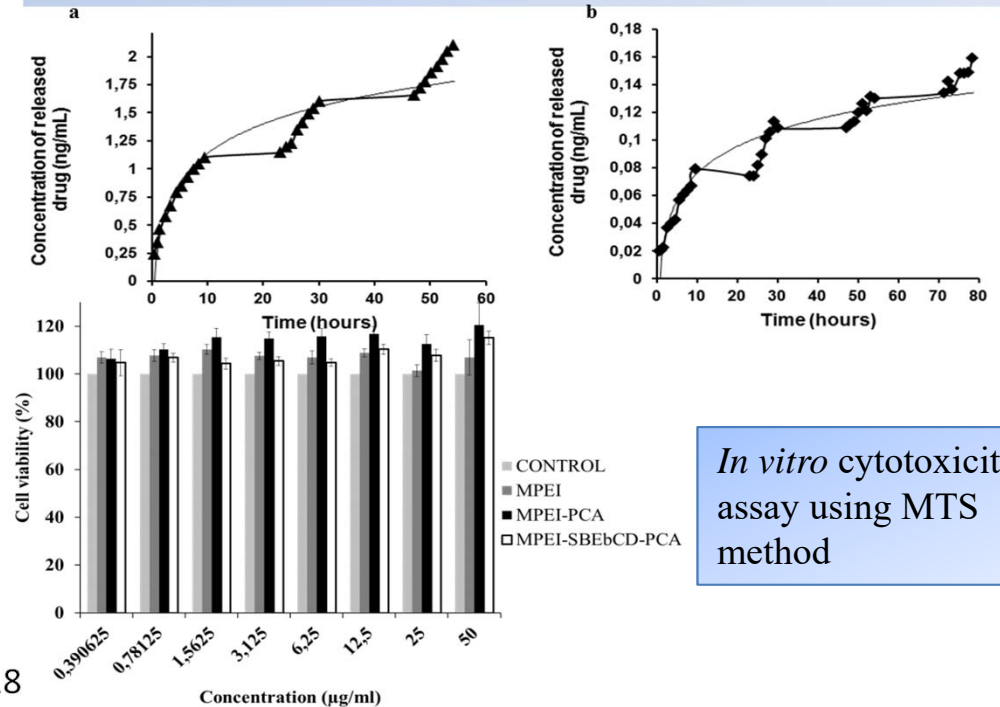


# Drug delivery systems...

## Multifunctional magnetic cargo-complexes with radical scavenging properties (protocatechuic acid)



### Antioxidant activity of PCA in different formulations (DPPH)



*In vitro* cytotoxicity assay using MTS method

# The promise...

To develop accurate know-how for producing bio-functional entities.

To make the preliminary steps for launching clinical trials.



Early steps towards  
real applicative projects,  
oriented to solve some of  
the problems raised by  
bio-pharma companies.

→ **5D-nanoP** ←  
nano-Platforms...  
Our teams suggest that the  
**dynamically assembled nanoplatforms**  
could be a viable and versatile solution.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 667387 WIDESPREAD 2-2014 SupraChem Lab

## Many thanks:

- Marc J.M. Abadie, Professor Emeritus - ERA CHAIR holder of SupraChem Lab project
- Acad. Maya Simionescu, Dr. Manuela Calin - Institute of Cellular Biology and Pathology "N. Simionescu"
- Prof. Stelian Maier and Prof. Geta David - "Gh. Asachi" Technical Univ.
- To all my colleagues

Nr. crt.	Numele și prenumele	Prezența la IntelCentru	Nr. crt.	Numele și prenumele	Prezența la IntelCentru
1	Dr. Mariana PINTEALĂ		16	Dr. Lilia CLIMA	
2	Dr. Teodora RUSU		17	Dr. Cristina URȚU	
3	Dr. Adrian FIFERE		18	Dr. Bogdan CRĂCIUN	
4	Dr. Irina ROȘCA		19	Dr. Gabriela PRICOPE	
5	Dr. Ioana MOLEAVIN		20	Dr. Irina CRUDU	
6	Dr. Alexandru ROTARU		21	Dr. Laura URSU	
7	Dr. Anca PETROVICI		22	Dr. Adina COROABĂ	
8	Dr. Ana-Lăcrămioara LUNGOCI		23	Dr. Sorin-Alexandru IBĂNESCU	
9	Dr. Dragoș PEPTIȚANARU		24	Dr. Cristian-Dragoș VARGANICI	
10	Dr. Dana BEJAN		25	Dr. Tudor VASILIU	
11	Dr. Lucian BĂHRIN		26	Dr. Radu ZONDA	
12	Dr. Monica SARDARU		27	Alexandra IACOBESCU	
13	Dr. Bogdan BRATANOVICI		28	Carmen BÎRSAN	
14	Dr. Narcisa MARANGOCI		29	Anca IFTENE	
15	Dr. Adina ARVINTE		30	Gheorghe IBĂNESCU	



