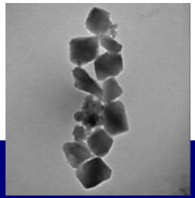
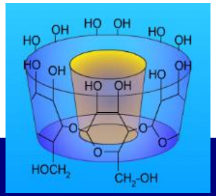
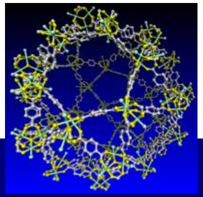





Project H-Nano

Hybrid nanoparticles for the treatment of resistant prostate cancers: characterization of individual nanoparticles and biological evaluation

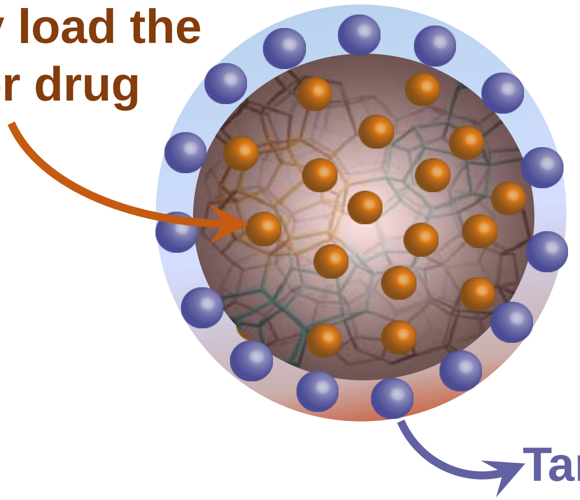
Céline JAUDOIN, Killian LAGUERRE and Ruxandra GREF

Institut des Sciences Moléculaires d'Orsay, Université Paris-Saclay

& Collaborators: Alexandre DAZZI, Ariane DENISET-BESSEAU, Jérémie MATHURIN, Giorgia URBINATI, Marta de FRUTOS, Maëva CHAUPARD

Journée Annuelle du LabEx NanoSaclay - Jeudi 13 janvier 2022

Multifunctional “cage” core-shell nanoparticles to fight cancer



“Green” technologies

Advanced characterization methodology

Interdisciplinary consortium

Institut des Sciences Moléculaires d’Orsay
UMR 8214 CNRS

Nanotechnology
- Dr. Ruxandra GREF
- Dr. Céline JAUDOIN
- Killian LAGUERRE

Institut Chimie Physique
UMR 8000 CNRS

Characterization: AFM-IR
- Dr. Alexandre DAZZI
- Dr. Ariane DENISET-BESSEAU
- Dr. Jérémie MATHURIN

Institut Gustave Roussy
UMR 9018 CNRS

Biological evaluation
- Dr. Giorgia URBINATI

Laboratoire de physique des Solides
UMR 8502 CNRS

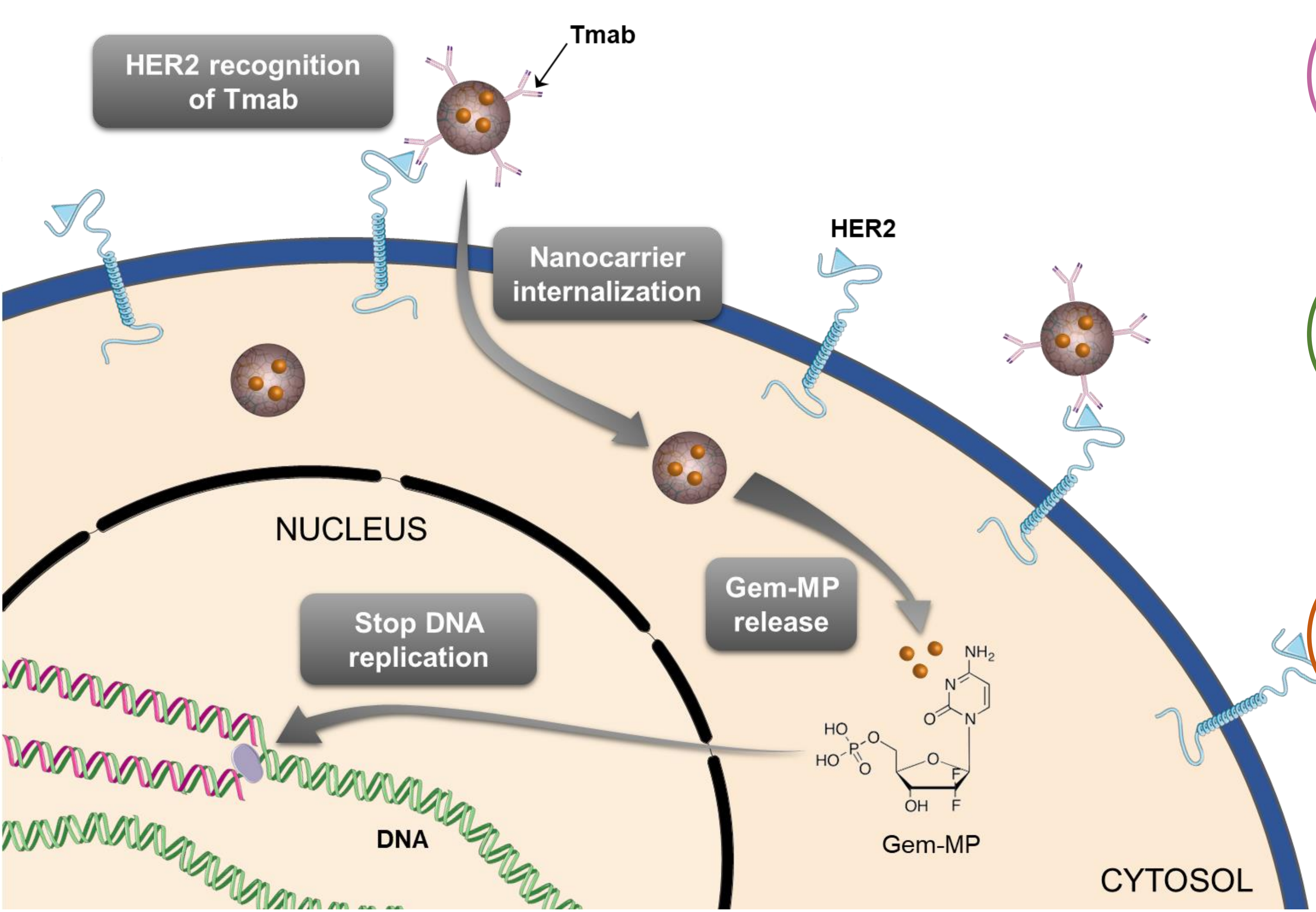
Characterization: STEM-EELS
- Dr. Marta de FRUTOS
- Maeva CHAUPARD

A new strategy to fight prostate cancer

Challenge of castration resistant prostate cancers

- Resistance to Androgen deprivation therapy (ADT or medical castration)
- Several mechanisms involved (ex: HER2-driven resistance)
- HER2 overexpressed in breast cancer but also in other cancers as prostate one
- HER2 overexpression → activate the androgen receptor in absence of androgens

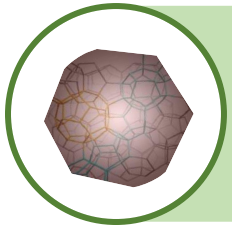
A new strategy to fight prostate cancer



Trastuzumab (Tmab)

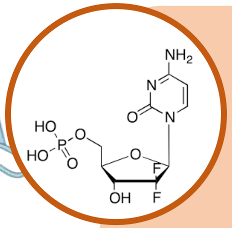
- Monoclonal antibody
- Target HER2
- Efficient on breast cancer

Nanocarrier



- High loading
- Loading efficiency
- Green technology

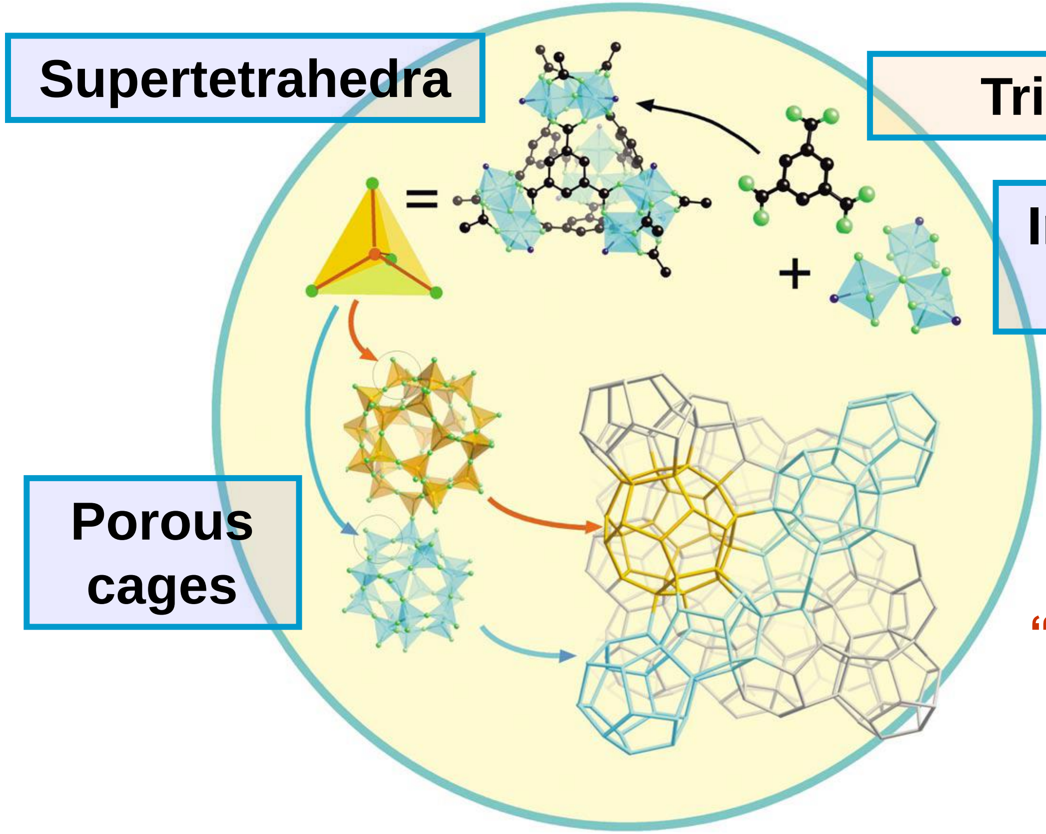
Gemcitabine monophosphate (Gem-MP)



- Anticancer drug
- Efficient in prostate cancer rodent model
- Does not cross cell membrane

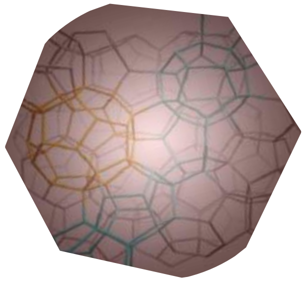
Porous hybrid MOF nanoparticles (nanoMOFs)

A "green" synthesis of MOF (Metal organic framework)

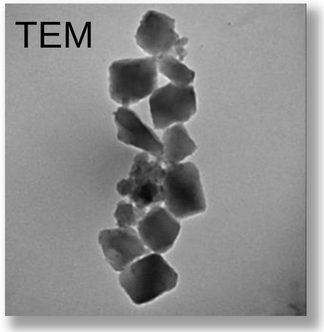


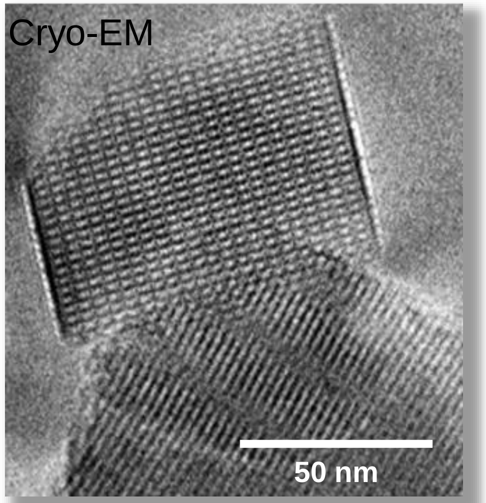
"Green" synthesis
H_2O, microwave, few minutes

MIL-100(Fe) NanoMOFs



100-200 nm
Cristalline structure
S BET ~ 1700-1800 m^2/g





P Horcajada, T Chalati, C Serre … G Férey, P Couvreur, R Gref
Porous nanoMOFs as a potential platform for drug delivery and imaging. *Nature Mater* **9,** 172–178 (2010)

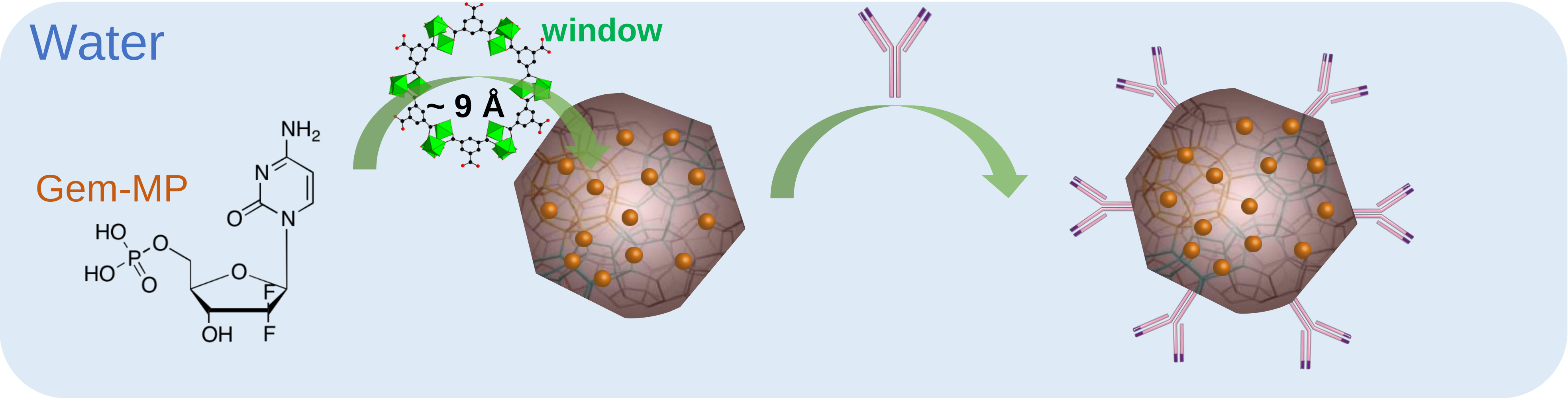
Chalati et al., J Mater Chem 21**,** 2220-7, 2011
Agostoni et al., Green Materials, 2013

Gem-MP loading & nanoMOF coating

Killian Laguerre, M1

Drug loading

Tmab coating



- Efficiency ~100%
- Loading up to 30 wt%
- Stable under storage

Agostoni et al., Adv. Heathcare Mater. 2013; Rodriguez et al., J Drug Target 2015; Li et al. ChemMedChem 2019; Li et al., Front. Bioeng. Biotechnol., 2020

- Tmab labelling with rhodamine
- Tmab functionalization ~ 230-450 Tmab/nanoparticle
- Morphology, size and cristallinity maintained after coating

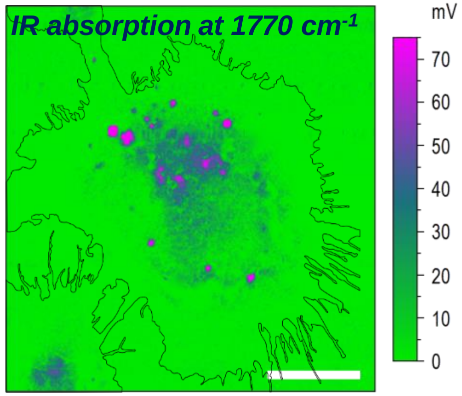
In-depth characterization by AFM-IR and STEM/EELS

Characterization of individual NPs

- ✓ Map the location of NP components
- ✓ Drug location
- ✓ NP location inside a cell
- ✓ No label

- AFM-IR:

A. Dazzi, A. Deniset-Besseau, J. Mathurin
Institut de Chimie Physique, U Paris-Saclay



E Pancani, J Mathurin, S Bilent, MF Bernet-Camard, A Dazzi, A Deniset-Besseau, R Gref. Part. *Part. Syst. Charact*. 3/2018

1^{st} application to investigate nanoMOFs

- STEM-EELS:

M. Chaupard, M. de Frutos
Laboratoire de Physique des Solides, U Paris-Saclay

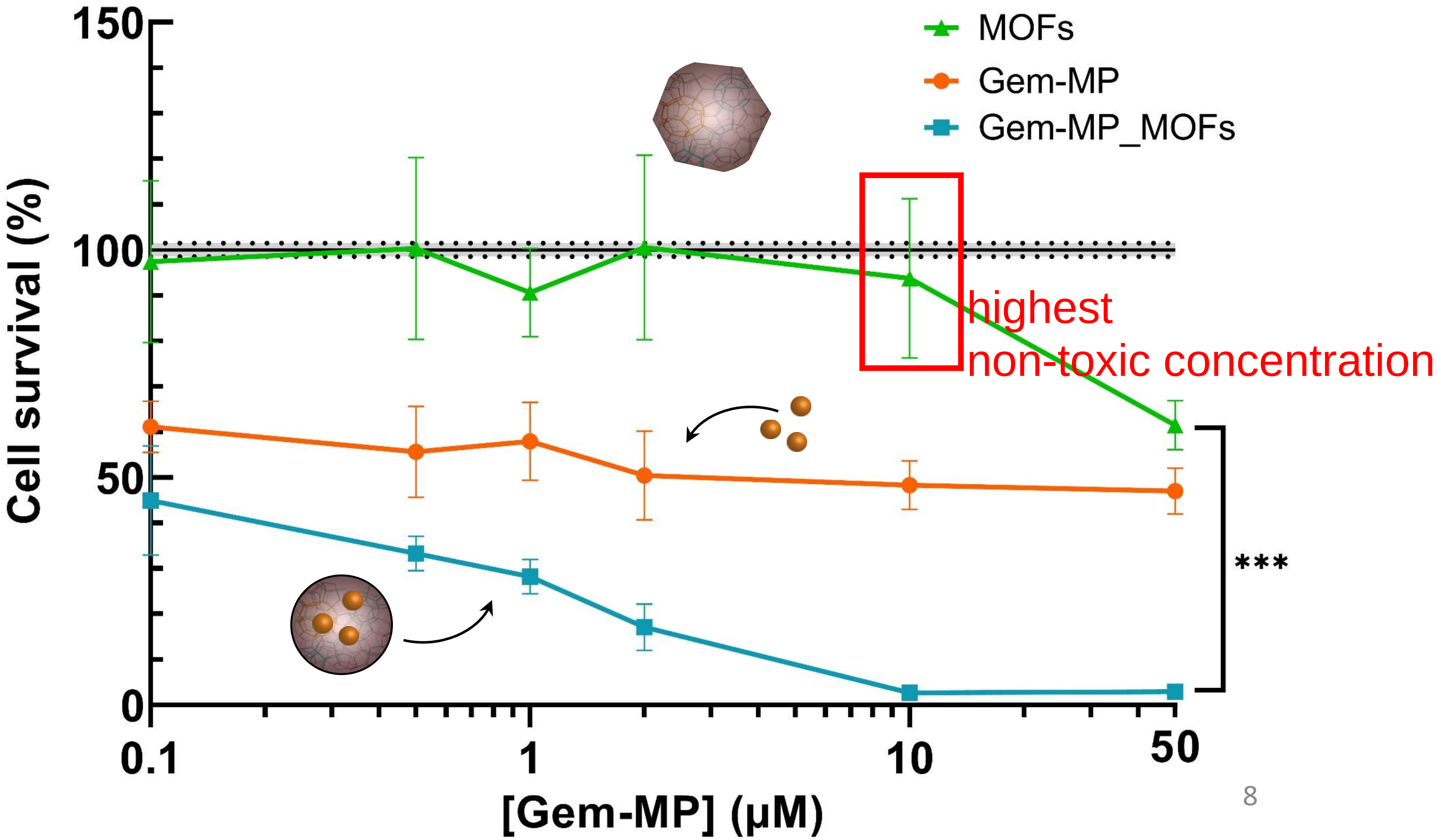
1^{st} application to investigate NPs

Biological evaluation

Impact of free Gem-MP, empty or Gem-MP loaded MOFs on DU-145 survival at 48h

GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS
METSY
Dr. Giorgia Urbinati

- DU-145 cells: castration resistant prostate cancer cells
- Survival 48h after exposition
- Determination of highest non-toxic [MOFs] = 17 µg.mL^{-1}
- $IC_{50(\text{loaded Gem-MP})} \approx 0.1$ µM
- Difference between Gem-MP loaded and empty nanoMOFs



Conclusion & Perspectives

Formulation

- Loading 20 wt% Gem-MP
- *Coating optimization*

***In vitro* evaluation**

- Effect on DU-145 cell viability
- *Tmab coating evaluation*
- *NPs internalization: difference between Tmab-coated and not-coated NPs*

***In vivo* evaluation**

- *Effect on tumor growth*
- *NPs biodistribution*

In depth characterization

- AFM-IR
- STEM-EELS

Aknowledgements

Institut des Sciences Moléculaires d'Orsay

Pr. Ruxandra Gref

Killian Laguerre
Dr. Céline Jaudoin
Dr. Xue Li
Dr. Mario Menendez
Dr. Jingwen Qiu
Dr. Giuseppina Salzano
Dr. Agostoni

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