

Magnetic hyperthermia coupled to siRNA deliverance to the cytosol for cancer treatment

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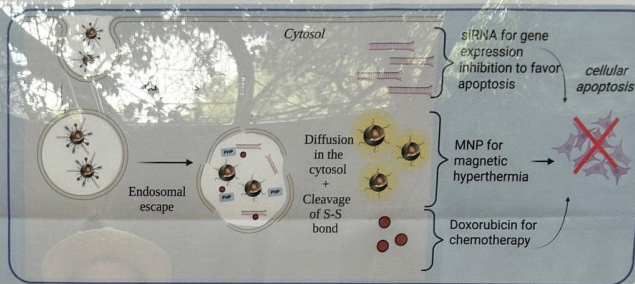
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Objectives:

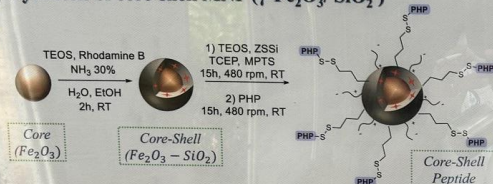
- Promote endosomal escape for diffusion of Magnetic Nanoparticles (MNPs)
- Induce cell death by magnetic hyperthermia combined with siRNA or chemotherapy agent delivery

By using:

Core (C)	Fe_2O_3
Core-Shell (CS)	$Fe_2O_3 - SiO_2$
Poly(Histidine) Peptides (PHP)	$C(TNP)_4H_4W$



2 Synthesis of core-shell MNP ($\gamma-Fe_2O_3 / SiO_2$)



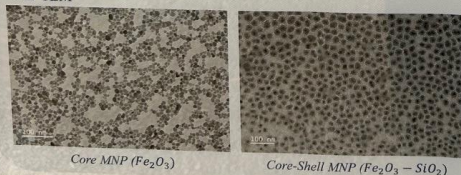
- ♦ Poly(histidine) peptide (PHP) → labile peptides for endosomal escape
- ♦ Zwitterions (ZSSi) → Colloidal stabilization

Characterization of the NP

- Dynamic Light Scattering (DLS)

NP	D_h (nm)	PDI	Zeta (mV)
Core	14.6	0.2	-50
Core-Shell (CS)	31.0	0.25	-33
CS-PHP	38.4	0.25	-28

- TEM



4 Confocal microscopy



- ✓ Diffusion of the peptides in the cytosol of cells
- Cleavage from MNP
- ✓ MNP aggregation
- Uncomplete endosomal escape

MCF-7 cells (Breast cancer) SHSY-5Y cells (Neuroblastoma)

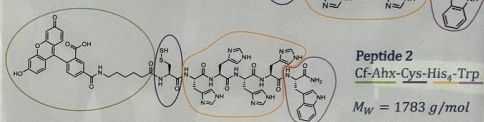
Zelus LSM710 inverted

3 Synthesis of peptide

Peptide 1

Cys-(TNP)-His₄-Trp

$M_w = 1009.3 \text{ g/mol}$



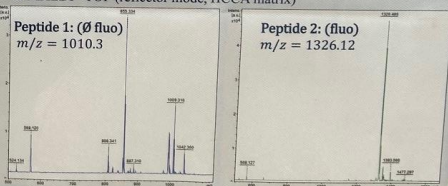
Peptide 2

Cf-Ahx-Cys-His₄-Trp

$M_w = 1783 \text{ g/mol}$

Characterization of the peptide

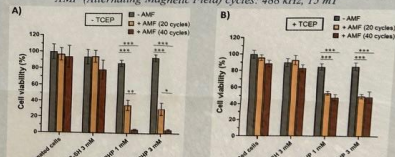
- HPLC: monopeak
- MALDI-TOF (reflector mode, HCCA matrix)



5 Magnetic hyperthermia

SHSY-5Y cells (Glioblastoma)

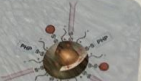
AMF (Alternating Magnetic Field) cycles: 488 kHz, 15 mT



- ♦ Better magnetic hyperthermia efficiency when functionalized with PHP
- ♦ TCEP treatment: to remove MNP on the cell surface
- ♦ CS-PHP at the surface of cells induce more cell death
- Optimization needed

Perspectives

- ♦ Attach doxorubicin for combined treatment
- ♦ Attach siRNA to silence anti-apoptotic genes
- ♦ SAXS analysis



Conclusion

- ✓ Synthesis of peptides PHP
- ✓ Functionalization of CS with the peptides
- ✓ Primary results in magnetic hyperthermia