Nanoparticules à luminescence persistante pour l'imagerie optique *in vivo*

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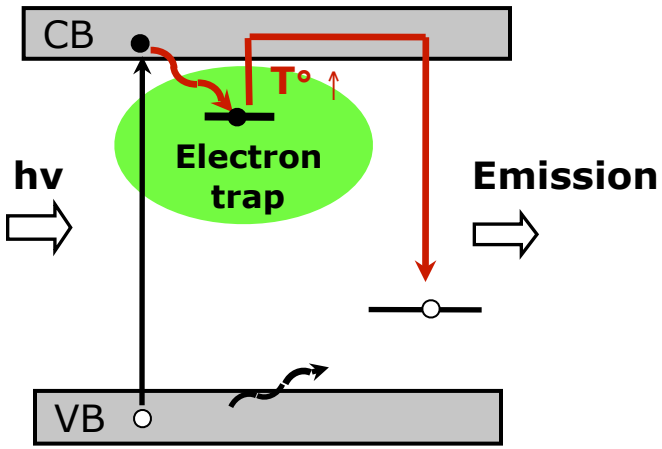
What is persistent luminescence ?

Optical phenomenon in which the **excitation** light is **stored** in traps, and is then slowly **released** upon **thermal activation**, producing a **light emission** which can last for **several hours**.



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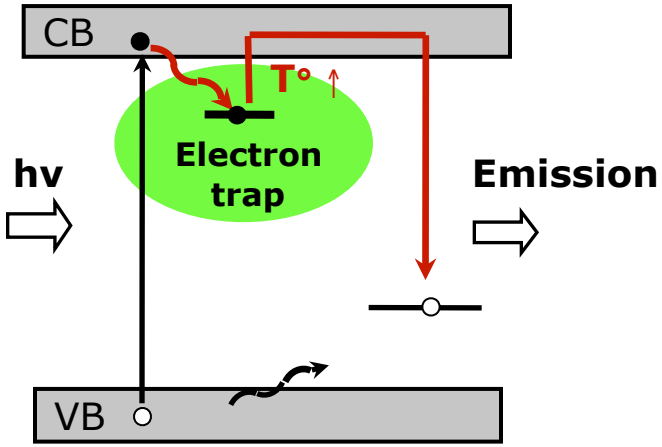
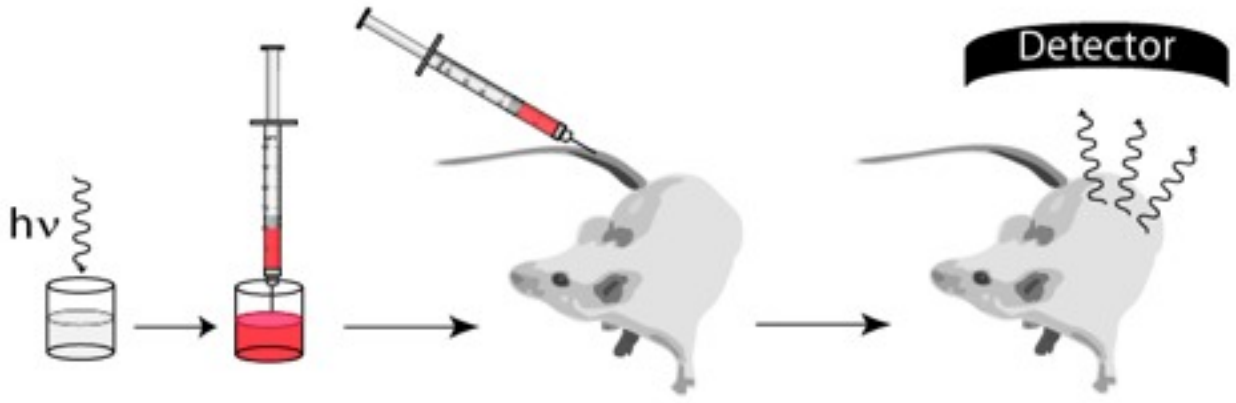


Main applications: traffic signs, emergency signage, watches, luminous paints, textile printing

Development of a new type of imaging probes



- Emission of light for several hours
- Probes excited before the injection ⇨ no autofluorescence
- Emission of light in the tissue transparency window (> 650 nm)
- Nanometric size

CNRS patent 2007, FR2892819

State of the art

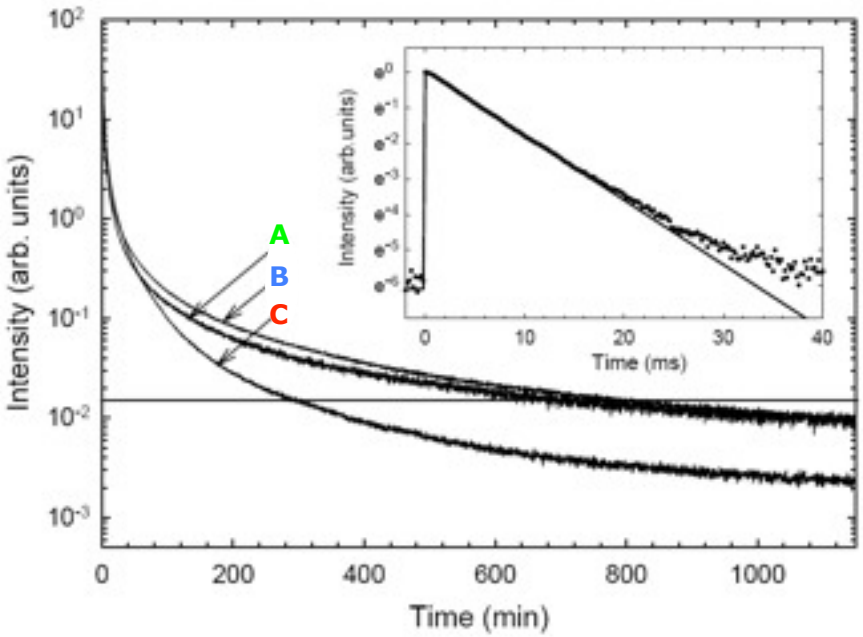
Wang et al., J Lumin 2003, 102-103, 34-37

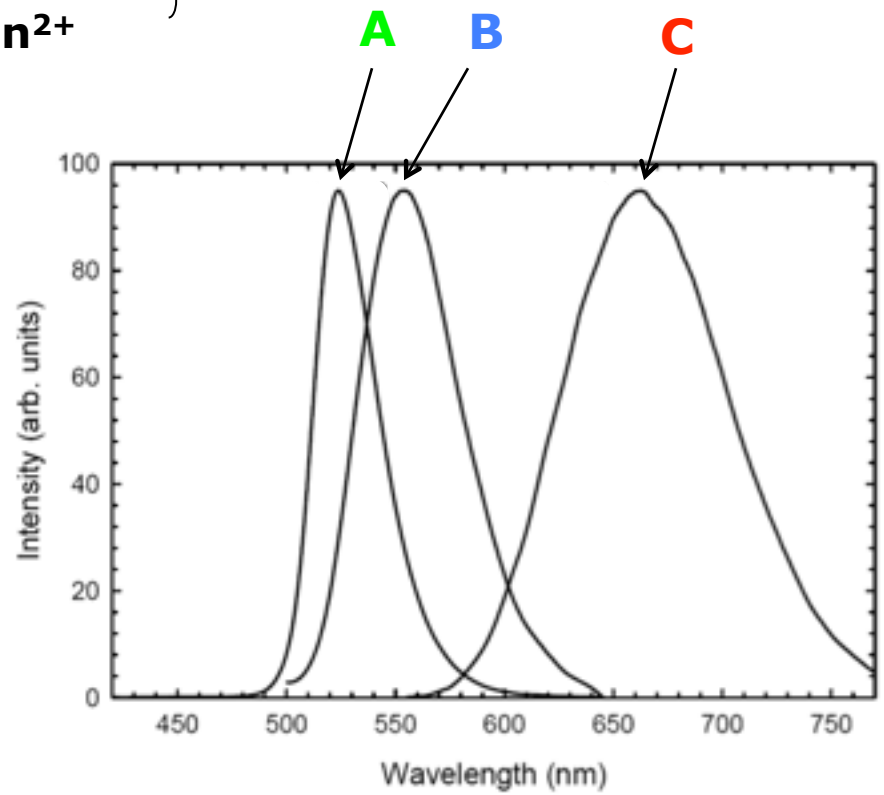
A = $CaAl_2O_4$: Mn^{2+}, Ce^{3+}

B = $Ca_2Al_2SiO_7$: Mn^{2+}, Ce^{3+}

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

} Solid state synthesis





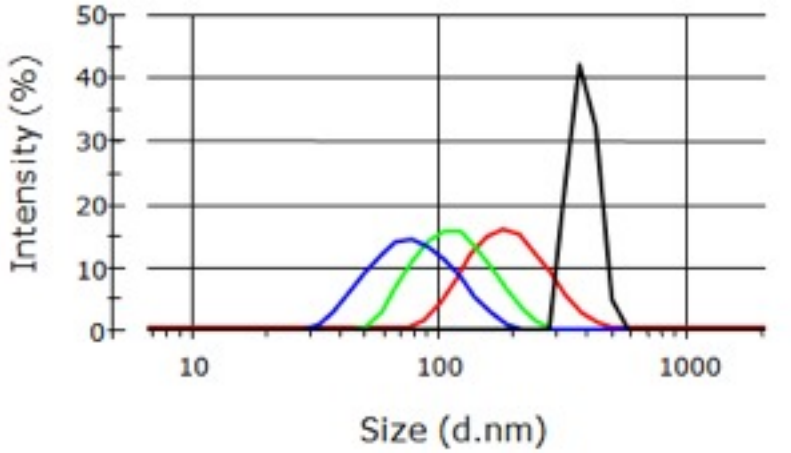
First generation of silicates for in vivo imaging

Small particles: Sol-gel process

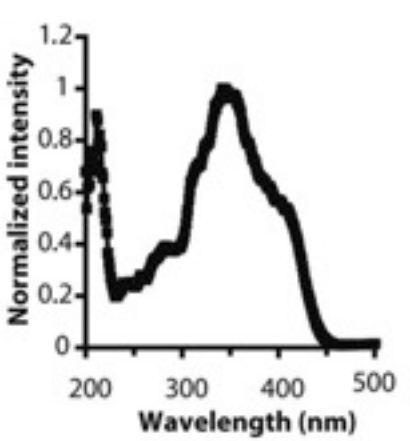
$MgSiO_3 : Eu^{2+}, Dy^{3+}, Mn^{2+}$

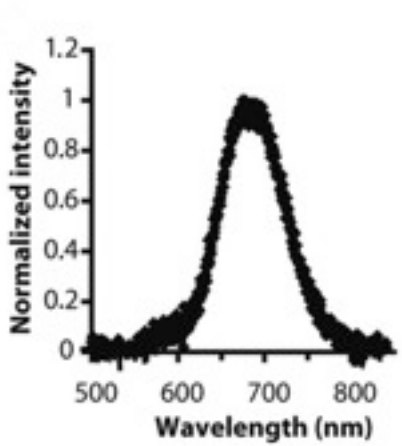
$ZnMgSi_2O_6 : Eu^{2+}, Dy^{3+}, Mn^{2+}$

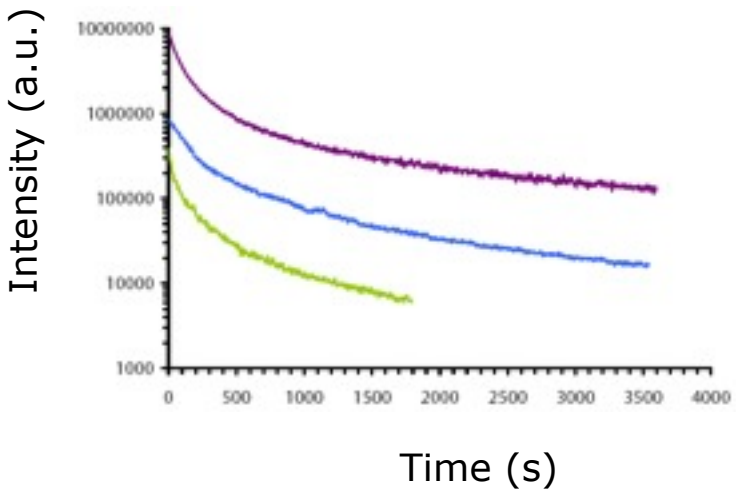
$Ca_{0,2}Zn_{0,9}Mg_{0,9}Si_2O_6 : Eu^{2+}, Dy^{3+}, Mn^{2+}$



Optical characteristics

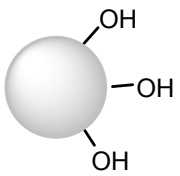




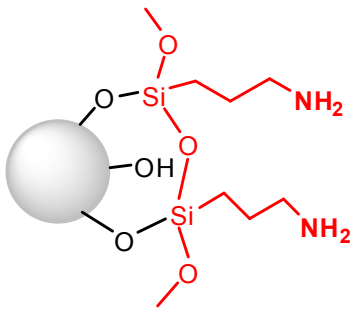


ACS Nano 2011, 5, 854-862

Surface modifications of the nanoparticles

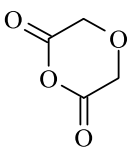


APTES
DMF

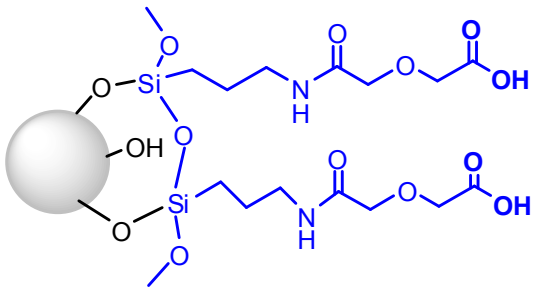


Amino-PLNP

Zeta Potential = +35 mV



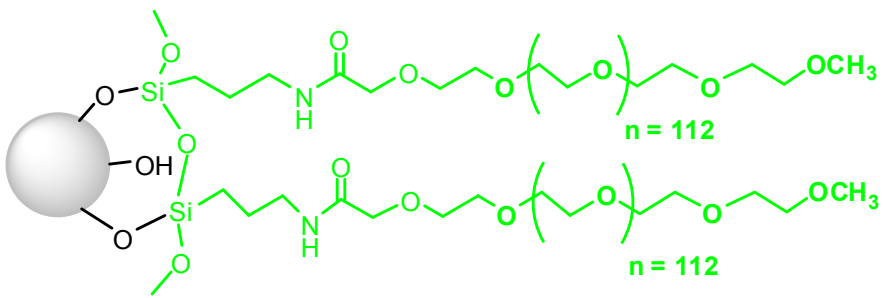
DMF



Carboxy-PLNP

ZP = - 25 mV

$MeO\text{-}PEG_{5000}\text{-}COOH$
BOP, TEA, DMF



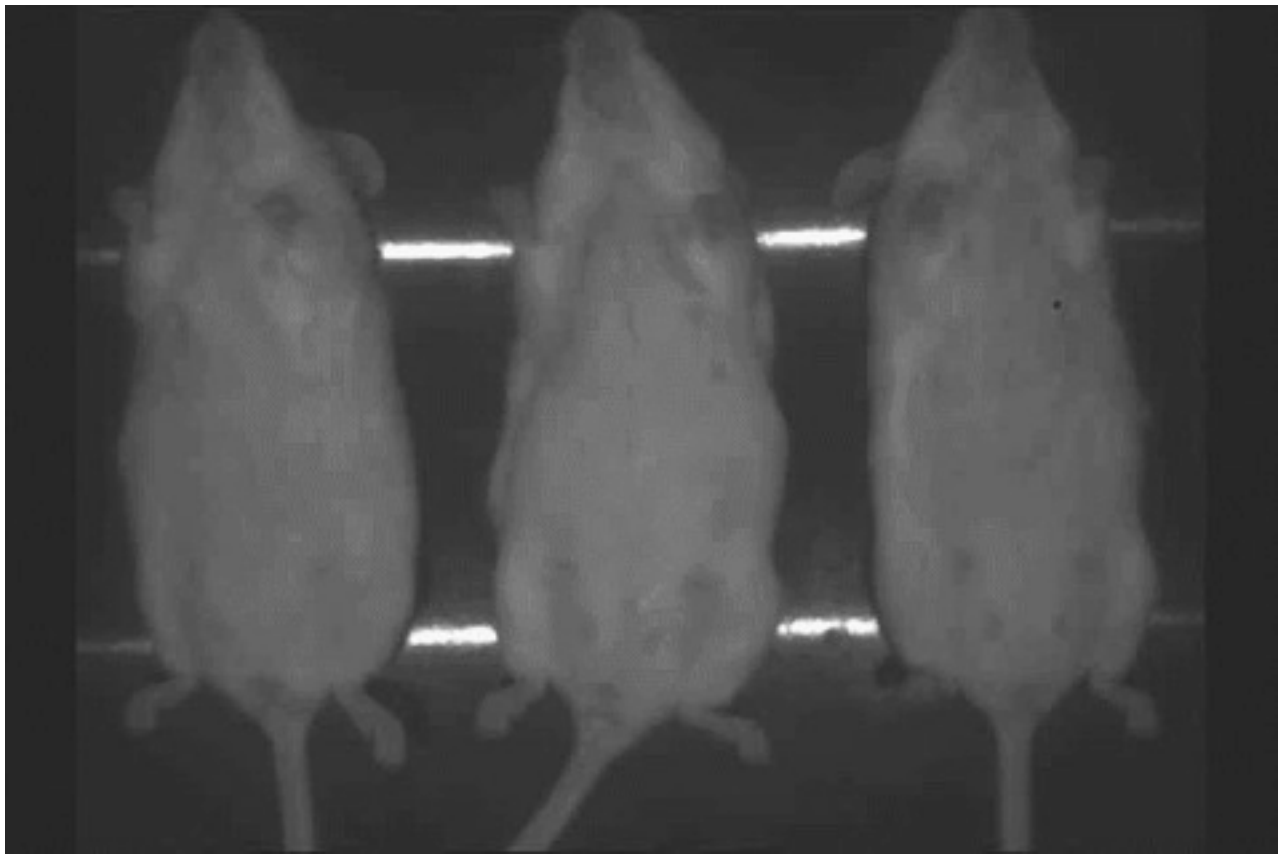
PEG-PLNP

ZP = 0 mV

Biodistribution of the chemically modified probes

- Dispersion in 150 mM NaCl
- Excitation for 2 minutes under UV light
- Injection in the tail vein

Amino-PLNP Carboxy-PLNP PEG-PLNP

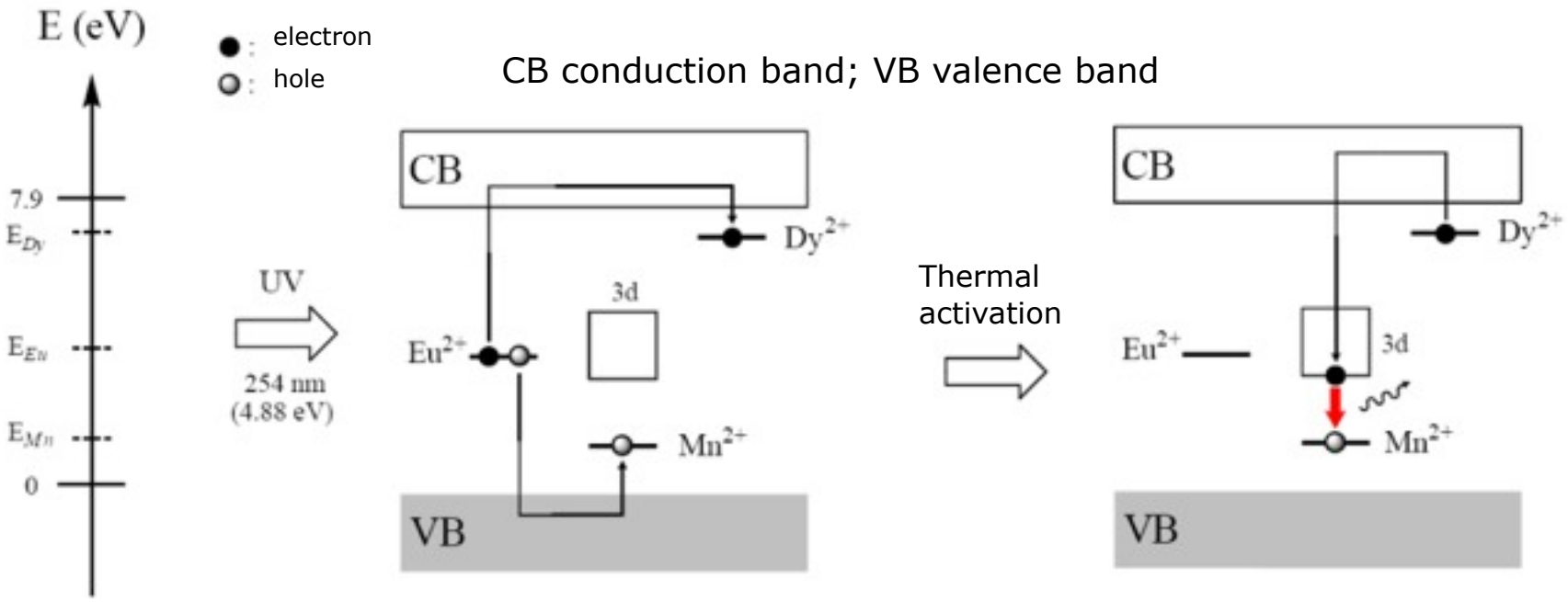


PNAS, 2007, 104, 9266-9271

Mechanism of persistent luminescence

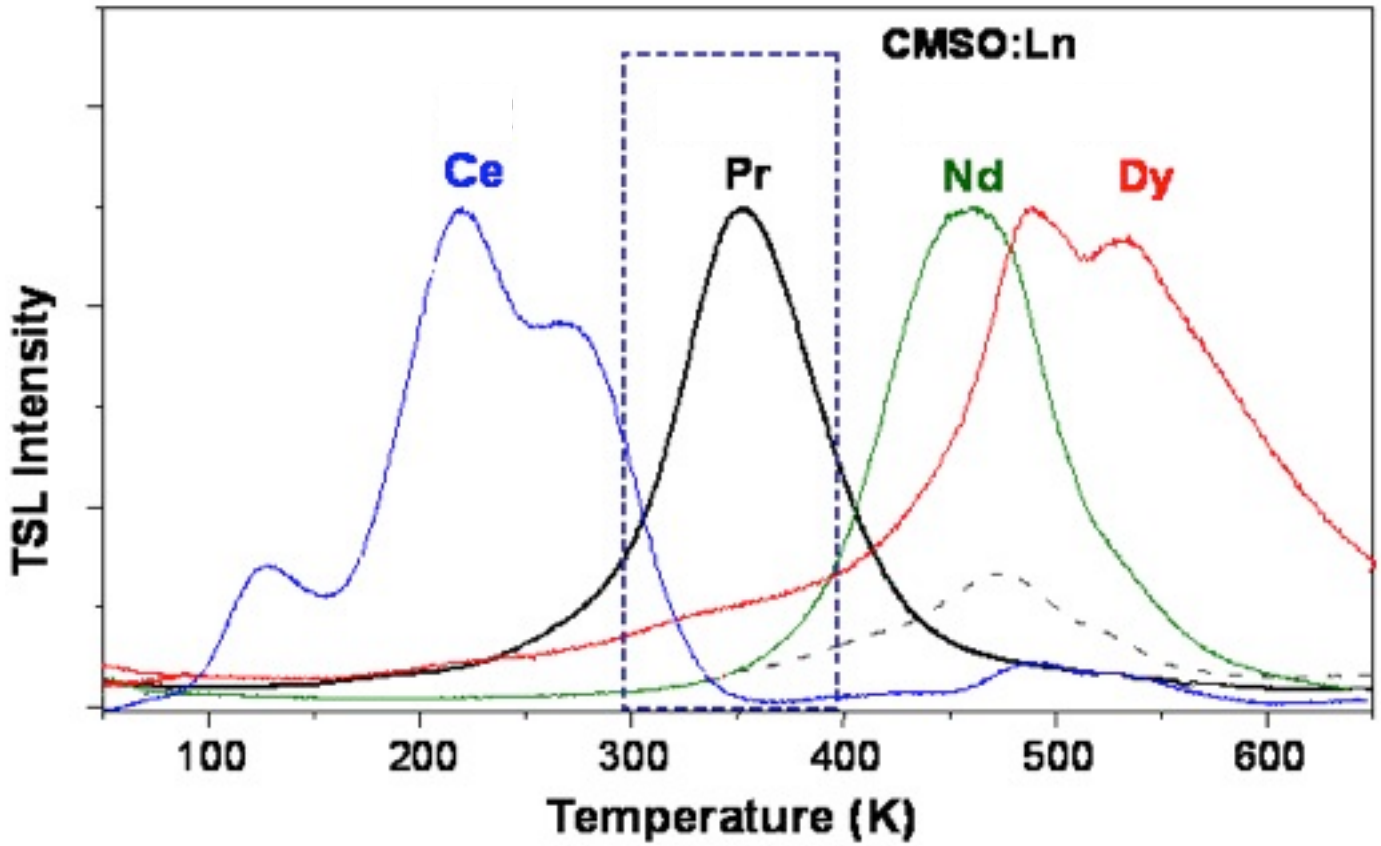
Excitation light is **stored** by **electrons traps**, and is then slowly **released** upon **thermal activation** of emitting centres, producing a light emission.

A. Bessière, B. Viana, D. Gourier, LCMCP



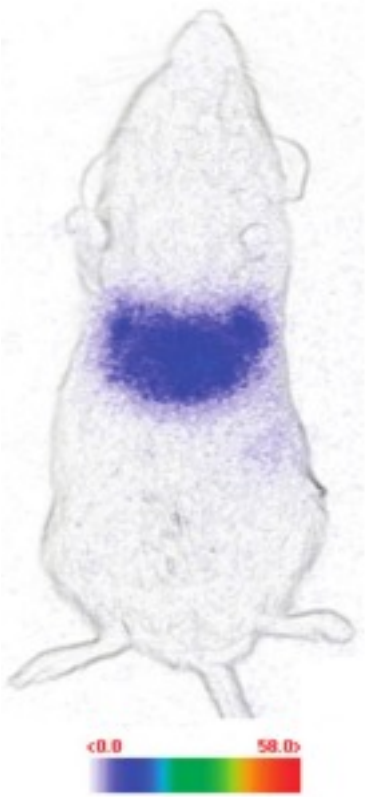
Influence of electron trap on persistent luminescence

- Synthesis of CMSO: Eu^{2+}, Mn^{2+}, Ln^{3+} (Ln^{3+} = Ce^{3+}, Nd^{3+}, Pr^{3+}, Dy^{3+})
- Observation of the different powders:

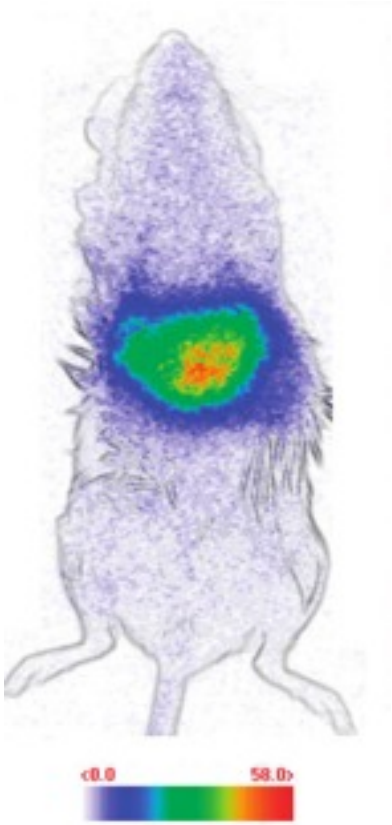


Comparative *in vivo* study of the two UV-excitable compositions

CMSO: Dy^{3+} doped

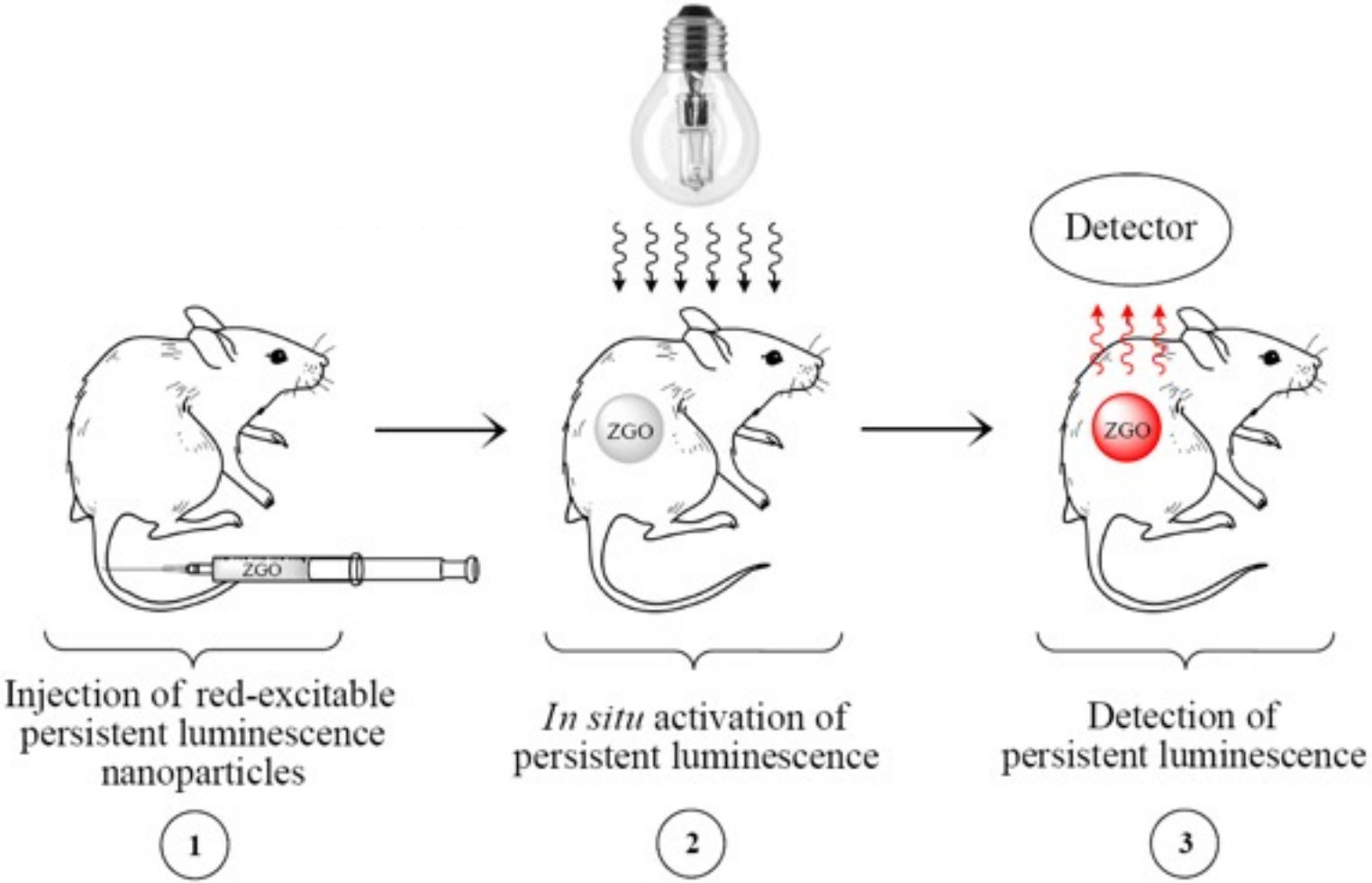


CMSO: Pr^{3+} doped



JACS 2011, 133, 11810-11815

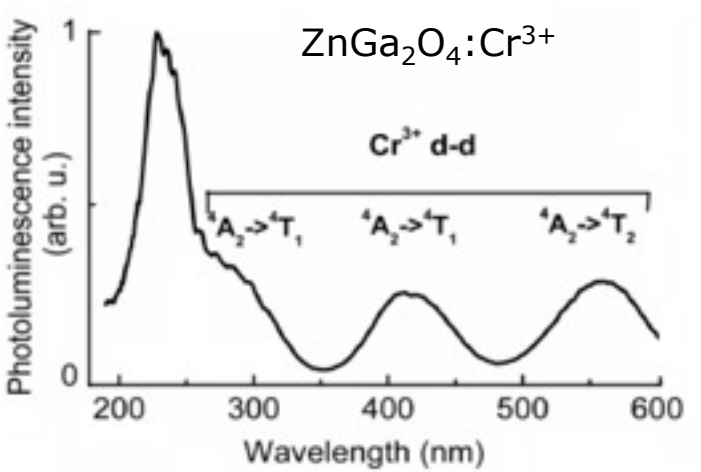
In vivo activation of persistent luminescence for long term imaging

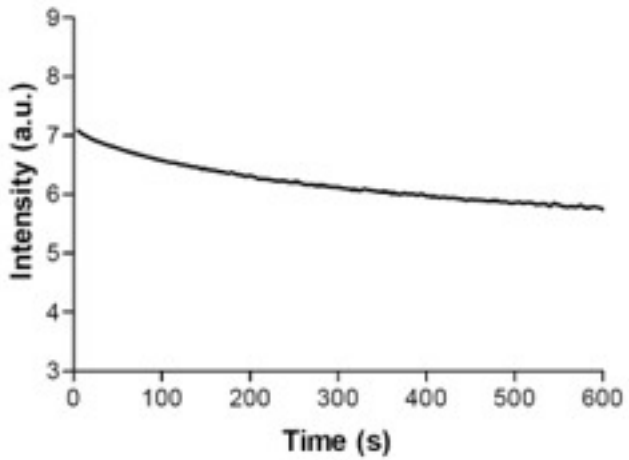


CNRS Patent, 2012, FR1250846

Second generation of persistent luminescence nanoparticles: $ZnGa_2O_4:Cr^{3+}$

A. Bessière et al,. Optics Express, 2011, 19(11), 10131-10137





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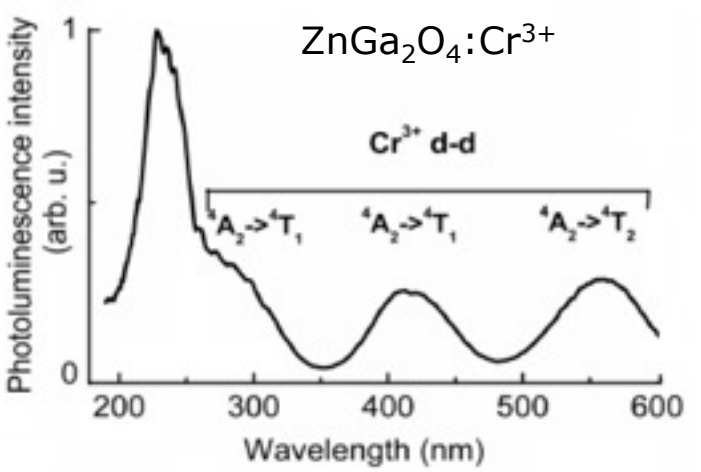
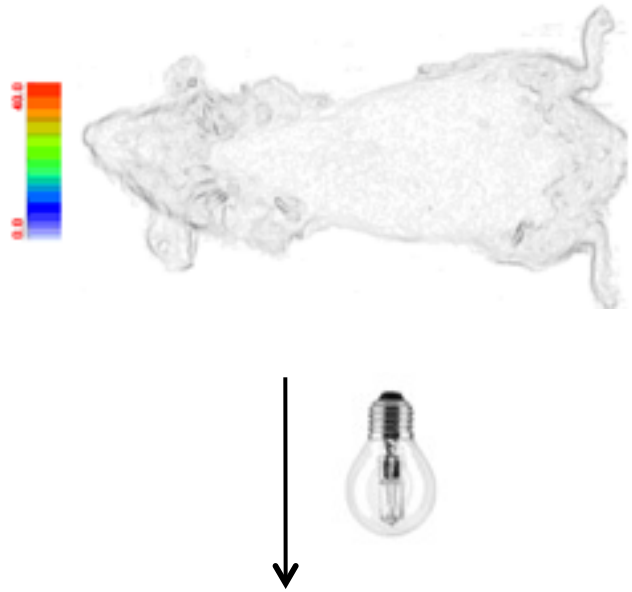
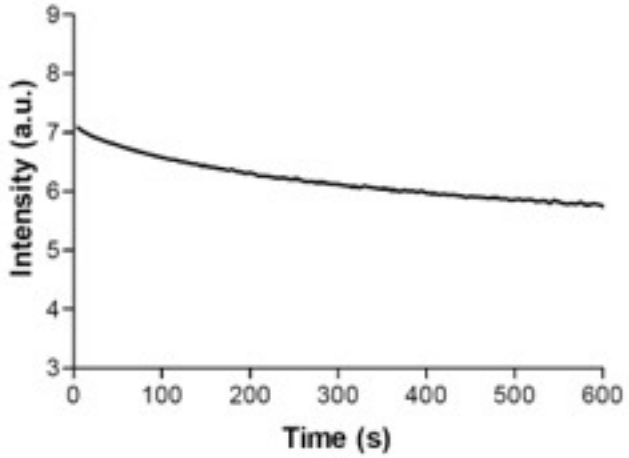
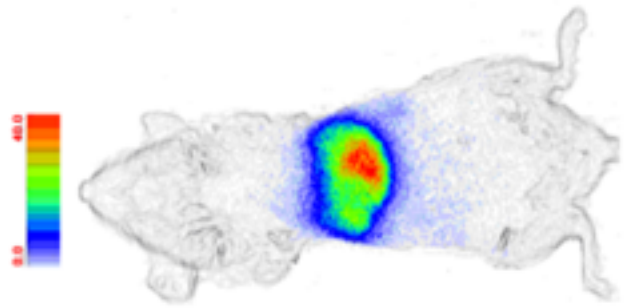
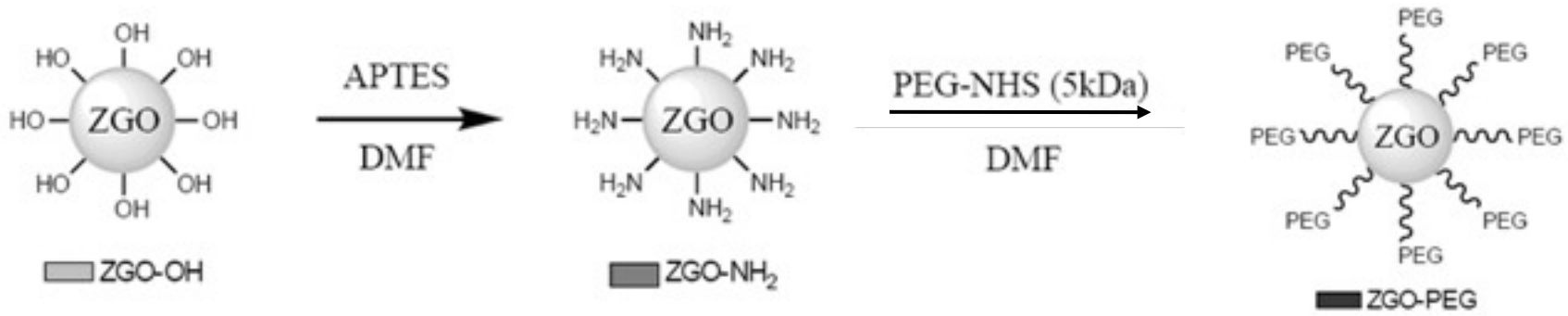








Surface modification and biodistribution studies



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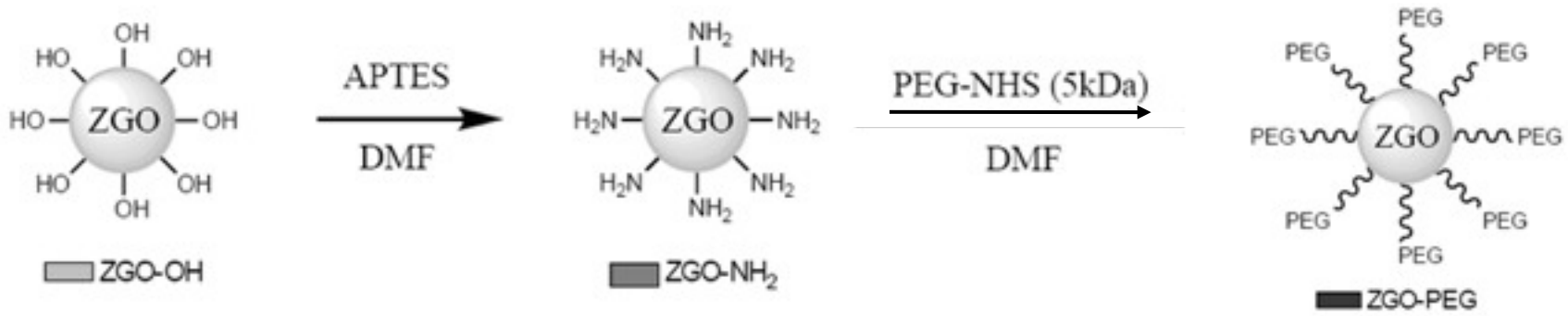
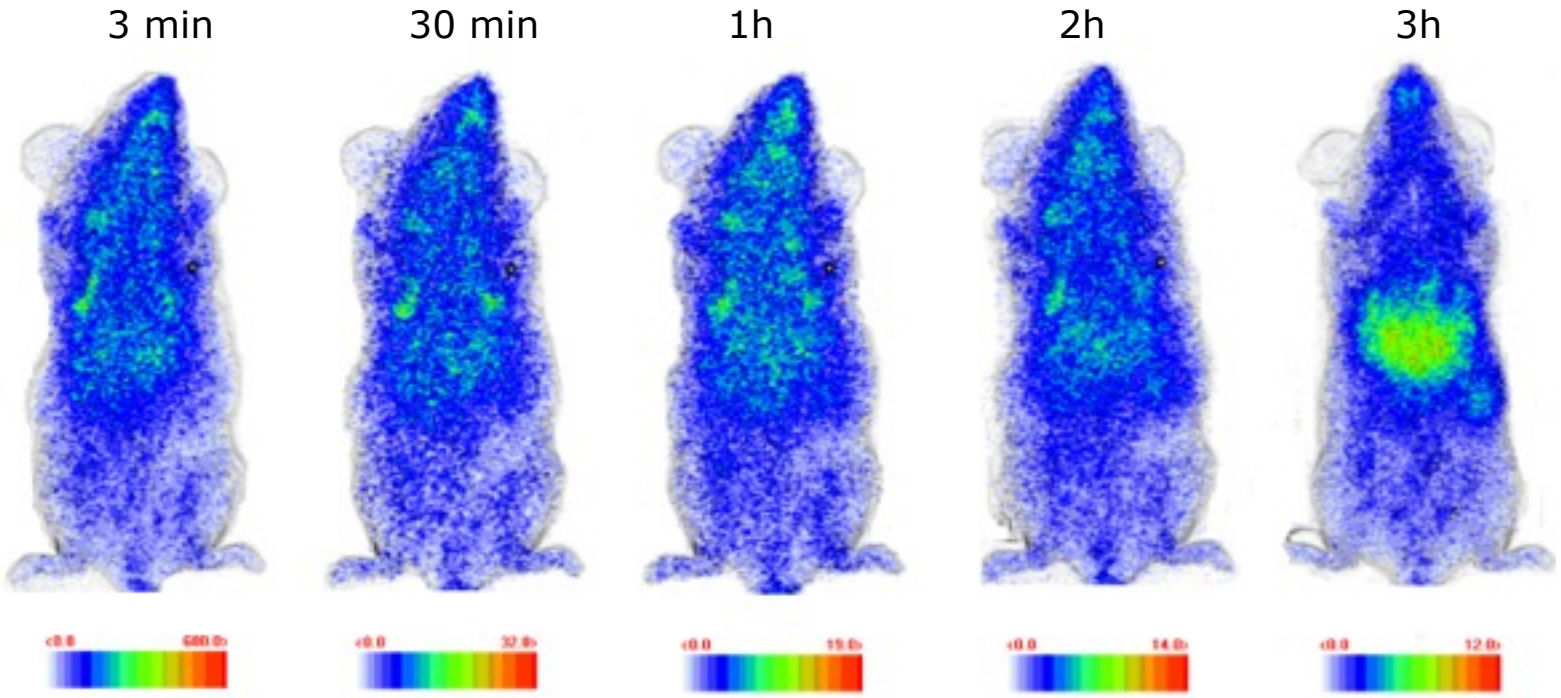
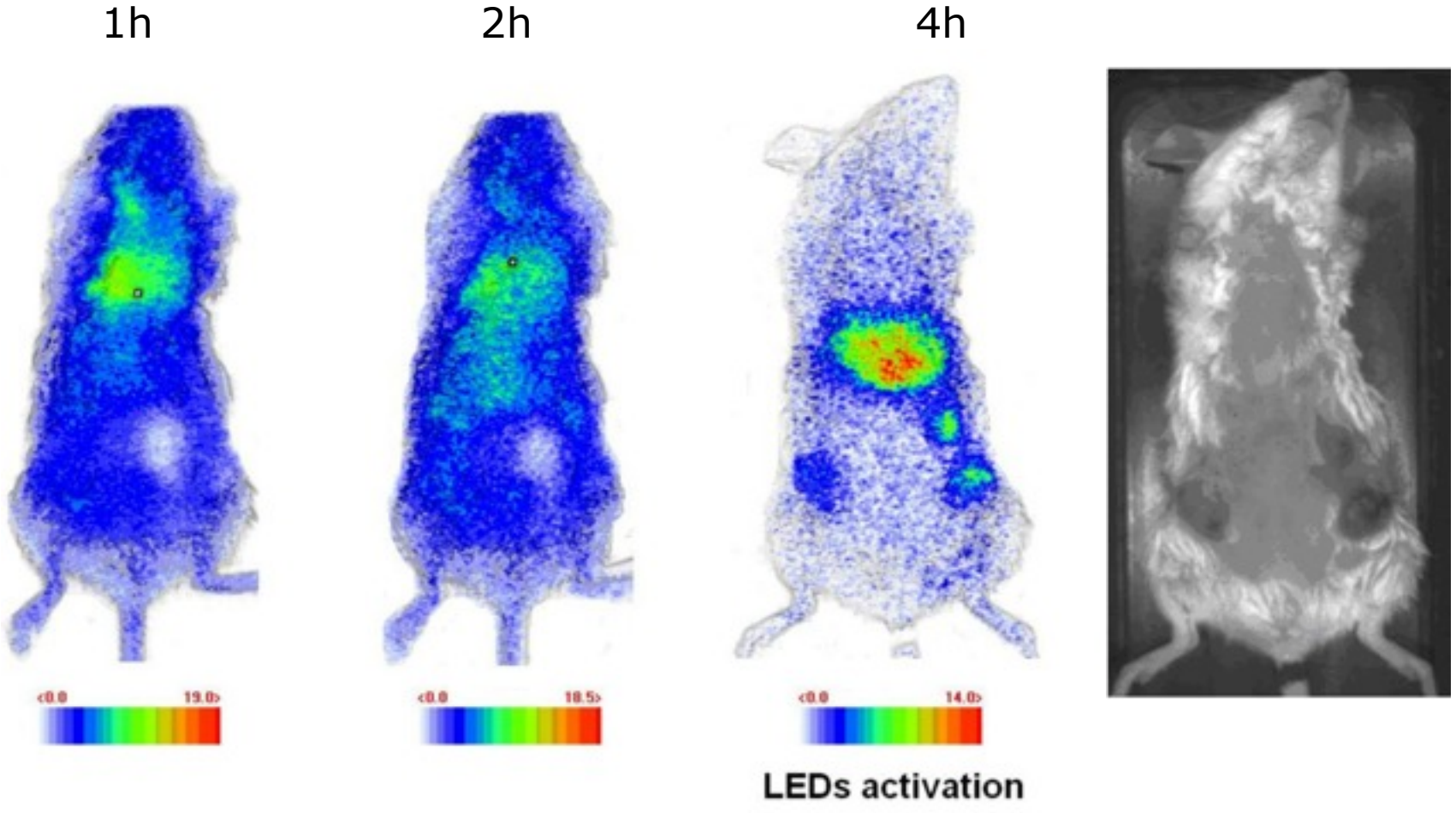


Biodistribution studies in healthy mice:



Biodistribution studies in tumor bearing mice



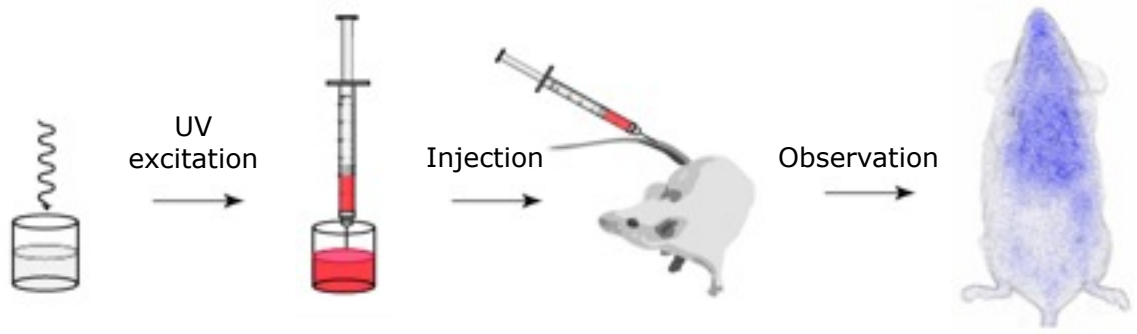
Nature Materials, under revision

Conclusion

Persistent luminescence nanoparticles for *in vivo* imaging applications

First generation:

Silicate



Time scale

0

hours

Conclusion

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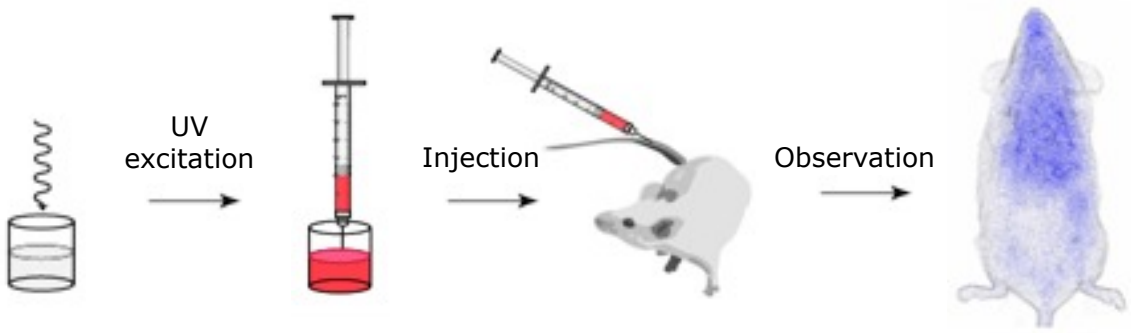
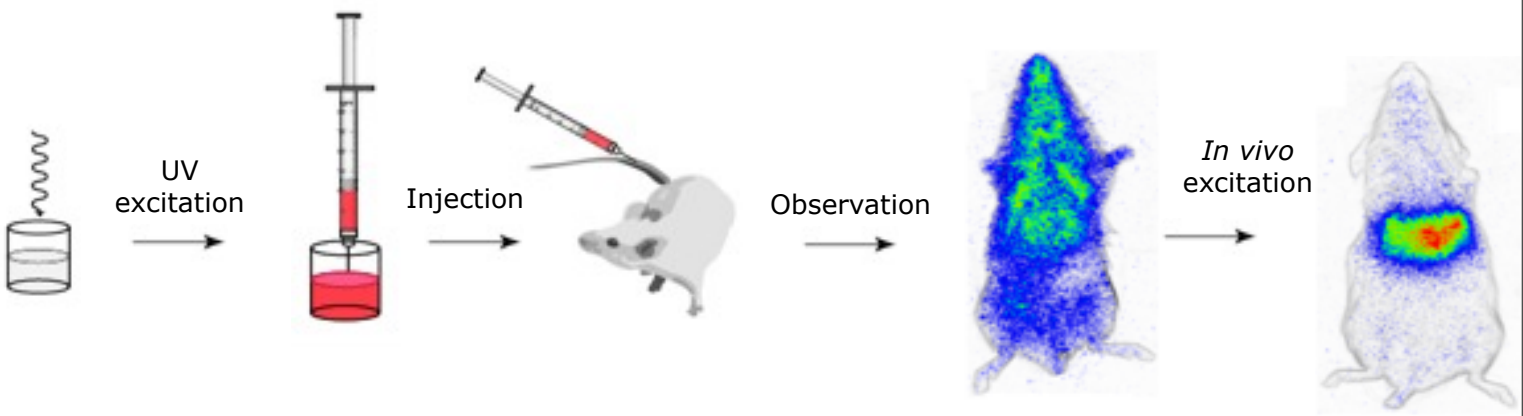


Time scale

0 → **hours**

Second generation:

Gallate



Time scale

0 → **hours** → **weeks**

Acknowledgements

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Quentin le Masne de Chermont (2004-2007)

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Collaborators:

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