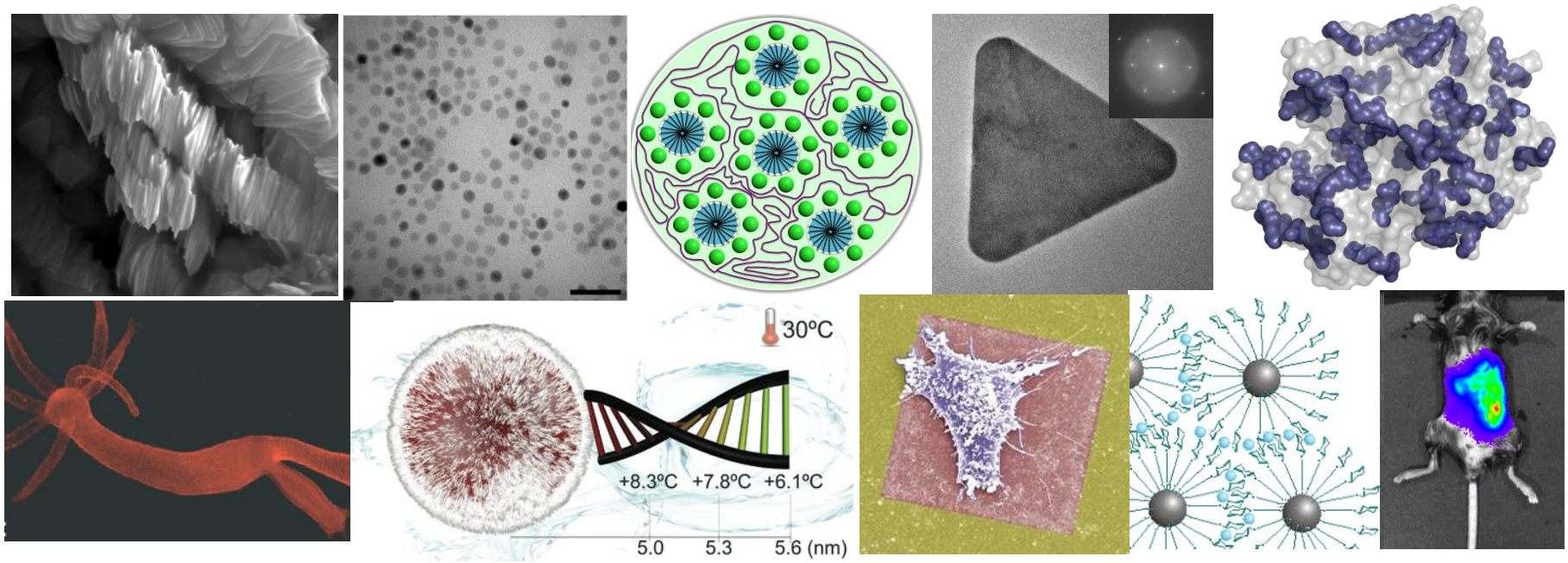
Nanoactuators for Therapy and Diagnosis



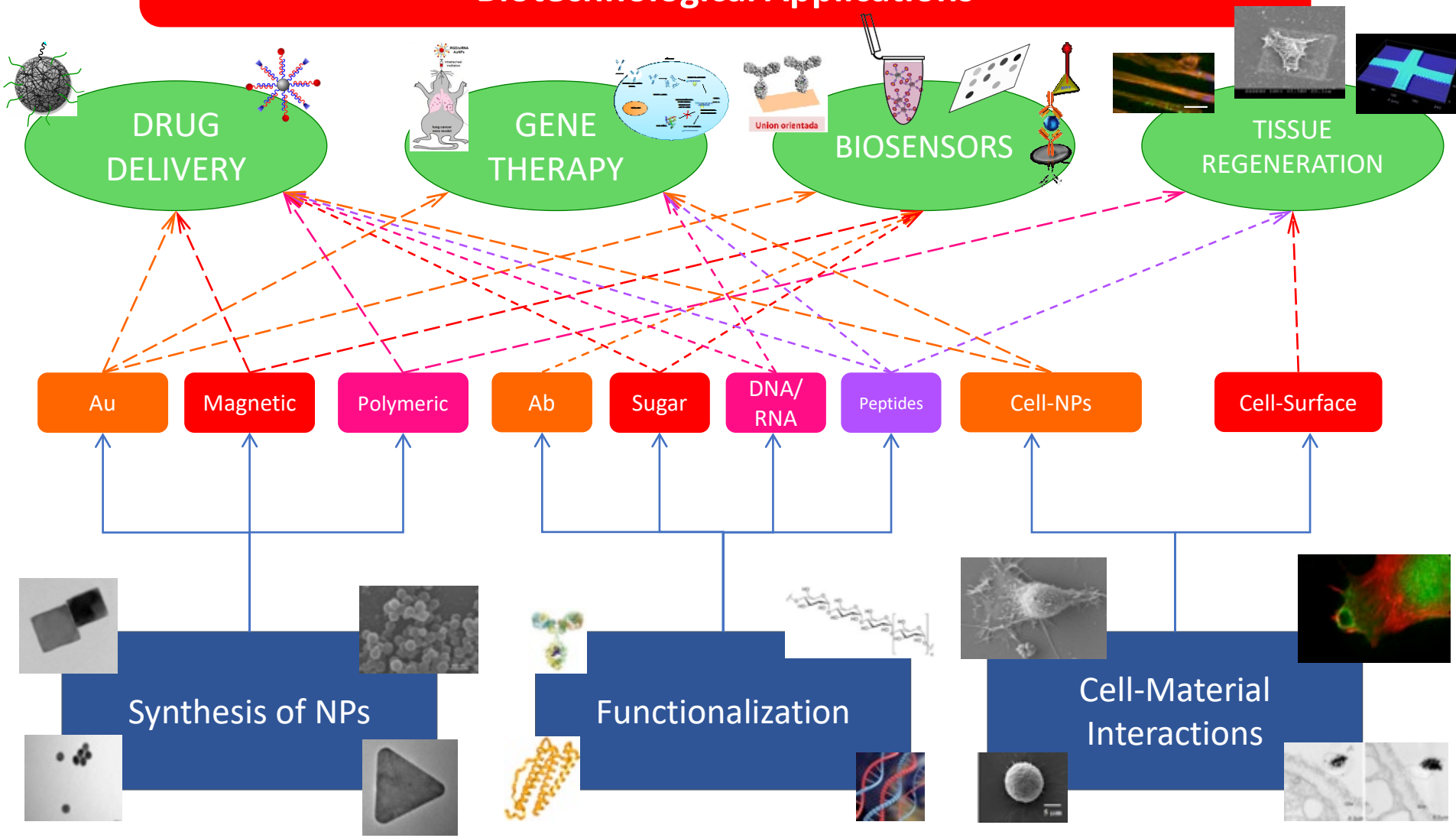
Prof. Jesús M. de la Fuente

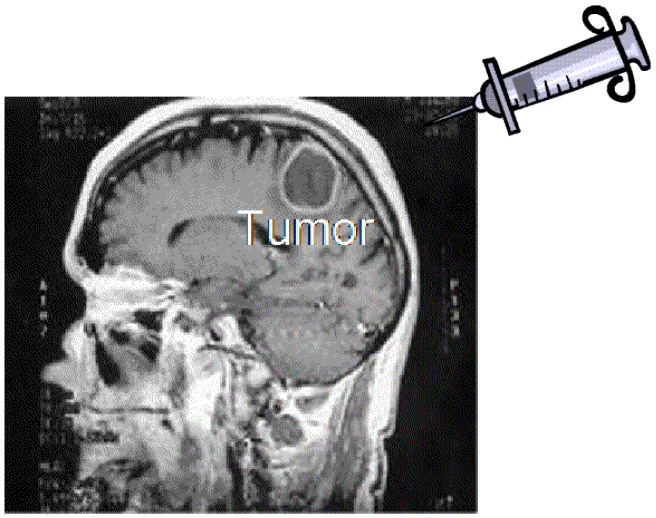
Instituto de Nanociencia y de Materiales de Aragón, CSIC/University of Zaragoza and CIBER-BBN, Spain

Bionanosurf

INMA
INSTITUTO DE NANOCIENCIA Y MATERIALES DE ARAGÓN

Our main interest: Design of Multifunctional Nanomaterials for Biotechnological Applications



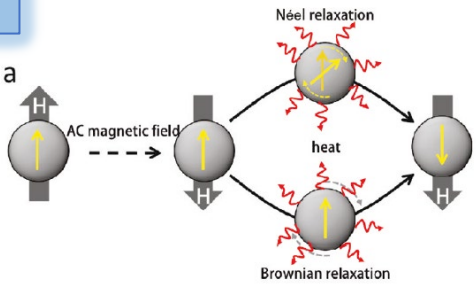


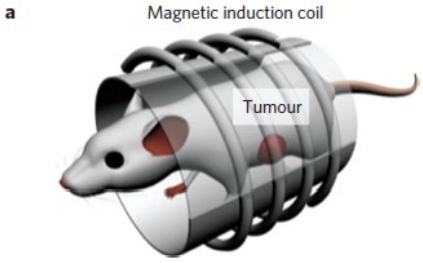
Magnetic Hyperthermia

Approved by EMA

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THE NANOMEDICINE COMPANY



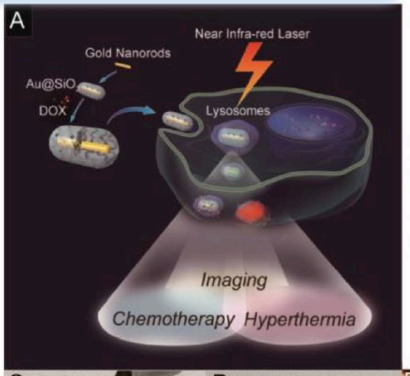


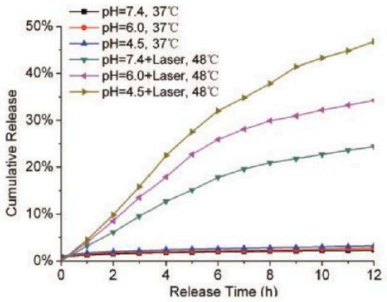


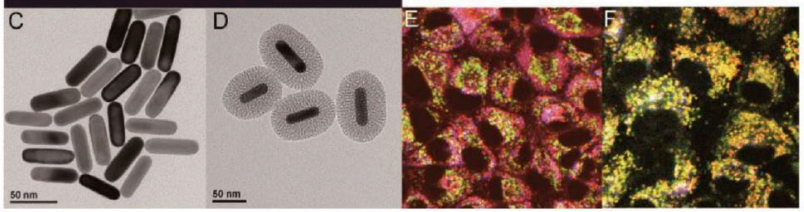
Lee *et al Nat Nanotechnol.* **2011**, *6*, 418

Photothermal Therapy

Nanospectra

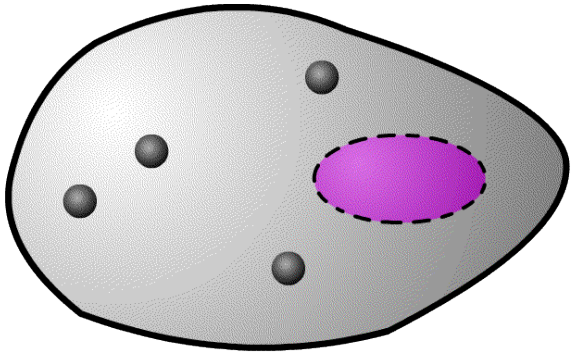




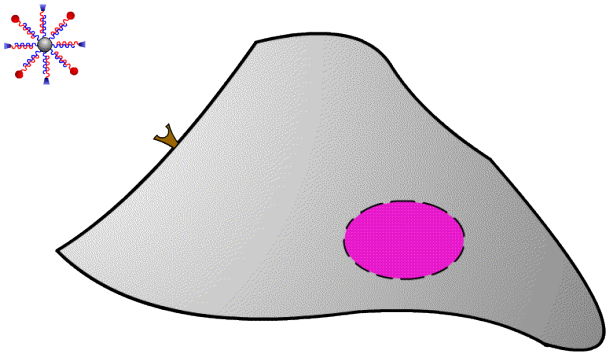


Zhang *et al Theranostics.* **2013**, *3*, 223

Magnetic Hyperthermia



Traditional Hyperthermia



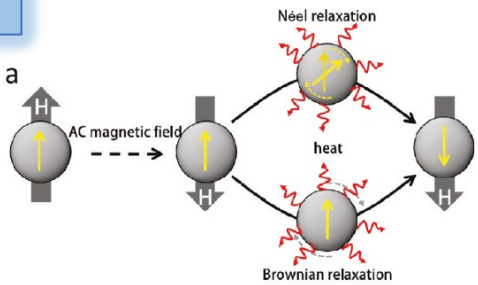
OUR Strategy

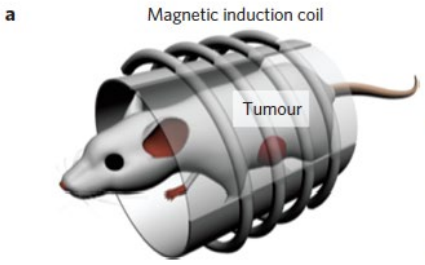
Magnetic Hyperthermia

Approved by EMA

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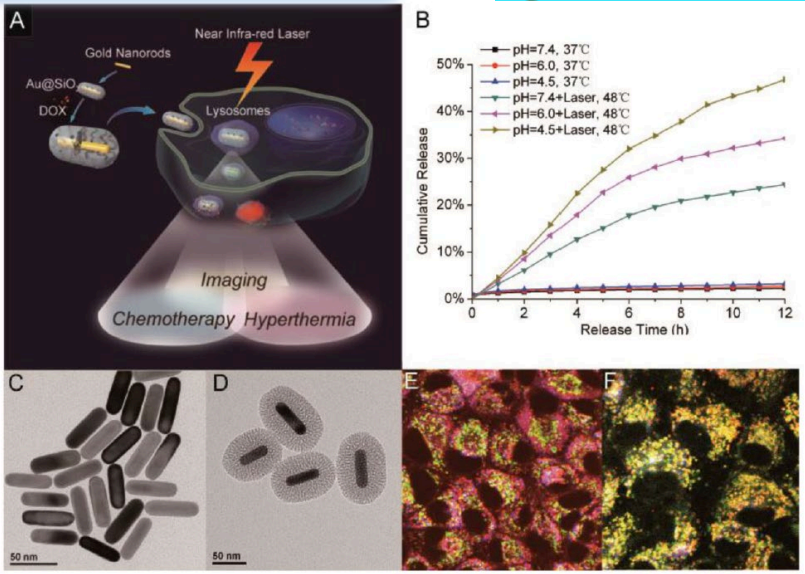




Lee *et al Nat Nanotechnol.* **2011**, *6*, 418

Photothermal Therapy

Nanospectra

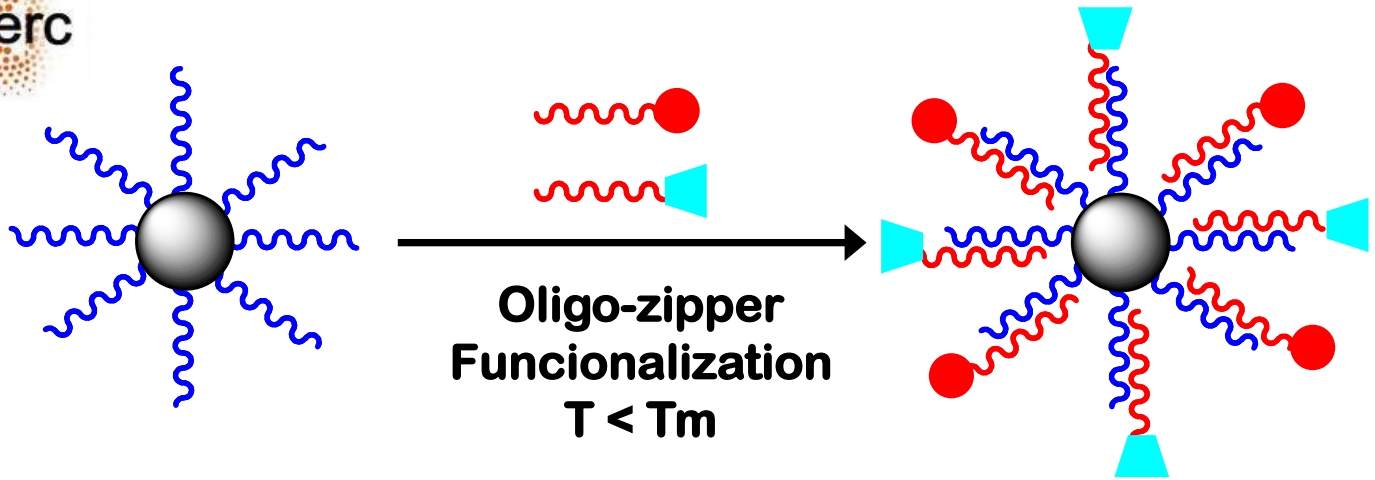


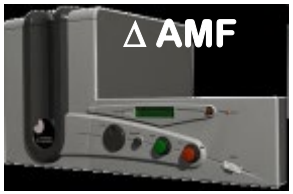
Zhang *et al Theranostics.* **2013**, *3*, 223

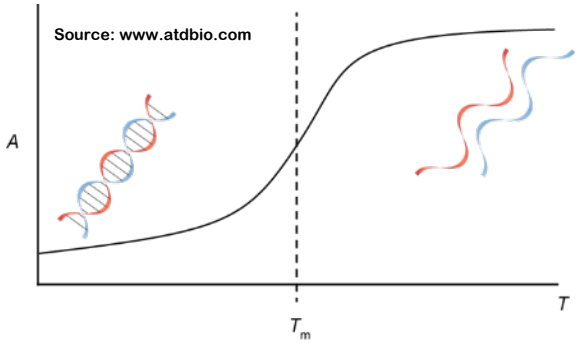
MAGNETIC NPs FUNCTIONALIZED WITH DNA
Functionalization and Controlled Release



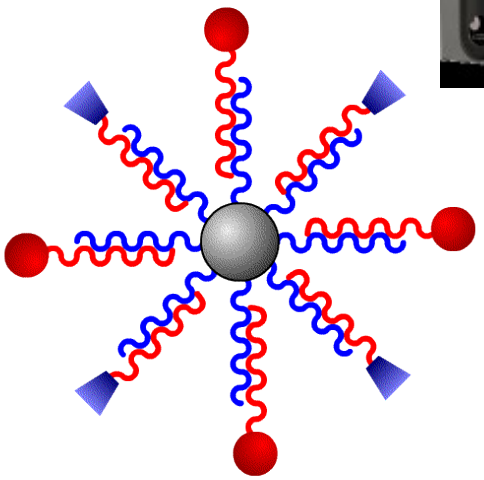
M Moros







Oligo-unzipper
Release
T > Tm



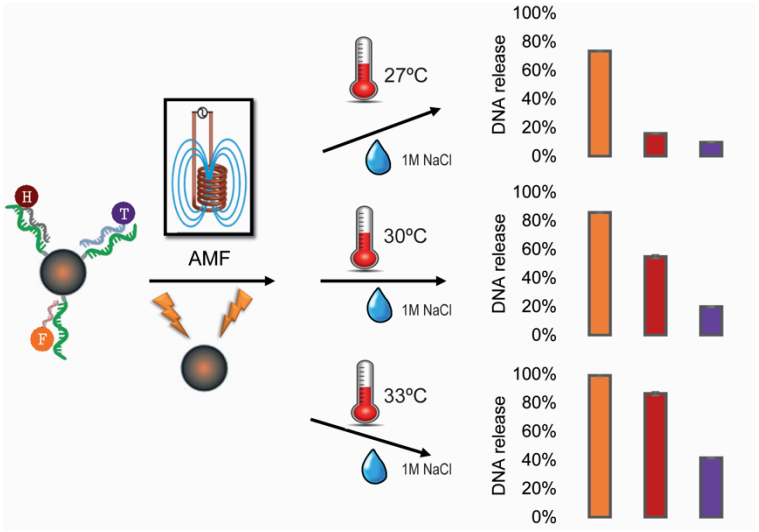
dsDNA is very rigid

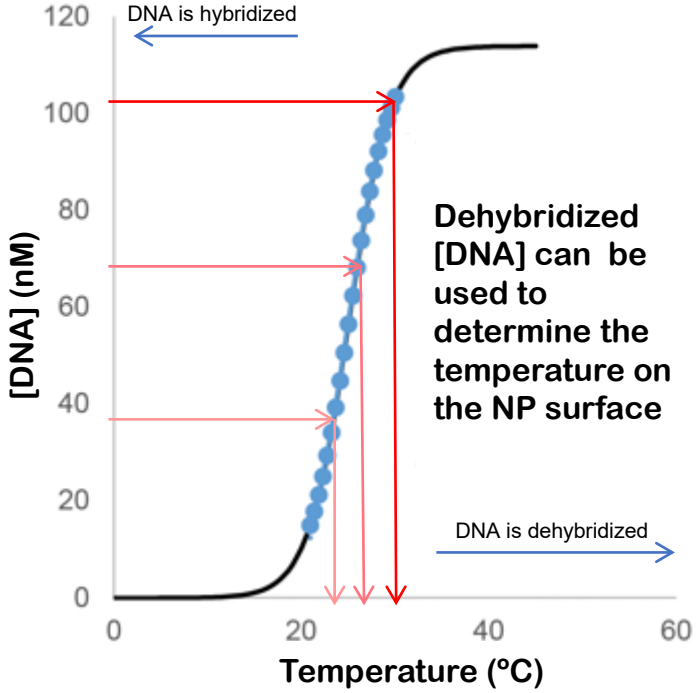
•Tm: Temperature at which a DNA double helix dissociates into single strands

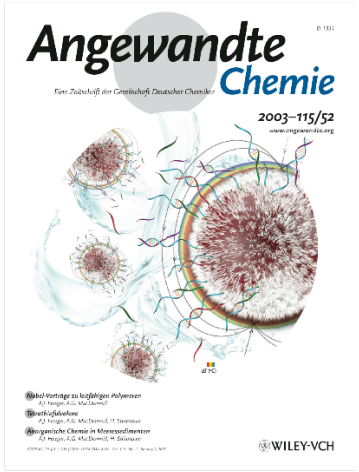
P. Del Pino *et al.* PCT, *WO2012/150373*

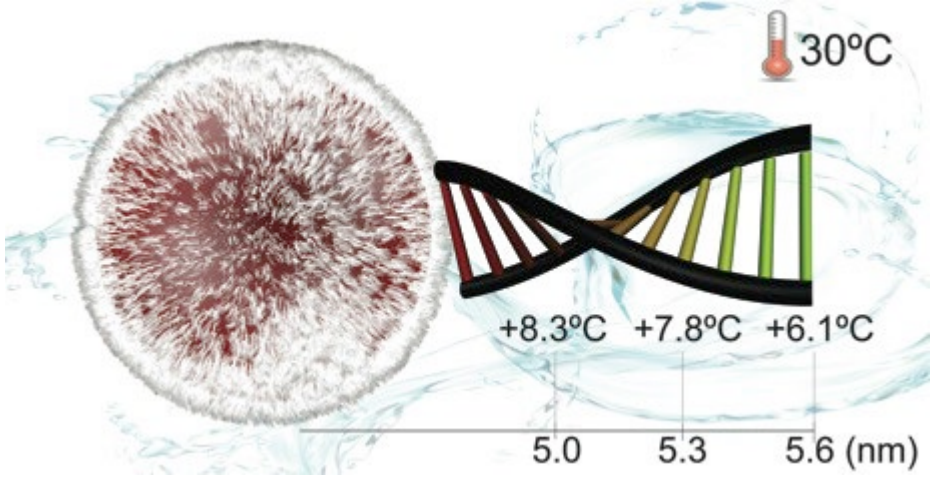
MAGNETIC NPs FUNCTIONALIZED WITH DNA
Controlled Release

Temperature Gradient induced by Magnetic Hyperthermia





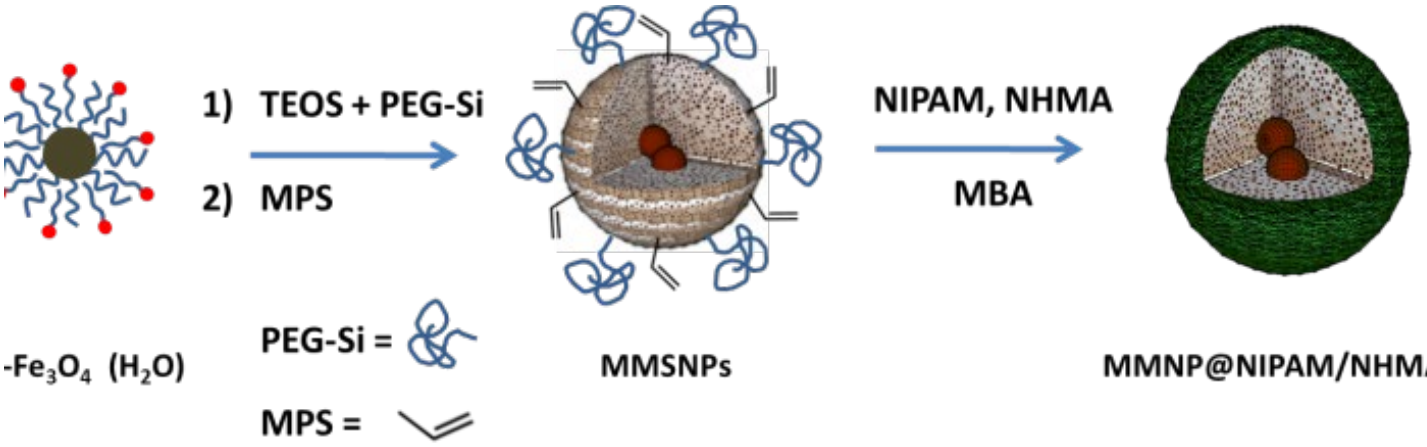


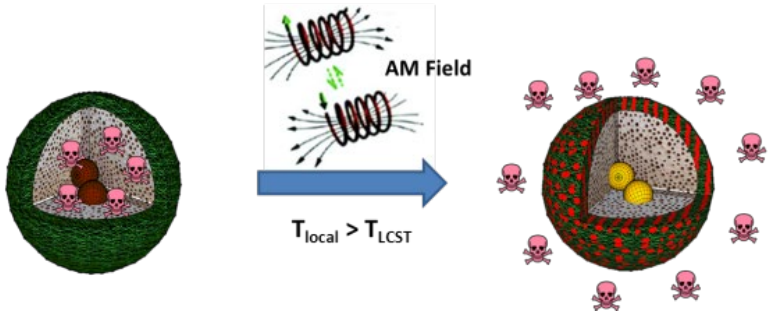


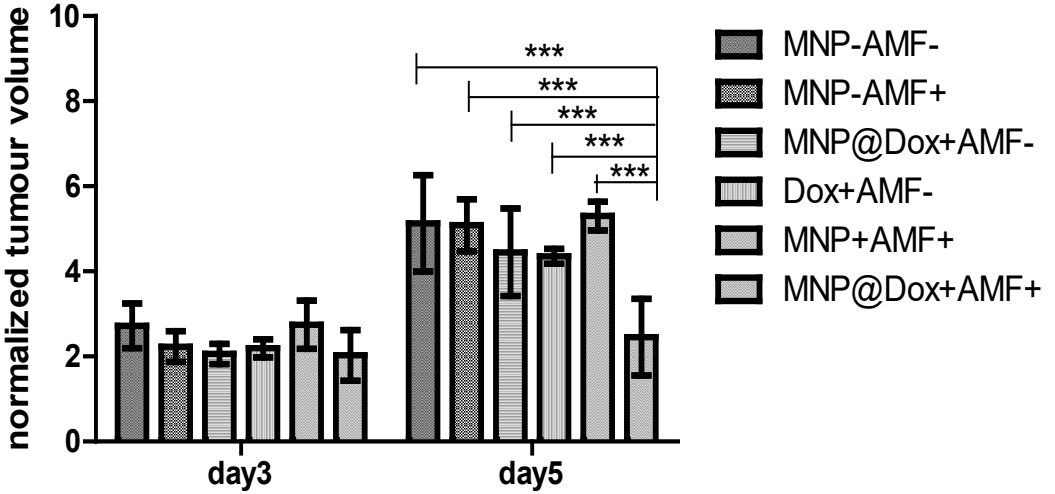
J. Dias *et al. Angew. Chem. (2013)*

Magnetic HT *in vivo*

Silica Mesoporous Materials





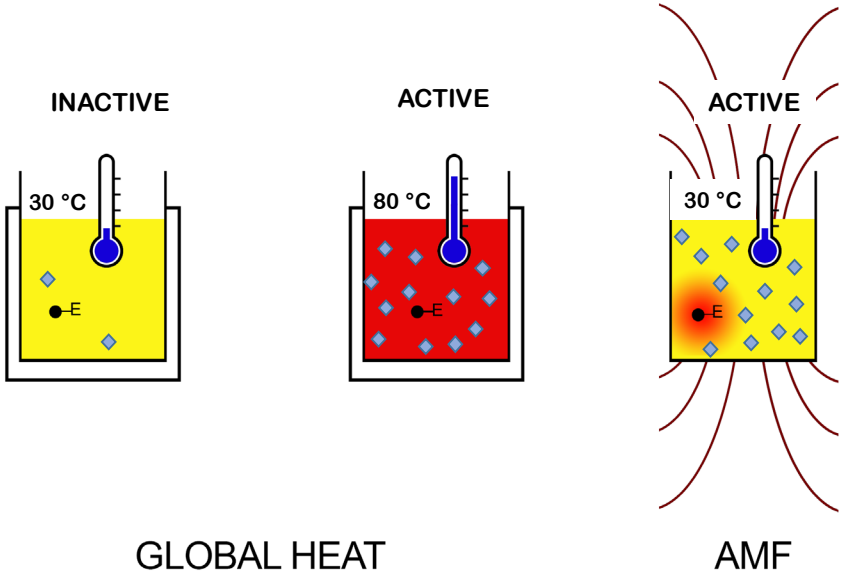


Guisasola et al., Langmuir (2015)

Guisasola & Asin et al., ACS Appl Mater & Interf (2018)

In collaboration with Prof M. Vallet (UCM)

Biocatalysis induced by Hyperthermia

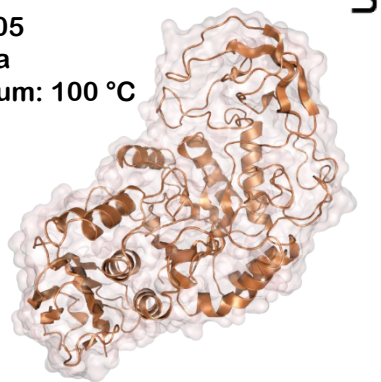


After enzymatic immobilization, the enzyme is activated by the heat produce by MHT, without detection of any external heating

α-Amylase (AMY)

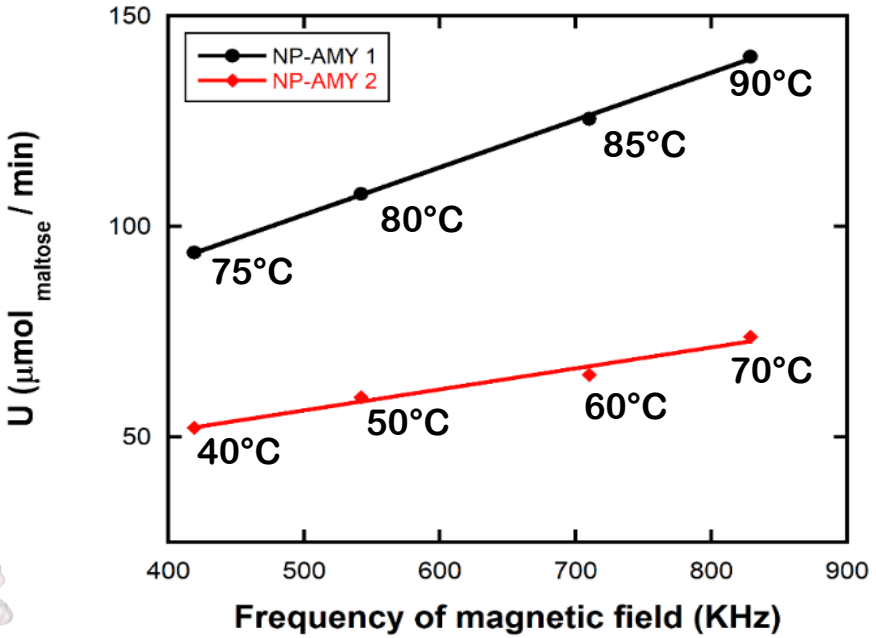
Endo-enzyme: cleaves the glycosidic bond within starch in the non-crystalline regions (cleaves a- 1-4 linkage). Products are DEXTRINS (small starch units), MALTOSE and MALTOTRIOSE

pKI 6,05
55 KDa
Optimum: 100 °C



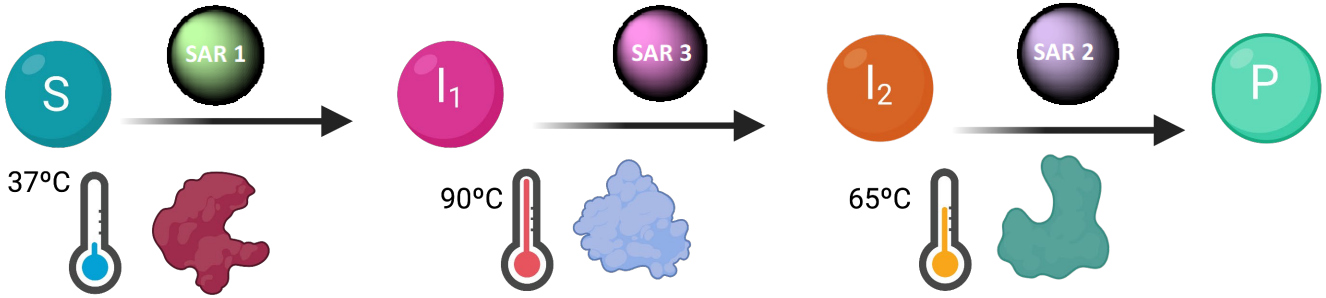


V Grazú & I Armenia

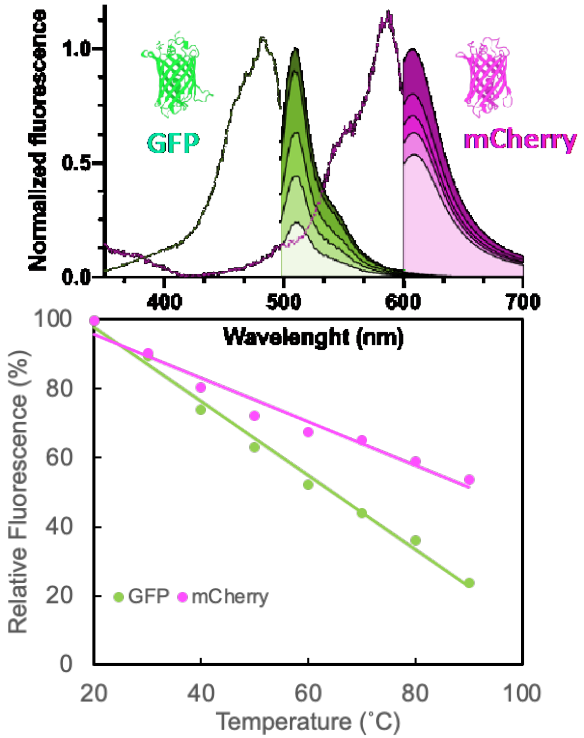


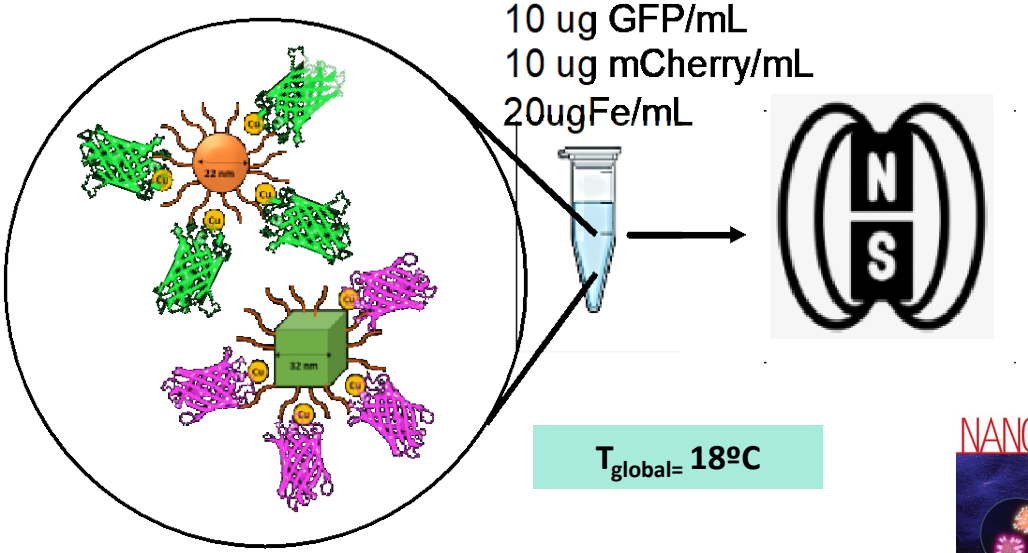
Armenia *et. al J. Colloid and Interface Science (2019)*
S. Correa *et al* Plos ONE (2019)

MAGNETIC HEATING FOR TUNING ENZYMATIC CASCADES



SAR. Specific Absortion Rate (W/g)

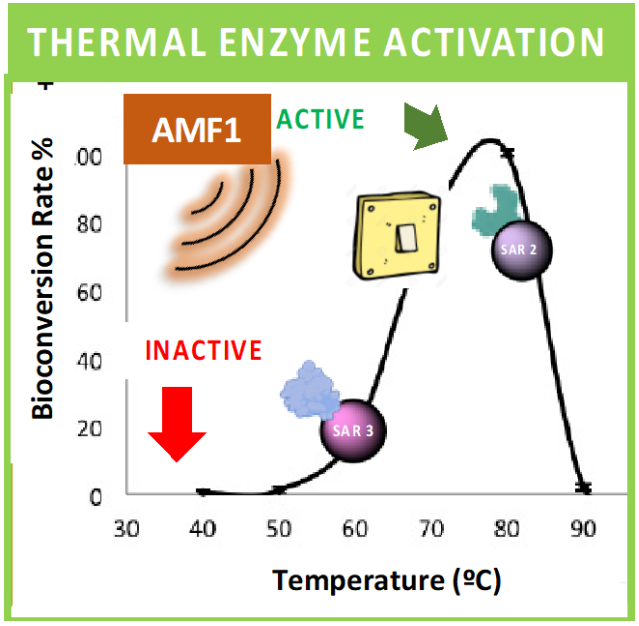


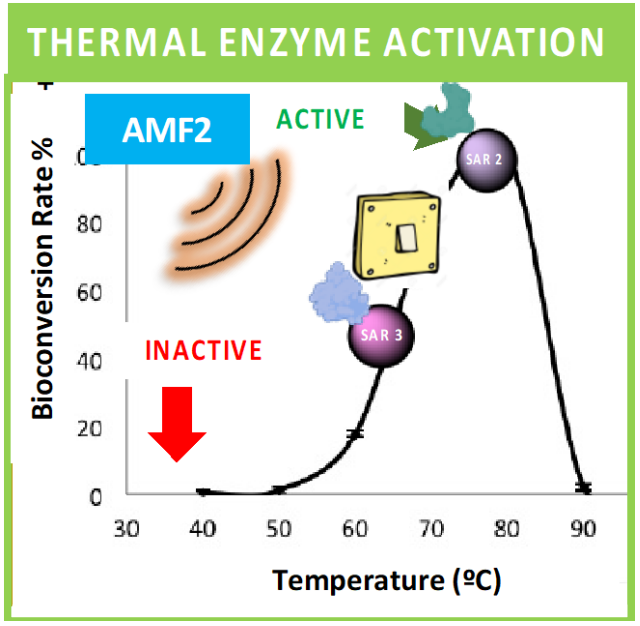


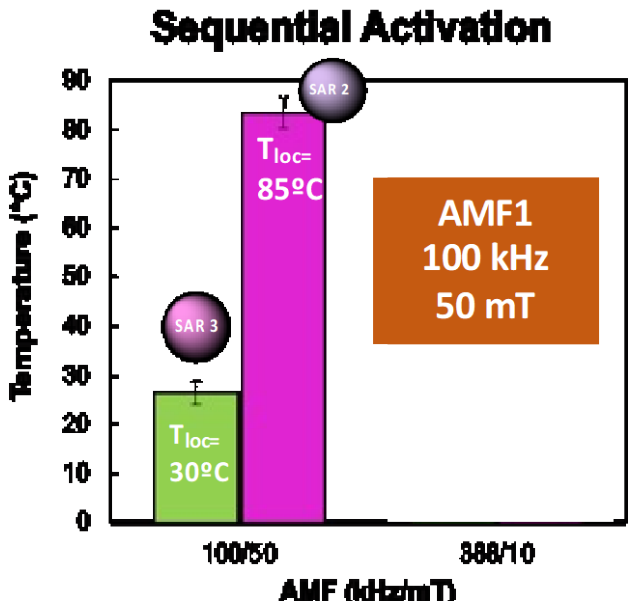
Ovejero, J.; Armenia I. *et. al Nano Lett. (2019)*

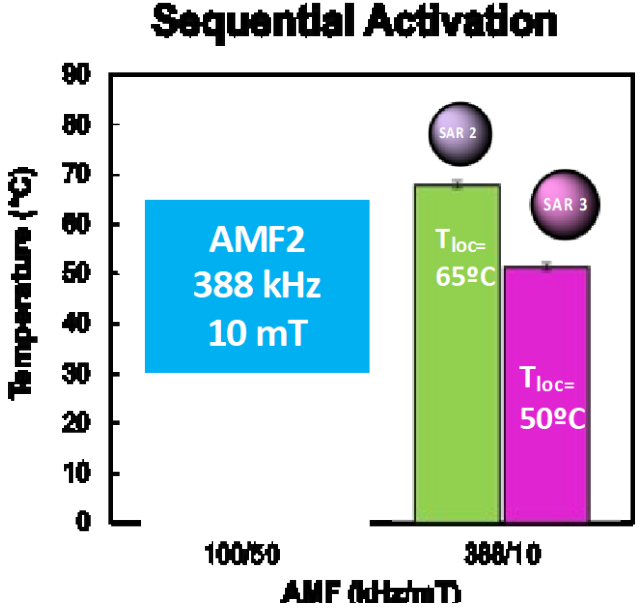


Biocatalysis induced by Hyperthermia - Bioprocesses



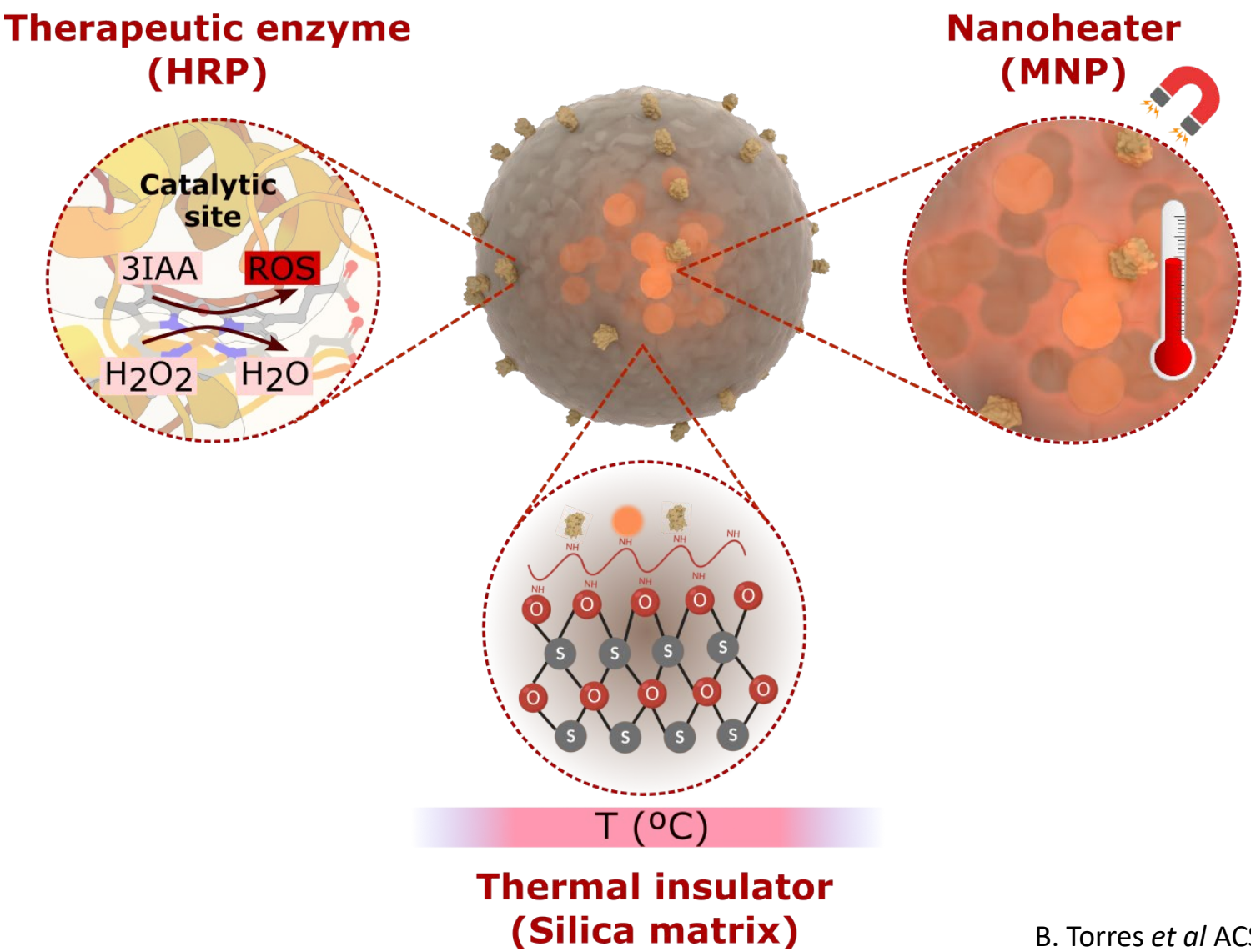






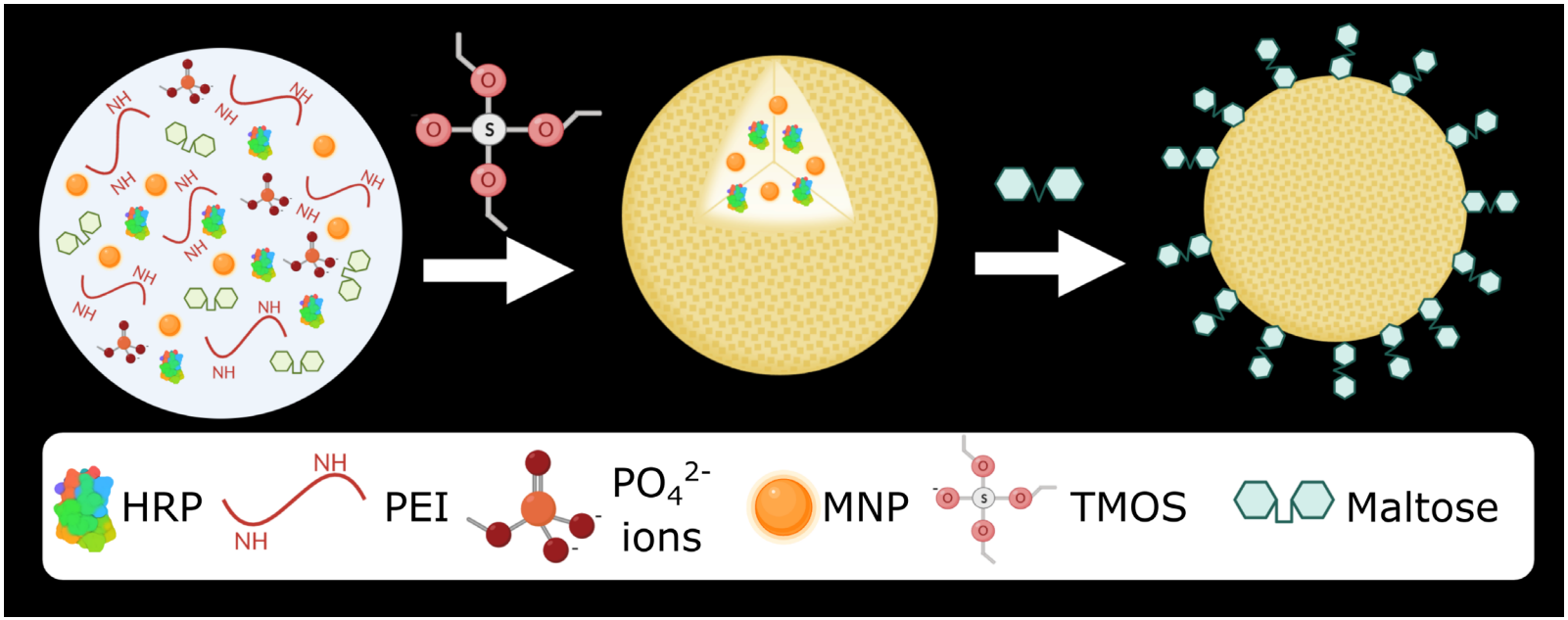
Biocatalysis induced by Hyperthermia - Enzymatic Therapy

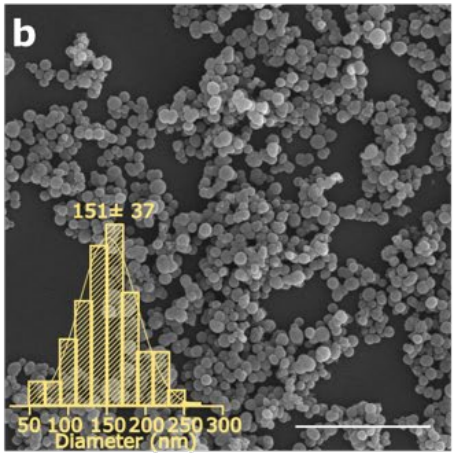
CONTROL OF ENZYME ACTIVITY BY NANOACTUATION

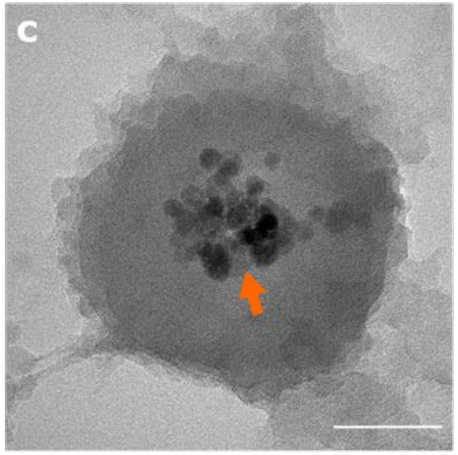


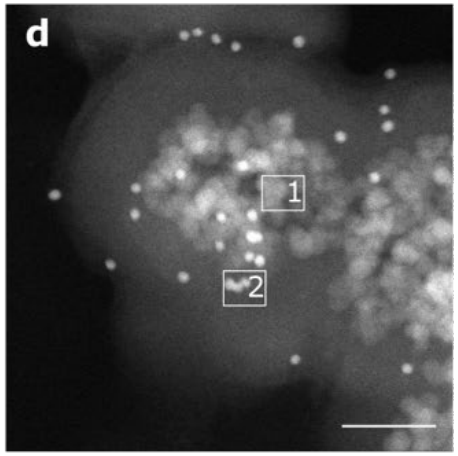
B. Torres *et al* ACS Nano 2023

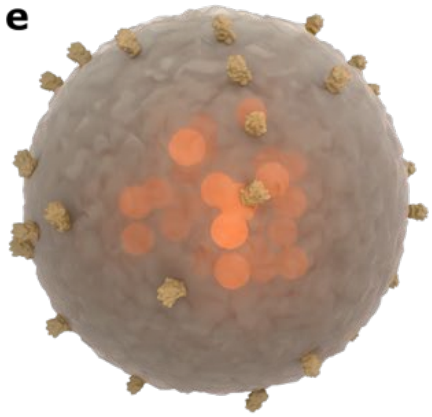
Biocatalysis induced by Hyperthermia - Enzymatic Therapy





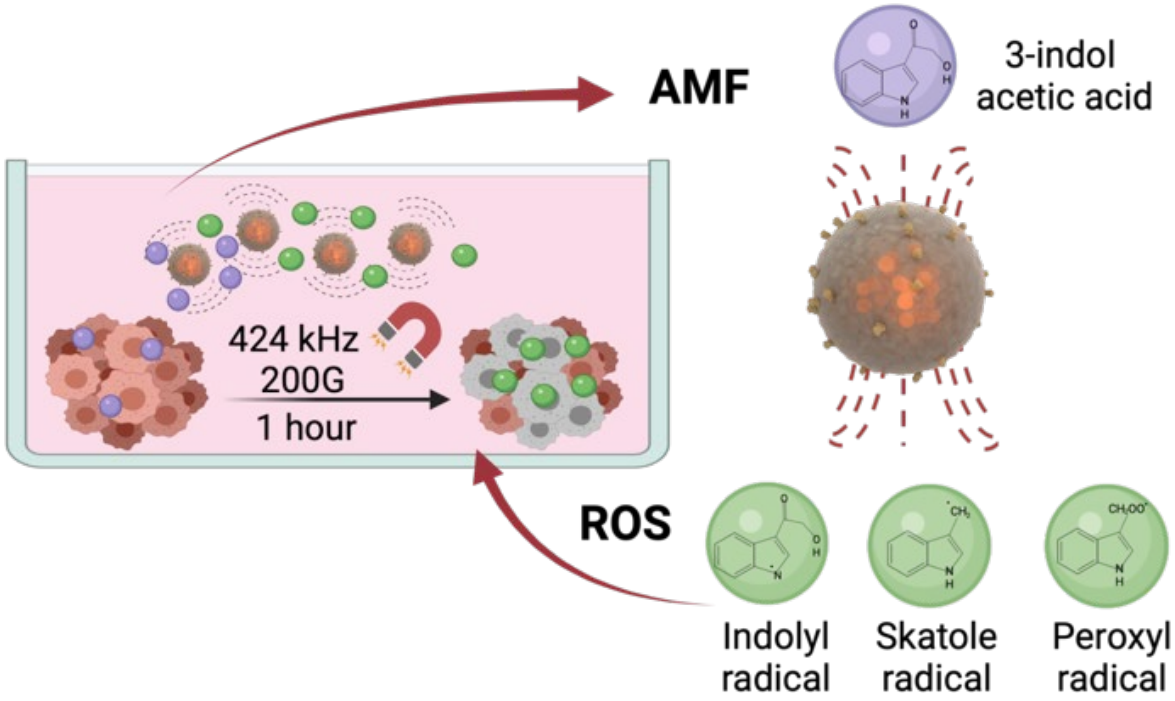


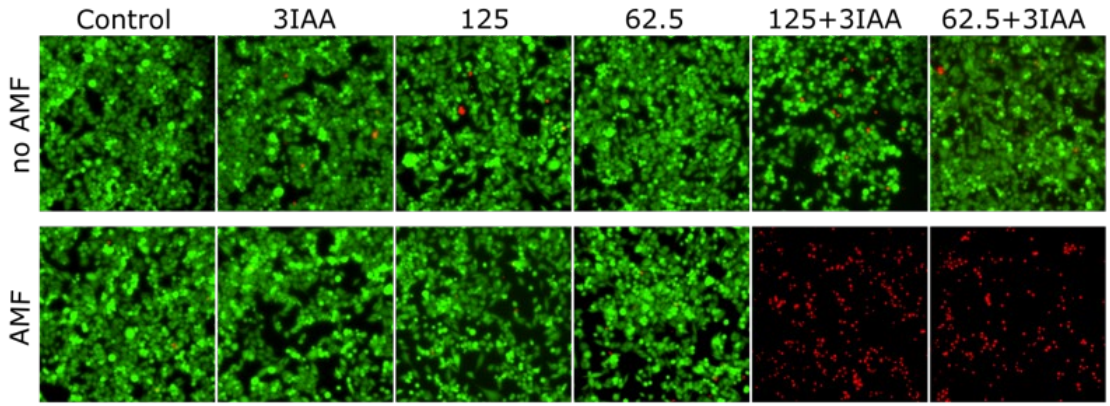


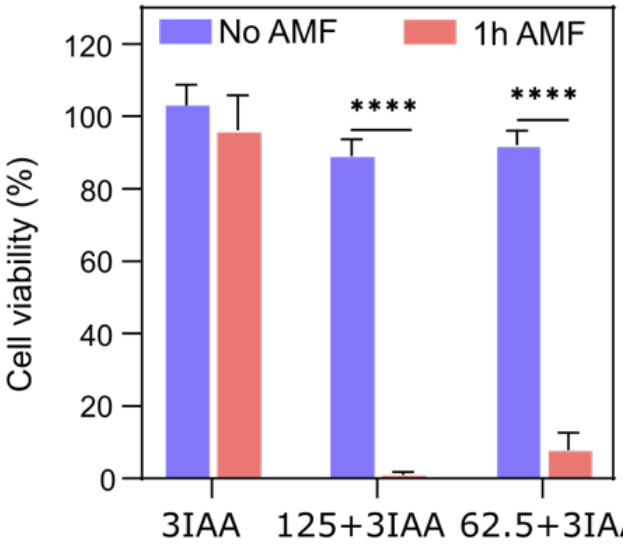


B. Torres *et al* ACS Nano 2023

Biocatalysis induced by Hyperthermia - Enzymatic Therapy

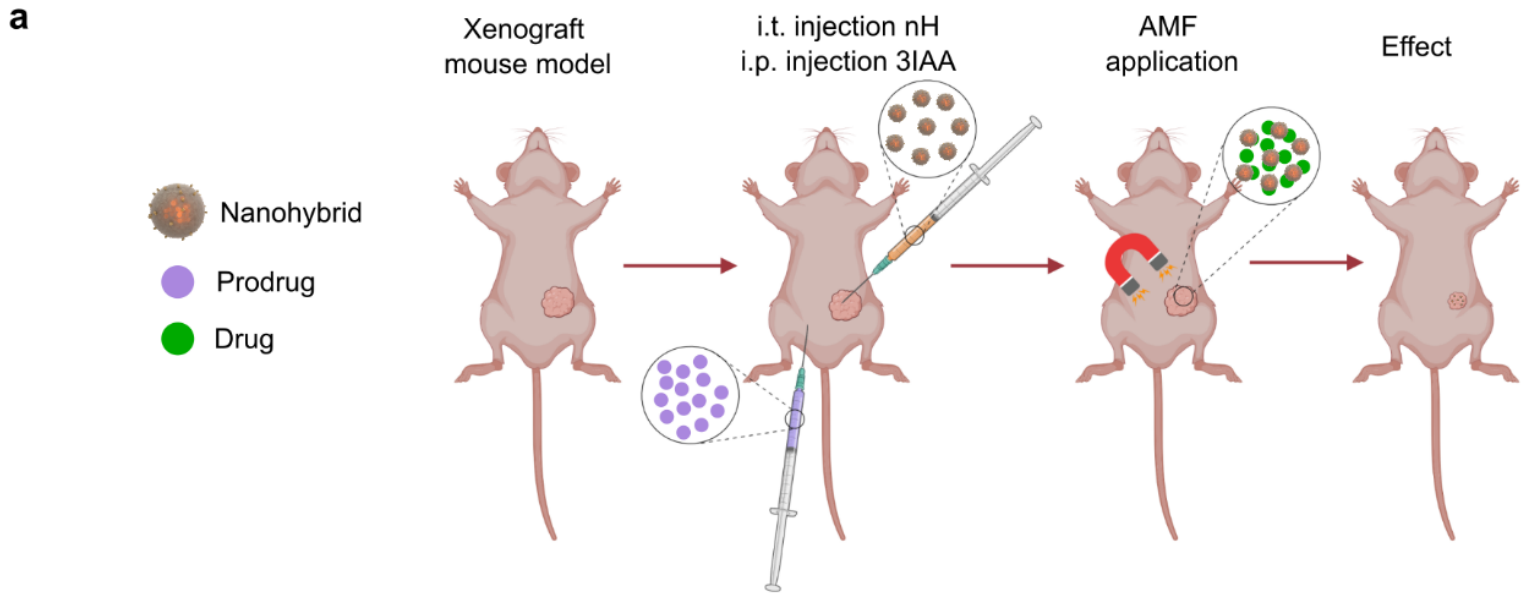


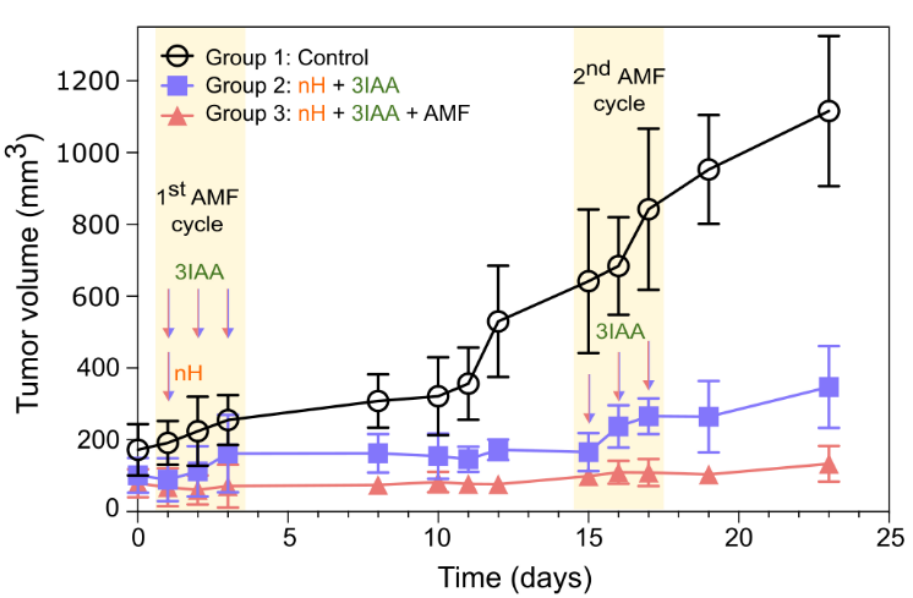


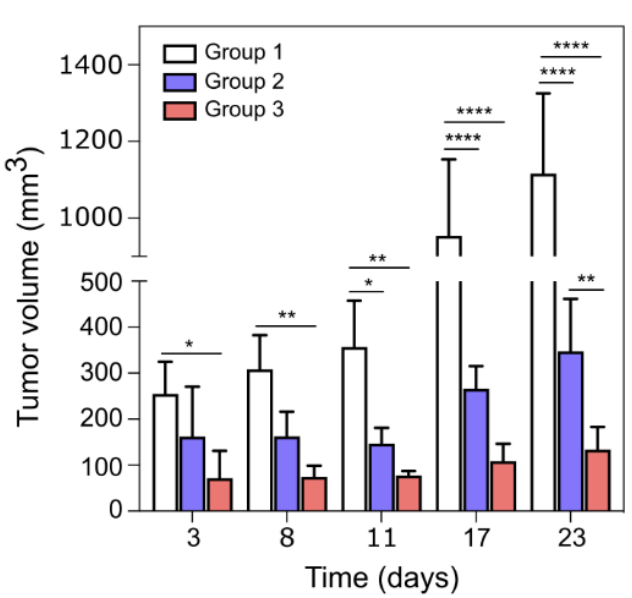


B. Torres *et al* ACS Nano 2023

Biocatalysis induced by Hyperthermia - Enzymatic Therapy





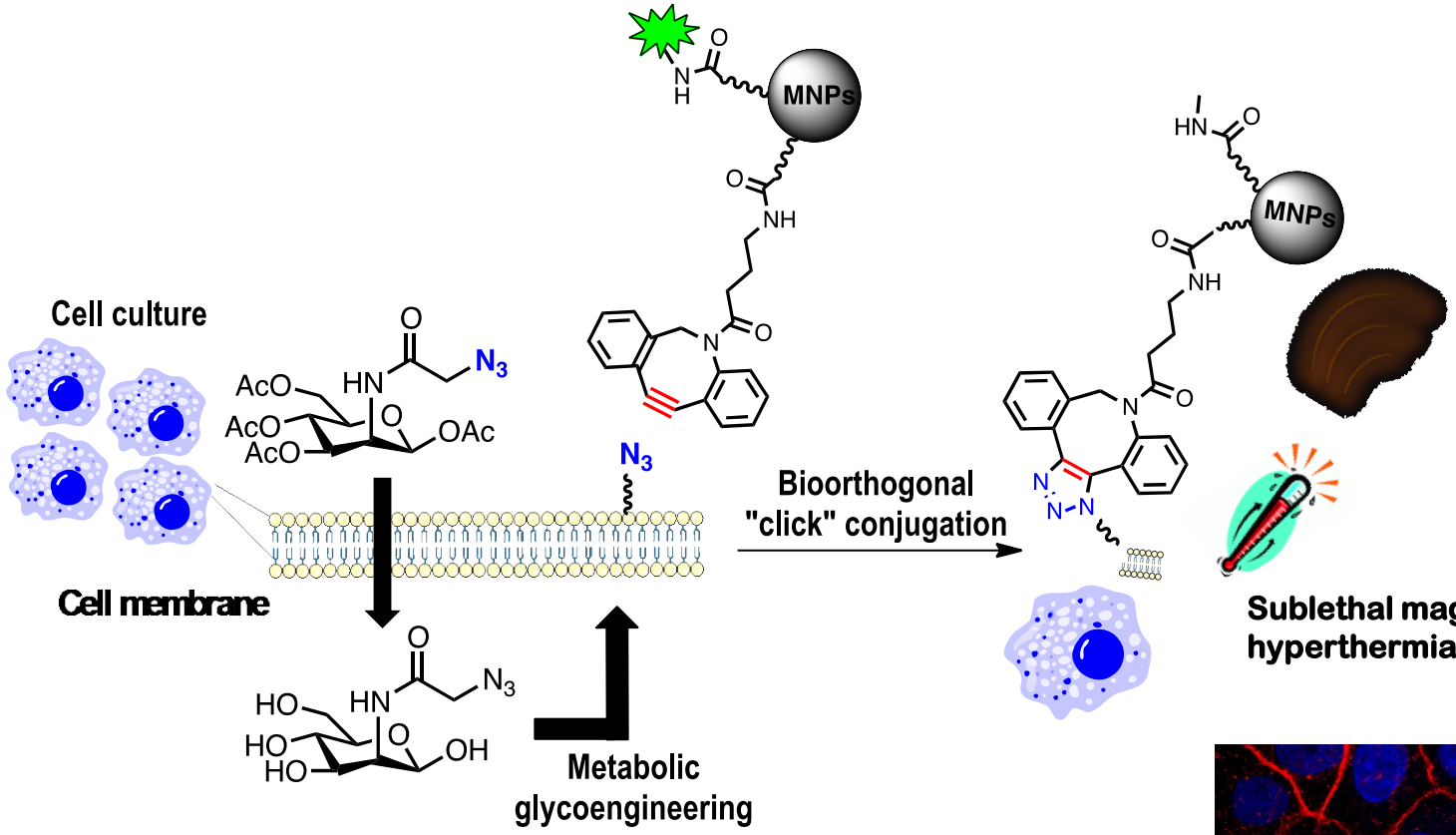


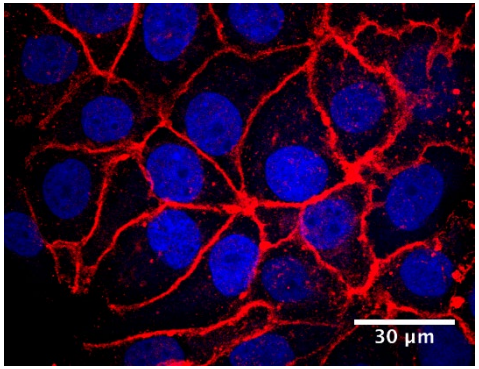
B. Torres *et al* ACS Nano 2023

Magnetic Nanoheater for Remote Control over the Permeabilization of Cellular Membranes.



R Fratila





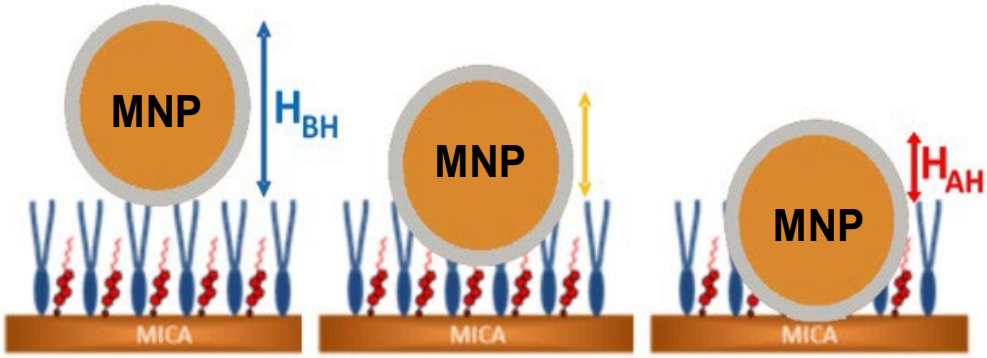
M-era.Net

J. Idiago-López *et al. Nanoscale Advances* (2021)

Magnetic Nanoheater for Remote Control over the Permeabilization of Cellular Membranes.



P Cea



Bare mica

(ii)

LB

35 mN·m^{-1}

DPPC: Chol

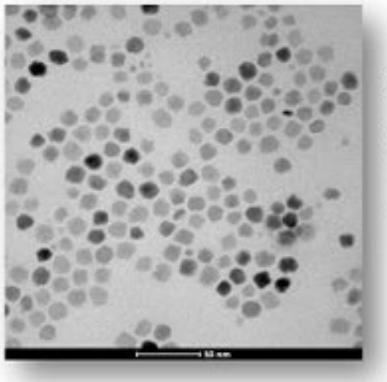
(iii)

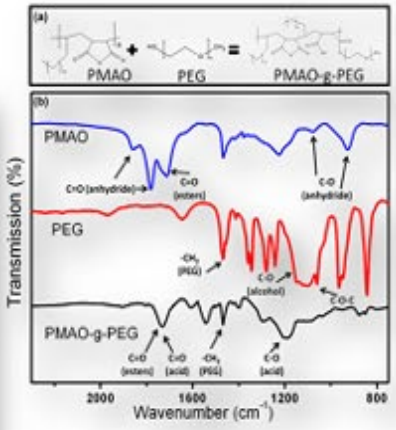
LB

15 mN·m^{-1}

MNPs on DPPC: Chol

(i)





(iv)

B = 252 Gauss

t = 45 min

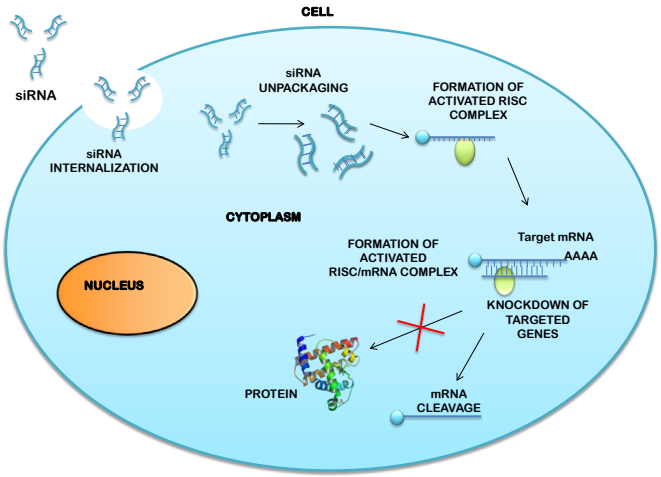
MNPs embedded into DPPC: Chol

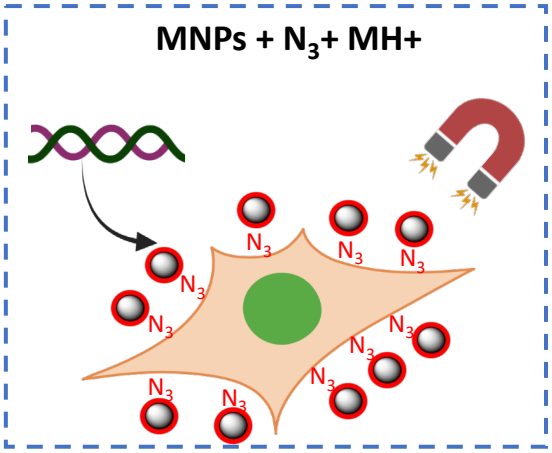


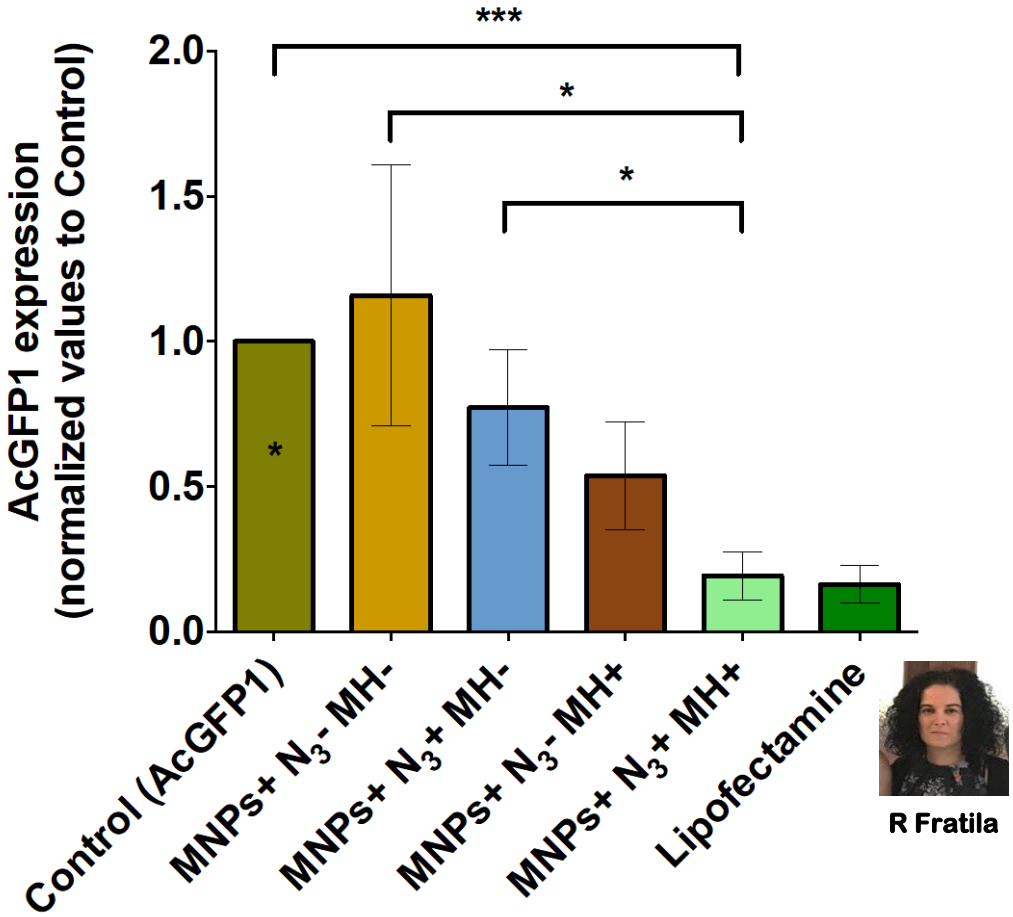
S. Ruiz *et. al Colloids and Surfaces B: Biointerfaces* (2020)

❖ ADVANCED THERAPIES: Local Heating induced by Hyperthermia

Magnetic Nanoheater for Remote Control over the Permeabilization of Cellular Membranes (siRNA Gene Silencing).







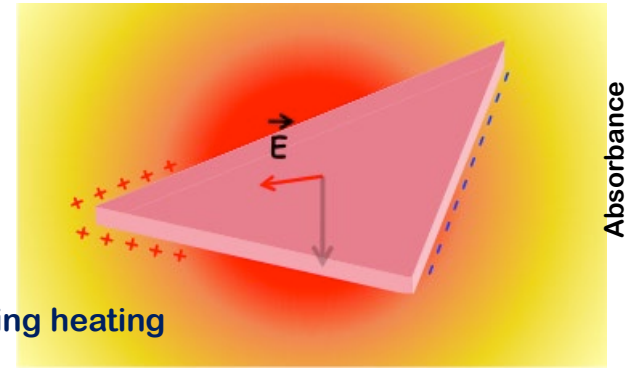
R Fratila

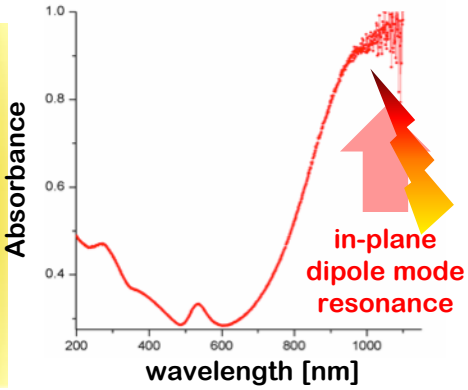
J. Idiago-López *et al. Nanoscale Advances* (2021)
J. Idiago.López *et al. Bioconjugate Chemistry* (2022)

Photothermal Therapy

for asymmetric nanoparticles ➔

700 – 1100 nm (biological window!!!)



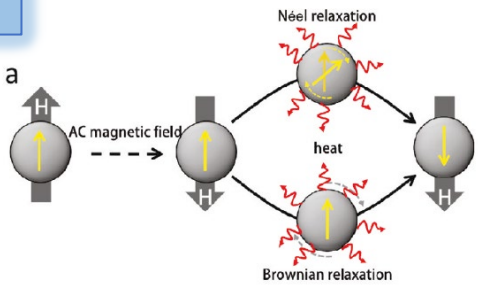


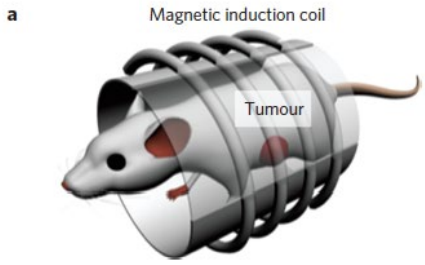
e⁻ cloud gained energy → hot crystal lattice → surrounding heating

Magnetic Hyperthermia

Approved by EMA

magforce®
THE NANOMEDICINE COMPANY





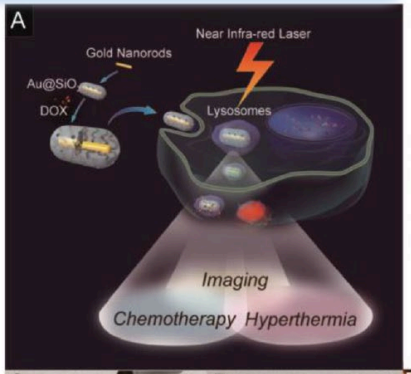


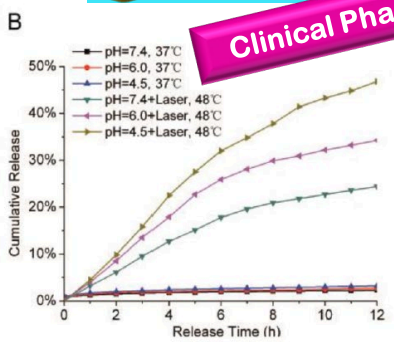
Lee *et al Nat Nanotechnol.* **2011**, *6*, 418

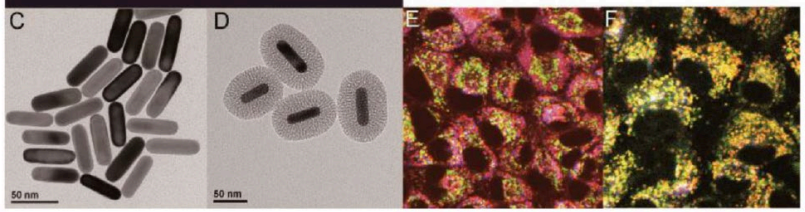
Photothermal Therapy

Nanospectra

Clinical Phase



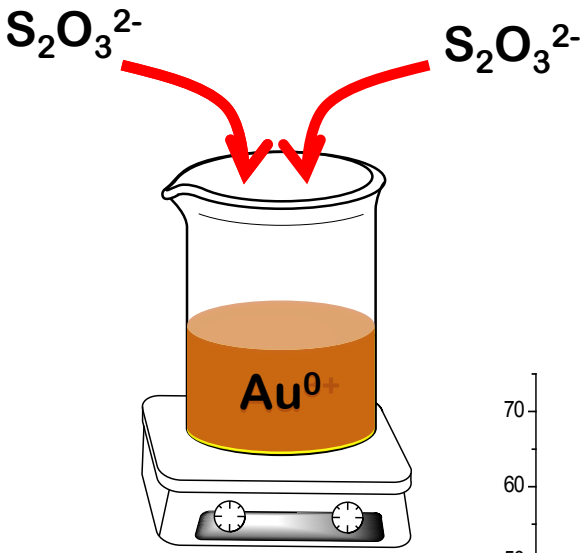


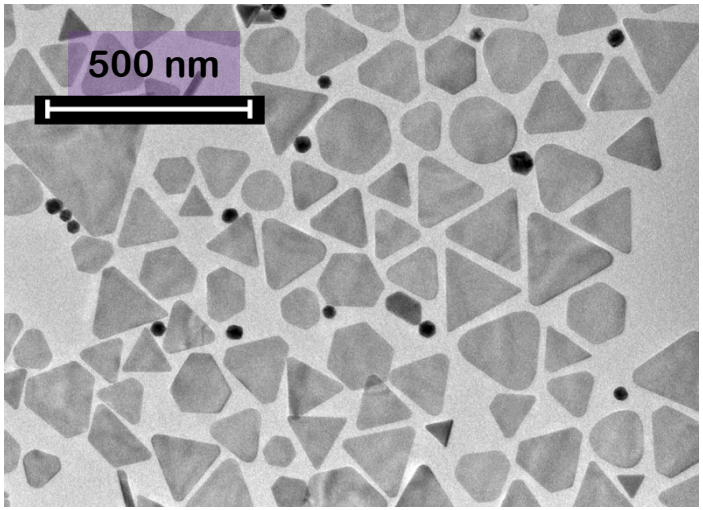


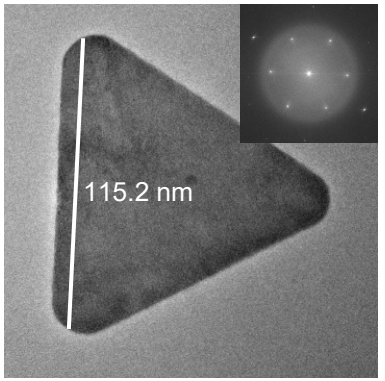
Zhang *et al Theranostics.* **2013**, *3*, 223

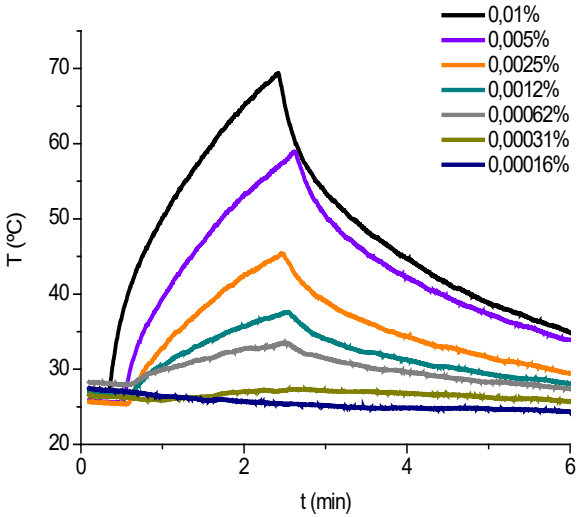
Synthesis of NanoPrisms

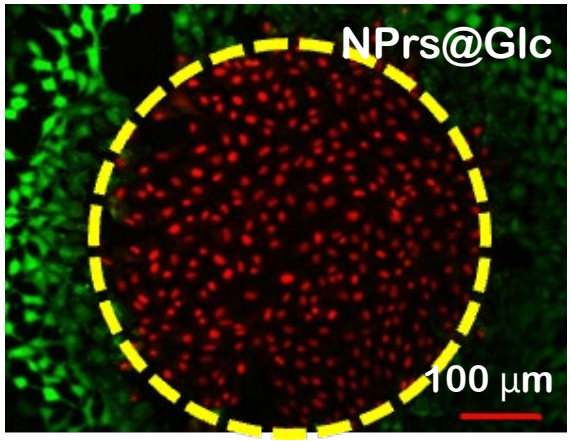
$Au^{3+} + S_2O_3^{2-}$ (two additions) → **NANOPRISMS**







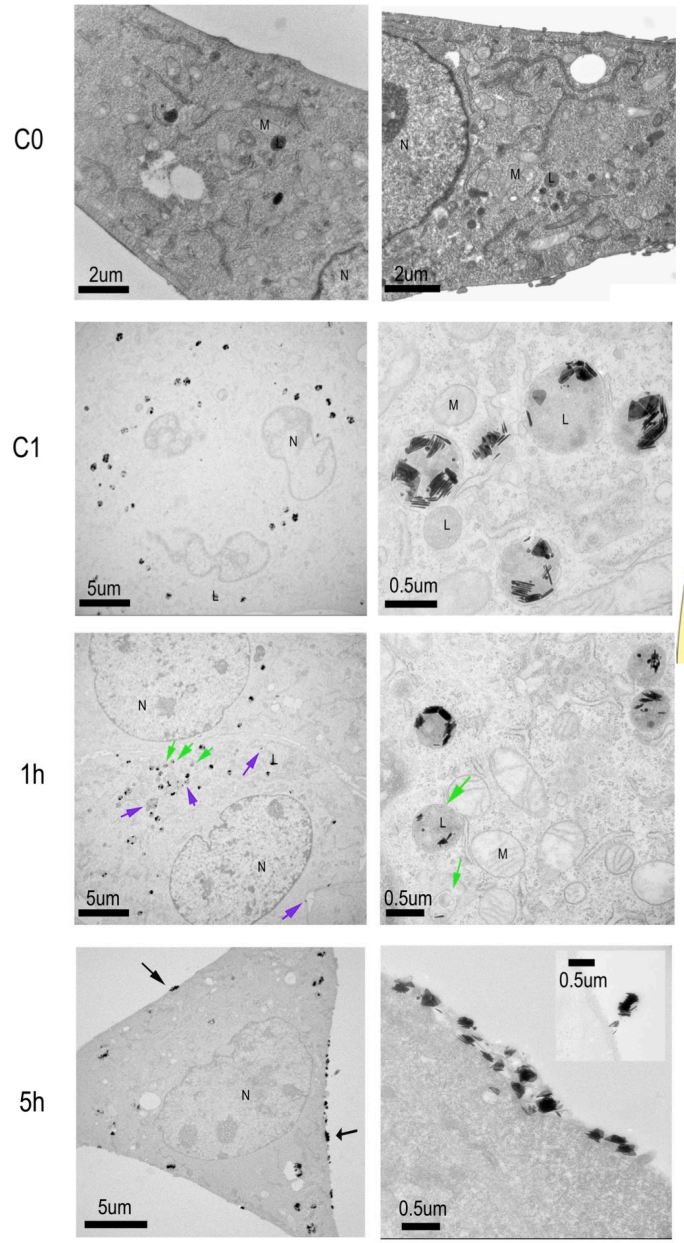


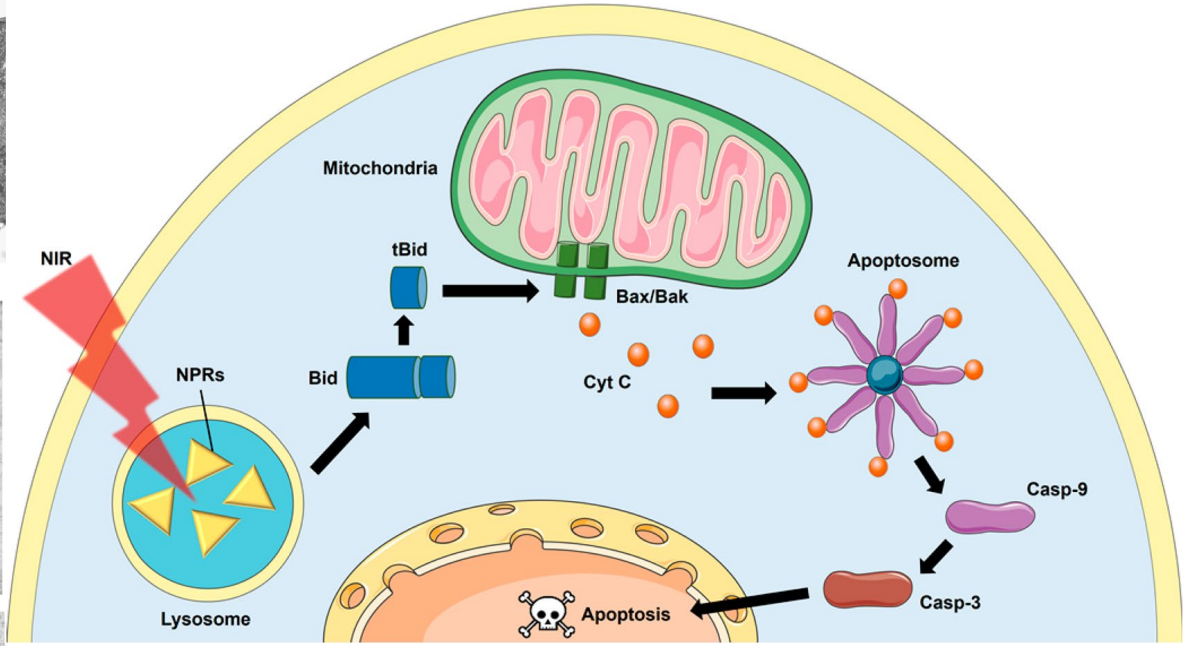


Dead/Live kit: **Red:** Etidium Bromide (Dead cells)
Green: Calcein (Living cells)

B. Pelaz et al. Langmuir (2012)

Deciphering Molecular Mechanism of Apoptosis





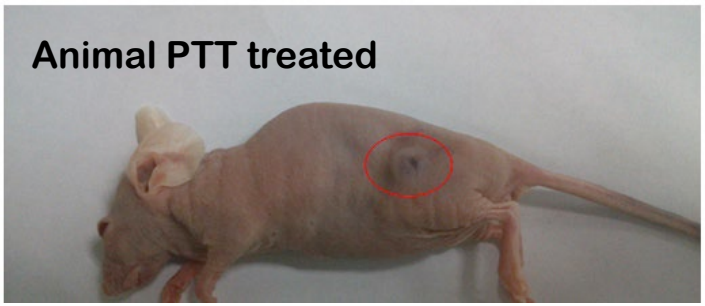
NPrs are localized in lysosomes. After irradiation, NPrs are released to cell cytosol. Lysosomal leakage can induce cathepsins release able to cleave Bid to tBid

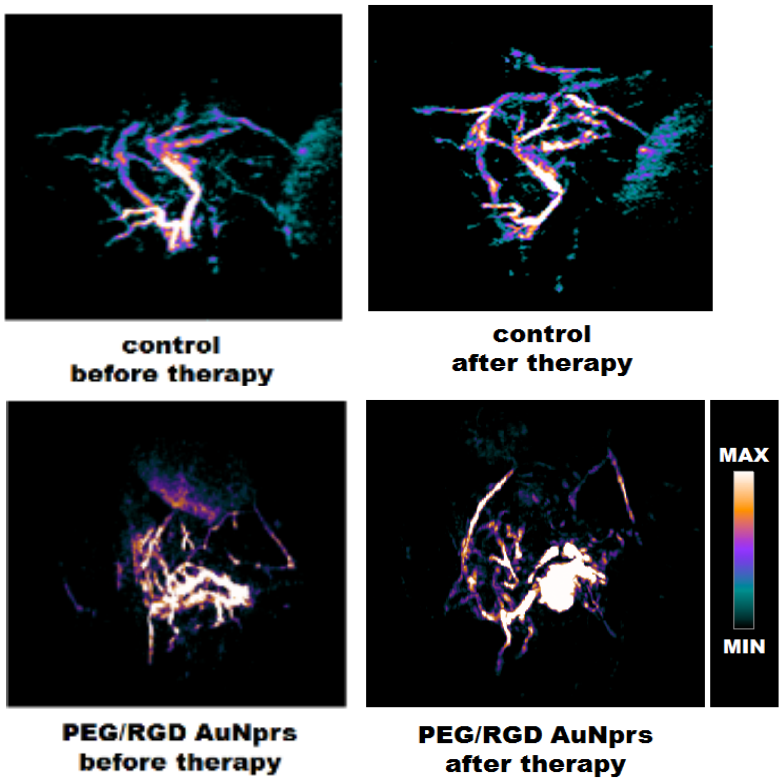
C0: Control Cells
C1: NPrs+, Laser-

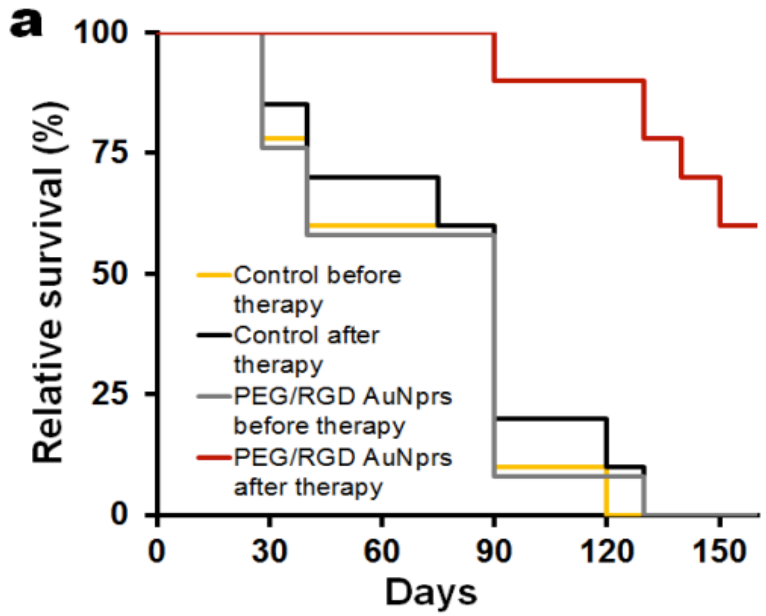
M. Perez et al. ACS Nano (2015)
M. Perez et al. Part. & Fiber Toxicol. (2018)

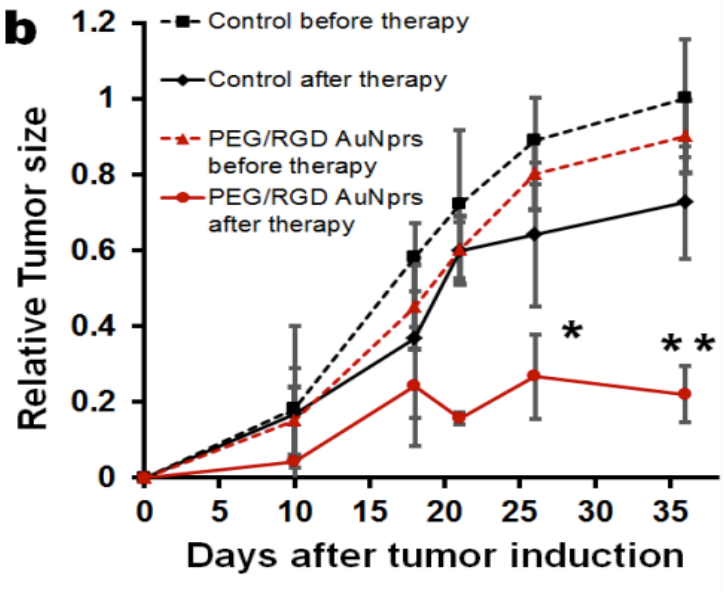
Au NPRs for Theranostics

In vivo PTT study using i.v. Injected NPrs@RGD.





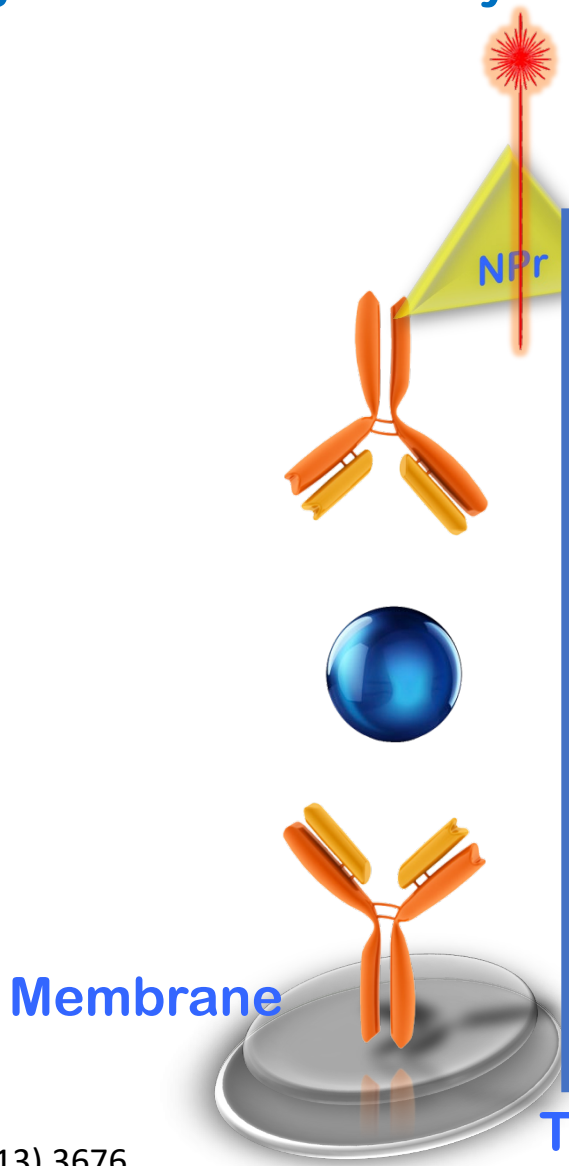




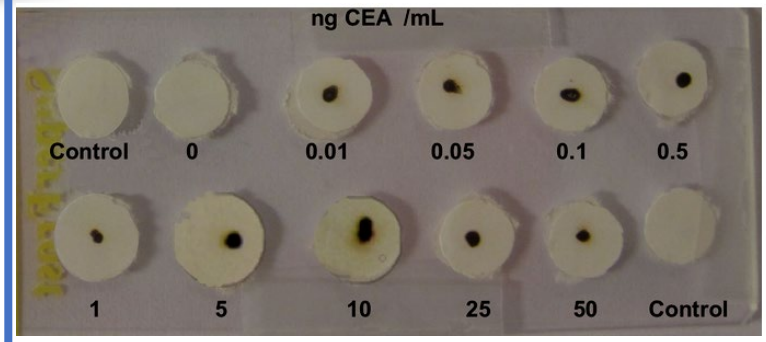
C. Bao et al. Small 2013

C. Bao et al. Nano Research (2016)

Gold-NanoPrisms as highly sensitive thermal biosensor against carcinoembryonic antigen



Serum from Patients with Cancer

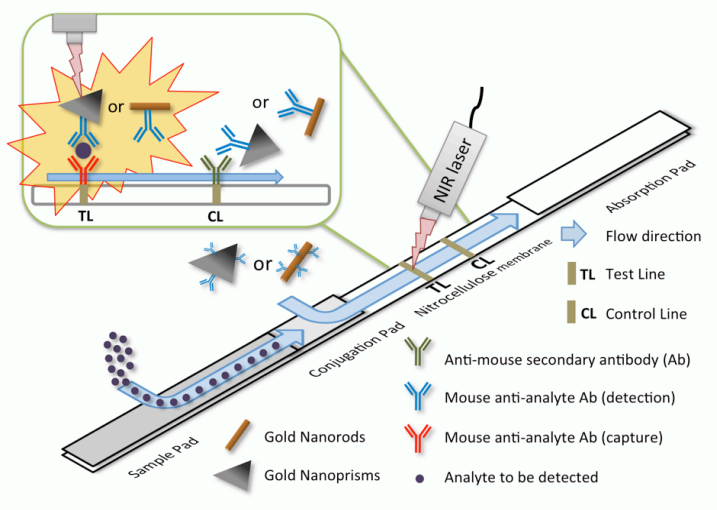


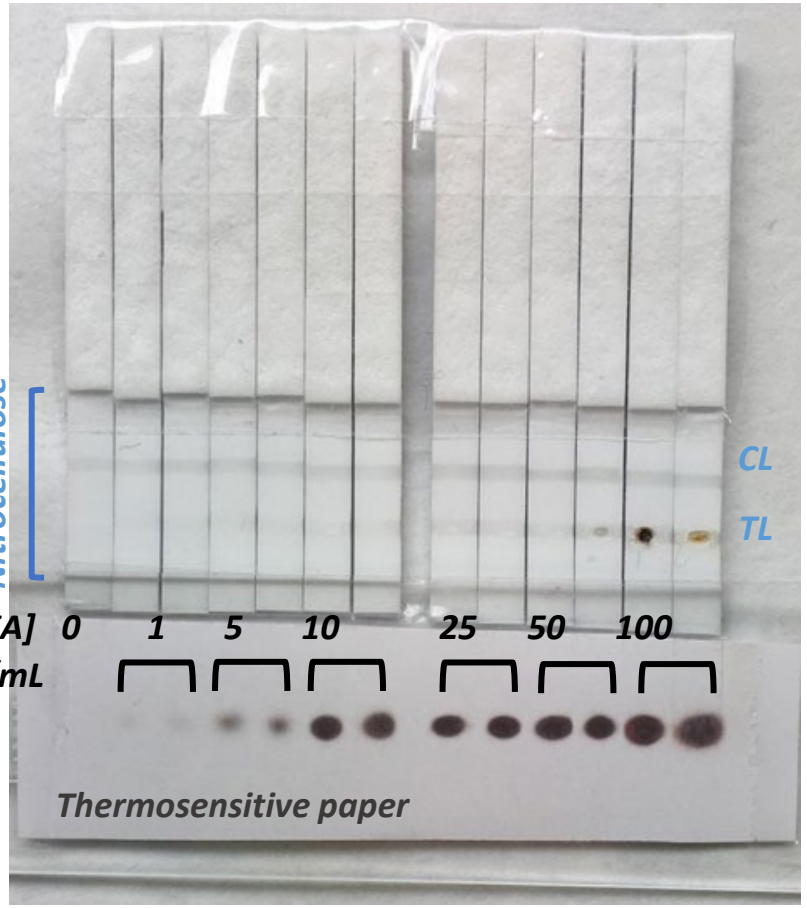
LOD 0.01 ng CEA/mL (aM range) in real samples from patient blood without any sample treatment

Thermosensitive paper

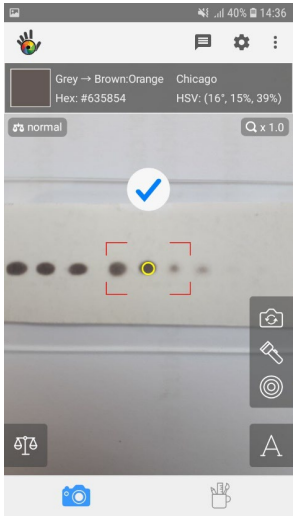
E. Polo *et al.* PCT, *ES2013/070549*
E. Polo *et al. Chem. Commun.*, **49**(2013) 3676

DETECTION OF COLON CANCER BIOMARKERS THROUGH THERMAL BIOSENSORS



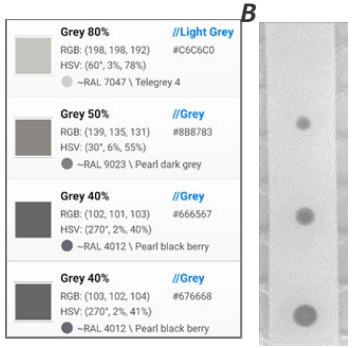


A





B



A) Color Grab App Interfaz B) Colour properties in RGB or HSV codes for each of the captured colours.

To be continued….

PRIME

Microfluidics in their PRIME:

Microfluidic Chips, Active Valves, Smart Sensors, and What Comes Next



14 Sept 2023
9:30-13:30

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Vienna, AUSTRIA

CSIC TU/e Universidad Zaragoza BNN BEOnChip

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