# Persistent Luminescent Nanoparticules for Optical Imaging Applications

**T. Maldiney, A. Lecointre, A. Bessière, F. Pellé**
**D. Gourier, C. Richard, D. Scherman, B. Viana**

*LCMCP; Chimie-ParisTech,*
*11 rue Pierre et Marie Curie, 75231 Paris Cedex 05, France*
*UPCG; Inserm, Faculté des Sciences Pharmaceutiques et Biologiques,*
*Paris, Chimie Paristech , Paris, F-75231 cedex France*

# Introduction

*in vivo* imaging : **non invasive** method

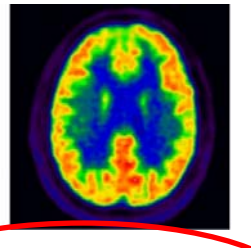
## Medicine

- Fast diagnostic
- Biodistribution of medicine
- Control of metabolisms

## Biomedical research

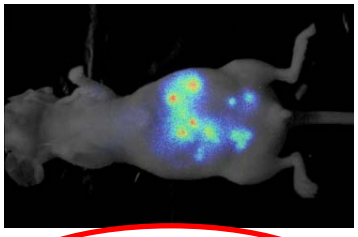
- Preclinic studies
- Longitudinal study
- Evaluation on small animal

## *in vivo* imaging

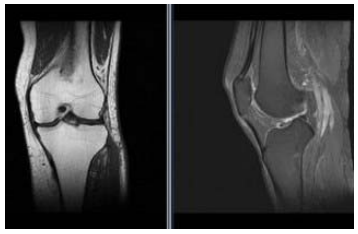


**Gamma rays imaging (scanner)**

**X-rays imaging**



**Optical imaging**



**IRM**

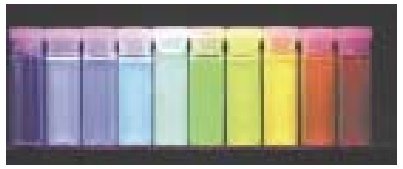

**Ultrasonic imaging**

# Introduction

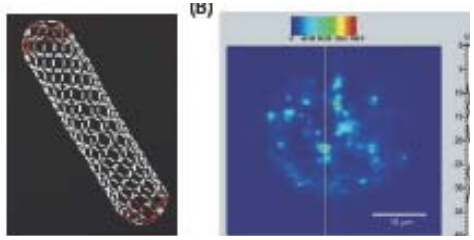
## Use of nanoprobes in optical imaging

**Inorganic probes are suitable for *in-vivo* optical imaging**

**QD (semiconductor Inorganic NPs)**



**Carbon nanotubes**

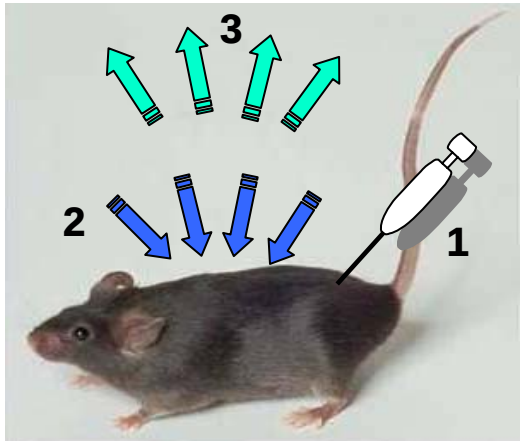


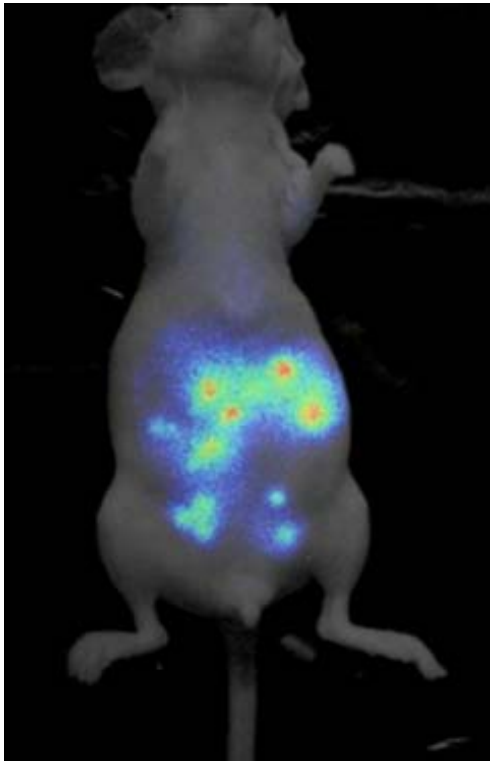
**Dielectric (large gap) inorganic NPs**

# Introduction

## Optical imaging

*Classical system*



Principle

**1**- Injection of a **chromophor** (organic QuantumDots...)

**2**- *in vivo* UV-VIS excitation or IR excitation in the case of multiphotonique process

**3**- Fluorescence detection

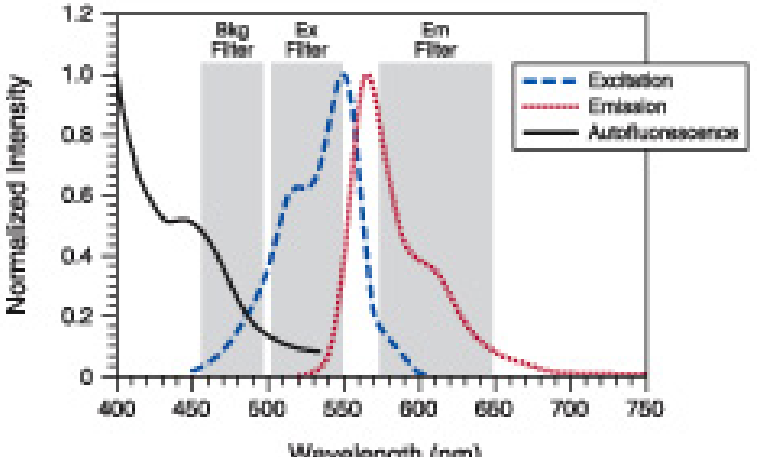
**Pb : tissues autofluorescence**

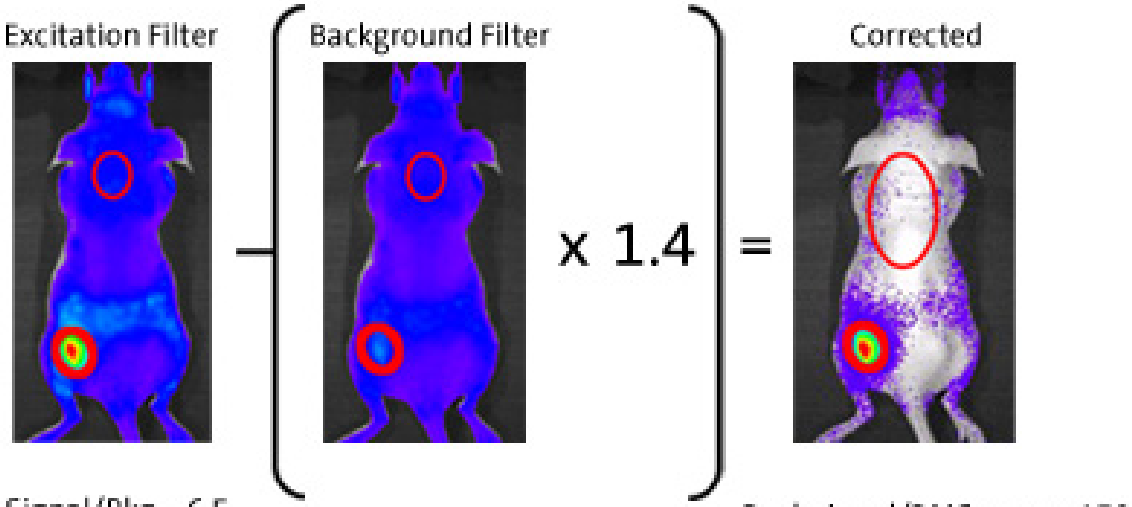
# Problems related to optical imaging

## Tissue autofluorescence

Excitation/emission

## Autofluorescent Subtraction with Filters



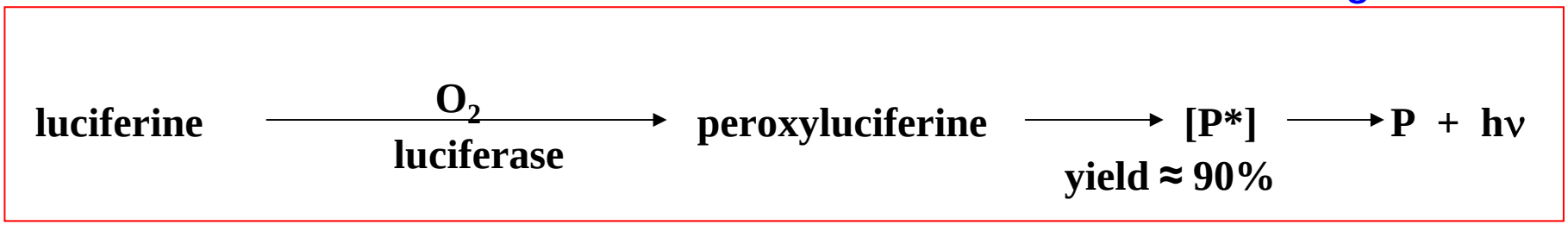
# *Is it possible to have emission without excitation ?*

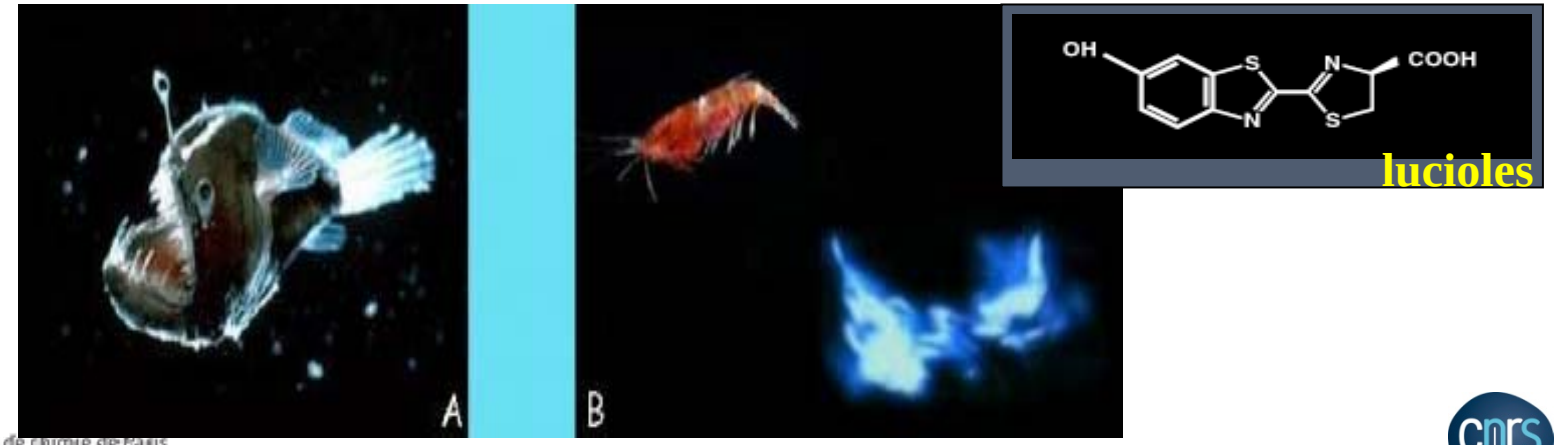
## Case of the Bioluminescence (Pr Rao talk):

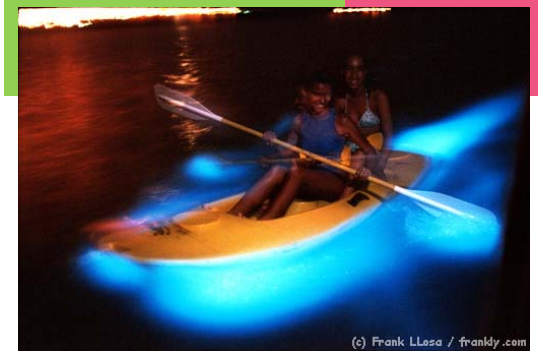
**oxydation of the luciferine with ATP**

**and with Mg as catalyst**

Oxydation and departure of adenosine phosphate, then relaxation and emission of light



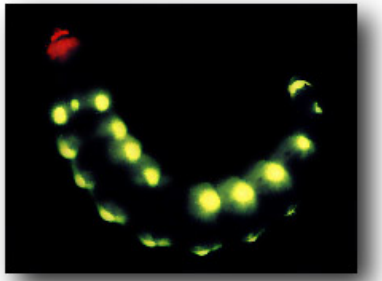







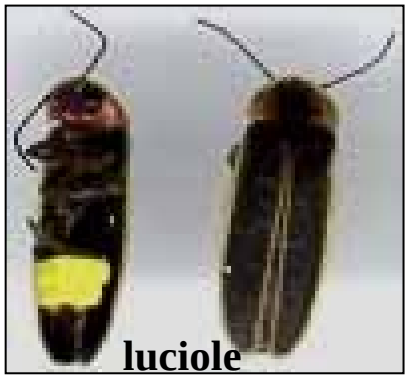
# Green Fluorescent Proteins

*Aequorea victoria*



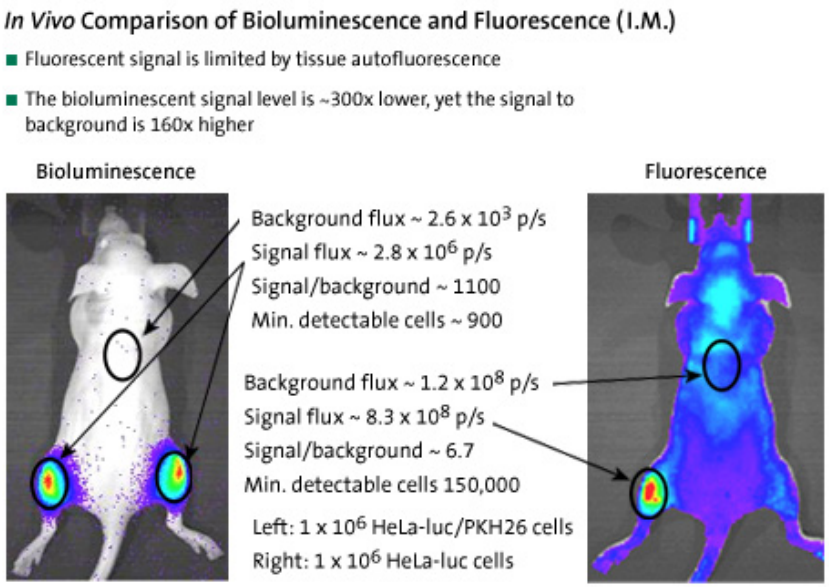
The railroad-worm *Phrixothrix hiatus* (actually abeetle larva) produces red light from its head, and green light along the rest of its body. © 1998 V. Viviani

**The ' railroad worm ' (*phengodidae*)**



**luciole**

The interest of the Bioluminescence is that there is no excitation required




No signal autofluorescence
But much smaller intensity !

From web

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# Solutions for in vivo imaging :

## Wavelength Management


## Up-conversion

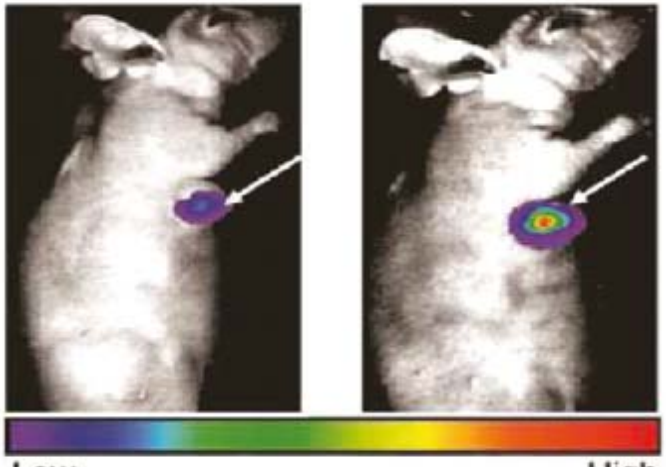
**(Pr Capobianco talk)**

NANO LETTERS
LETTER
pubs.acs.org/NanoLett

Mesoporous Multifunctional Upconversion Luminescent and Magnetic "Nanorattle" Materials for Targeted Chemotherapy

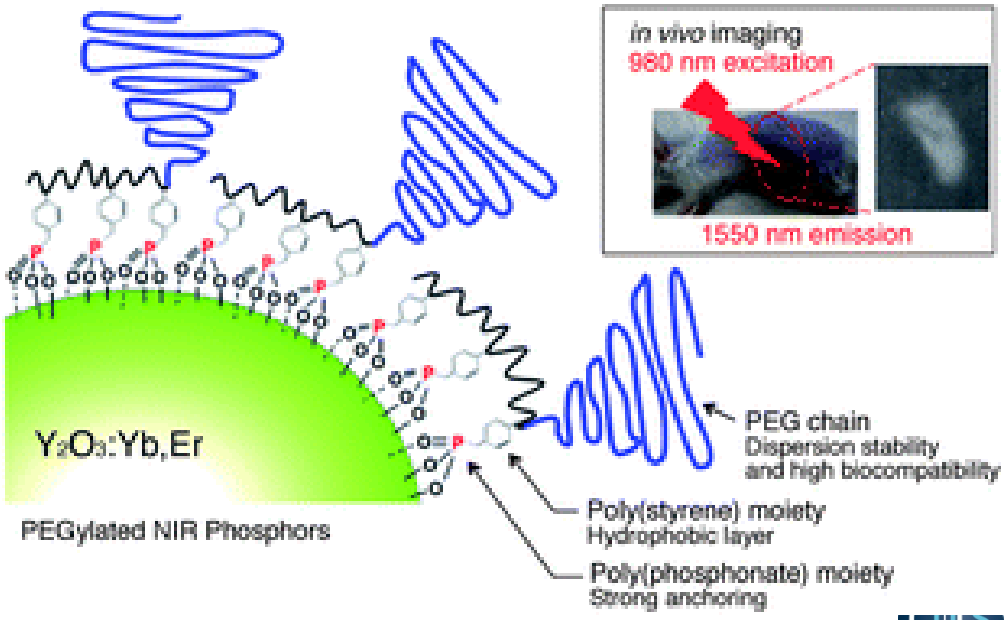
Fan Zhang,*,† Gary B. Braun,† Alessia Pallaoro,† Yichi Zhang,† Yifeng Shi,† Daxiang Cui,§ Martin Moskovits,† Dongyuan Zhao,† and Galen D. Stucky*,†

*Nano Lett. (2012), 12, 61-67*



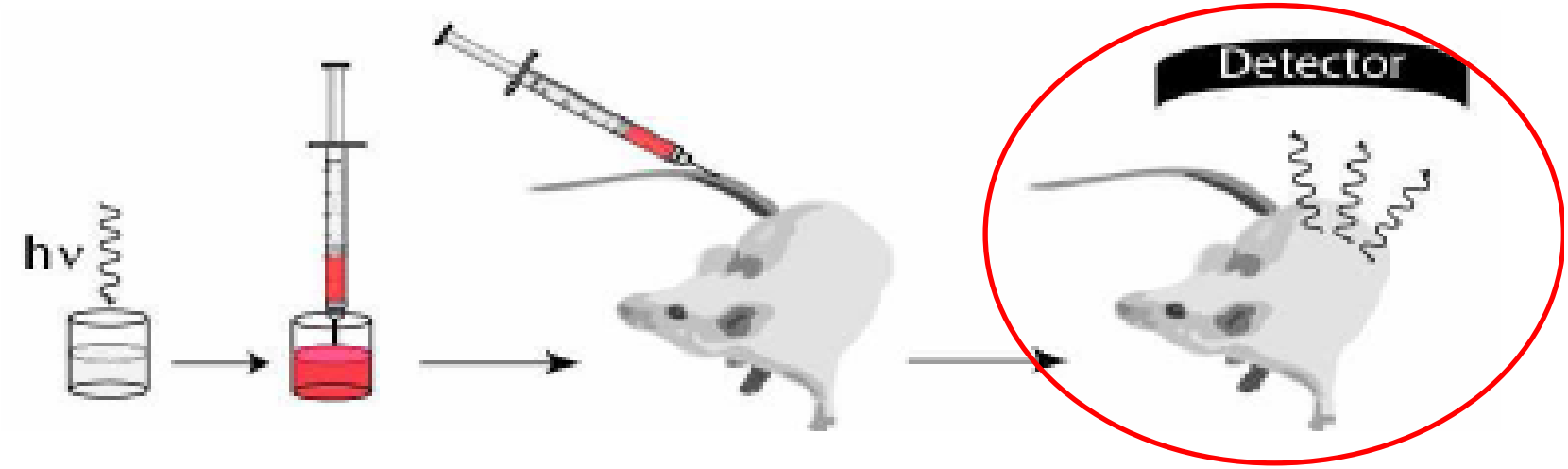

## Down-conversion
## IR-conversion

*Nanoscale*, 3, 3705-3713 (2011)



# Solutions for in vivo imaging :

Time Management


Long decay and/or enhancement of the decay with temperature

Persistent luminescence

# Requirement for efficient persistent luminescence

- **Efficient luminescent materials :**
  - **Need to avoid non radiative processes**
- **For applications :**
  - **Avoid or enhance point defects?**

No traps

Phosphors for cathodic tubes

Scintillators in medical imaging

# Requirement for efficient persistent luminescence

❖ Efficient luminescent materials :

↳ Need to avoid non radiative processes

❖ **For applications :**

↳ Avoid or **enhance point defects?**

No traps

Control of traps

Phosphors for cathodic tubes

Scintillators in medical imaging

Storage phosphors

Persistent luminescent materials in medical imaging

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# This is possible with materials with persistent luminescence

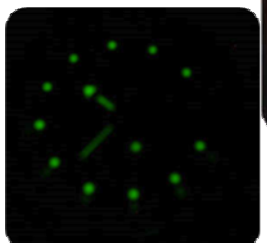
## Principles of the persistent luminescence

Emission of visible light for hours after exposure to light energy (sunlight, UV light, fluorescent lamp, *etc*)

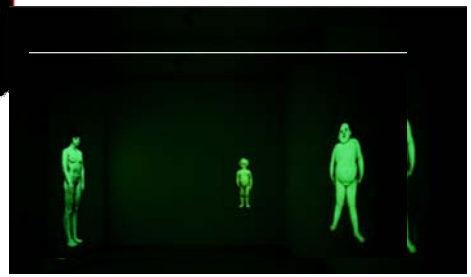
Energy « stored » in the materials

Light emission during several hours

Applications







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cnrs

# Outline

1) Introduction

2) Part 1 : Interest of the persistent luminescence in optical imaging

3) Part 2 : Persistent luminescence in the red range :case of $CaMgSi_2O_6$:Mn NP's and exemples of optical imaging

4) Part 3 : New materials and interest for *in-vivo* optical imaging

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# Interest of the persistent luminescence

Materials

$MAl_2Si_2O_8 : Eu^{2+}$ (M : Ca, Sr, Ba)

$M_2MgSi_2O_7 : Eu^{2+}, Dy^{3+}$ (M : Ca, Sr, Ba)

$Ca_2Al_2SiO_7 : Ce^{3+}$

$Ca_2P_2O_7 : Eu^{2+}, Y^{3+}$

$CaAl_2O_4 : Eu^{2+}, TR^{3+}$ (TR : Nd, Tm, Dy)

$SrAl_2O_4 : Eu^{2+}, Dy^{3+}$

$CaAl_2O_4 : Mn^{2+}, Ce^{3+}$

$ZnS: Cu^{+}, Co^{2+}$

$Y_2O_2S : Ti^{4+}$

$ZnS : Mn^{2+}$

$BaMg_2Si_2O_7 : Eu^{2+}, Dy^{3+}, Mn^{2+}$

$Ca_2SSi_4 : Eu^{2+}, Nd^{3+}$

**$MgSiO_3 : Eu^{2+}, Dy^{3+}, Mn^{2+}$**

$CaS: Eu^{2+}, Tm^{3+}$

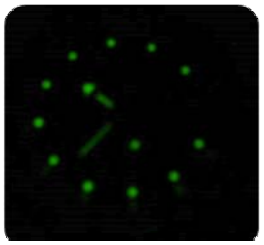
$Ca_2Si_5N_8 : Eu^{2+}$

$CaTiO_3 : Pr^{3+}$

**$Ca_2Si_5N_8 : Tm^{3+}, Eu^{2+}$**

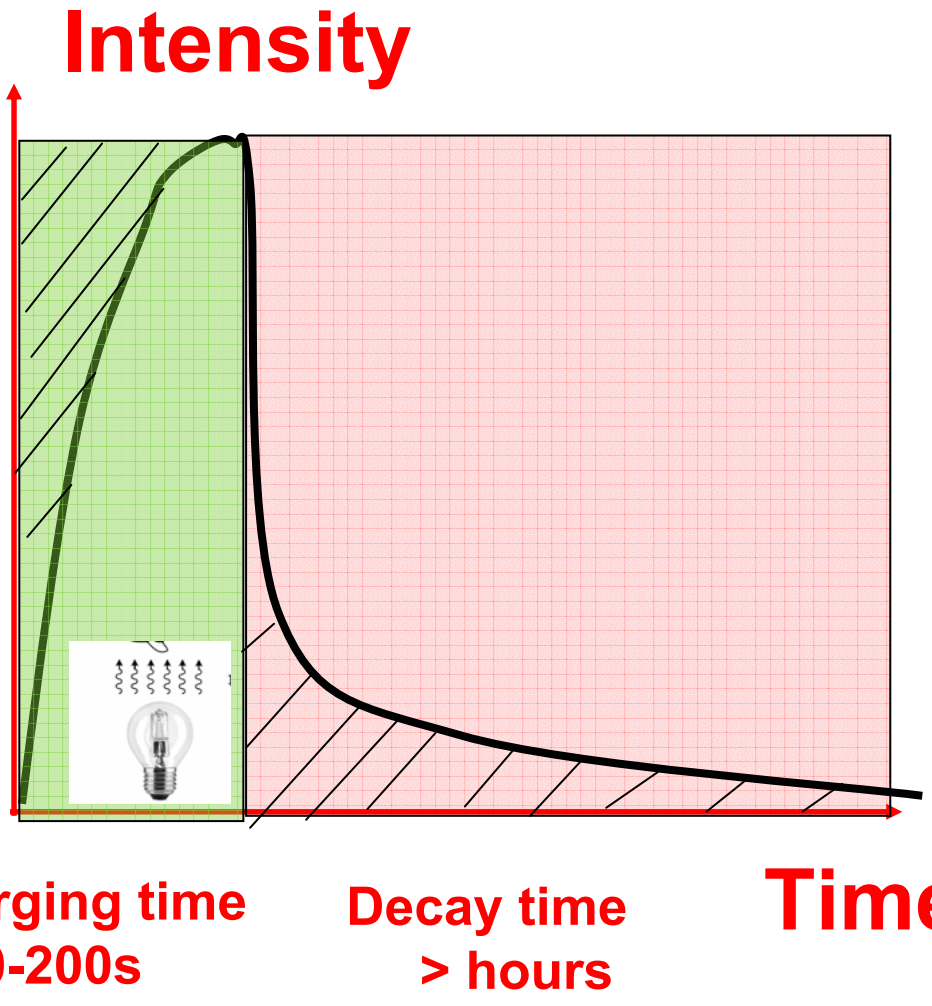
$Y_2O_2S : Eu^{3+}, Mg^{2+}, Ti^{4+}$

**$ZnGa_2O_4 : Cr^{3+}$**



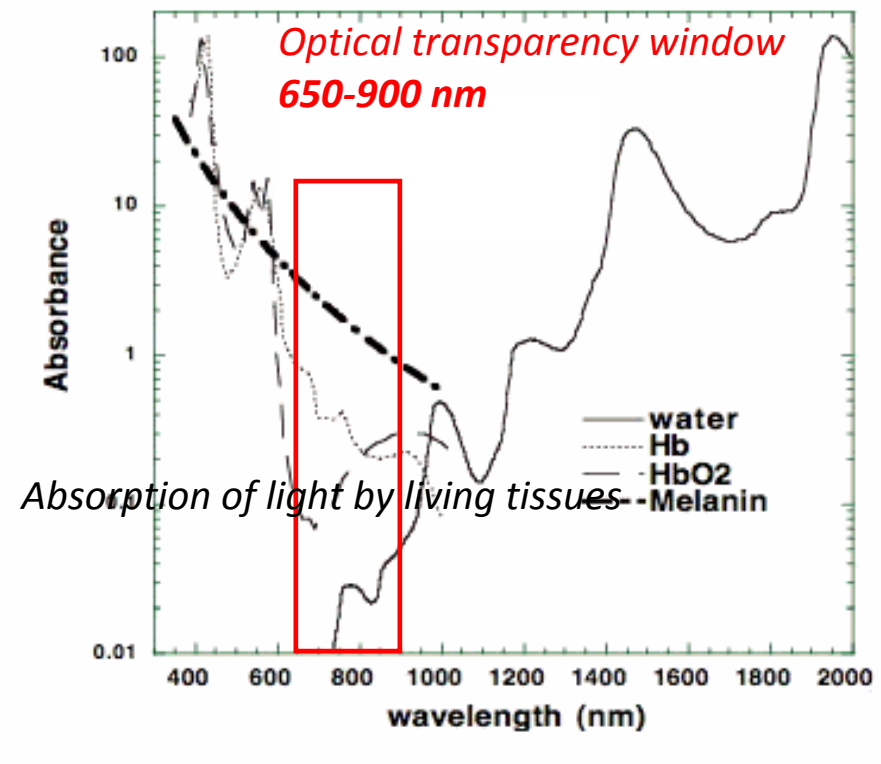

# Interest of the persistent luminescence

## Optical « battery » : storage of the light in traps/defects

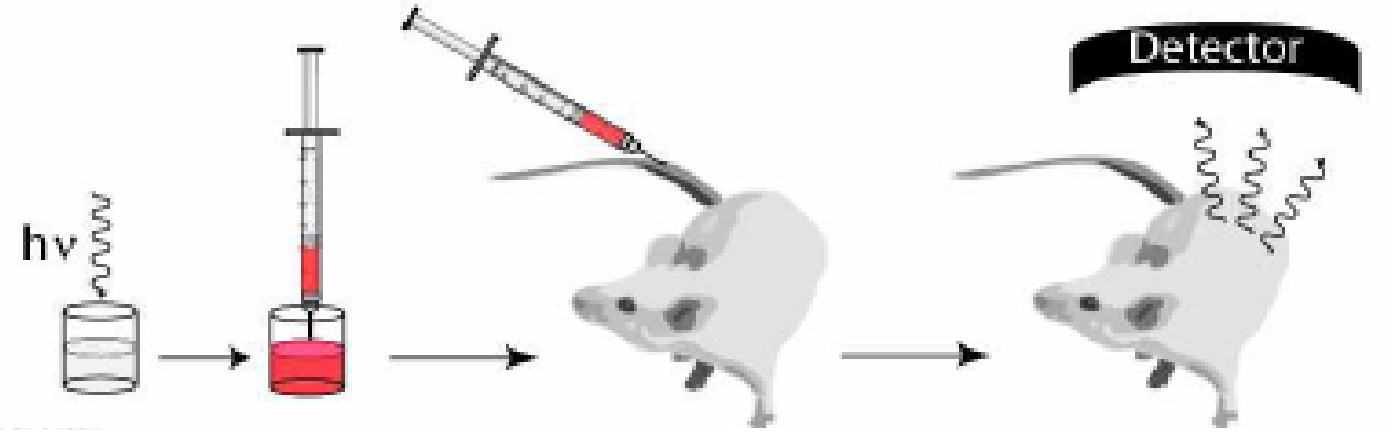



# Interest of the persistent luminescence

- NPs Synthesis
- Functionalization
- Persistent luminescence in the red/NIR




*Absorption of light by living tissues*

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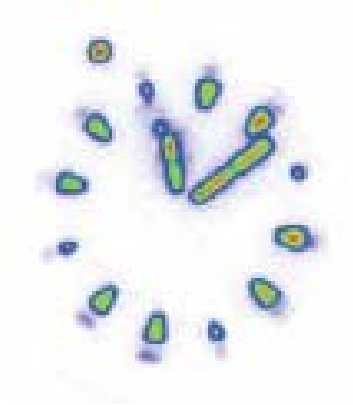
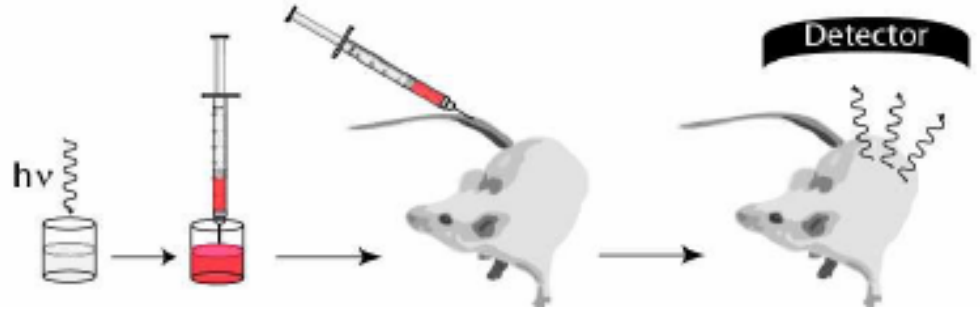
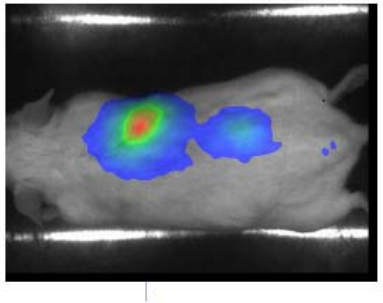
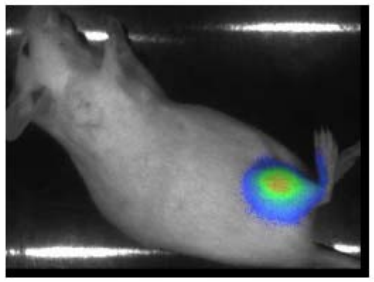
# Interest of the persistent luminescence for in-vivo imaging

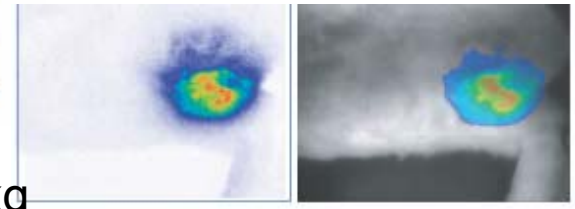
## Red and NIR LLP NPs









Rabbit 4,5 kg

Intramuscular injection on a rabbit

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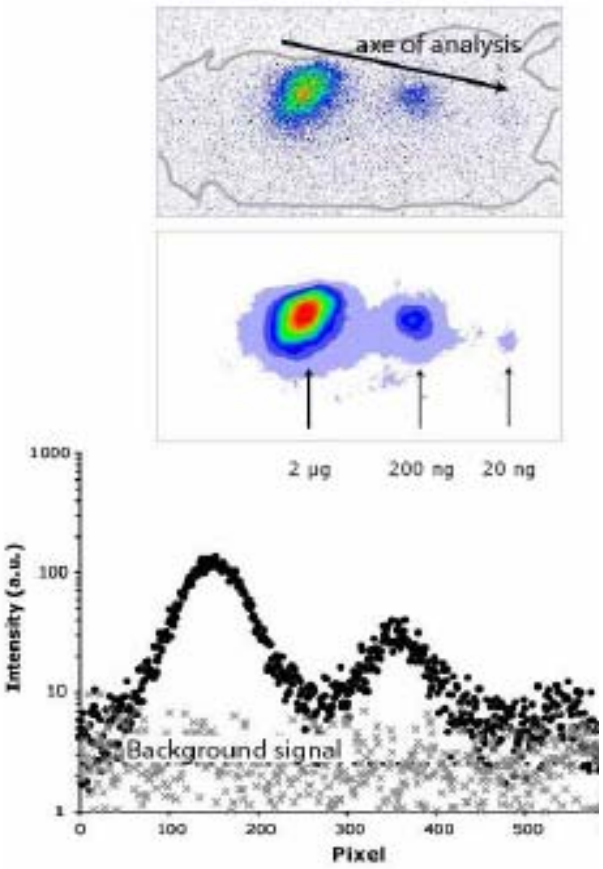
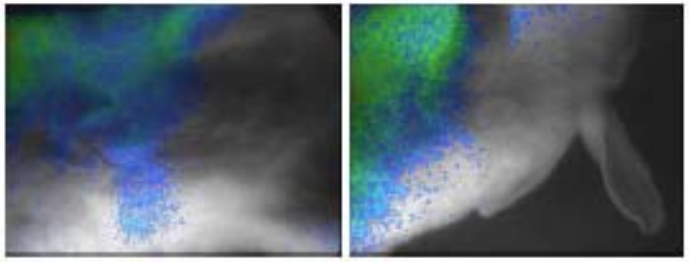
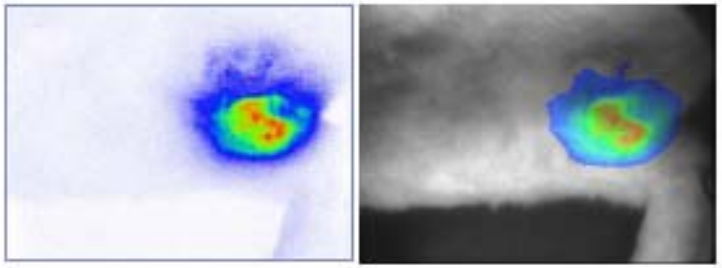
# Interest of the persistent luminescence for in-vivo imaging

## *Sensitivity*



Intraveinal injection



Intramuscular injection

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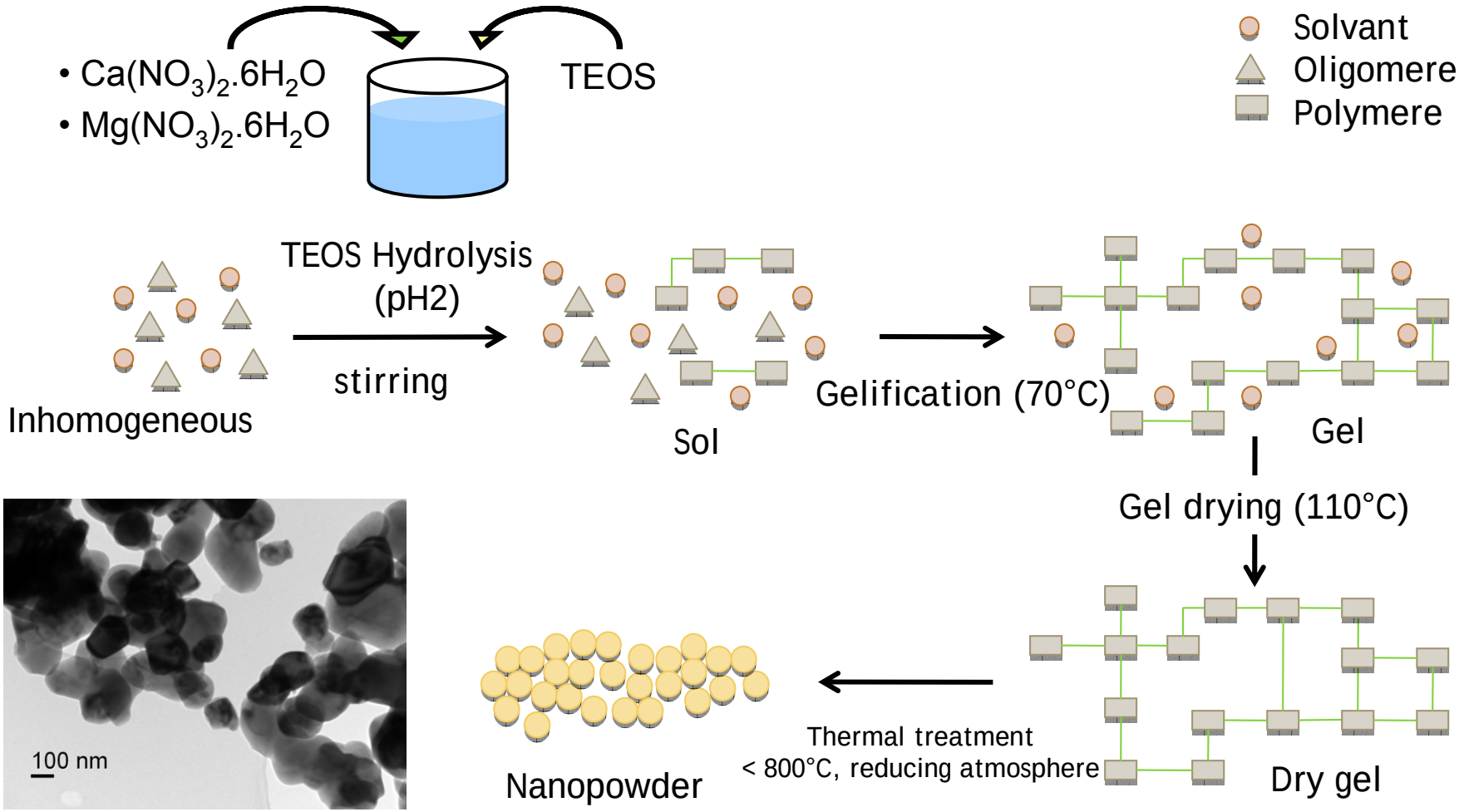
# Material synthesis

## The long-lasting fluorescent material

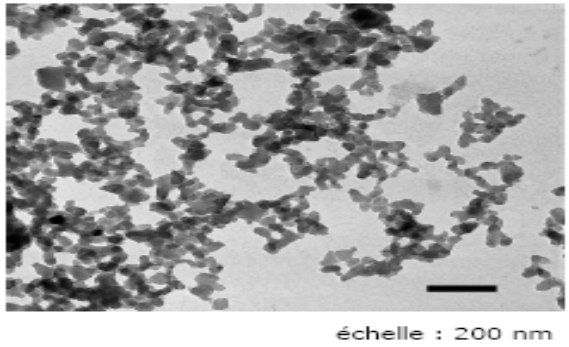
For instance : Sol-gel synthesis

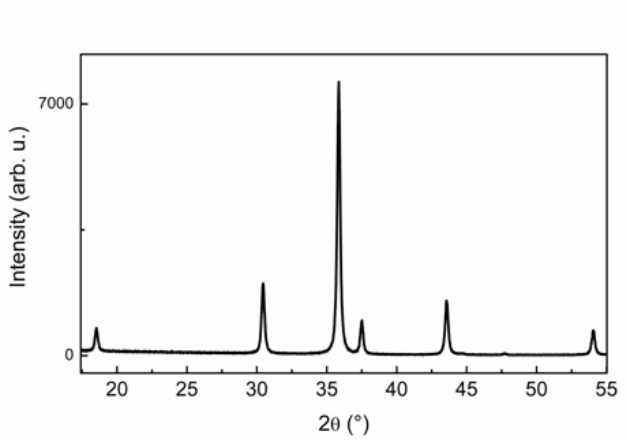



XRD, TEM

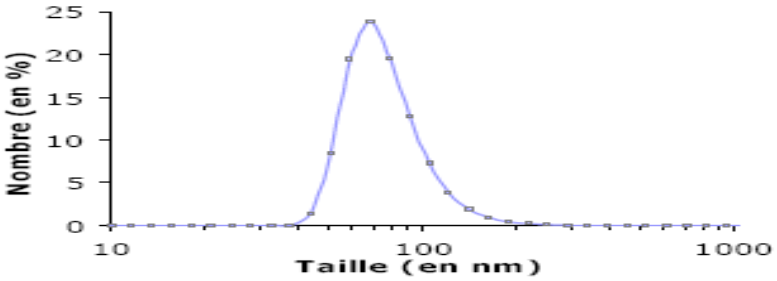
# Material synthesis

## Matérials Characterization




NPs :Preparation, size and cristallinity,




NPs : charge and dispersion

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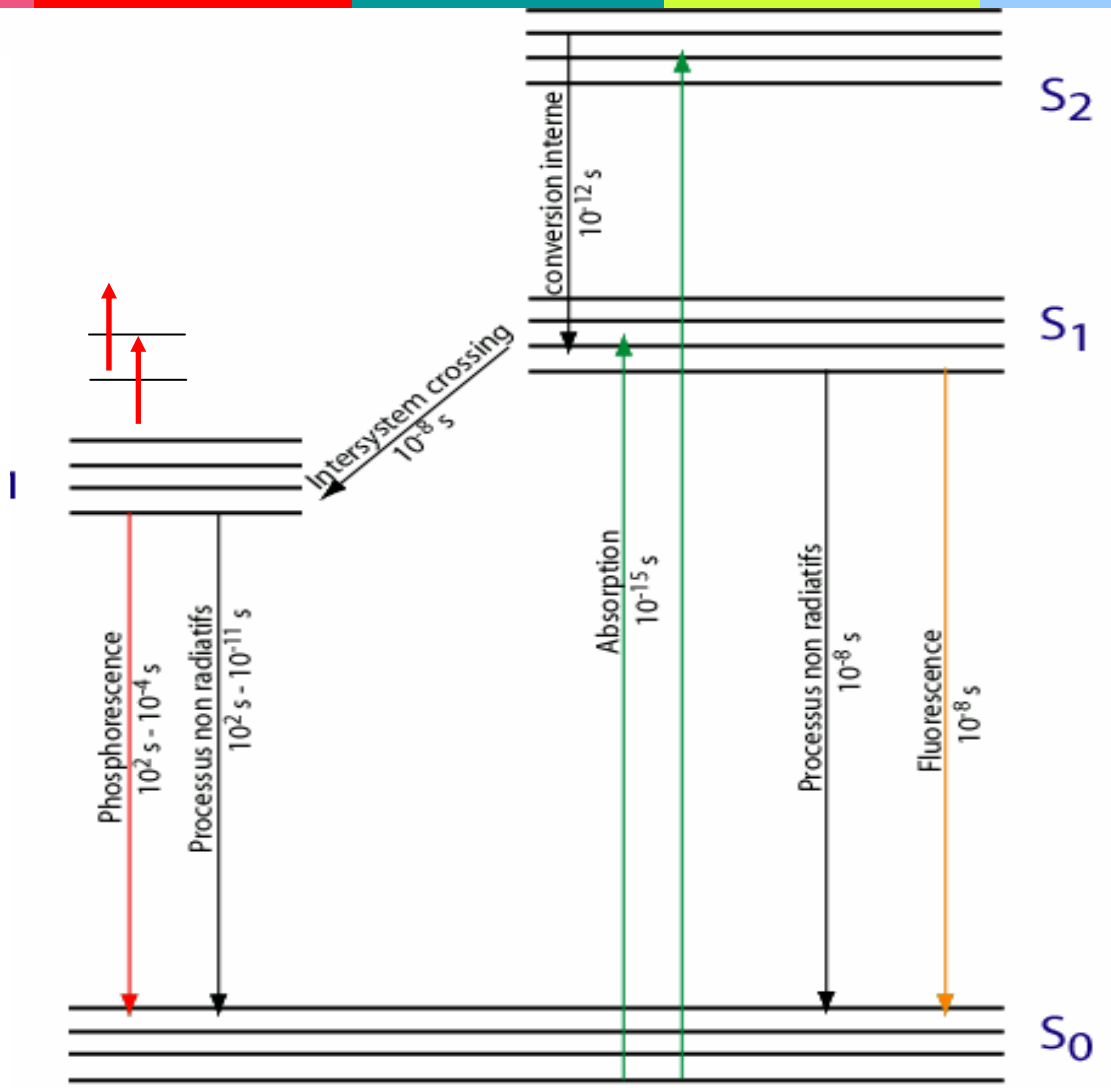
# Origin of the emission

**Allowed transition (fast decay) when :**
**i) $\Delta S = 0$**
**(non spin variation)**

**ii) $\Delta l = +/- 1$**
**(charge transfer, s-p Transition, f-d transition, etc...**

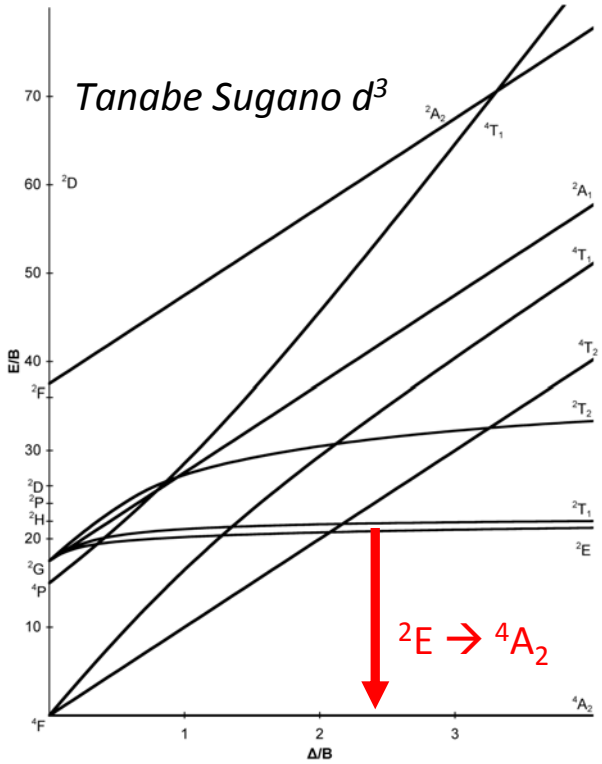
**iii) Vibration between two close energy levels**

**iv) Energy transfer with resonant levels**




Characteristic times for the absorption, the fluorescence, the phosphorescence and the non radiatifs processes

# Origin of the emission




3d-3f (Mn, Cr)

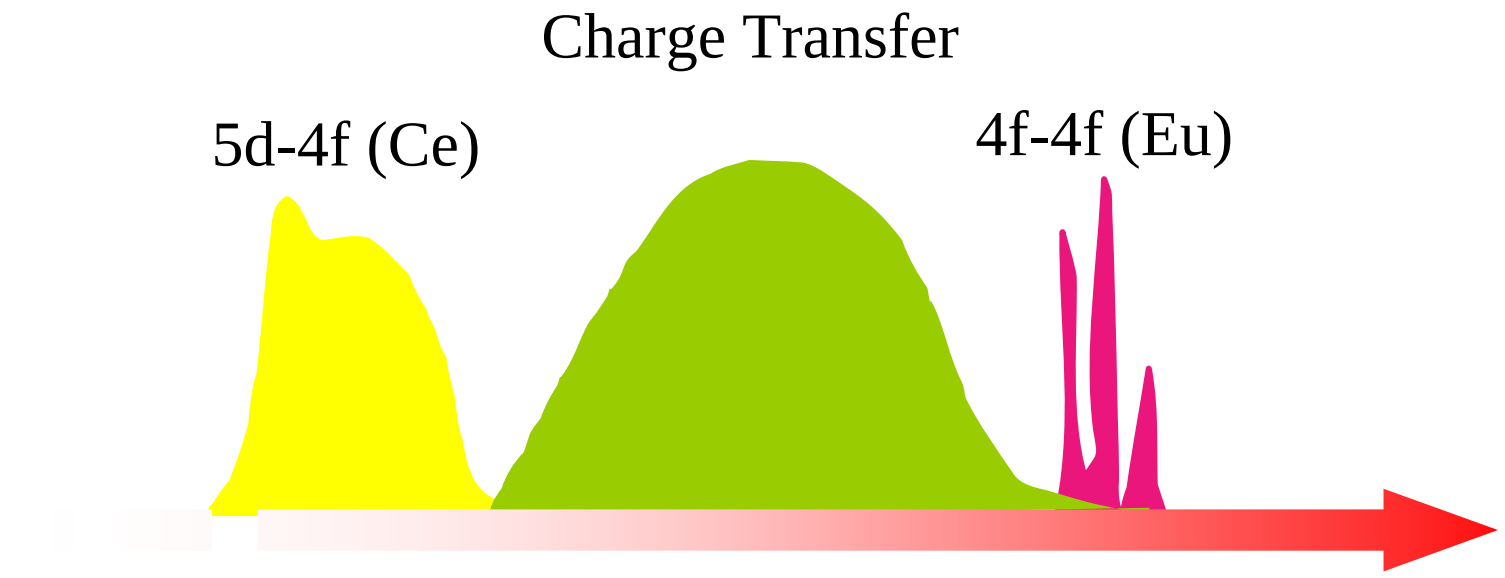
400 nm

600 nm

Broad band
Tau > ms
Not very intensive

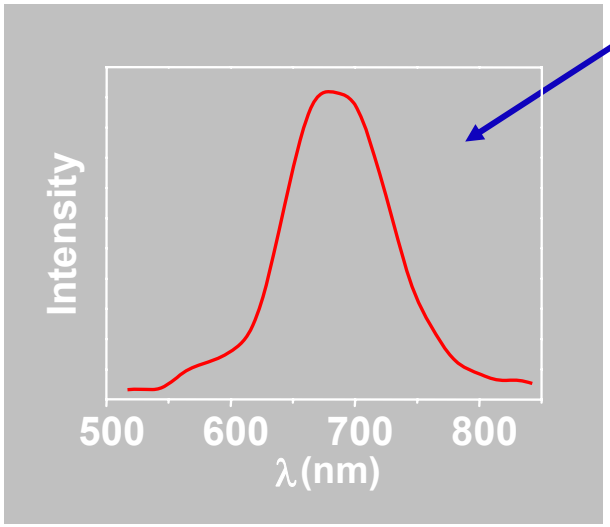
# Origin of the emission

No « classical » emission can explain such long emission time !!



# Persistent luminescence : a different origin !!

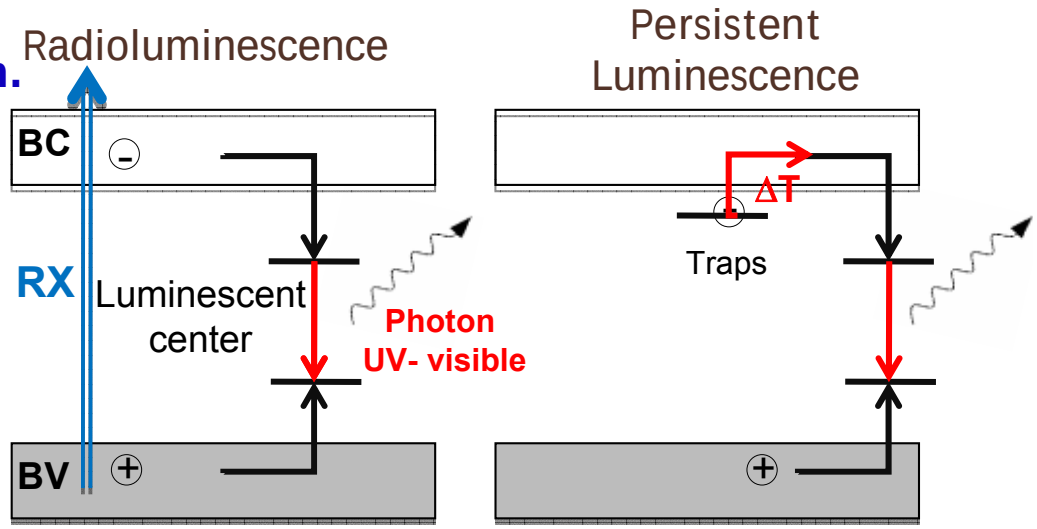
Traps at the origin of the Persistent luminescence of $CaMgSi_2O_6:Mn^{2+}$




**Persistent lum.**

**685 nm**

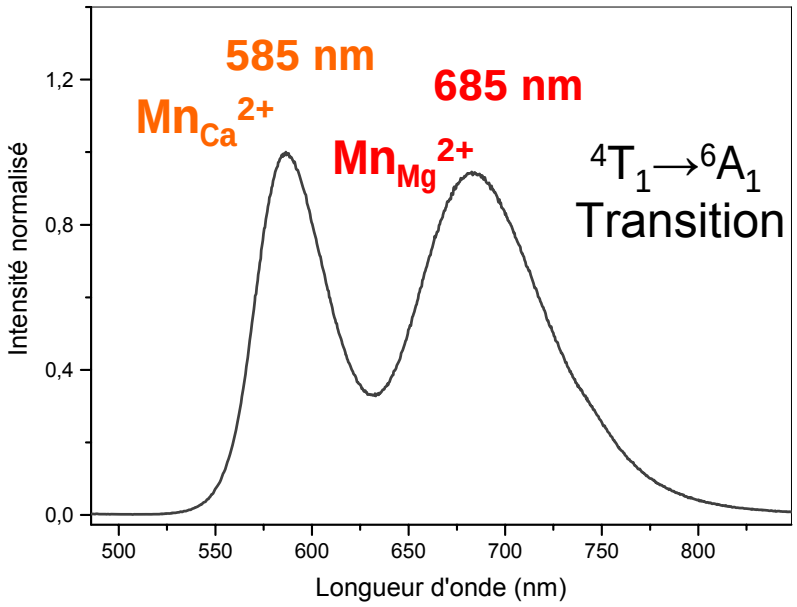
**$Mn_{Mg}^{2+}$**



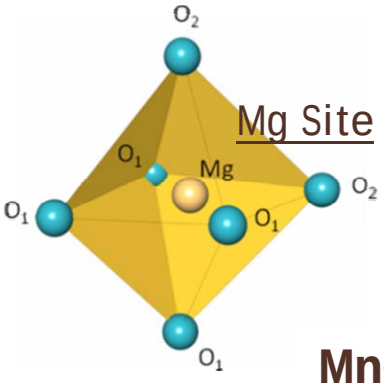

- $Mn^{2+}$ participate to the capture step + energy transfer
- $Mn^{2+}$ : recombination center & hole traps
- Electron traps at the origin of the persistent luminescence

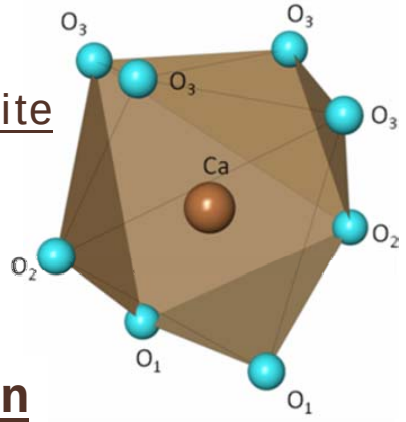
# Material characterization

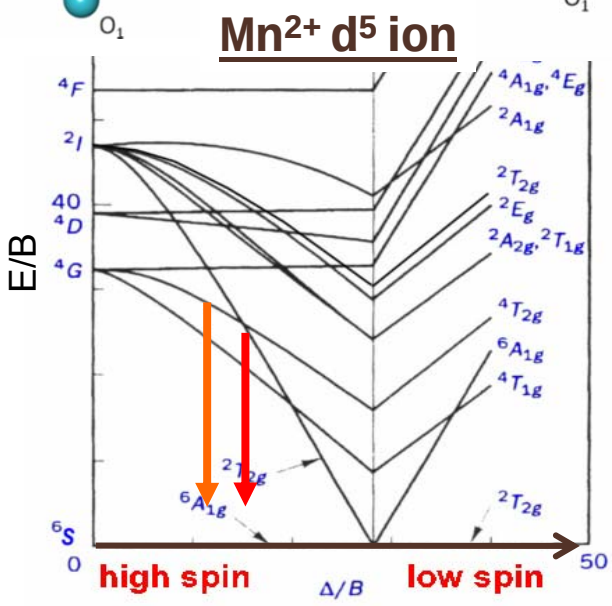
**better understanding of the optical properties and traps origin**
**Luminescence of $CaMgSi_2O_6:Mn^{2+}$ (CMSO:Mn)**




2 surrounding for Mn




Increase crystal field

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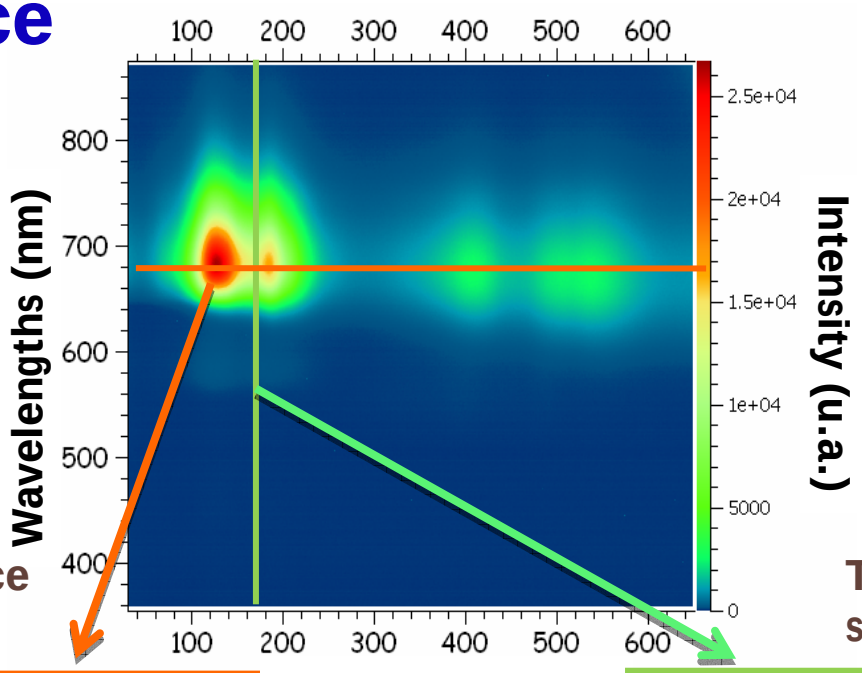
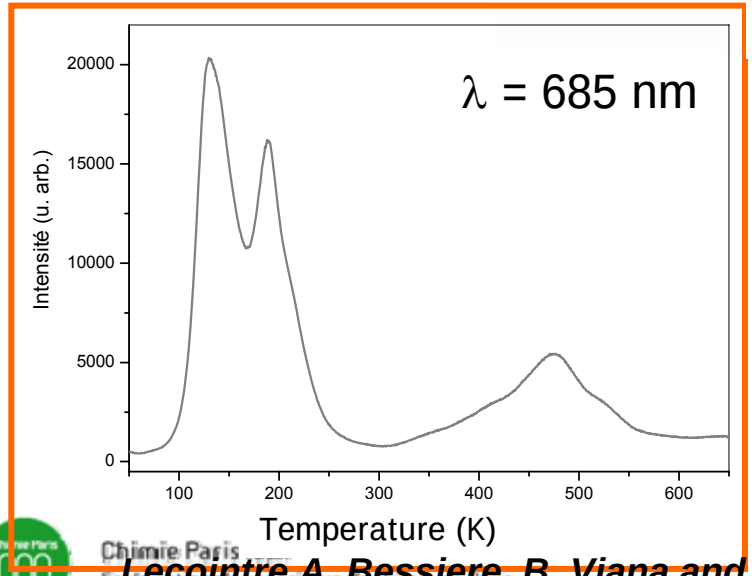
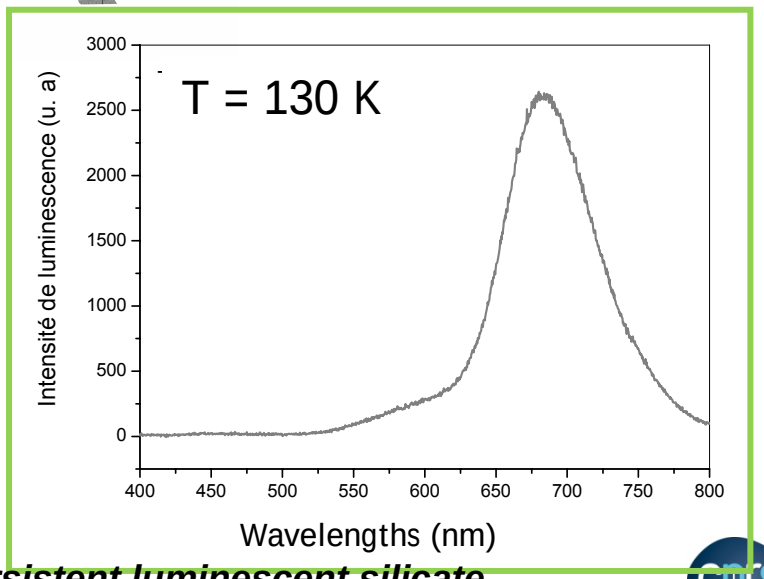
# TSL a good tool to investigate the persistent luminescence




**Thermoluminescence curve**




**Thermoluminescence spectrum**

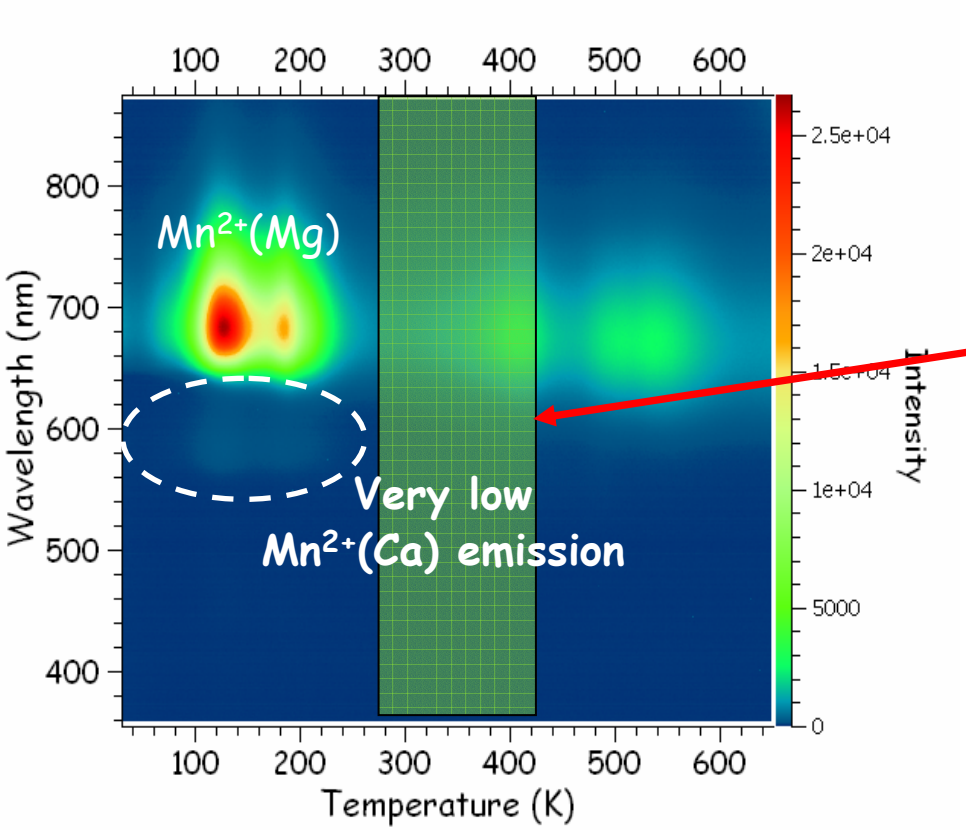



*Lecointre A. Bessiere, B. Viana and D. Gourier "Red persistent luminescent silicate nanoparticles" Radiation Measurements 45, 3-6; 497-499 (2010)*

# TSL a good tool to investigate the persistent luminescence

## 3D Thermally stimuled luminescence spectra

$CaMgSi_2O_6 : Mn^{2+}$

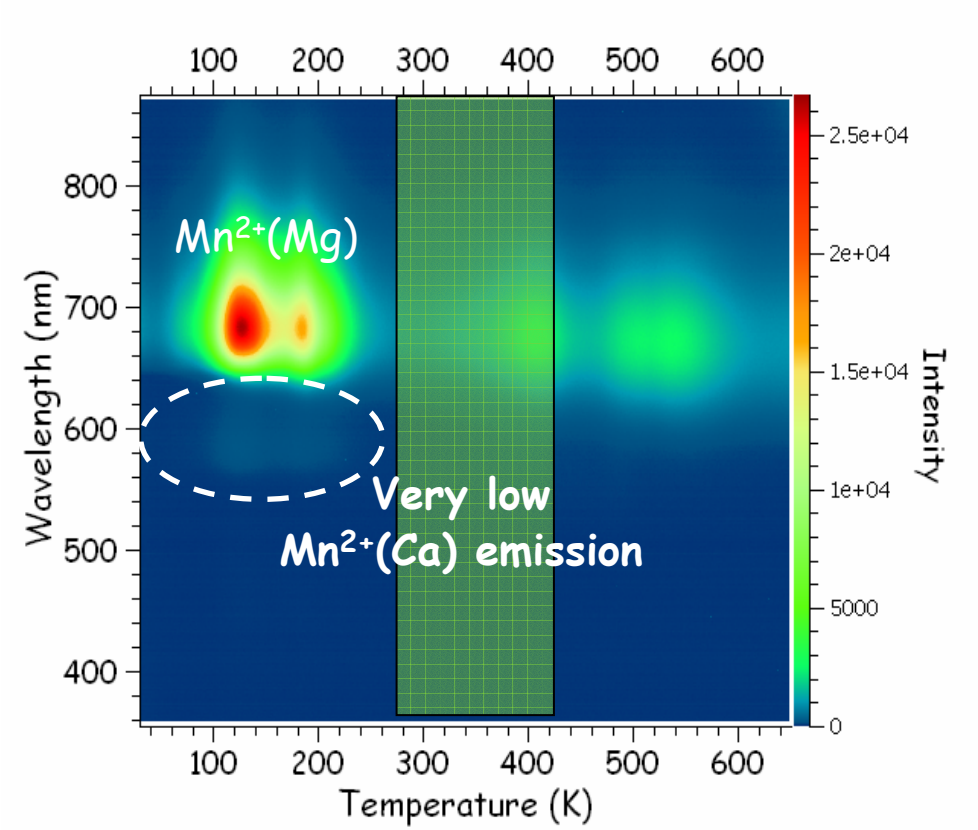



**Better temperature range for intensive persistent luminescence**

# TSL a good tool to investigate the persistent luminescence

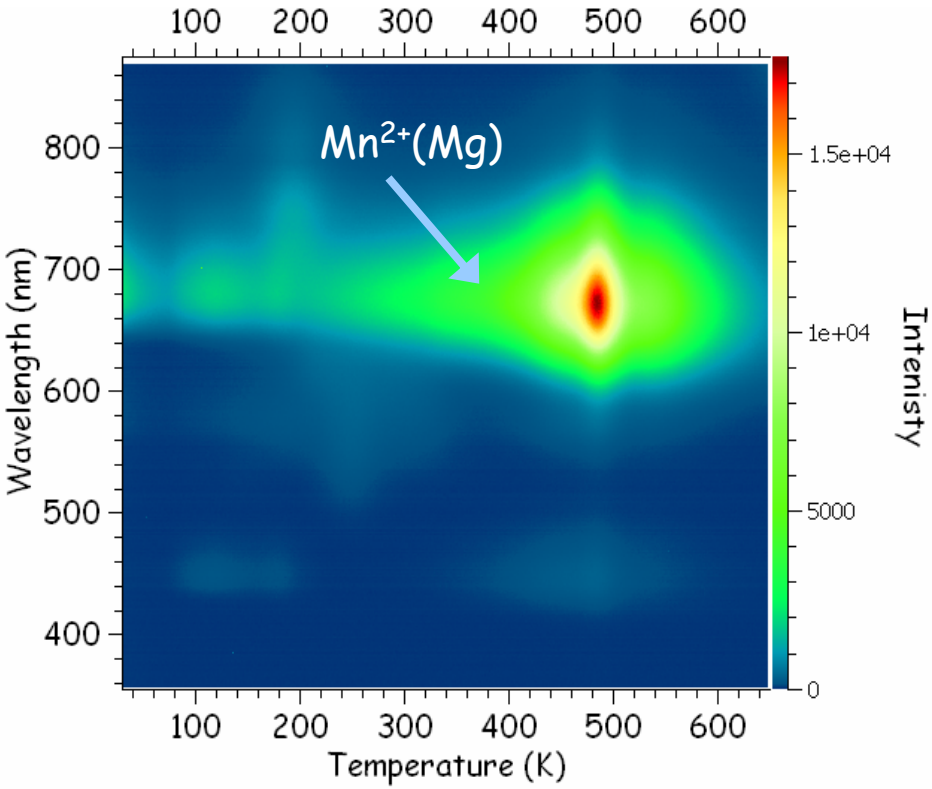
## 3D Thermally stimuled luminescence spectra

$CaMgSi_2O_6 : Mn^{2+}$




$CaMgSi_2O_6 : Mn^{2+}, Dy^{3+}$

$Dy^{3+}$ : good electron trap




Introduction of $Dy^{3+}$ strongly modifiy the TSL peaks

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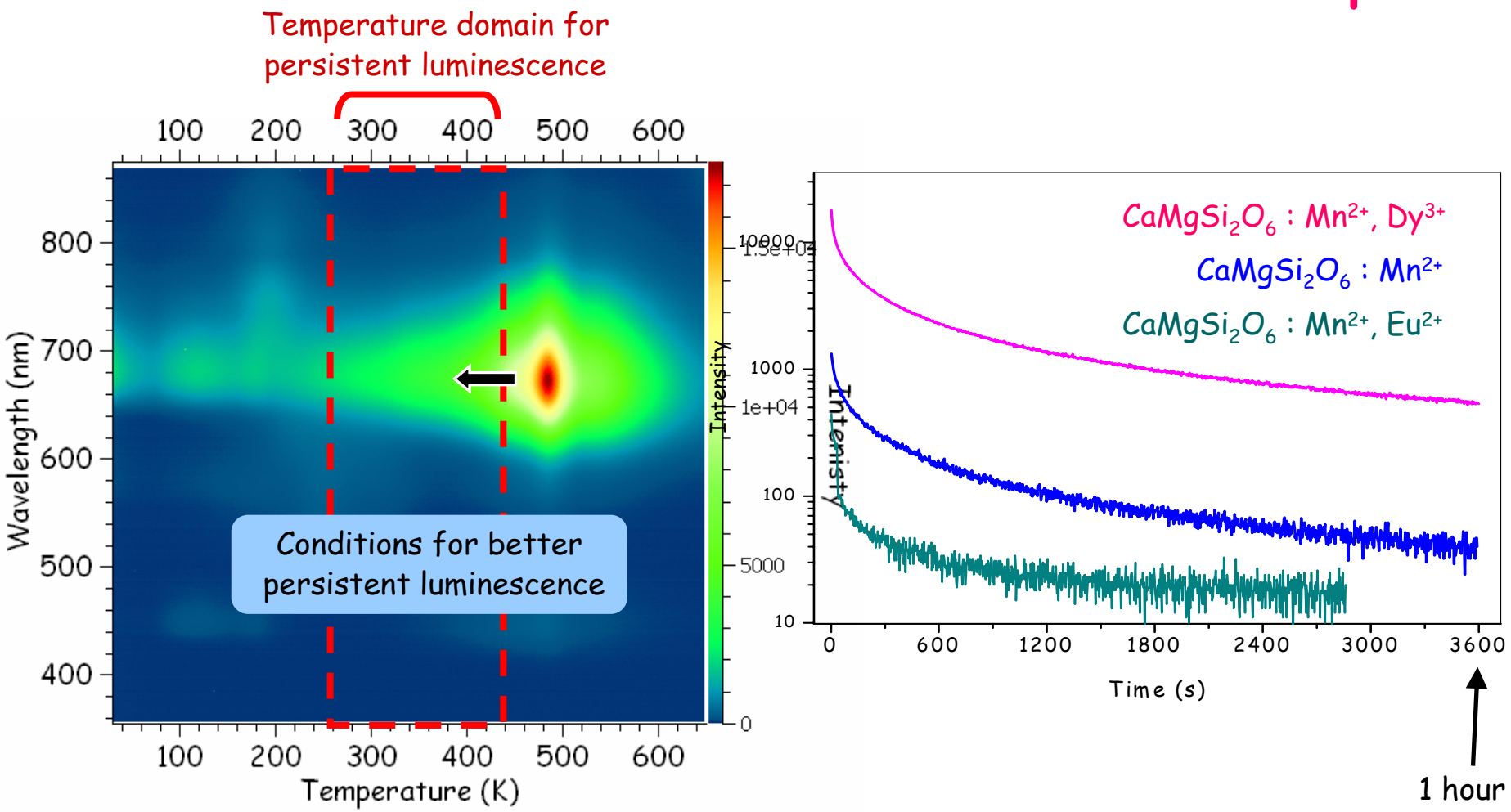
# TSL a good tool to investigate the persistent luminescence

$CaMgSi_2O_6 : Mn^{2+}, Dy^{3+}$

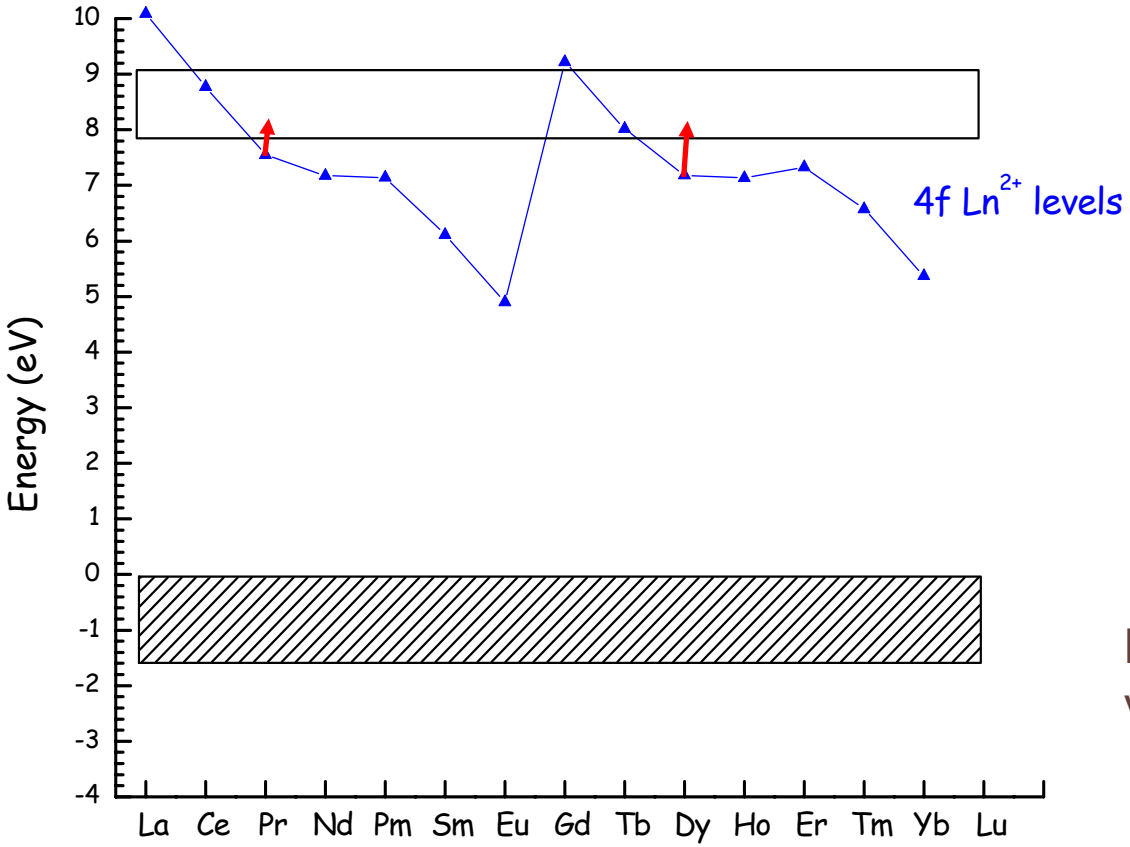
## Persistent luminescence spectra

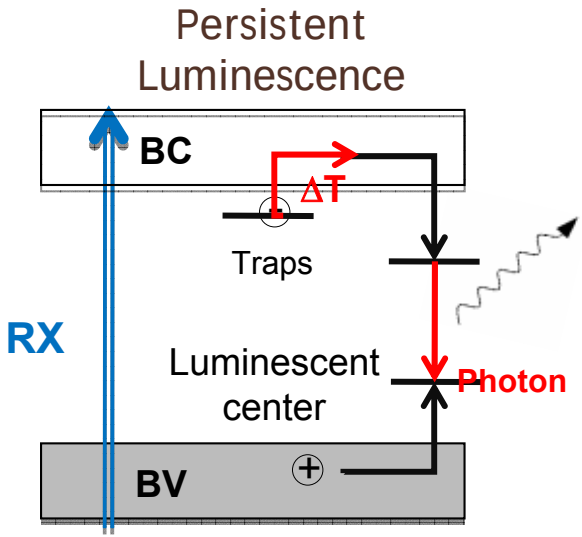


# Mechanisms

## Increase of the persistent Luminescence ?

other codopant ? Other $e^-$ traps ?




Dopant and Oxygen vacancies :

electron traps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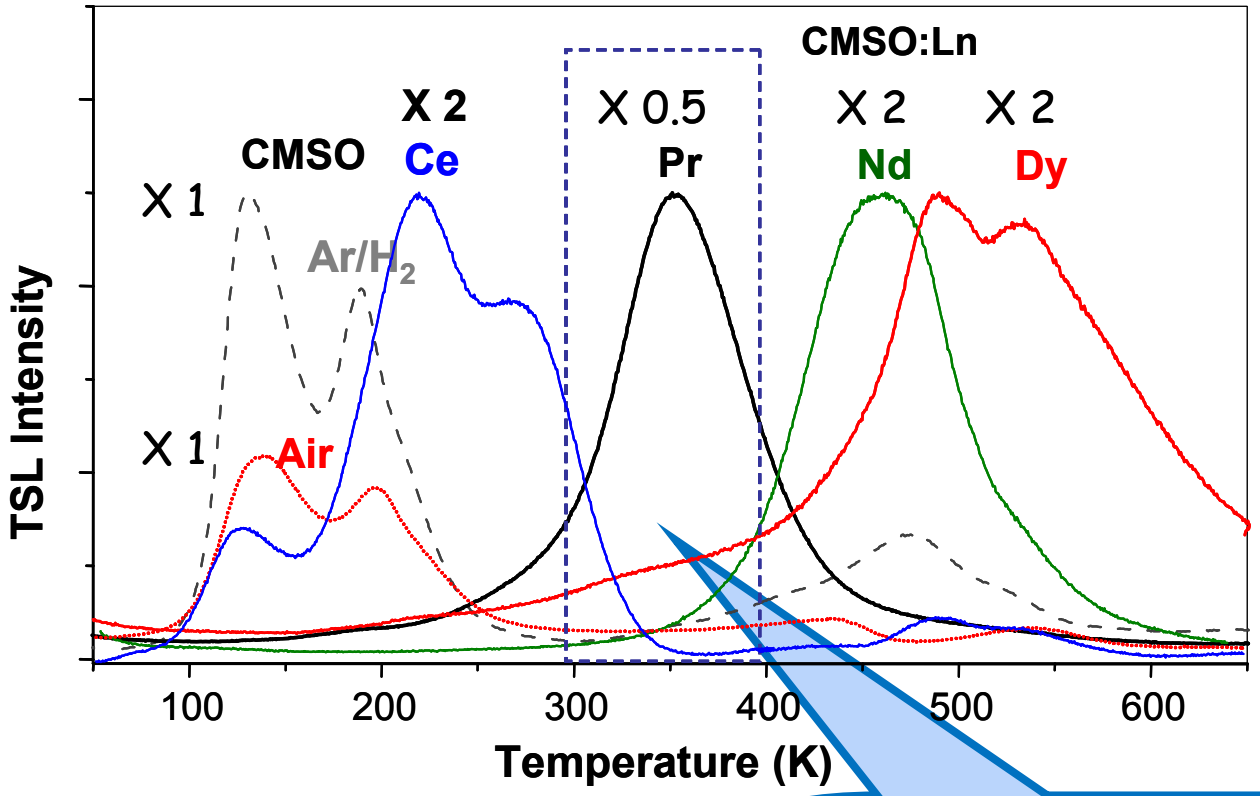
*A.Lecointre; A. Bessiere; A.J.J. Bos; P. Dorenbos, B. Viana and S. Jacquart*
*Journal of Physical Chemistry C 115, 10, 4217-4227 (2011)*

# Mechanisms

Variation of the RE codopant in $CaMgSi_2O_6$:RE,$Mn^{2+}$

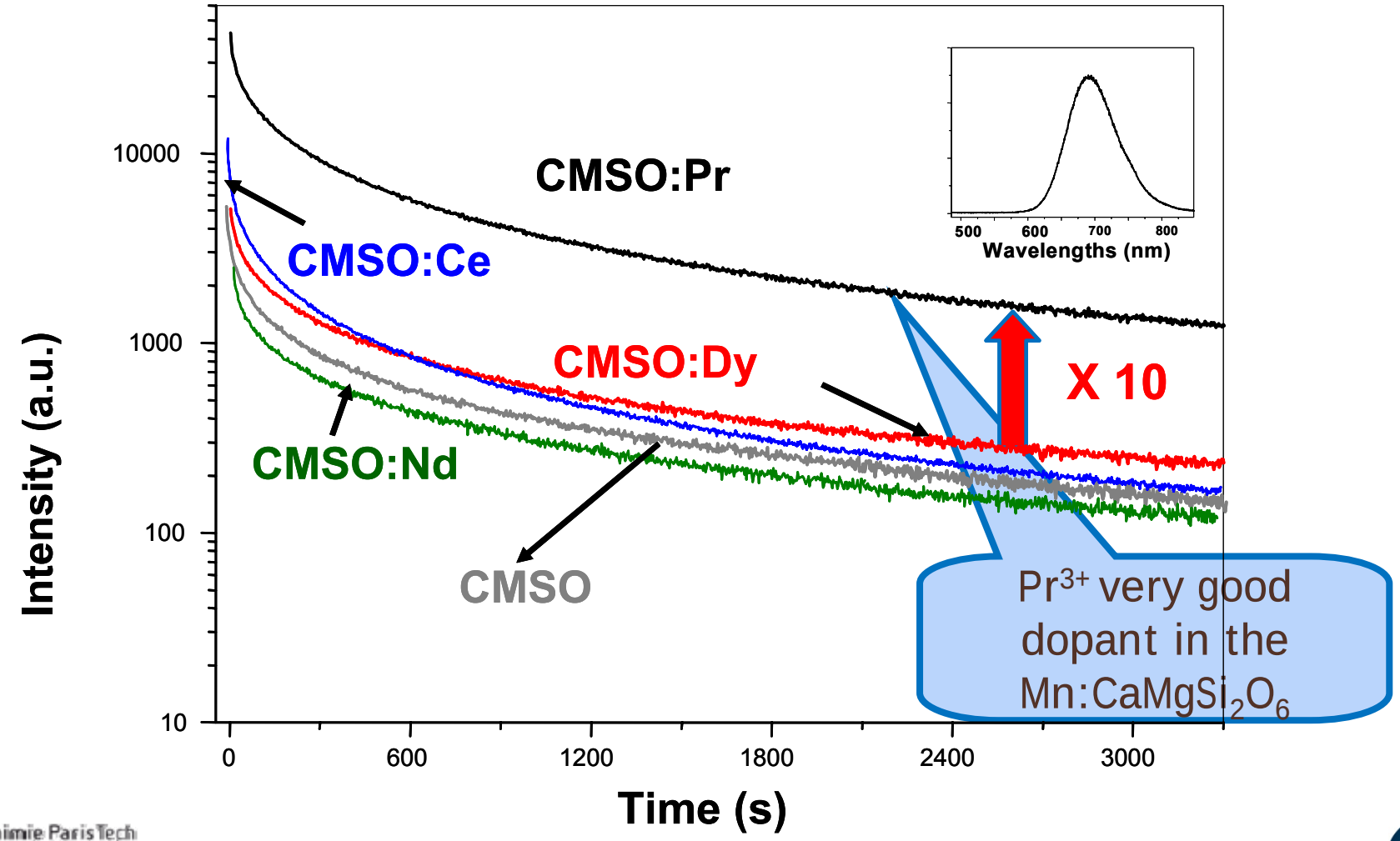



Pr : good candidat

# Improved Materials

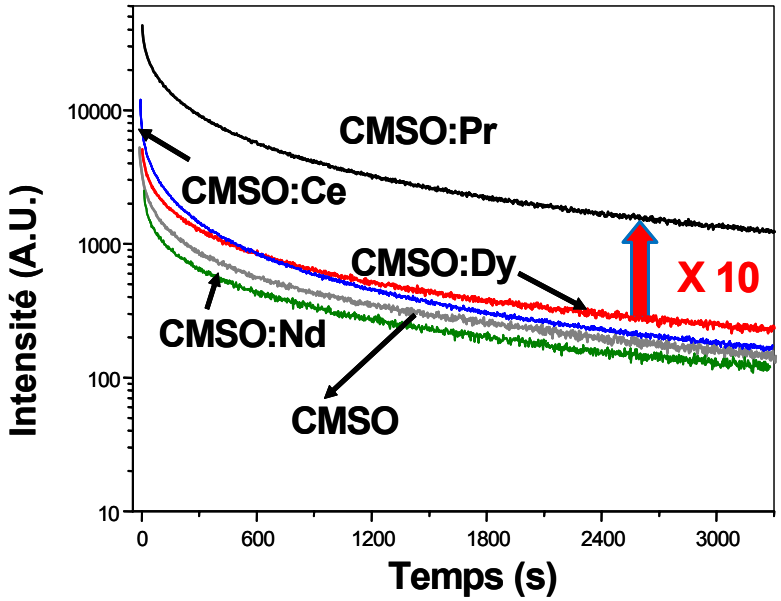
## Persistent luminescence in $CaMgSi_2O_6:Mn^{2+}, Ln^{3+}$

***T. Maldiney et al.*, J Am Chem Soc. (2011), 133 (30) 11810-11815.**

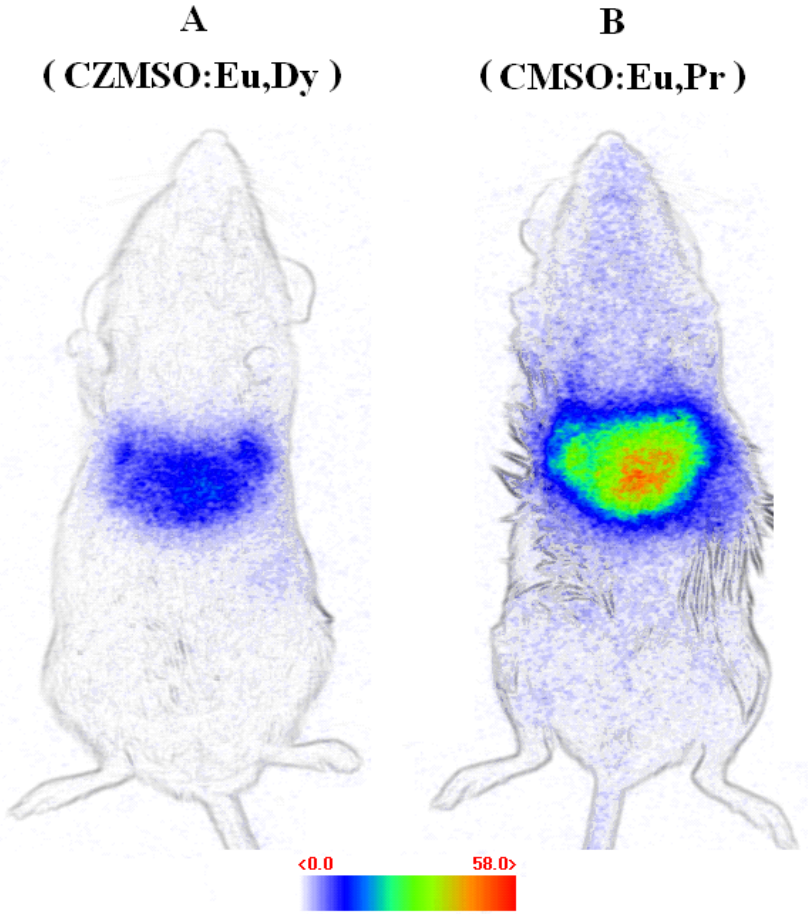


# Improved Materials

## Results on small animals imaging

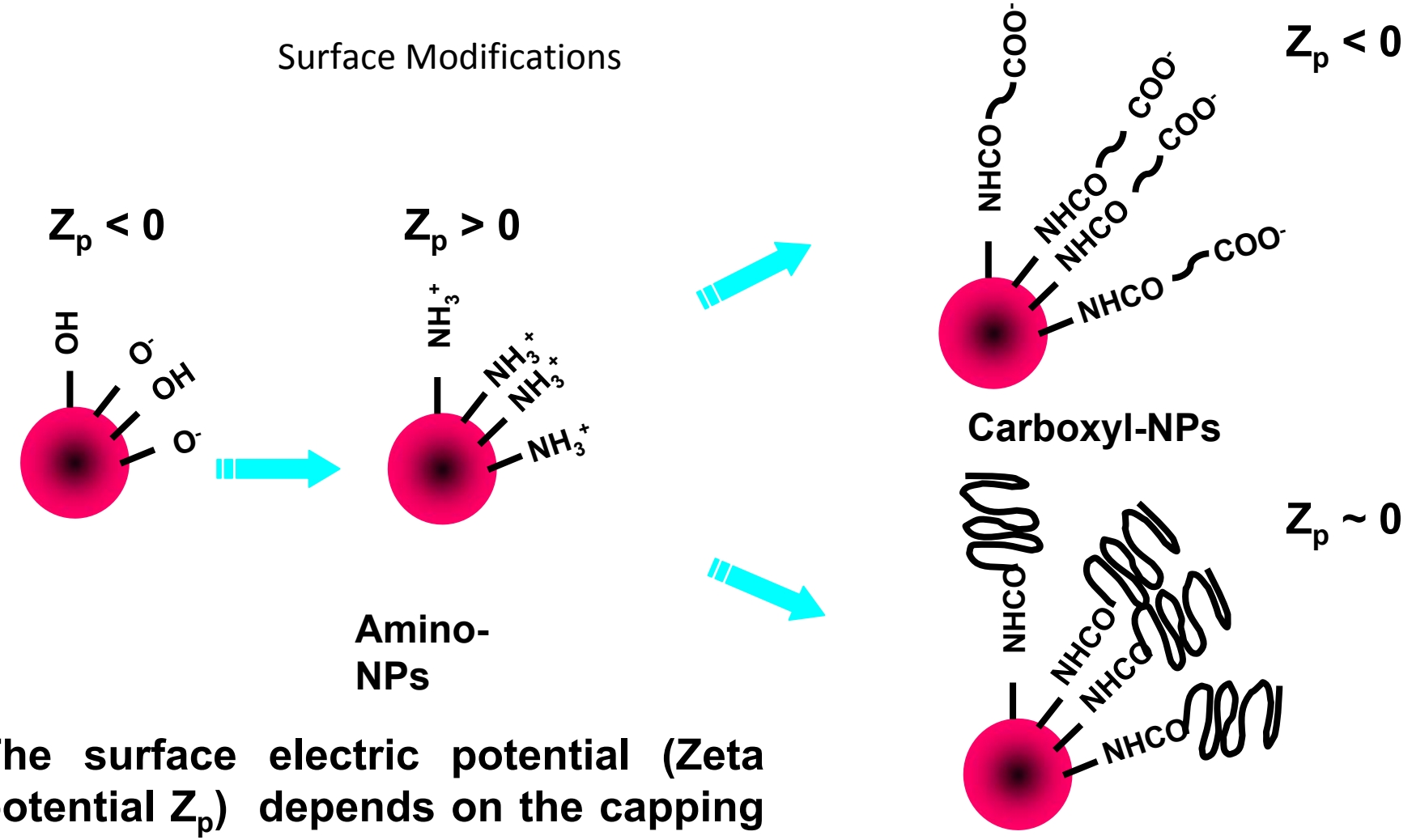



**Luminescence after 30 min.**



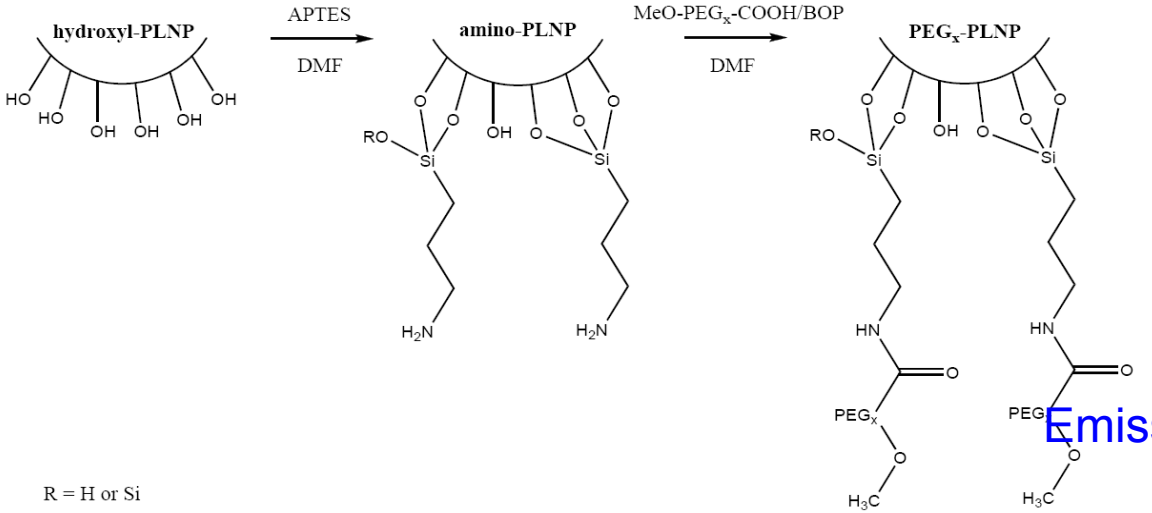
# Improved Materials

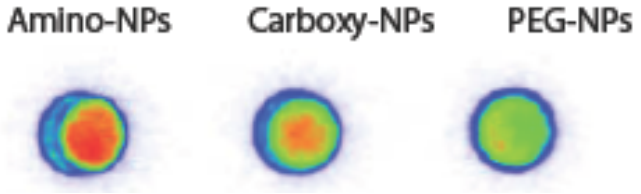
## Persistent luminescence nanoprobes for *in vivo* imaging



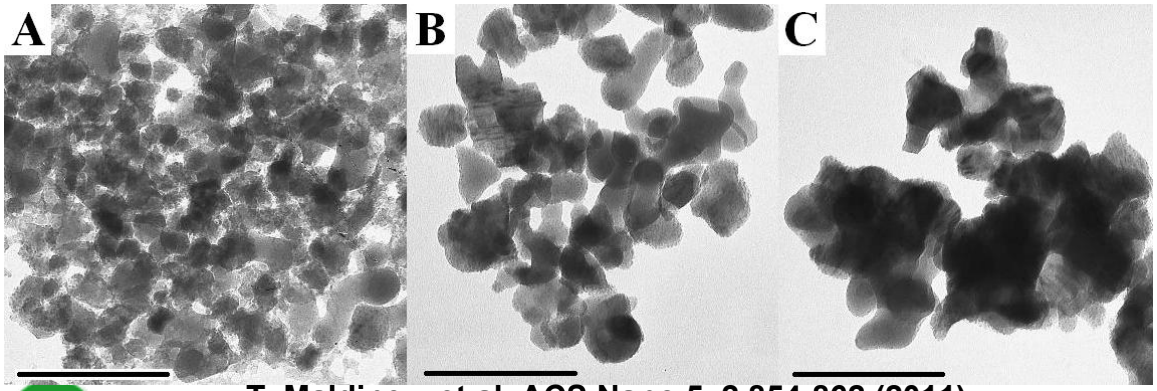

**The surface electric potential (Zeta potential $Z_p$) depends on the capping agent**

# Are the NPs after functionalization still efficient ?




Emission intensity after functionalization




T. Maldiney, et al. ACS Nano 5, 2 854-862 (2011)

**Selection of 3 size populations:**
**80 nm ; 120 nm ; 180 nm**
**(hydrod. diameter of crude PLNP)**

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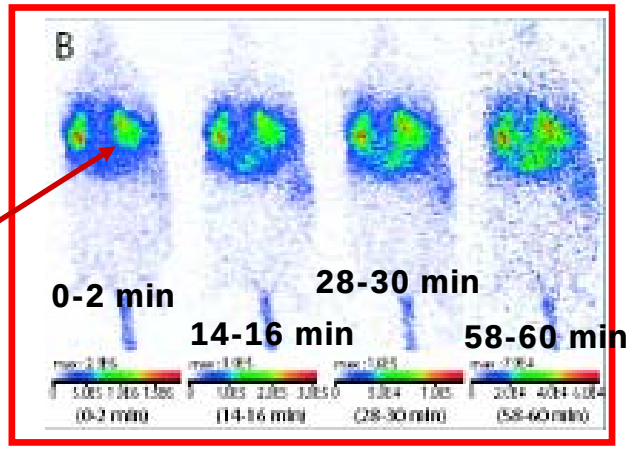
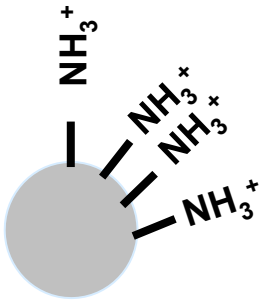
# Exemples of optical imaging

## Small Animal Imaging

lungs

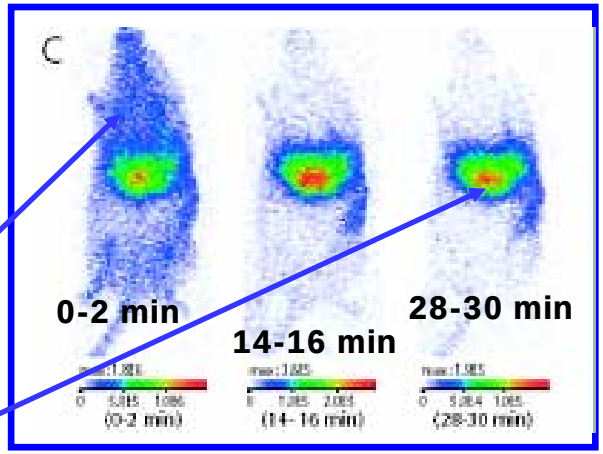


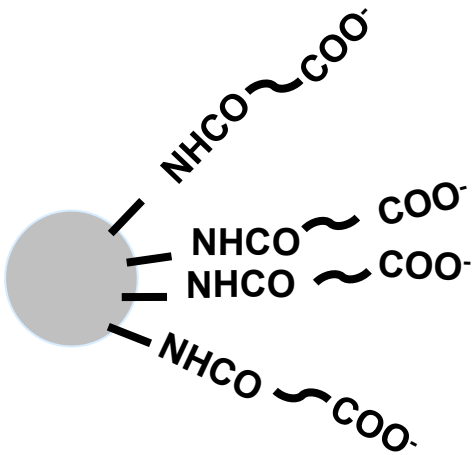

**$NH_3^+$** = electric surface potential **>0**




**$COO^-$** = electric surface potential **<0**

=>better circulation, then liver uptake

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# Outline

1) Introduction

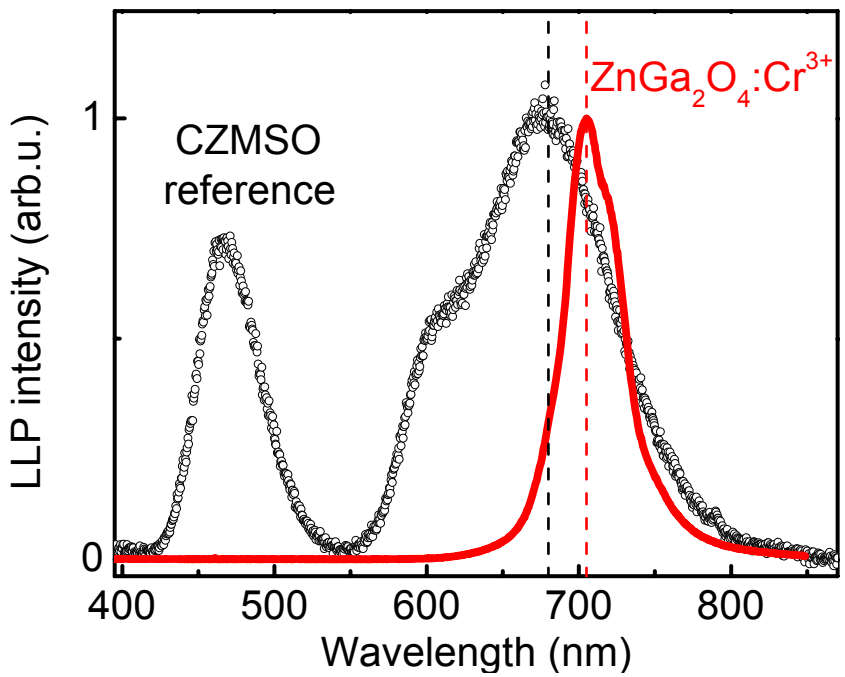
2) Part 1 : Interest of the persistent luminescence in optical imaging

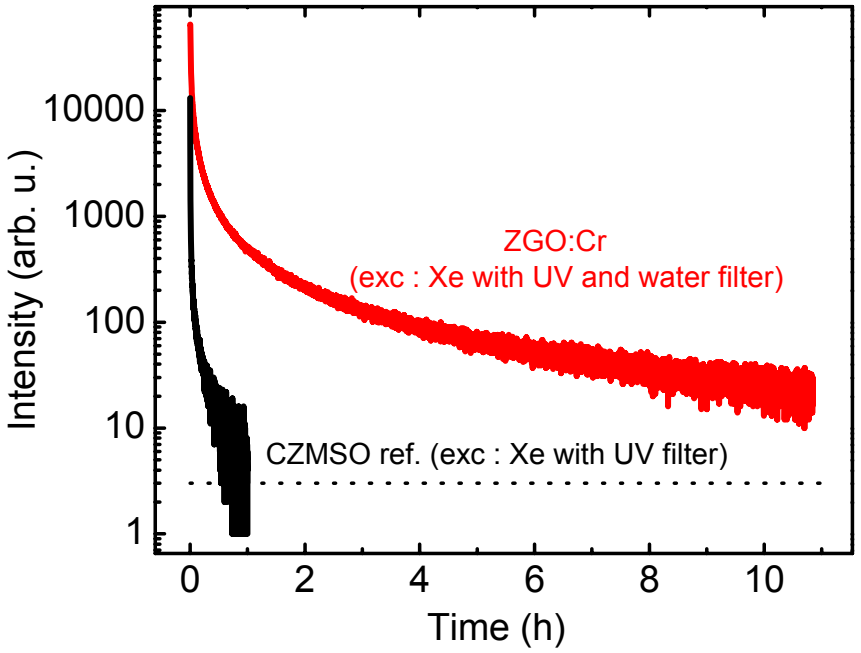
3) Part 2 : Persistent luminescence in the red range :case of $CaMgSi_2O_6$:Mn NP's and exemples of optical imaging

**4) Part 3 : New materials and interest for *in-vivo* optical imaging**

# Search of others new materials

## $ZnGa_2O_4:Cr^{3+}$

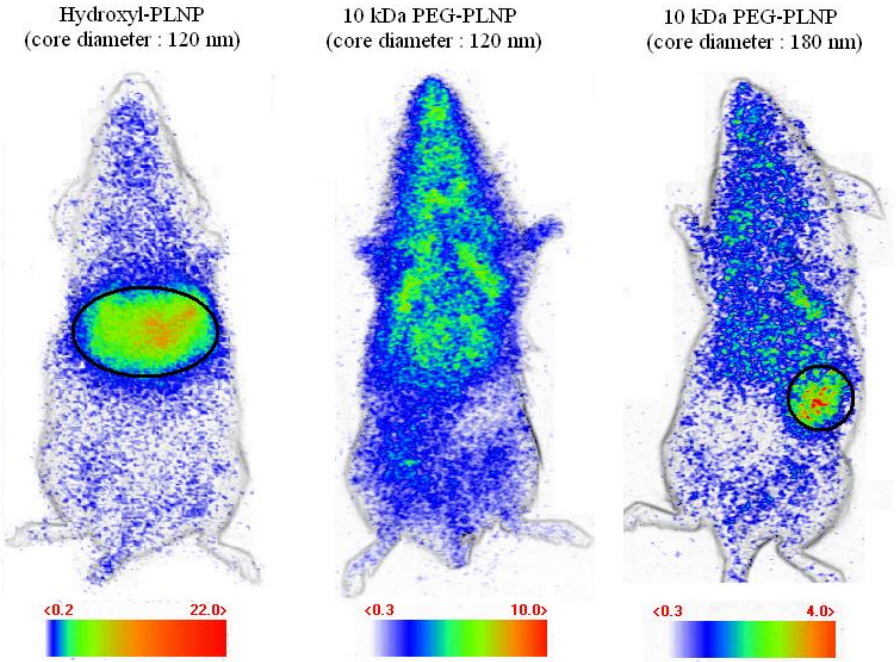



A. Bessière, S. Jacquart, K. Priolkar, A. Lecointre, B. Viana, D. Gourier, "$ZnGa_2O_4:Cr^{3+}$ : a new red long-lasting phosphor with high brightness", ***Opt. Exp. 19(11) (2011) 10131-10137***

# Search of others new materials

Persistent luminescence emitted **through $Cr^{3+}$ distorted and composition variation (stœchiometry effect)**



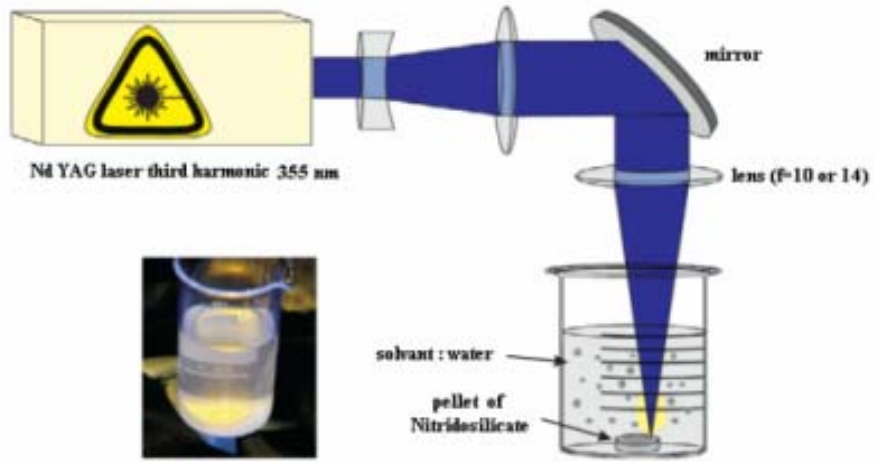

- *in vivo* injection of NPs (100 µg)
- healthy mice
- biodistribution after 15 minutes
  (ROI drawings on liver and spleen)

Maldiney *et al.* ***CNRS patent, Num. 1000138662, 2012***.

# Search of others new materials

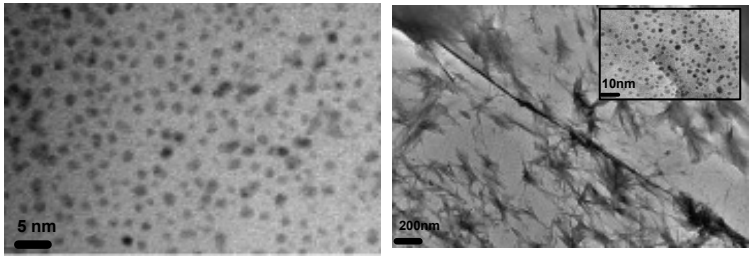
## *Higher LLP and new devices in $Ca_2Si_5N_8 : Tm^{3+},Eu^{2+}$ ?*

### Material preparation

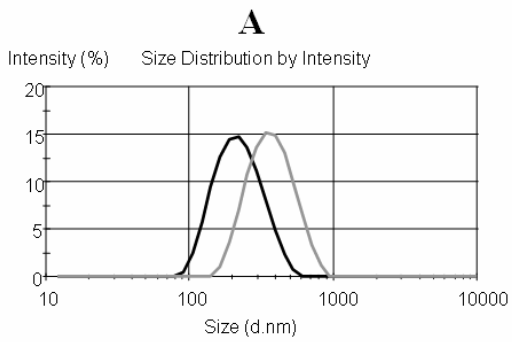


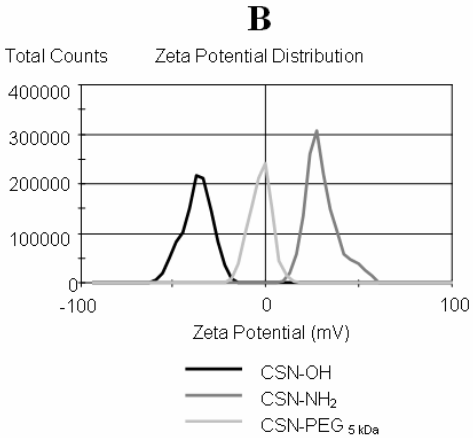

### NPs by Pulsed Laser Ablation in Liquids

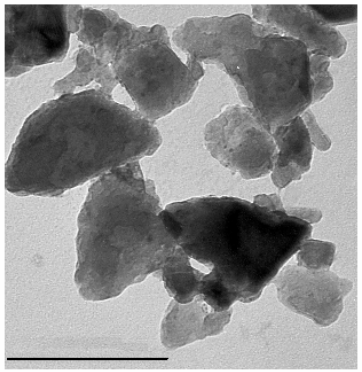
*G. Ledoux et al. Nanotechnology, 20, 445605 (2009).*




### NPs by top-down size selection

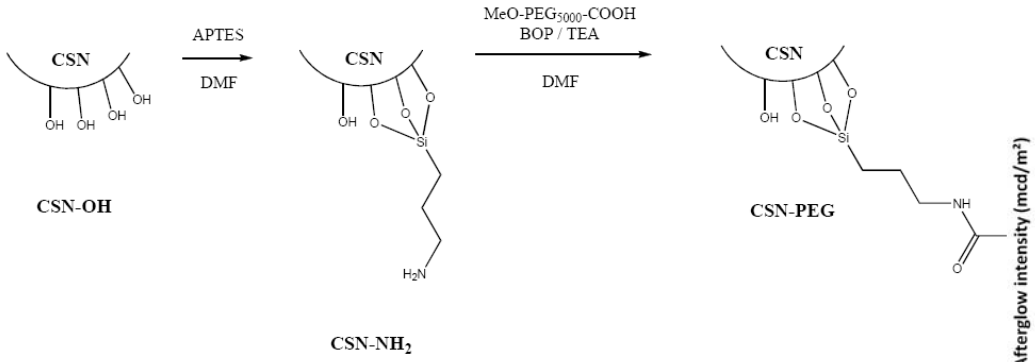


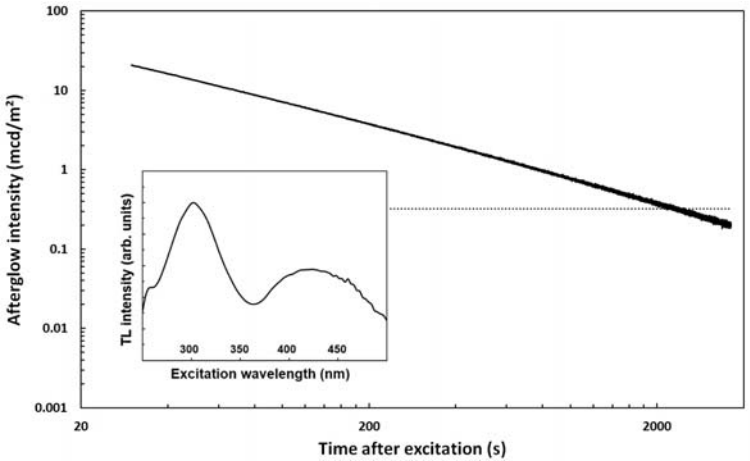



# Search of others new materials

## $Ca_2Si_5N_8 : Tm^{3+},Eu^{2+}$



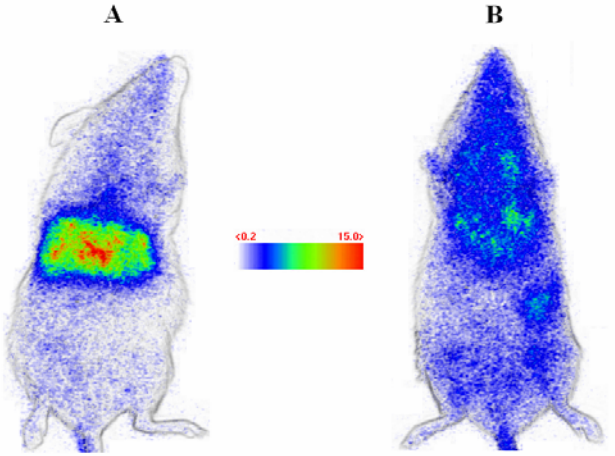




**CSN-OH (mouse A) and CSN-PEG (mouse B), 15 minutes after tail vain injection**

## $Ca_2Si_5N_8 : Tm^{3+},Eu^{2+}$

## *f-d* type intensive transitions:

## Emission in the red and excitation in the green




*(Coll Ph. Smet et al.*

*Ref T. Maldiney et al. Opt. Mat. Express (Vol. 2, Iss. 3, pp. 261–268 (2012))*

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**5) Conclusions**

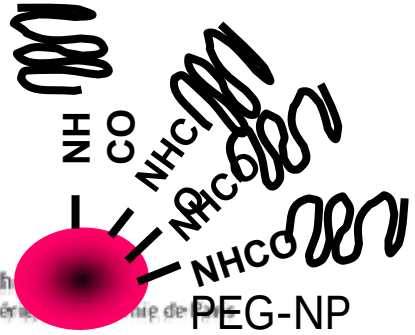
# Conclusions

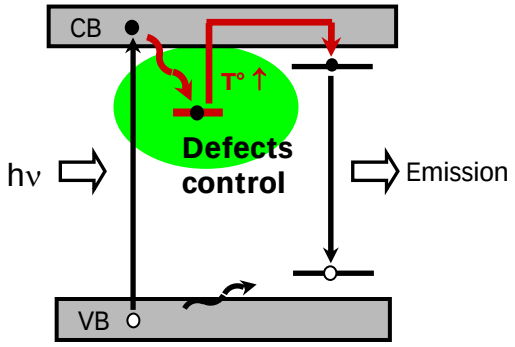
## Summary : our purpose

- Find new materials for optical imaging or optimization of functional materials
- Control of the kinetic processes

(codoping and/or thermal treatment)

- Increase of the luminescence yield
- Mechanisms study
- Concept transfer to biologists for developments



# Thanks to :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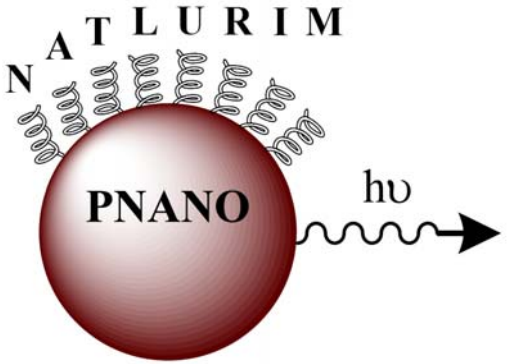
UPC&G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