Radiation engineering - on the fast track towards the development of smart nanodrugs

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International Atomic Energy Agency Scientific Forum

ATOMS IN INDUSTRY

Radiation Technology for Development

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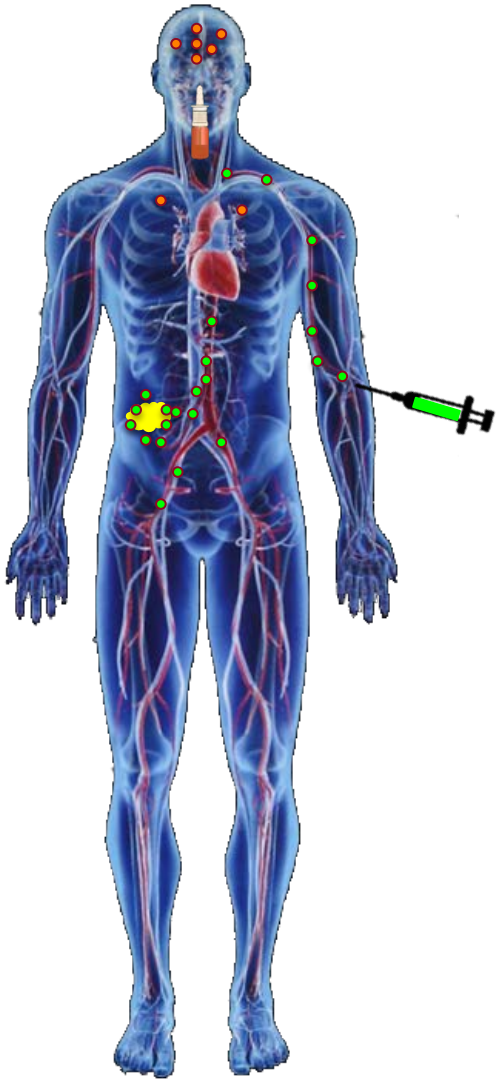
The nanotechnology revolution in drug delivery

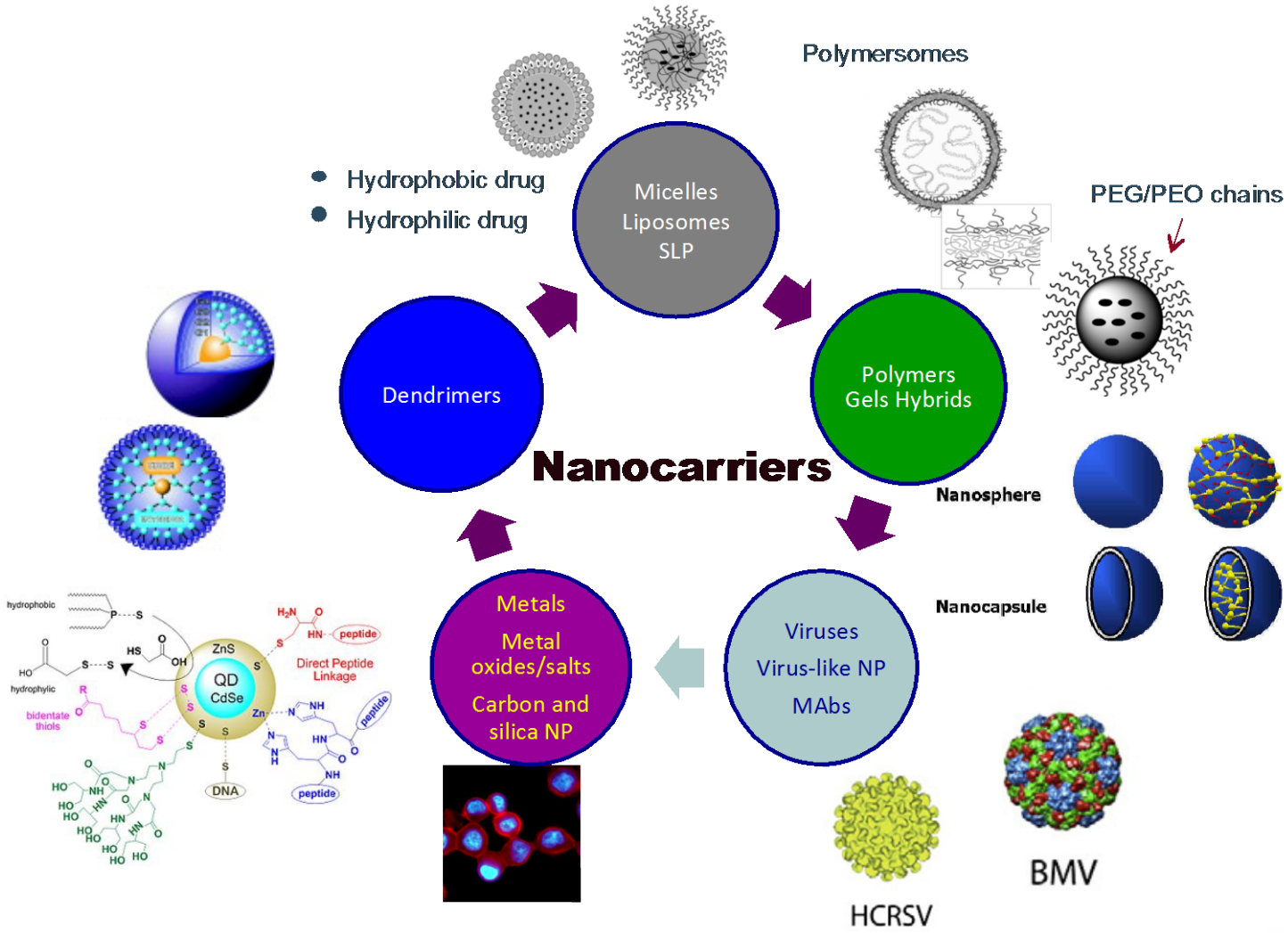


- Stable and durable drug carriers, 1-100 nanometers in size, hold the promise of enhancing the in vivo efficiency of many drugs.

CHALLENGES

- PROTECTION: Minimize drug degradation and inactivation upon administration.
- RECOGNITION: Increase the fraction of drug delivered in the pathological area, by the ability to specifically recognize and bind target tissues or cells.
- ACTUATION: Activate drug release upon an external or internal stimulus.
- DIAGNOSTIC OR TRACKING FUNCTIONS

Material platforms for nanocarriers



Often, difficult to synthesize and to scale-up to industrial production.

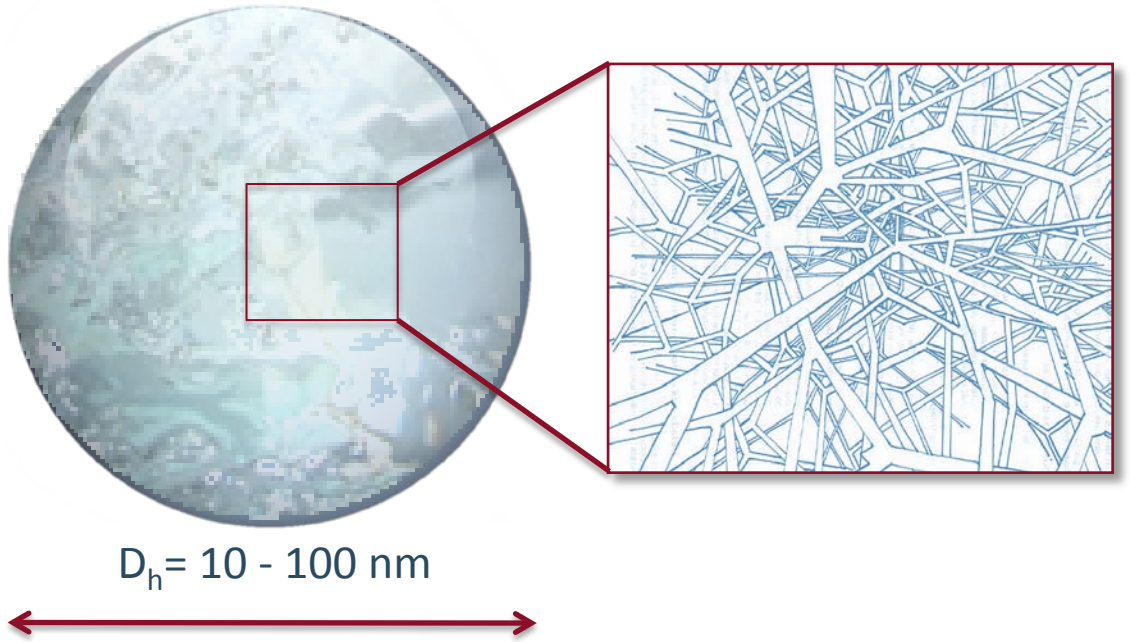
Nanogels

Water-loving, crosslinked polymer nanoparticles

SOFT

WET

SMART



D_h= 10 - 100 nm

KEY REQUIREMENTS

- Controlled particle size and surface electrical charge.
- Controlled physical and chemical structure: mesh size (or crosslinking density) and chemical functionality (responsiveness and reactivity).

Functional decoration of nanogels

Physical entrapment

Molecular drug

Biomolecule

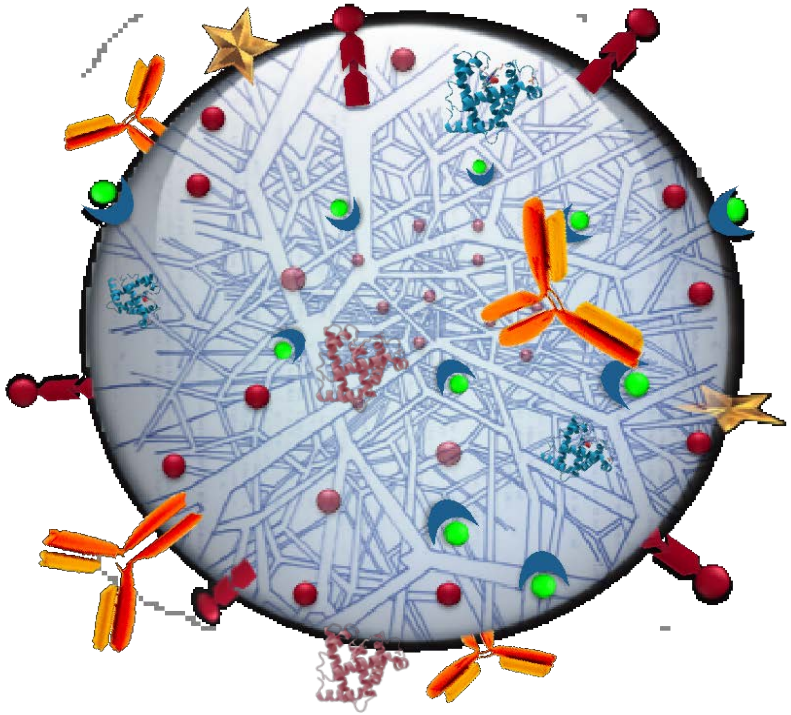
Chemical binding

Targeting moiety

Fluorescent tag

Imaging agent

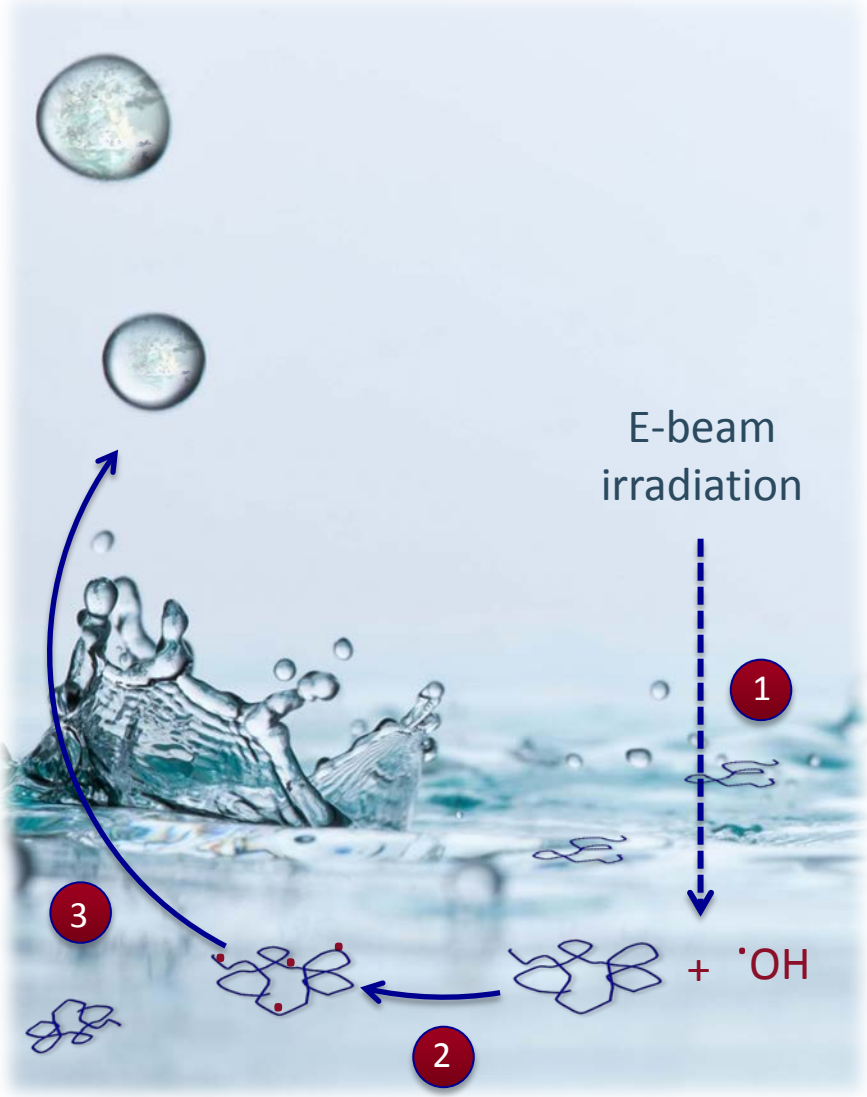
Biomolecule



Drug with stimuli-sensitive linker

Enabling one or many functions: DRUG PROTECTION – SITE RECOGNITION – TRIGGERED DRUG DELIVERY – TRACKING – IMAGING

Radiation engineered nanogels



1. Pulsed, e-beam irradiation of an aqueous polymer solution.

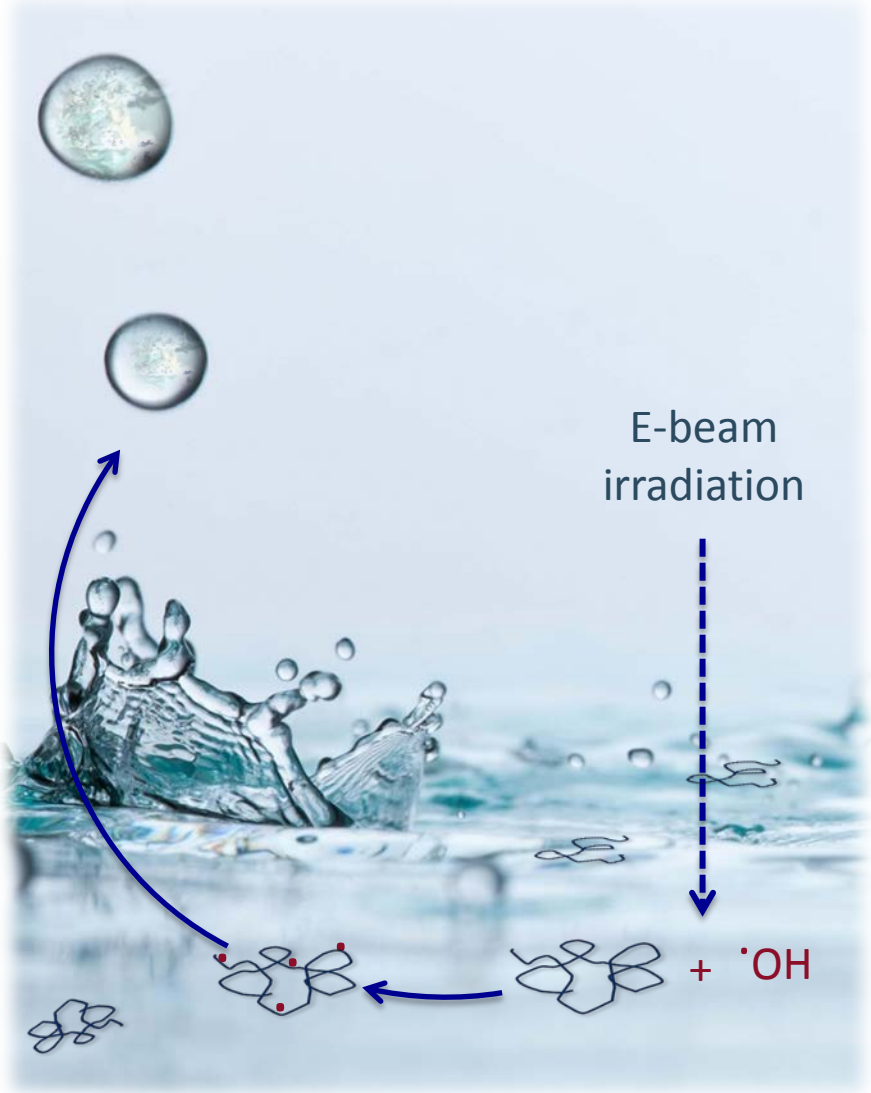
2. Water radiolysis products ($^{\cdot}OH$, $^{\cdot}H$, e^-_{aq} H_3O^+, H_2O_2, …) react with the polymer, forming polymer radicals.

3. Their chemical follow-up reactions lead to the formation of crosslinked polymer nanoparticles with controlled size and functionality.

NO CATALYSTS OR INITIATORS, ORGANIC SOLVENTS AND SURFACTANTS REQUIRED!

SIMULTANEOUS STERILISATION.

Radiation engineered nanogels



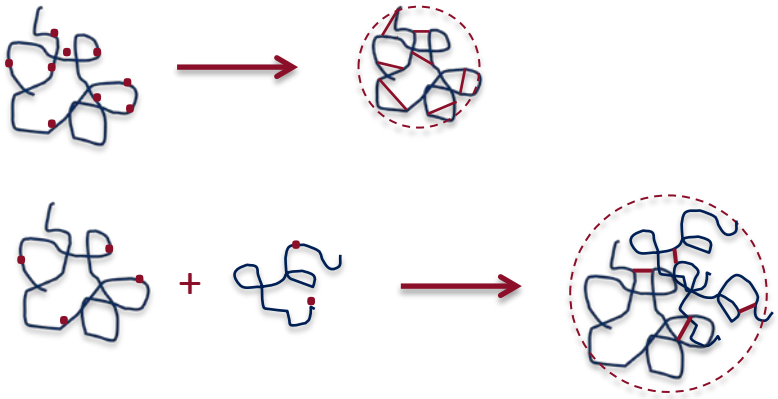
MANUFACTURING PROCESS:
FAST – SIMPLE – VERSATILE - EFFICIENT

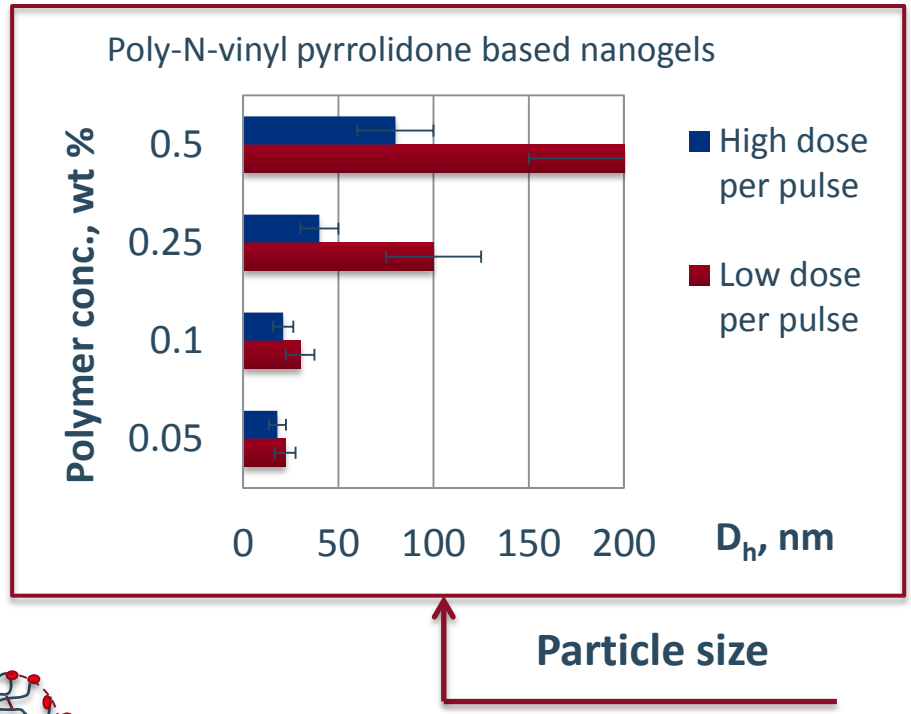
Poland's Institute of Nuclear Chemistry and Technology (INCT), in Warsaw

Nanogel properties are fine tuned by Radiation Chemistry

CONTROL OF SIZE

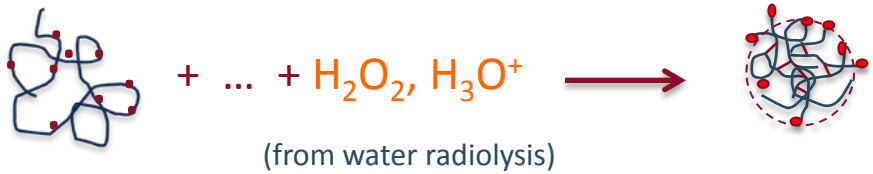
CROSSLIKING





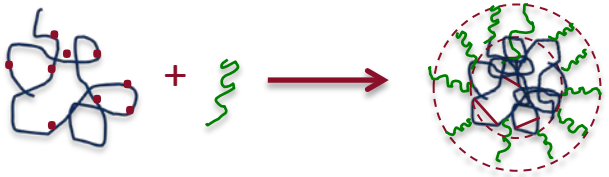
CONTROL OF CHEMICAL STRUCTURE

OXIDATION



= -COOH; -OH

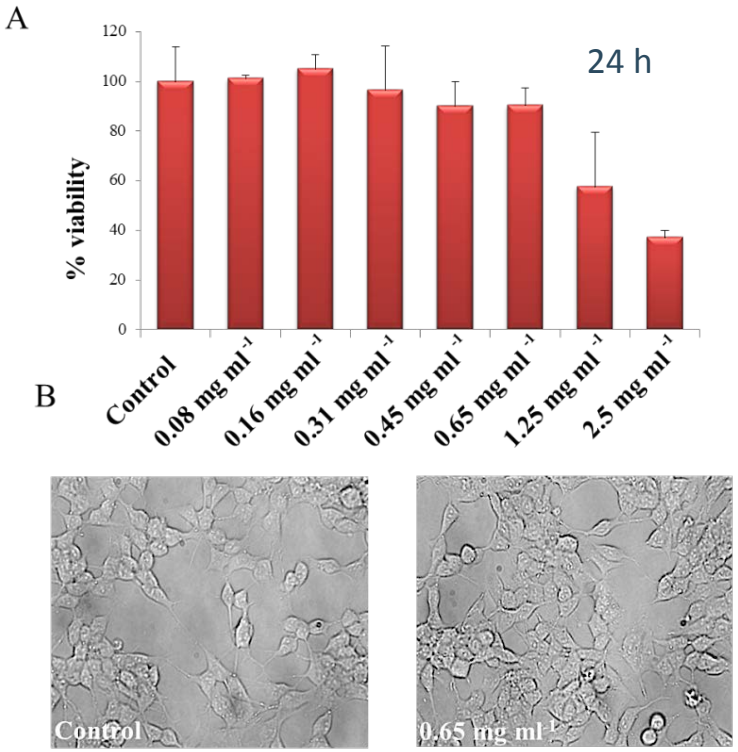
GRAFTING



= functional acrylic monomer

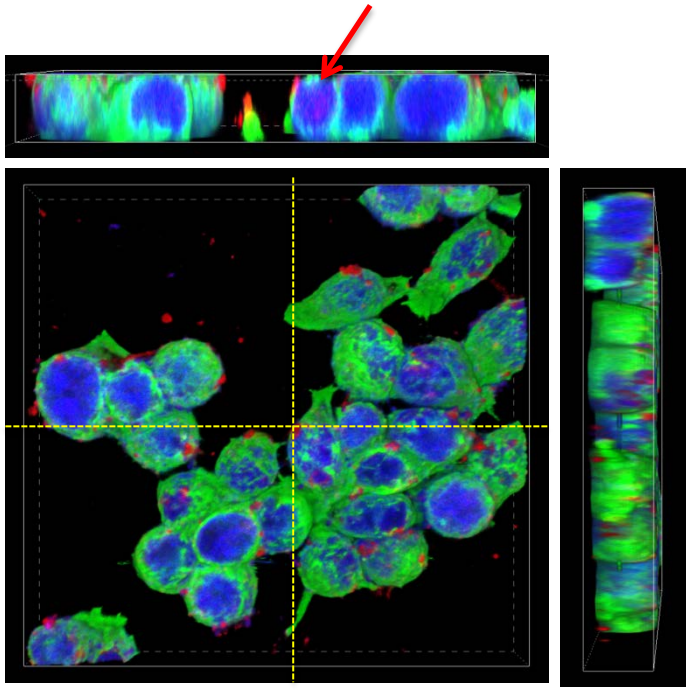
Biocompatibility of radiation engineered nanogels

MTS cell metabolic activity test



Absence of cytotoxicity

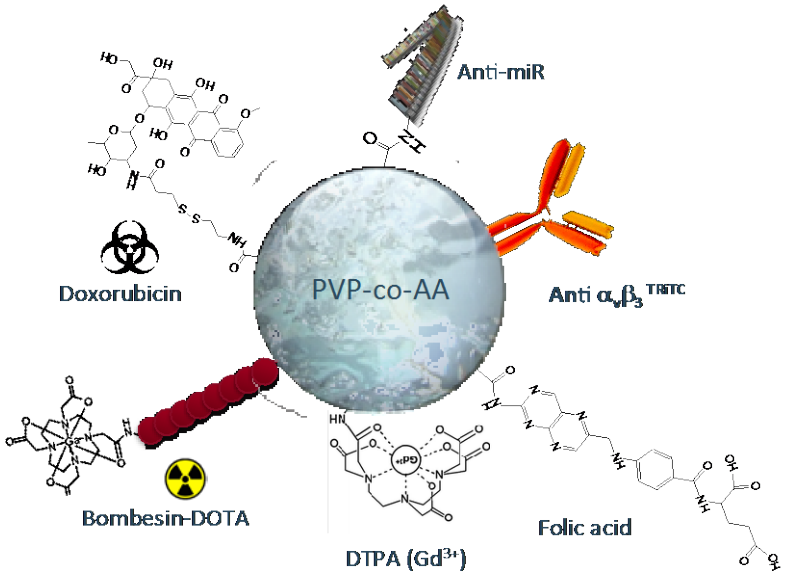
Poly-N-vinyl pyrrolidone based nanogels

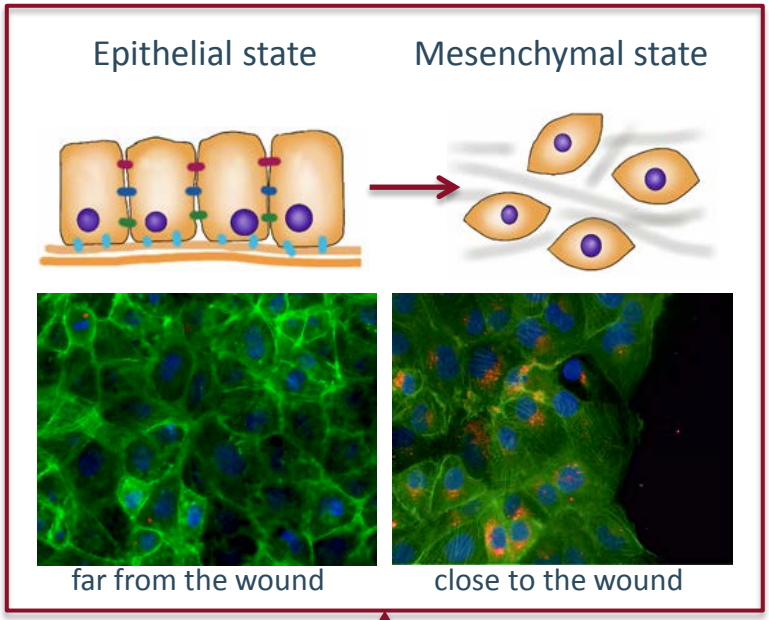


Cellular uptake
and **nuclear localisation**

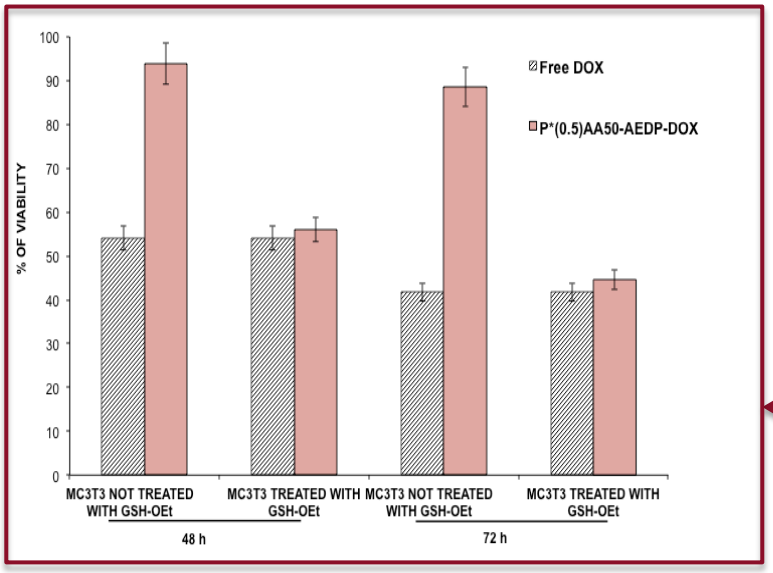
Absence of proliferative, immunogenic, thrombogenic and inflamatory responses.
Hemocompatibility.

Opportunities for radiation engineered nanogels in cancer therapy





Targeting function

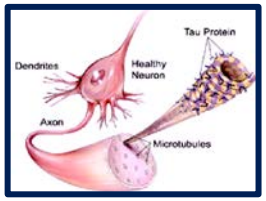


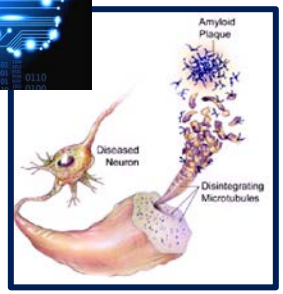
Intracellular smart drug release

Stimulus: Glutathione monoester (GSH-OEt)

Opportunities for radiation engineered nanogels in AD therapy

Alzheimer Disease (AD)





Insulin resistance

Intranasal insulin-NG delivery to the brain

Opportunities for radiation engineered nanogels in AD therapy

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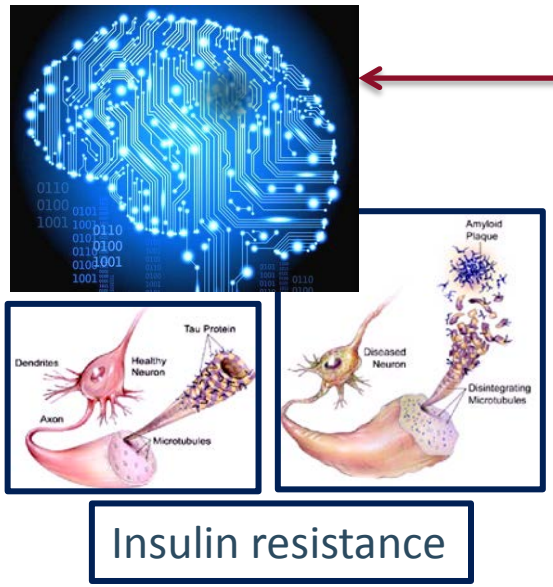
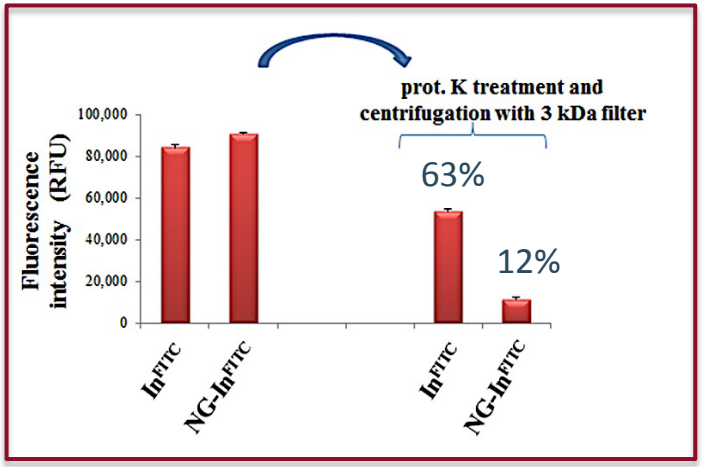


Insulin resistance

Intranasal insulin-NG delivery to the brain

- NG protects insulin by protease degradation



- NG-In bypasses the blood brain barrier (BBB).
- NG-In binds to insulin receptors
- Insulin signalling is activated.
- Toxicity caused by amiloid fibrils β is almost completely recovered.
- ROS production reduced.

Conclusions and outlooks

Functional polymer nanoparticles can be manufactured in a simple and effective way by exploiting the great versatility of polymer aqueous systems in combination with pulsed electron beam irradiation.

Straighten science foundations

Continue to address healthcare and societal challenges

Expand the application range of these functional nanoparticles

Acknowledgements

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THANK YOU!