CHEMISTRY: MOLECULES TO MATERIALS

Institut Charles Gerhardt Montpellier

MultifunctiOnal NanOparticles for microGlia Modulation

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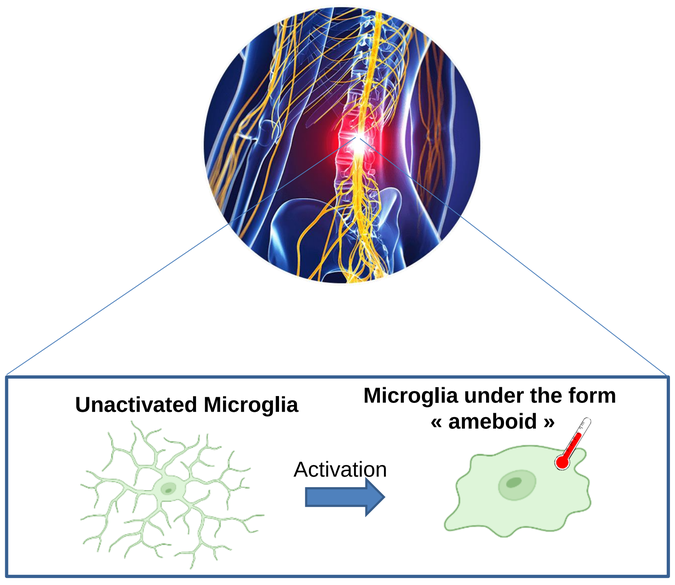
Microglia, the central nervous system (CNS) immune cells, exert many functions. Under physiological conditions, microglia survey the environment to protect the CNS. During development, microglia participate in sexual differentiation and display gender differences in number and functionality.



Why Microglia ?

⊕ ➢ Spinal cord injury: activation and accumulation of microglia = > contribution to immune responses, and involvement in tissue repair.

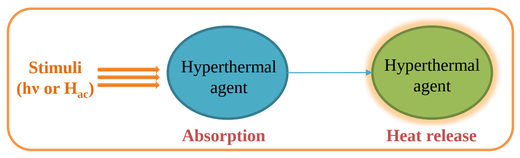
Hypothesis: Increase in the internal temperature of microglia related to its activation ?

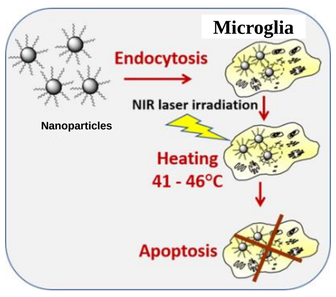
Strategy 1 => Establishment of the relationship between microglia internal temperature and degree of activation.

⊖ ➢ Excessive accumulation of activated microglia => creation of a scar: limitation of neurological connections + inflammation.

Strategy 2 => hyperthermia to trigger apoptosis

A promising therapy : Hyperthermia





- **Painless**
- **Non-invasive**
- **Few or no side effects**
- **Effective and lasting results**
- **Natural and deep tissue stimulation**

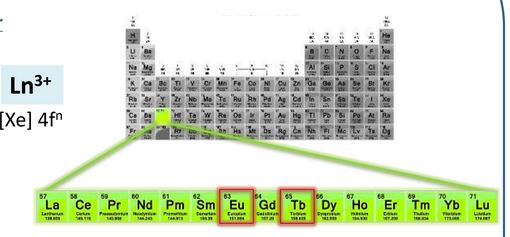
GOALS: Design of multifunctional nanoparticles able to work as nanothermometers and/or nanoheaters and in monitoring the thermal dynamic inside microglia during their activation and modulation of their responses by heating from inside the cells

Lanthanides as sensor

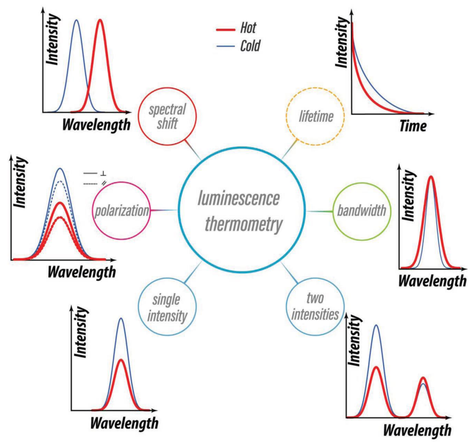
Lanthanides for thermometry

Ln → Ln^{3+}

[Xe] $6S^2$ $4f^{n+1}$ → [Xe] $4f^n$

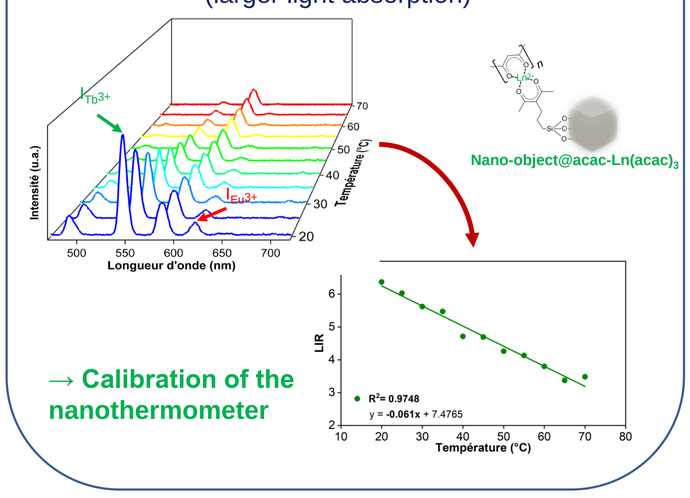


- Narrow photoluminescence peaks.
- Long emission lifetimes (μm-ms).
- Tunable emission lines from UV to IR.
- The intensity of the luminescence lines depends on many parameters: pressure, pH, oxygen, Temperature.



Luminescence by direct excitation of Ln dopant is not efficient (shielding 4f orbitals)

Sensitization of lanthanide luminescence via ligands (larger light absorption)



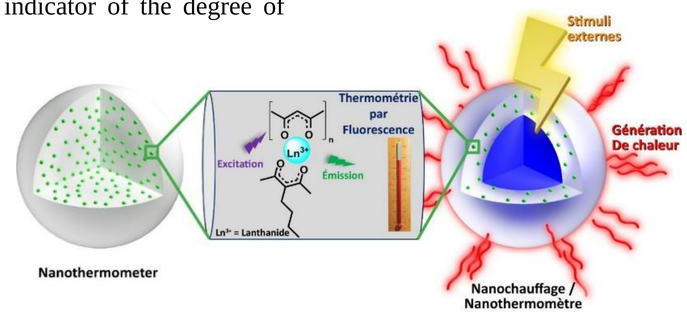
→ **Calibration of the nanothermometer**

Nanothermometer

- T° measurement in "normal" and activated microglia
- T° as an indicator of the degree of activation

Nanoheater/Nanothermometer

- Controlled hyperthermia of activated microglia *via* "hot spot" effect



Ln^{3+} complex incorporated in polymer or SiO_2 NPs

- Fe_3O_4@polymer or SiO_2
- Prussian blue@polymer or SiO_2

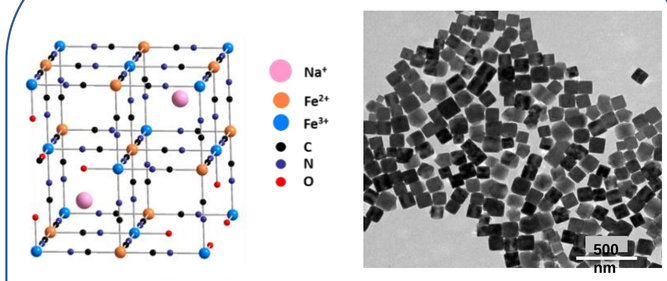
Ln^{3+}=Tb^{3+}/Eu^{3+} (visible)

Yb^{3+} or Nd^{3+} (NIR)

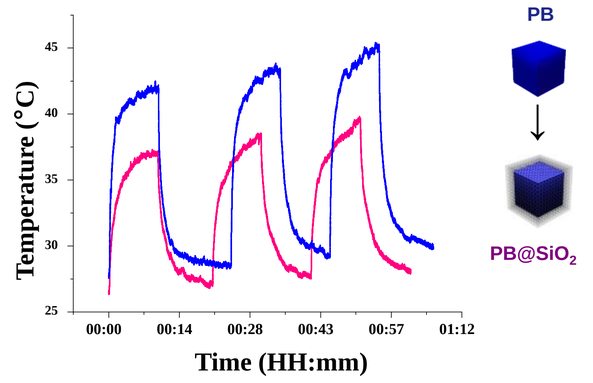
Acquired skills & knowledge

- ➢ Materials chemistry (nanoparticles, sol-gel, …)
- ➢ Characterization : FTIR, PXRD, UV Spectroscopy, TGA, Electronic Microscopy, Dynamic Light Scattering, N_2 Porosimetry, …
- ➢ Fluorescence studies
- ➢ Photothermal properties
- ➢ Biomedical studies in collaboration

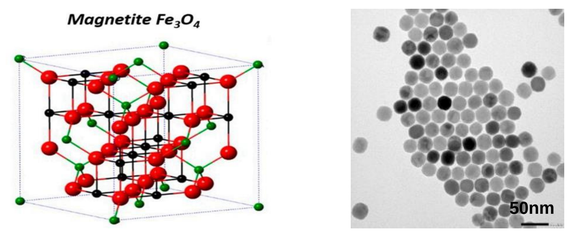
Prussian blue as heater



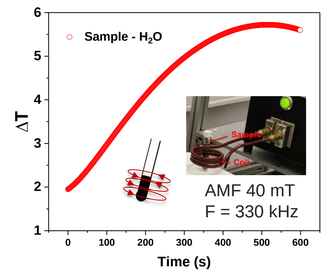
$Na_{1-x}Fe^{III}[Fe^{II}(CN)_6]_{1-\frac{x}{4}}.nH_2O$



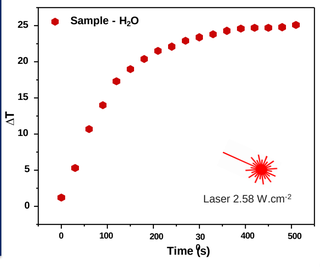
Iron Oxide as heater



Magnetothermia



Photothermia



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To address fundamental questions on the lifetime differential response after Spinal Cord Injury (SCI), as well as the response to microglia modulation, a combination of multimodal approaches will be utilized. This research collaboration aims to evaluate the following hypotheses: (1) vectorized nanoparticles can be phagocytosed by microglia, (2) microglia exhibit increased temperature upon activation, and (3) the response of microglia and subsequent recovery can be altered by an induced temperature increase caused by nanoparticles.

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