

HYBIOTAG : Towards generation of new luminescent and multifunctional hybrid nanoparticles for bioimaging and biosensing

project (ANR-10-P2N-001 01/04)

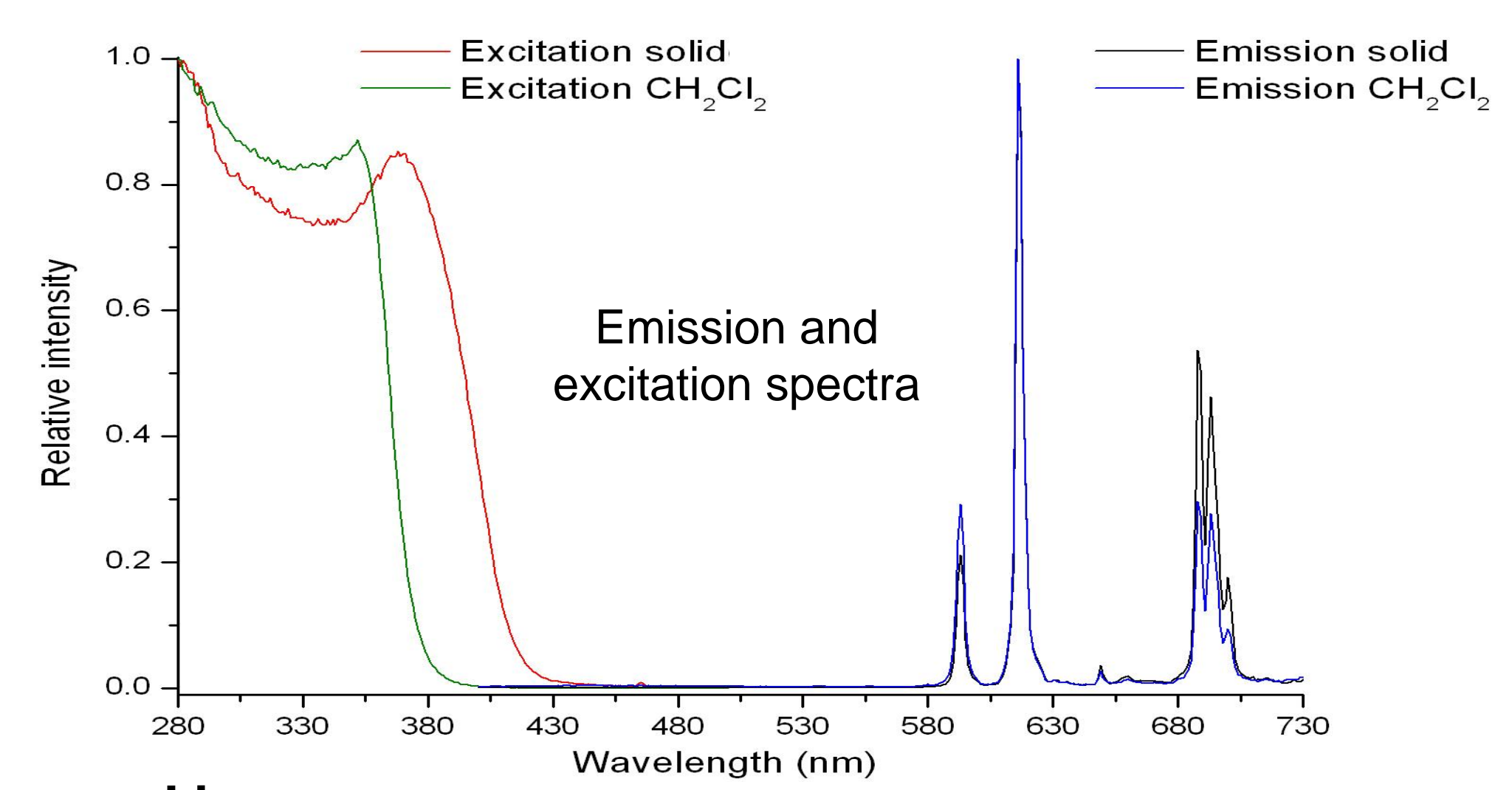
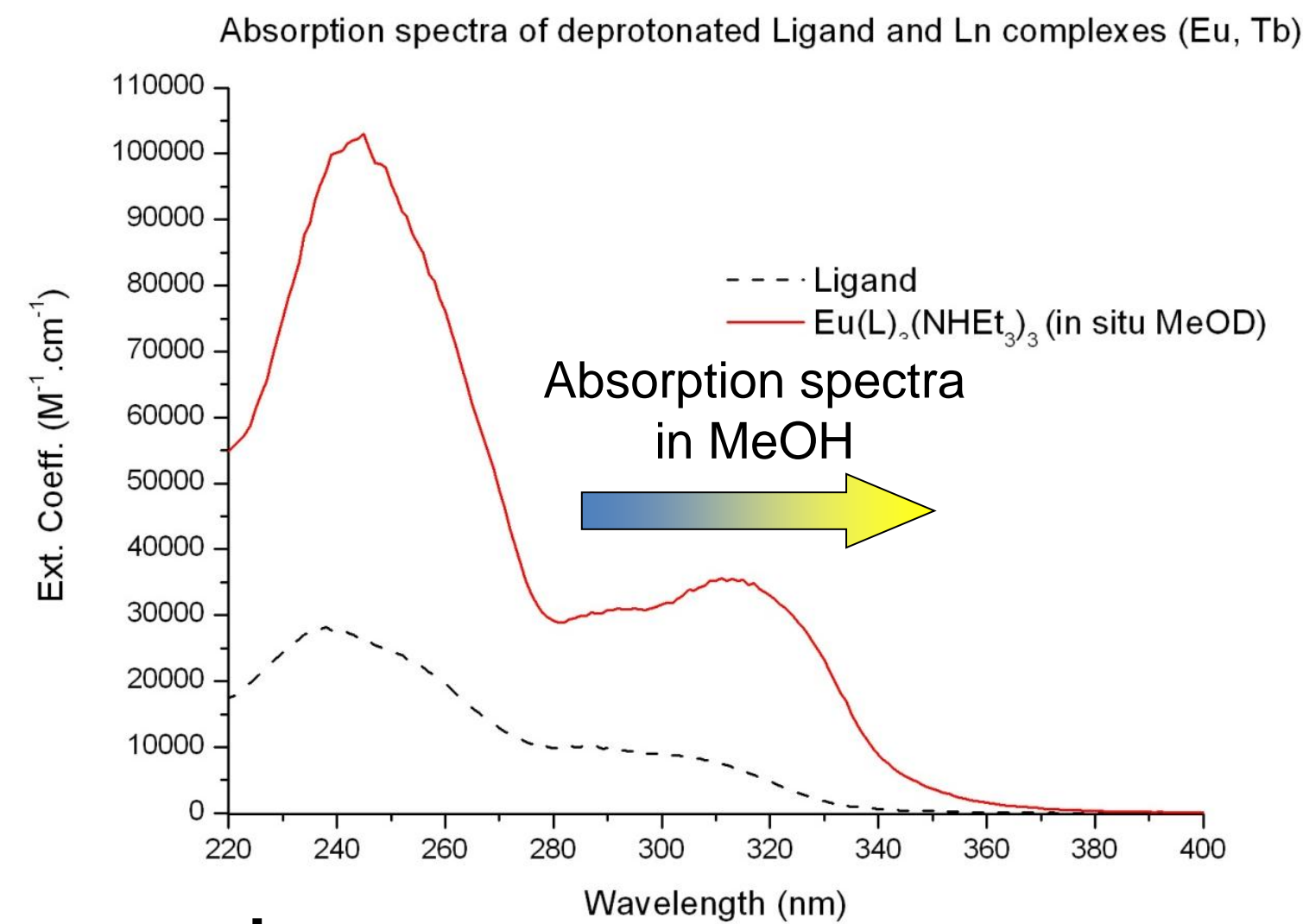
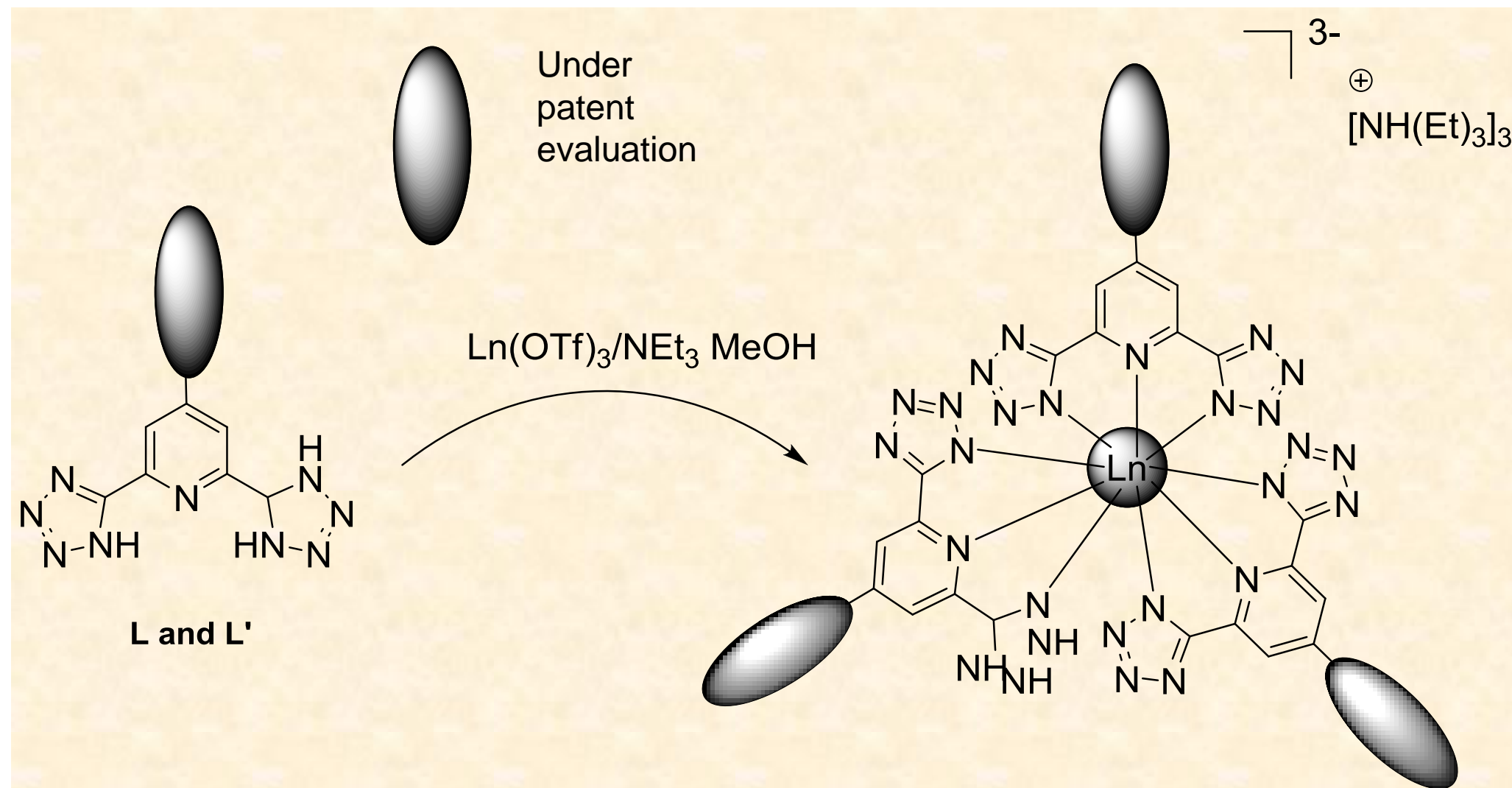
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CEA LITEN-INAC

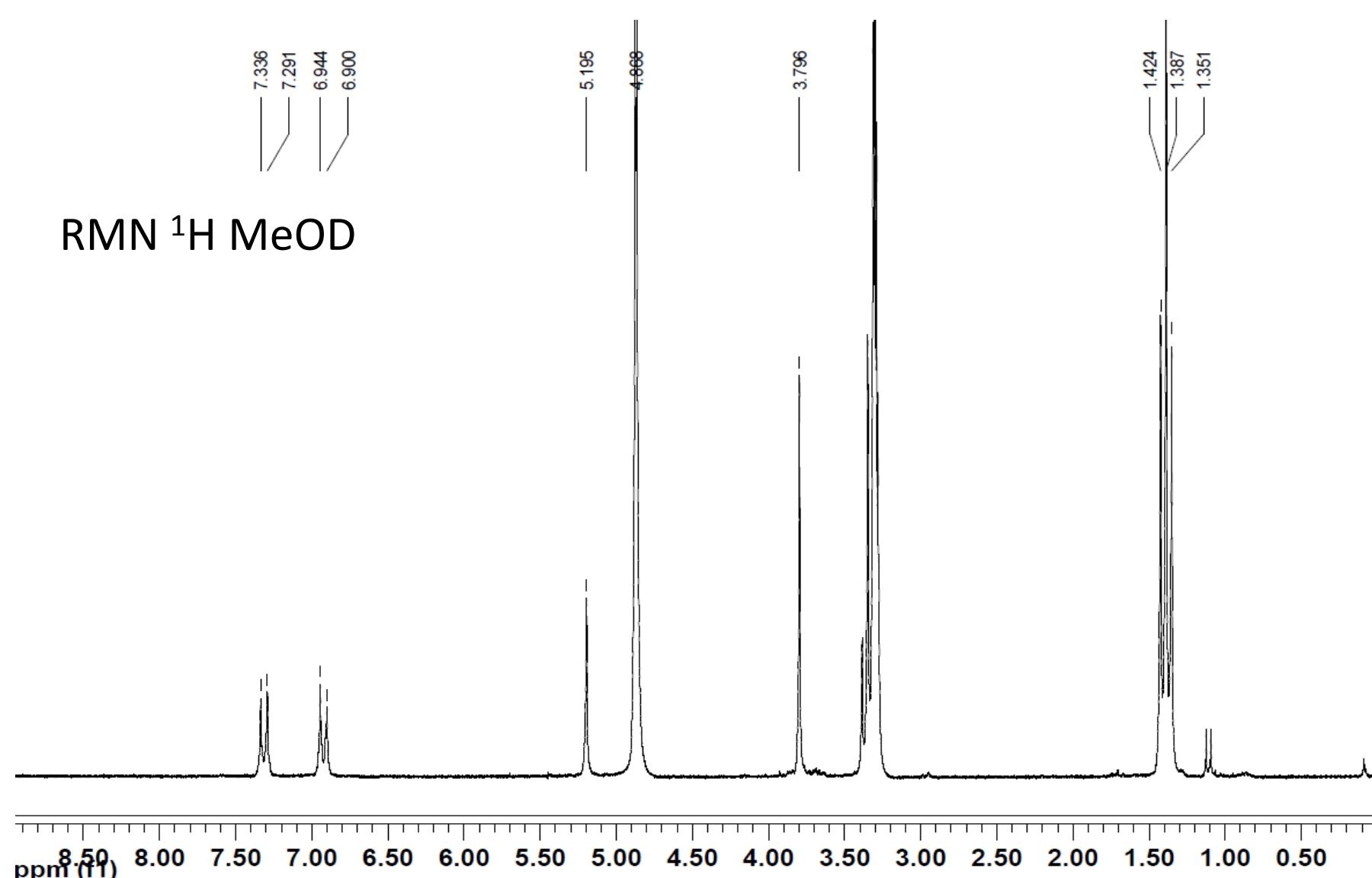
Two new tridentate dianionic ligands in good yield which self-assemble to form **robust triple helical** tris-chelate lanthanide(III) complexes. Good sensitization of Eu(III). **Shift of the absorption window** of the lanthanide complexes towards the visible region (up to 370 nm) with respect to the **dpa²⁻** and **ptz²⁻** analogues



L :
 Φ (λ_{exc} 340 nm); σ (ms)
Solid: 46.6 % ; 2.65 ms

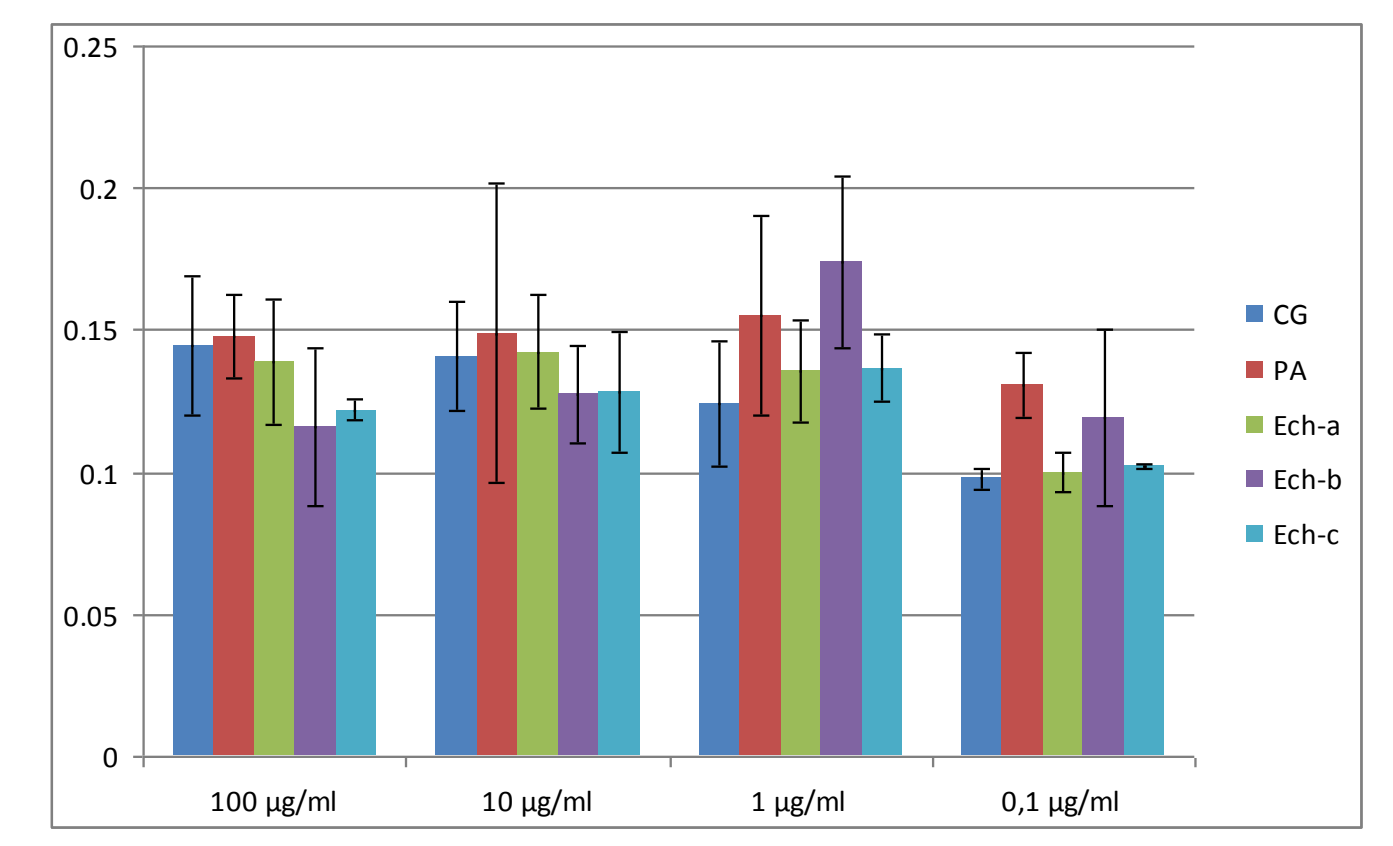
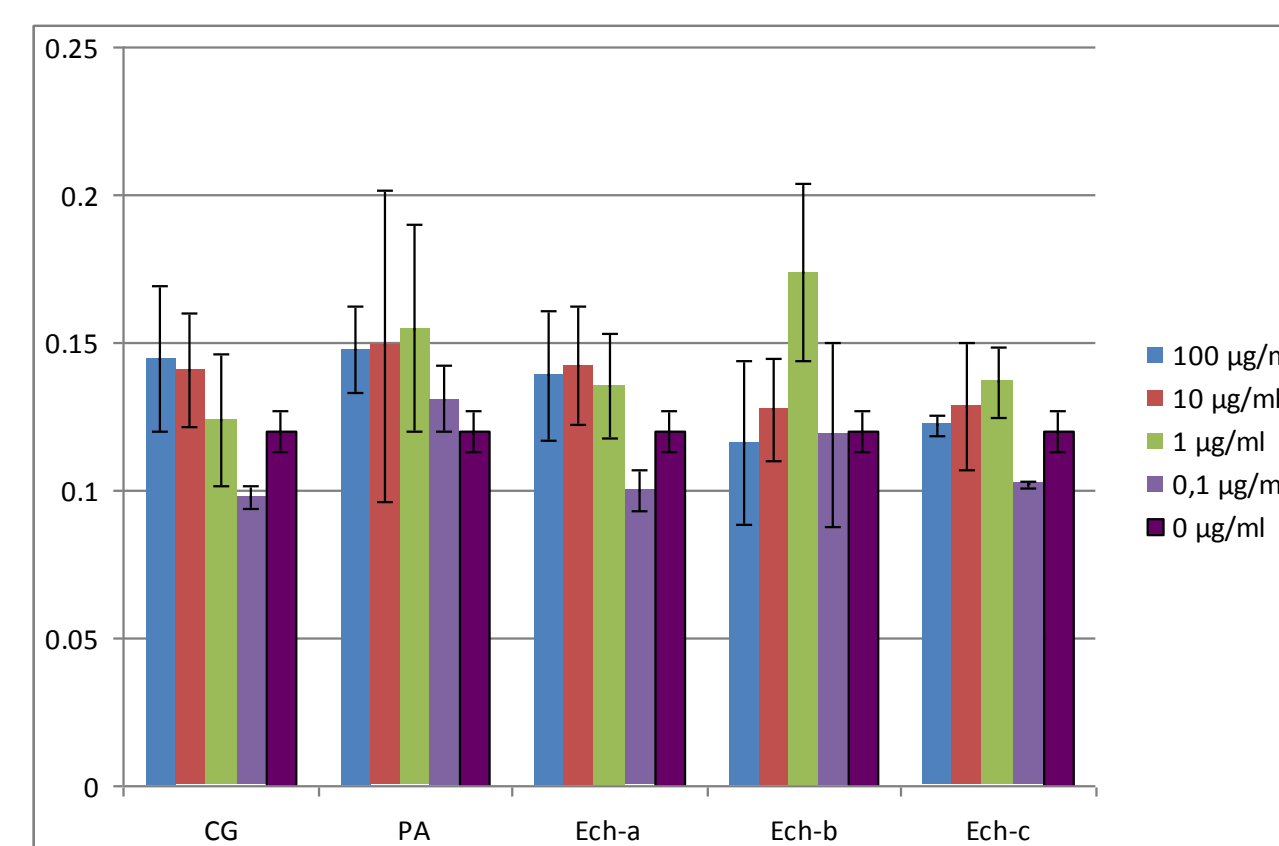
L' :
 Φ (λ_{exc} 370 nm); σ (ms):
Solid: 21 % ; 1.87 ms

RMN ¹H MeOD



One species in solution for the Eu(L)₃ complex

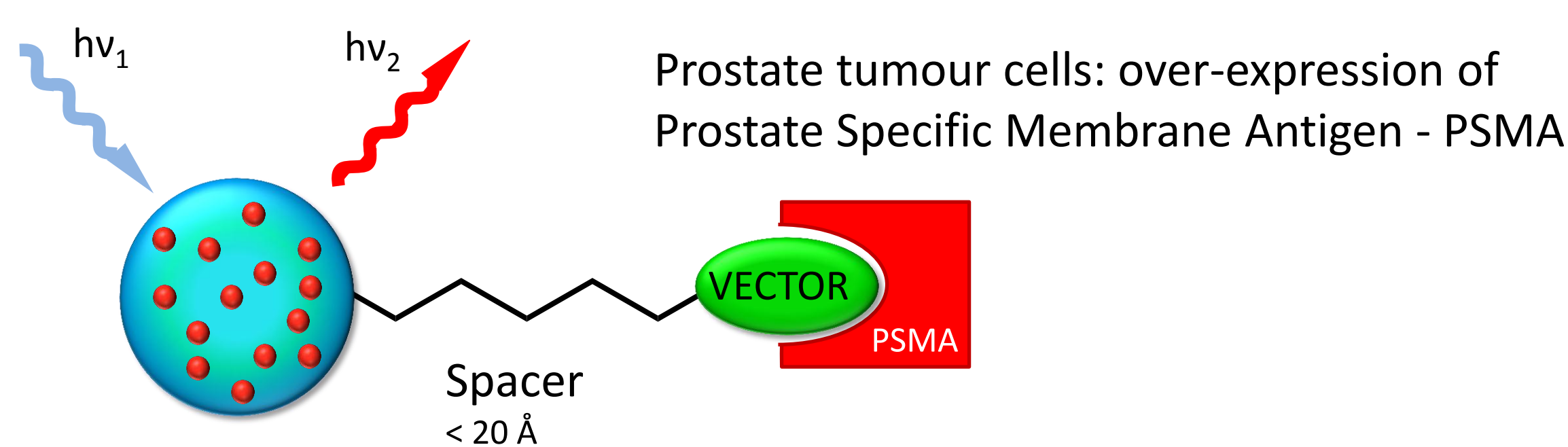
Cytotoxicity assessment of luminescent Lanthanides doped silica nanoparticles by biological tests (GReD)



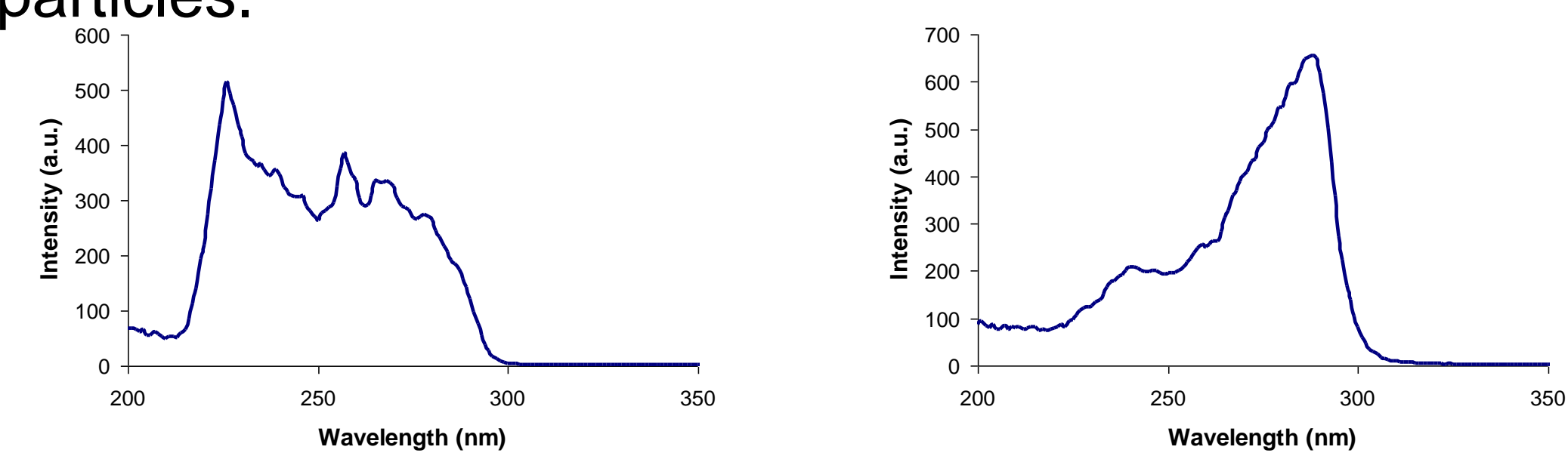
Ech a, b and c correspond to 15, 50 nm and 60 nm amine-functionalized nanoparticles, respectively (CEA). CG and PA correspond to non-functionalized nanoparticles (MI-SEESIB)

ICCF MI-SEESIB

Objective: Synthesis of luminescent nanoprobe for targeting PSMA

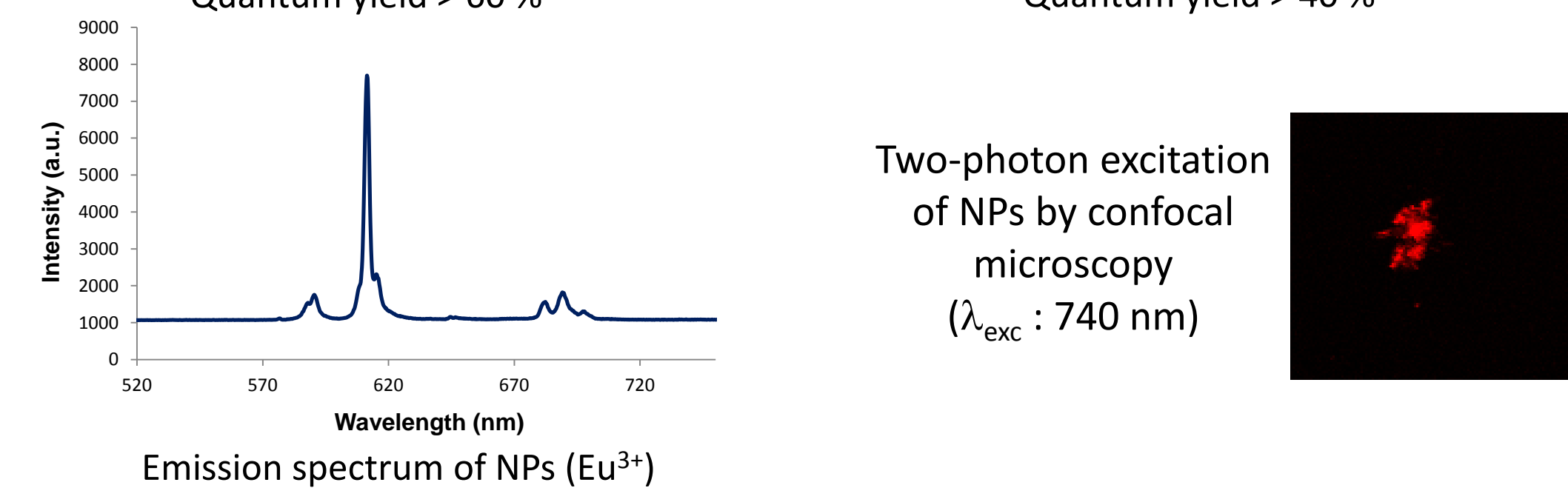


Luminescence properties of Ln complexes and corresponding nanoparticles.



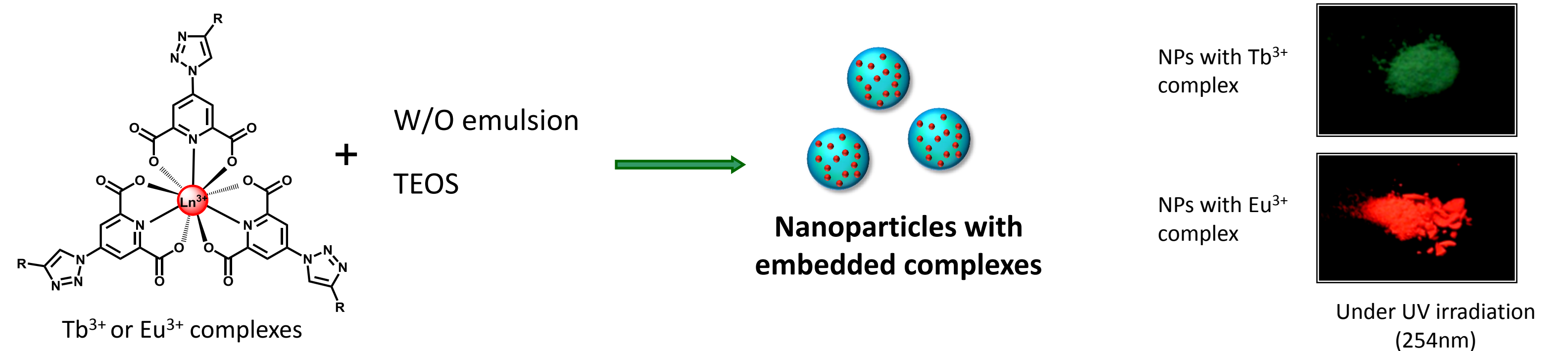
Excitation spectrum of Eu³⁺ complex in solution
Quantum yield > 60 %

Excitation spectrum of NPs
Quantum yield > 40 %

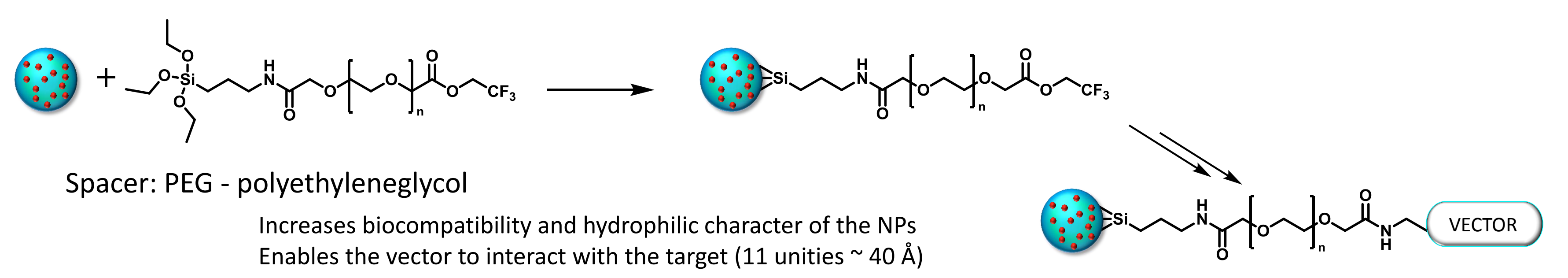


Two-photon excitation of NPs by confocal microscopy
(λ_{exc} : 740 nm)

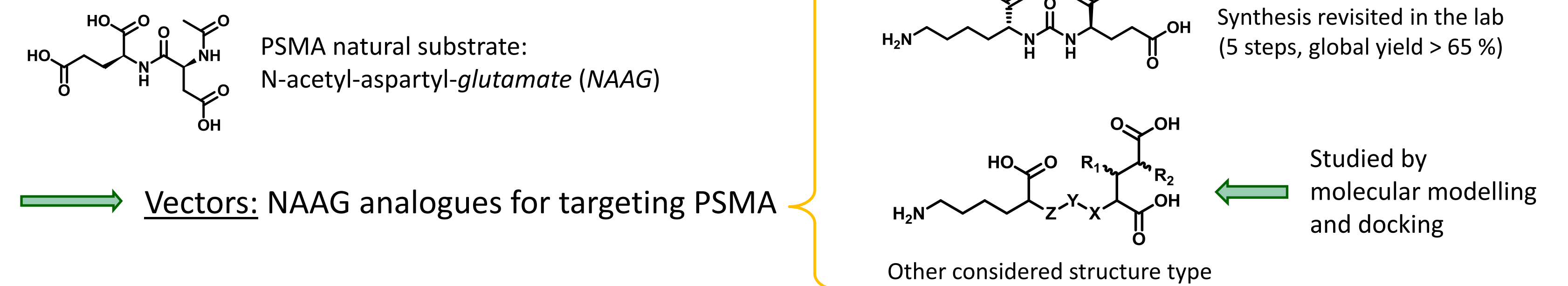
Luminescent nanoparticles synthesis by water in oil emulsion



PEGylation of nanoparticles



Vectorisation in progress



Vectors: NAAG analogues for targeting PSMA

Vector described in literature
Synthesis revisited in the lab
(5 steps, global yield > 65 %)

Studied by
molecular modelling
and docking

Scientific Record (publications, communications, patents)

- "Water-in-oil microemulsion preparation of fluorescent lanthanide complexes doped silica nanoparticles for applications as imaging biomarkers" C. Gaillard, P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, E-MRS 2011 Spring Meeting, Nice, 9-12 May 2011
- "Sol-gel microemulsion synthesis of fluorescent lanthanide complexes embedded in silica nanoparticles for bio-labelling applications" C. Gaillard, P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, XIVth International Sol-Gel Conference, Hangzhou (China), 28 Aug. - 2 Sept. 2011
- "Luminescent Lanthanide Complexes In Silica Nanoparticles For Biolabeling" C. Gaillard, P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, International Symposium on Advanced Complex Inorganic Nanomaterials, Namur (Belgium), 11-14 Sept. 2011.
- "Luminescent Lanthanide Complexes In Silica Nanoparticles For Biolabeling" C. Gaillard, P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, Colloque Interfaces Vivant / Matériaux nanostructurés, Clermont-Ferrand, 16 Sept. 2011
- "Towards generation of new luminescent and multifunctional hybrid nanoparticles for bioimaging and biosensing" P. Adumeau, C. Gaillard, J.-L. Canet, A. Gautier, V. Théry, L. Nauton, T. Gefflaut, D. Boyer, A.C. Franville, L. Morel, C. Beaudoin, F. Tardif, O. Raccurt, M. Mazzanti, D. Imbert, R. Mahiou, J3N, Strasbourg, 7-9 Nov. 2011.
- "sol-gel emulsion synthesis of luminescent nanohybrids for early prostate cancer diagnosis" P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, Journées scientifiques du CLARA, Lyon, 20-21 mars 2012.
- "Sol-gel emulsion synthesis of luminescent nanoparticles for precocious prostate cancer diagnosis" P. Adumeau, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, 8^{ème} Journée sol-gel Rhône-Alpes-Auvergne, Saint-Etienne, 5 avril 2012.
- "Lanthanide based luminescent nanohybrids by water-in-oil microemulsion, for early prostate cancer diagnosis" P. Adumeau, C. Gaillard, D. Boyer, J.-L. Canet, A. Gautier, R. Mahiou, E-MRS 2012 Spring Meeting, Strasbourg, 13-17 May 2012.
- "Encapsulation of lanthanide complexes into functionalized silica nanoparticles by water-in-oil emulsion for early prostate cancer diagnosis" P. Adumeau, D. Boyer, J.-L. Canet, L. Nauton, V. Théry, T. Gefflaut, L. Morel, C. Beaudoin, A. Gautier, R. Mahiou, Colloids and nanomedicine, Amsterdam, 15-17 July 2012.
- E. S. Andreiadis, D. Imbert, J. Pécaut, R. Demadrille, M. Mazzanti, Dalton Trans., 2012, 41, 1268-1277.
- "Sensitization of luminescence lanthanide doped nanocrystals with organic ligands for photovoltaic applications", N. Gauthier, D. Imbert, M. Mazzanti, O. Raccurt, 19th International Symposium on the Photophysics and Photochemistry of Coordination Compounds, Strasbourg, France, 3-7 July, 2011
- "Coordination and Photophysical Properties Homo- and Hetero-metallic Complexes, Multimodal Imaging Agents", D. Imbert, M. Mazzanti, COST Action CM1006, EUFEN 1, Tarragona, Spain, 2-4 April 2012
- "Luminescent Terbium/Europium chelates-based Silica Nanoparticles : Stability and Incorporation Efficiency measured by Radioactive Probe", N. Wartenberg, O. Raccurt, D. Imbert, M. Mazzanti, E. Bourgeat-Lami, Nanotech , Santa Clara, USA, 18-21 June 2012
- Application for a french patent (involving partner 1 – ICCF) n°115 90 06 the 06-10-2012 regarding "New rare earth complexes and luminescent organic inorganic hybrid materials" D. Boyer, R. Mahiou, A.C. Franville, J.-L. Canet, A. Gautier, P. Adumeau, R. Deloncle, J. Deschamps. PCTE in progress.

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