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



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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)



Iasi University
(1860)

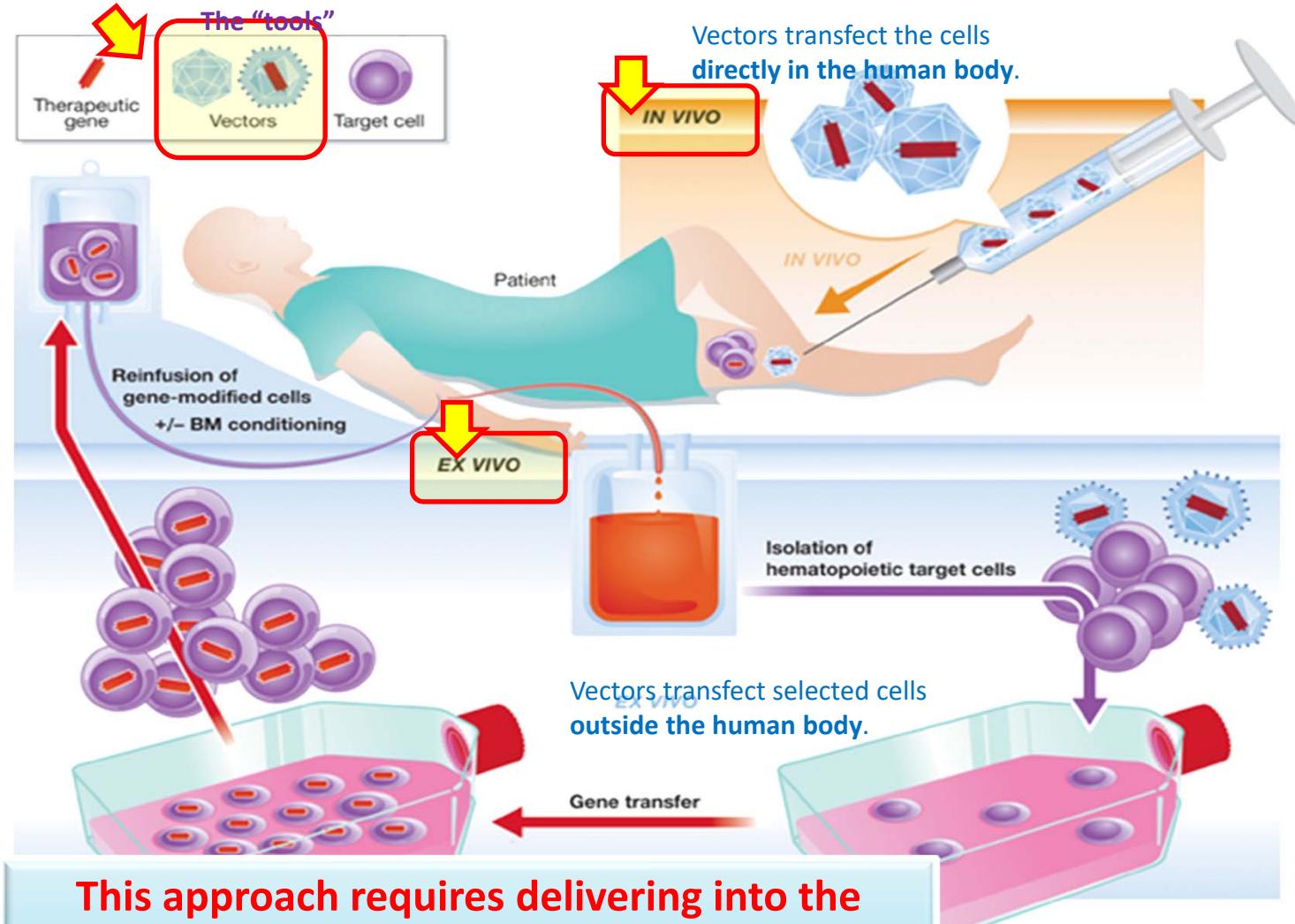


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Gene delivery: The “philosophy”...

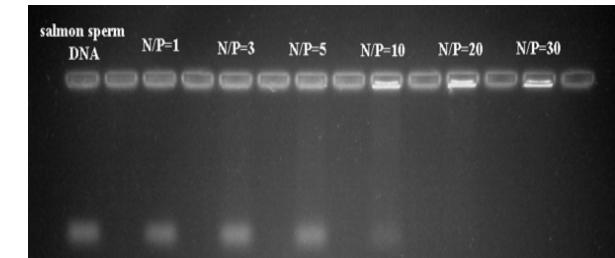
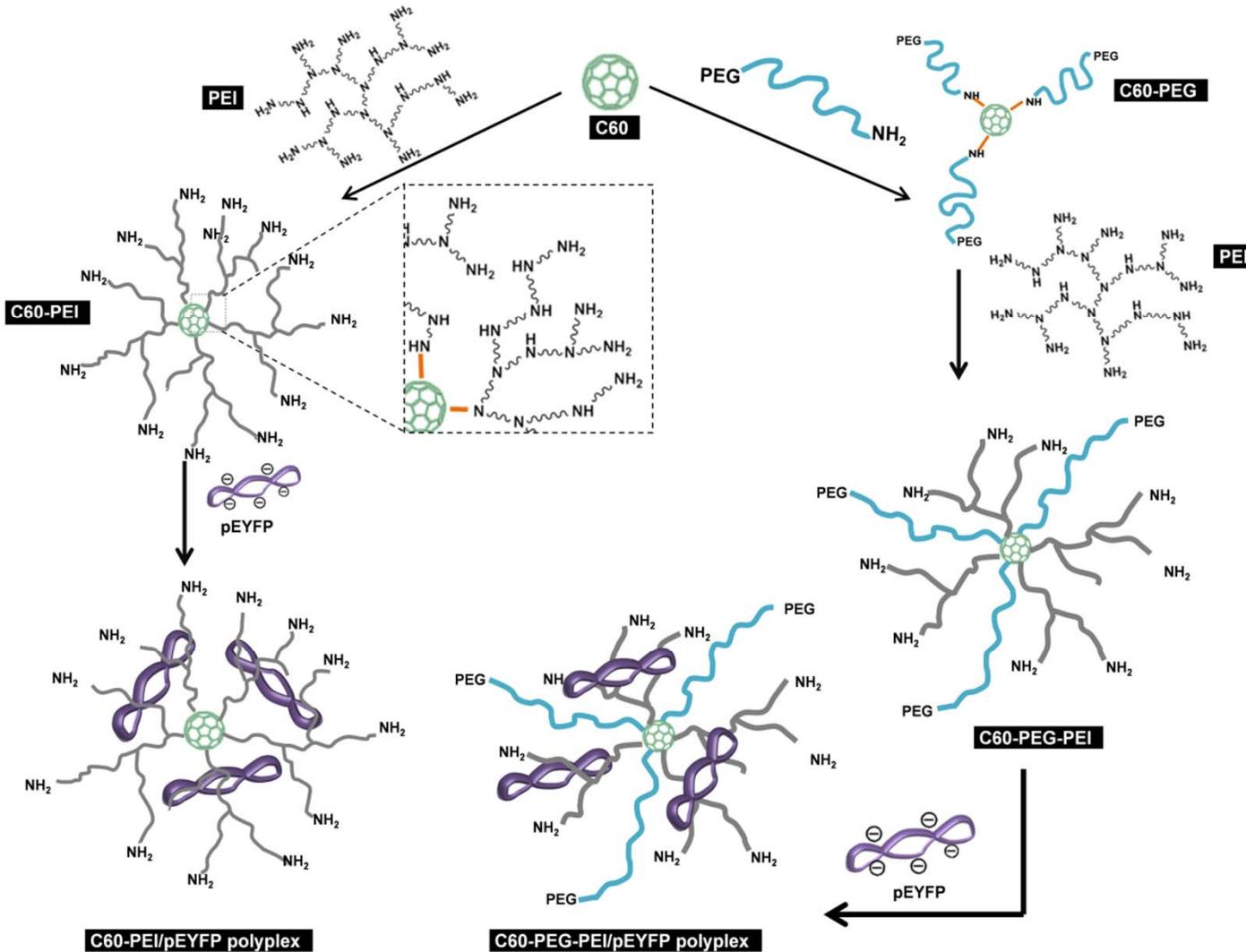


This approach requires delivering into the targeted cells a complete gene, with thousands of nucleotides !

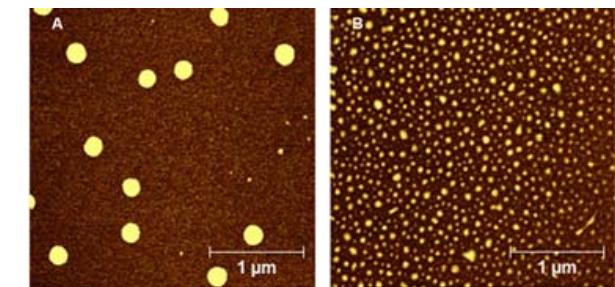
Kerstin B. Kaufmann et al.,
EMBO Mol Med., 2013, 5, p.1642-1661.

Gene delivery: The “tools”...

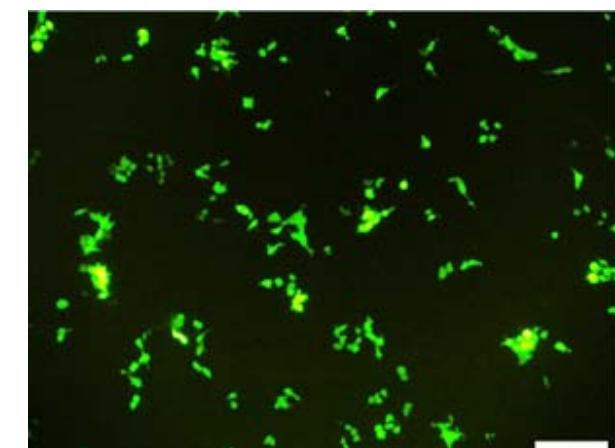
C60 Fullerene-Polyethyleneimine



Gel retardation assay



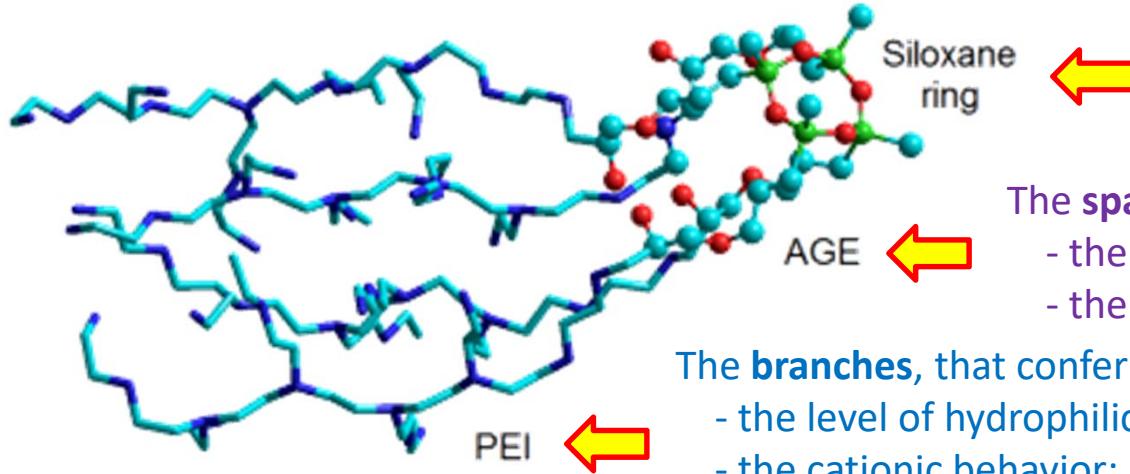
AFM



Transfection HEK 293T
(reporter gene: pEYFP)

Gene delivery: The “tools”...

Cyclic siloxane -Polyethyleneimine



The **core**, which induces:

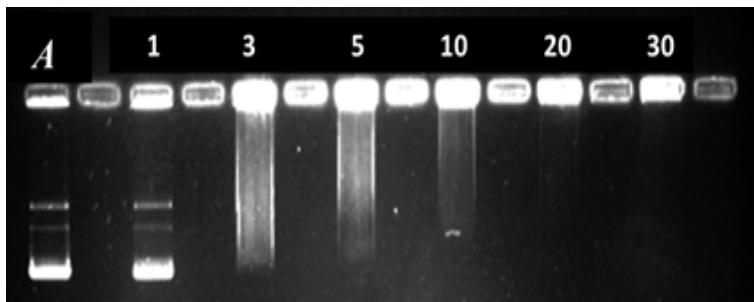
- the level of hydrophobicity;
- the biochemical inertia;
- the articulation flexibility.

The **spacer**, which ensures:

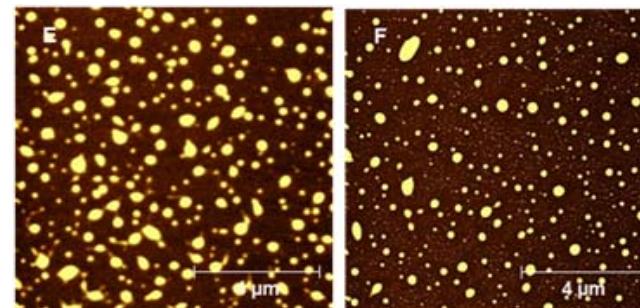
- the biochemical inert elongation;
- the enhancement of amphipathic behavior.

The **branches**, that confer:

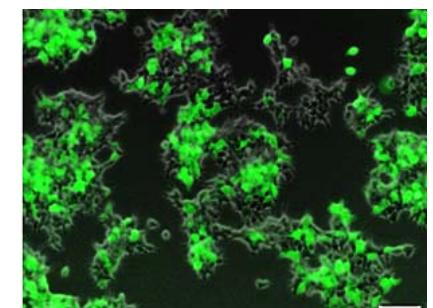
- the level of hydrophilicity;
- the cationic behavior;
- the affinity for (negatively charged) nucleic acids .



Gel retardation assay



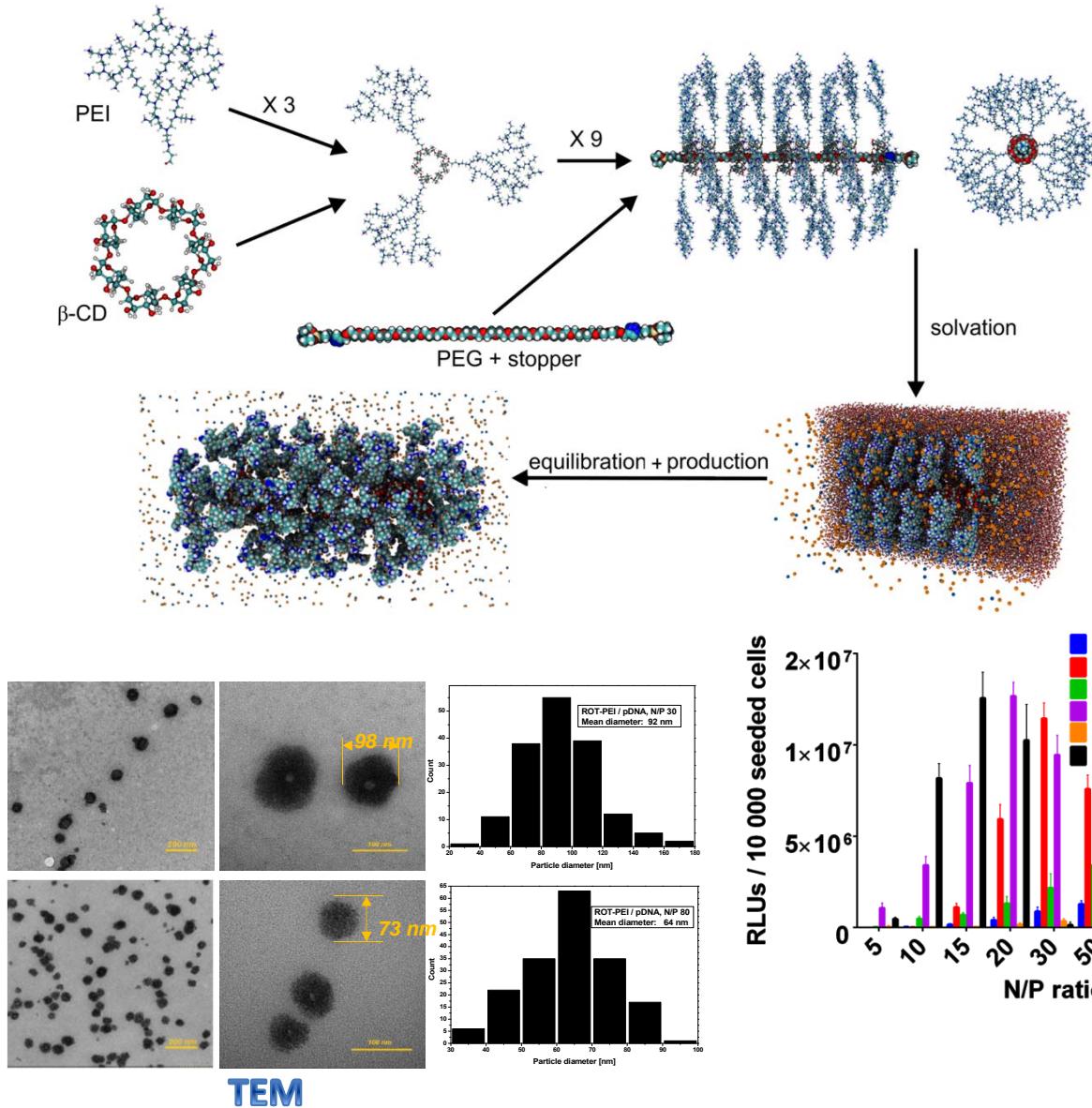
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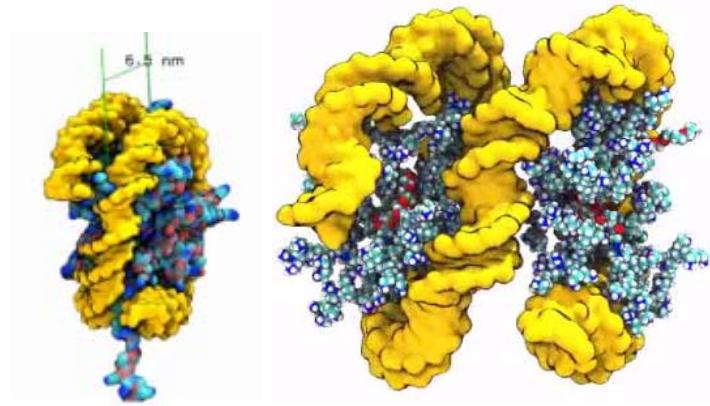
Transfection HEK 293T
(reporter gene: pEYFP)

Gene delivery: The “tools”...

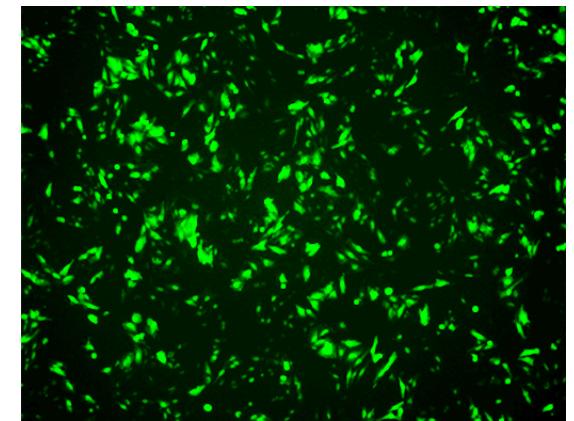
Supramolecular structures



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



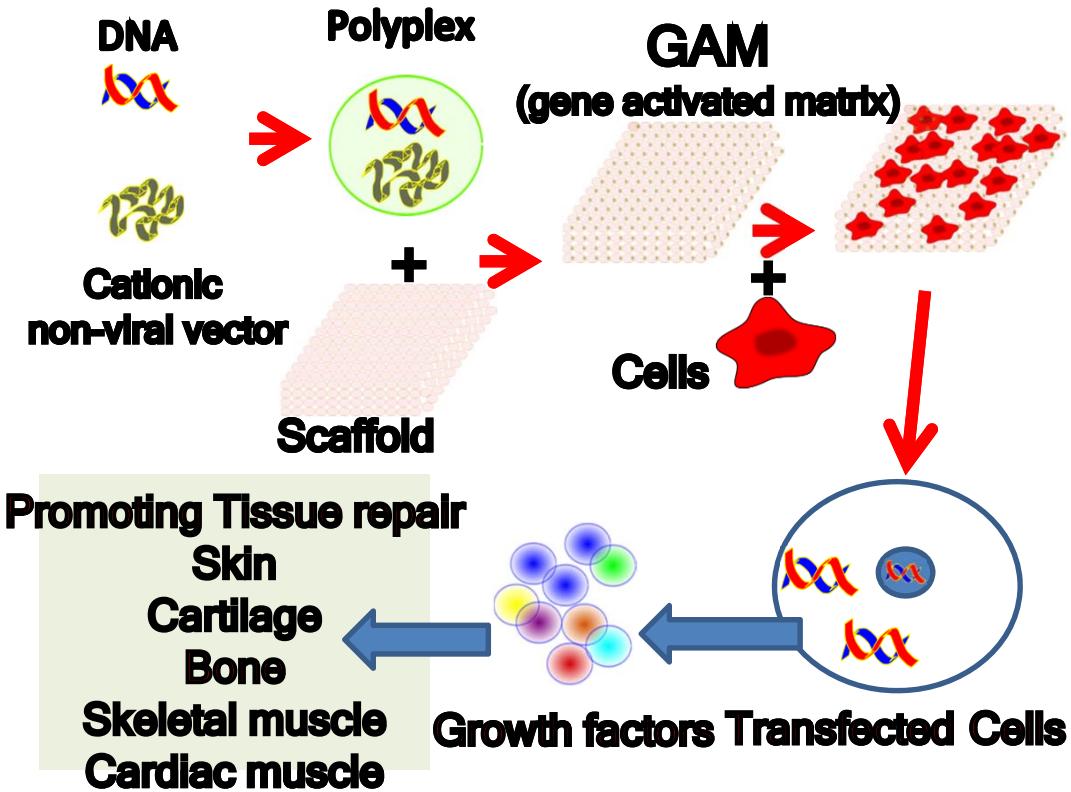
Luger, K.; Mäder, A. W.; Richmond, R. K.; Sargent, D. F.; Richmond, T. J. Crystal structure of the nucleosome core particle at 2.8 Å resolution. *Nature*. 1997, 389(6648), 251–260;
Clima L *Organic & biomolecular chemistry*, 2015, 13(36), 9445-56.



Transfection HEK 293T
(reporter gene: pEYFP)

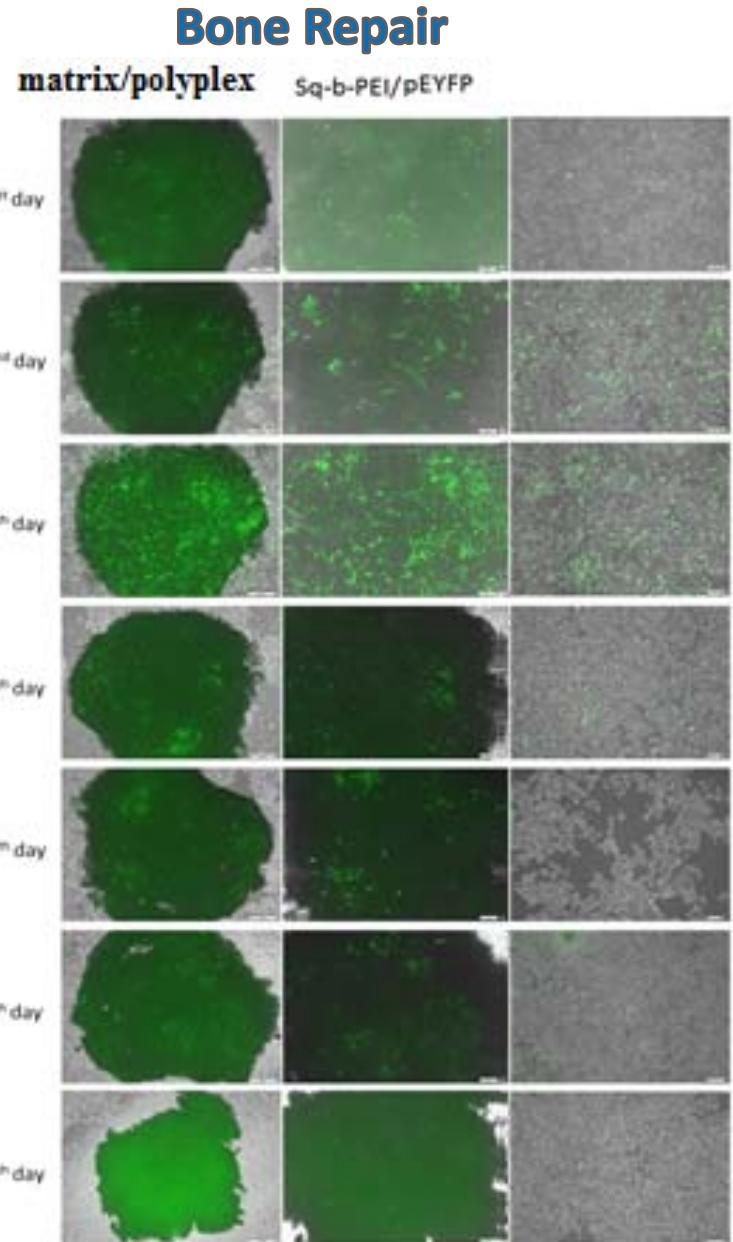
Gene delivery: Application...

Gene-activated Matrix (GAM)



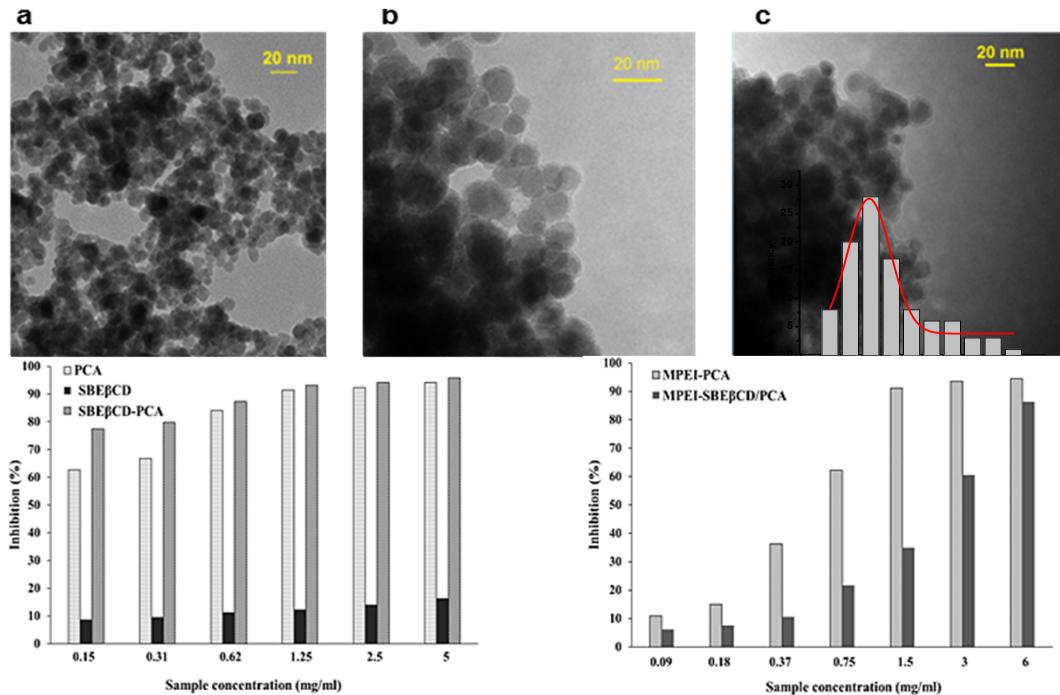
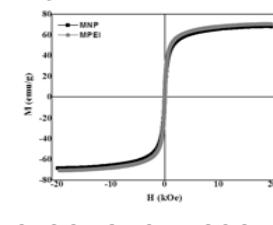
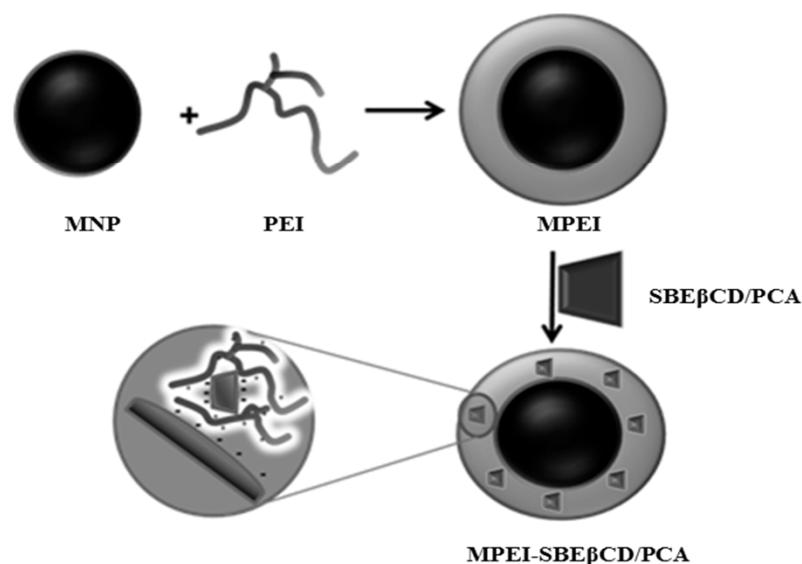
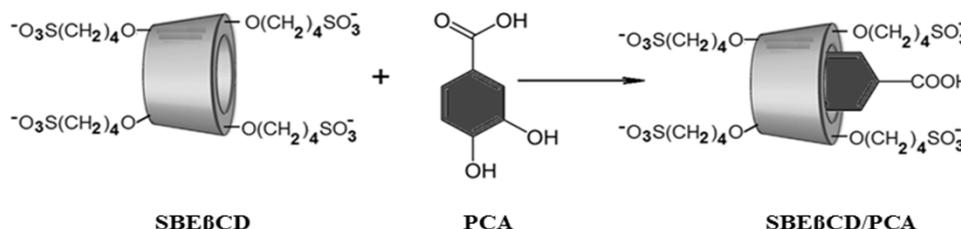
GAM: Novel solution for the restoration of structure and function of damaged or dysfunctional tissues, combines gene therapy and tissue engineering .

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

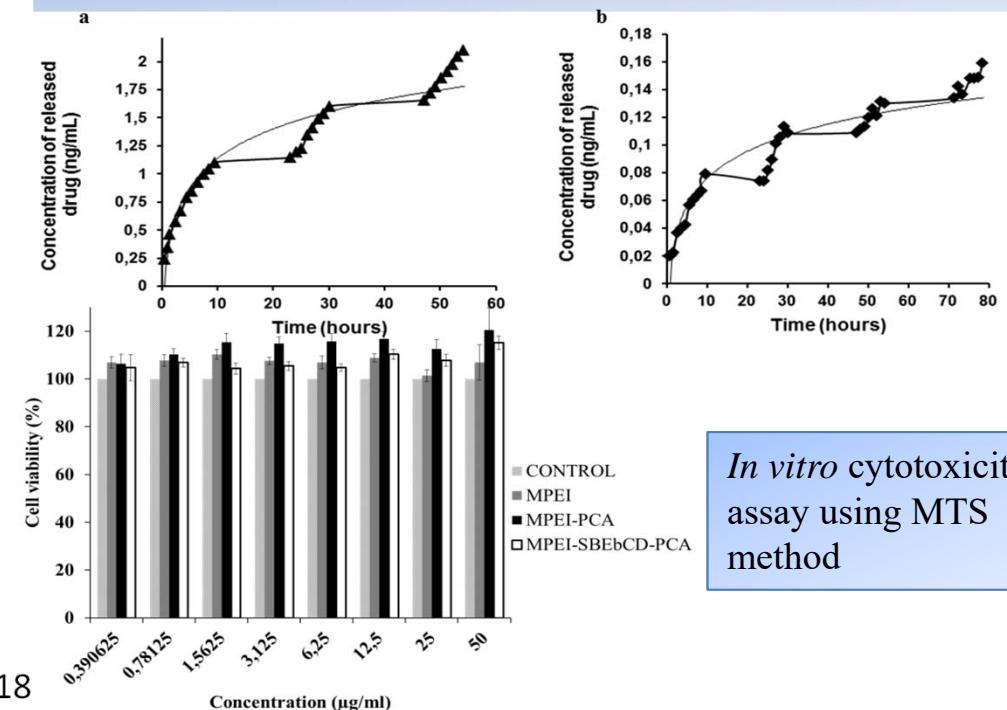


Drug delivery systems...

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.



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- To all my colleagues

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شكرًا جزيلاً شکرًا جزیلًا
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dank je dankon ačiu go raibh maith agat dakujem
gracias gracies arigatō merci
spas sulpáy grazie xiexie
welalin tack tanemirt rahmet shukriya mercs
marsi vinaka diolch trugarez
barka blagodaram dhanyavadagalu
kia spas shukriya
matondo misaotra mercs
paldies grazzi matodo mercs
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kam sah hamnida dankon ačiu mercs
তোমাকে ধন্যবাদ dankon ačiu mercs
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