

APPEL A PROPOSITIONS 2016 DU CANCEROPOLE DU GRAND-EST
« EMERGENCE STRUCTURANTE »

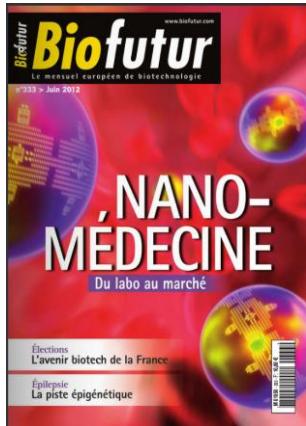
E-NANORX

NANOParticules multimodales excitables par rayons X

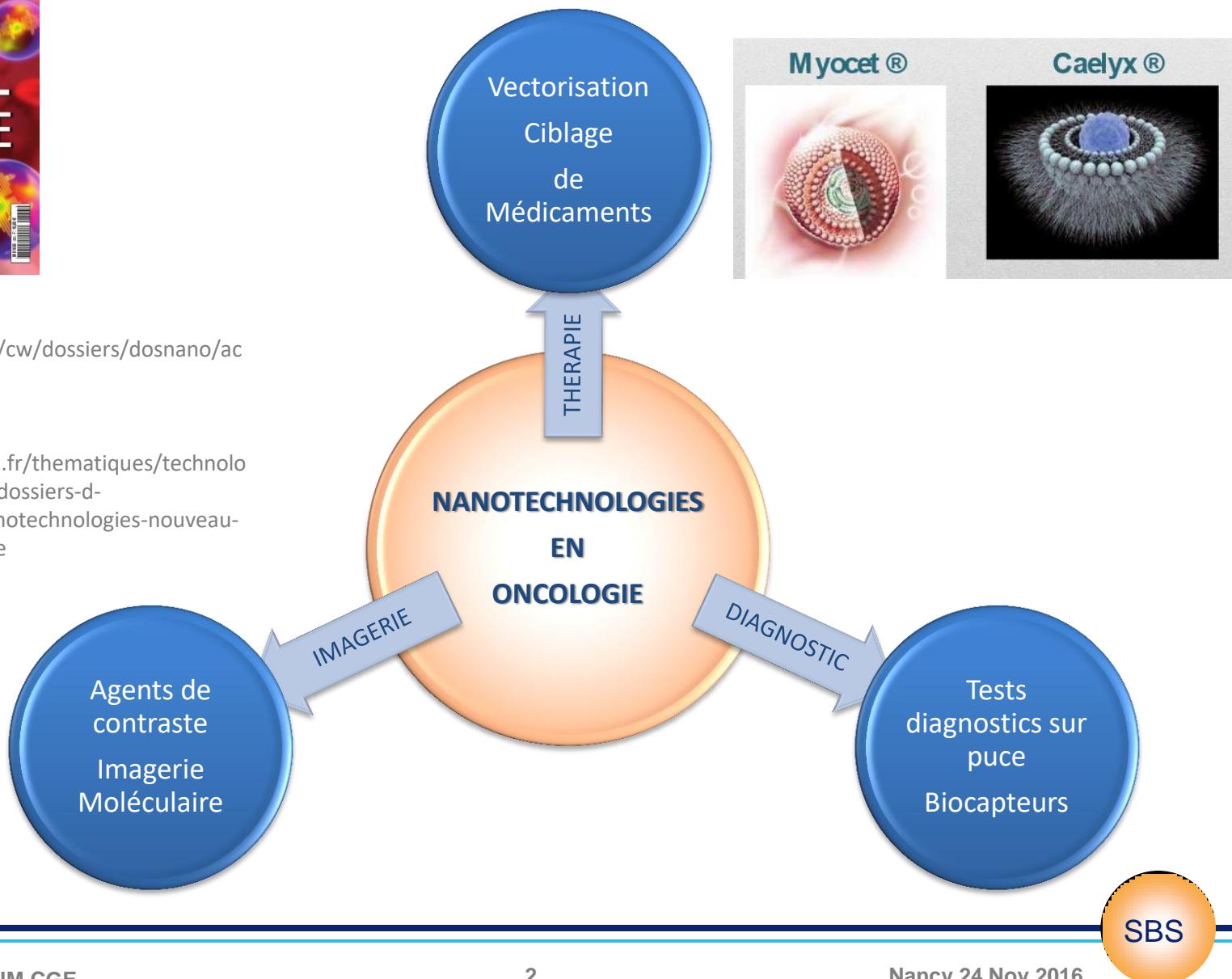
De la conception à la validation préclinique

Coordination du projet : **Sophie PINEL, MCF**
sophie.pinel@univ-lorraine.fr

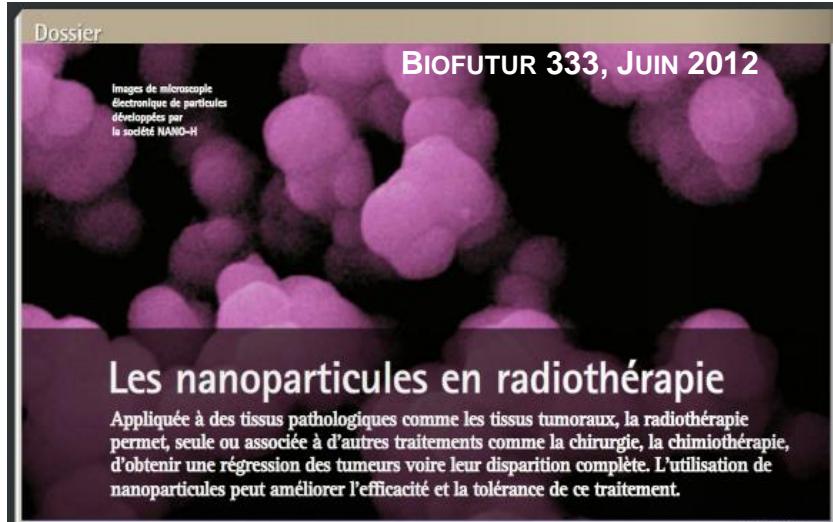
CONTEXTES CLINIQUE & SCIENTIFIQUE



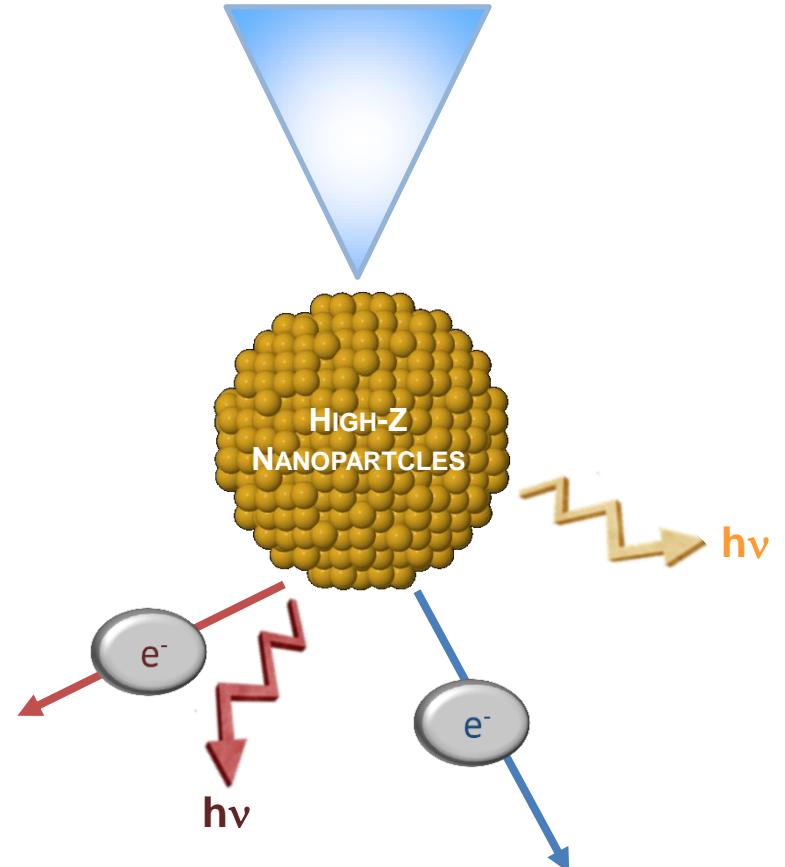
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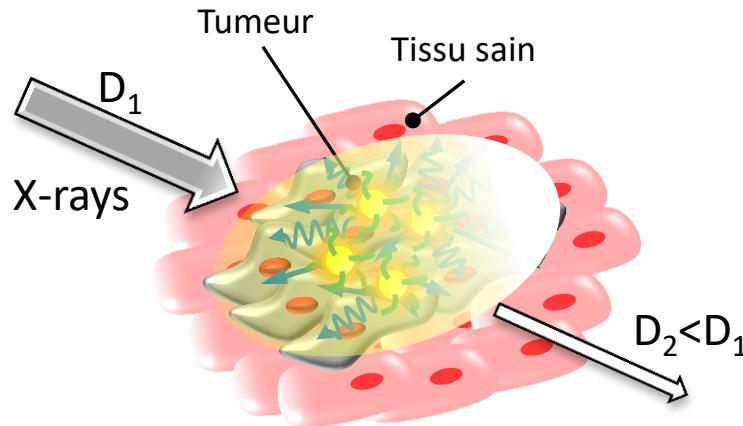
CONTEXTES CLINIQUE & SCIENTIFIQUE



RAYONS X



CONTEXTES CLINIQUE & SCIENTIFIQUE



Différence d'absorption des photons X entre tissu tumoral et tissu adjacent sain

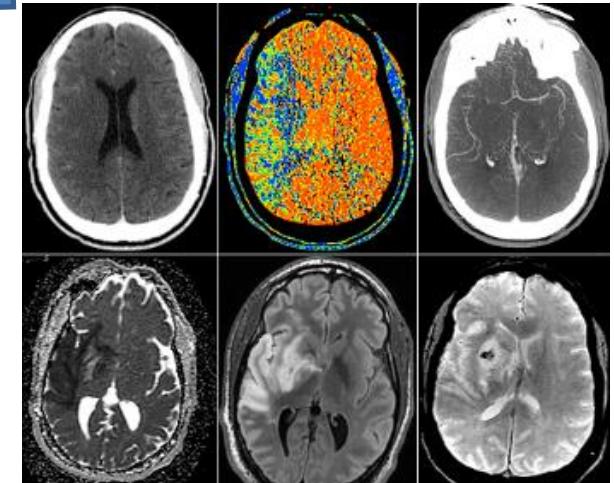
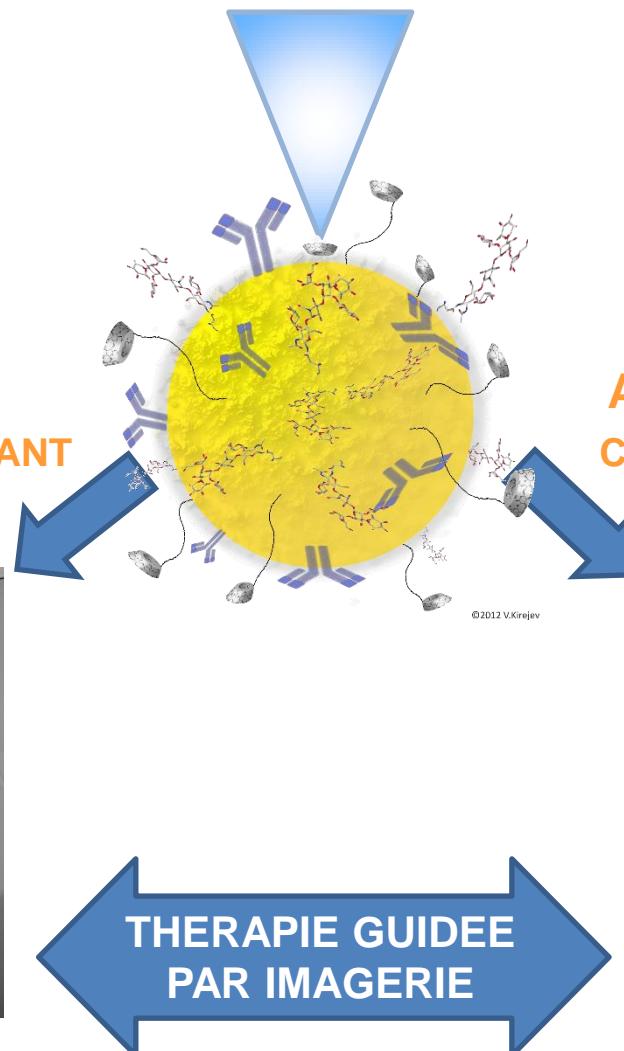
Accumulation préférentielle des nanoparticules dans le tissu tumoral pour :

- ▶ Augmenter la densité du tissu cible
- ▶ Favoriser les interactions photons X et tissus
- ▶ Multiplier les espèces secondaires produites
- ▶ Amplifier les dommages cellulaires et tissulaires

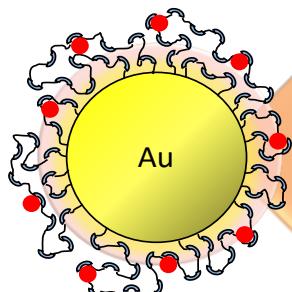
*Adaptée de Roux et al., rapport ANR TheraGulma 2012

CONTEXTES CLINIQUE & SCIENTIFIQUE

RAYONS X



LES CONTOURS DU PROJET E-NANORX



NANOPARTICULES MULTIMODALES
(Nanoparticules hybrides et Z élevé)



RAYONNEMENTS X
(Imagerie & Thérapie)



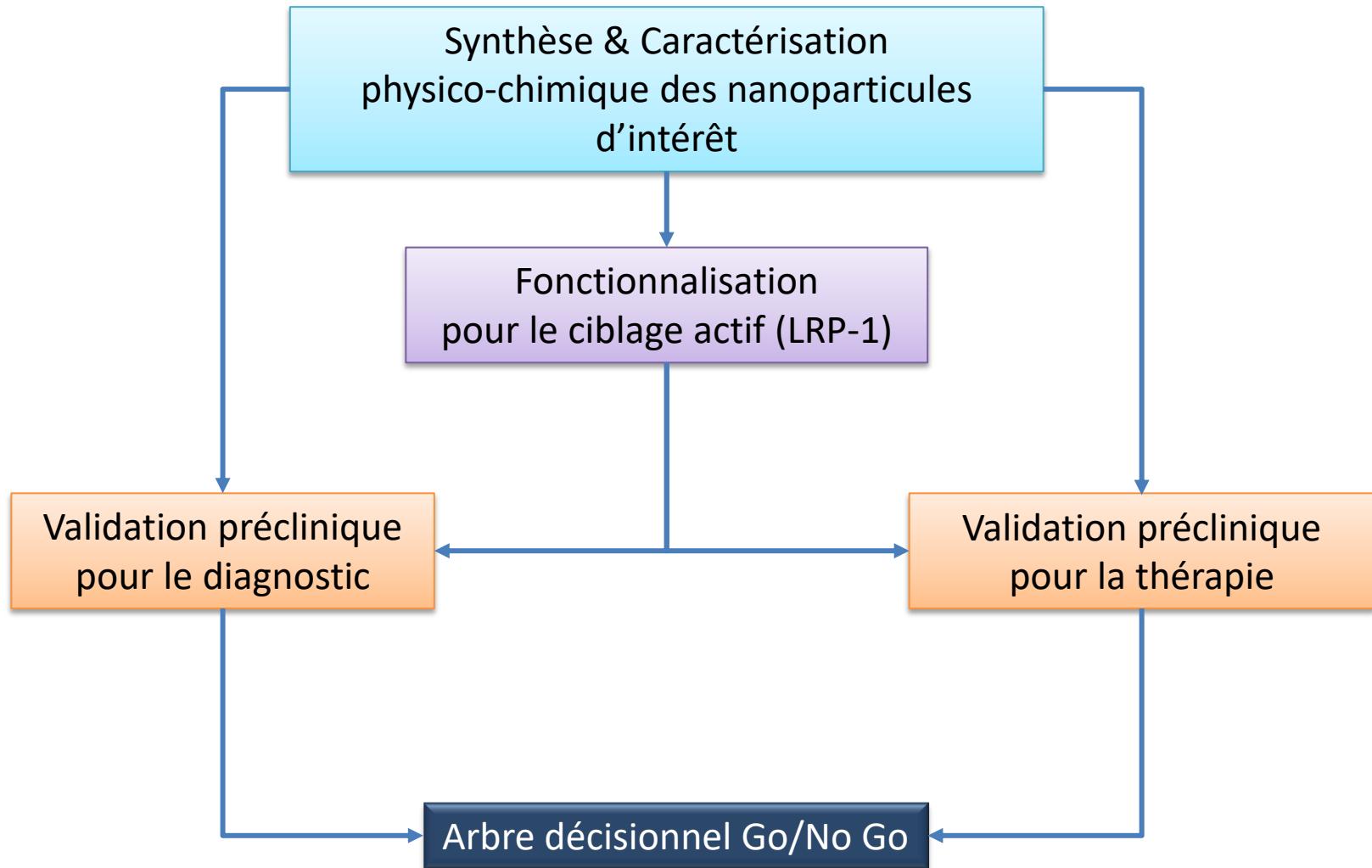
TUMEURS DU SNC
(Gliomes de haut grade & Métastases cérébrales)



MODÉLISATION &
SIMULATION NUMÉRIQUES

SBS

LES TÂCHES DU PROJET E-NANORX



LES PARTENAIRES DU PROJET E-NANORX

MEDyC UMR CNRS 7369



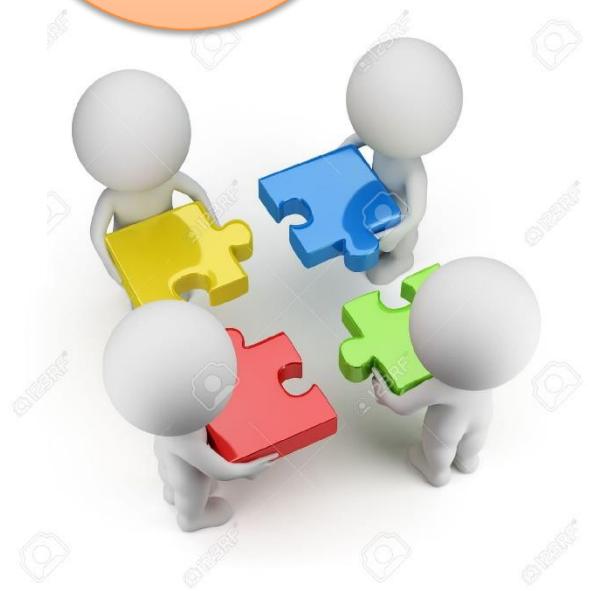
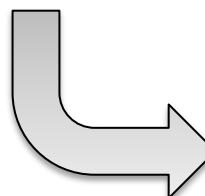
UNIVERSITÉ
DE REIMS
CHAMPAGNE-ARDENNE



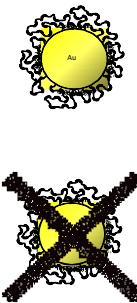
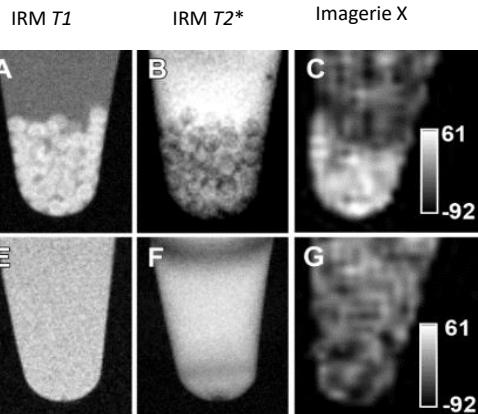
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DE LORRAINE



UNIVERSITÉ
DE LORRAINE

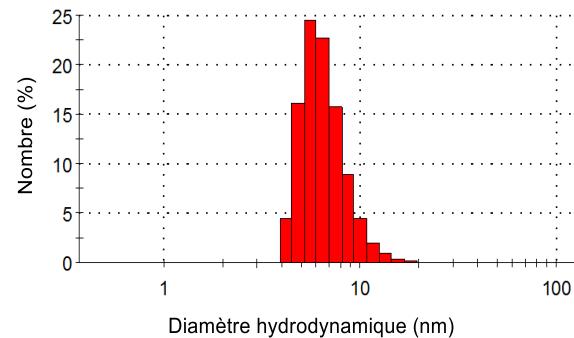
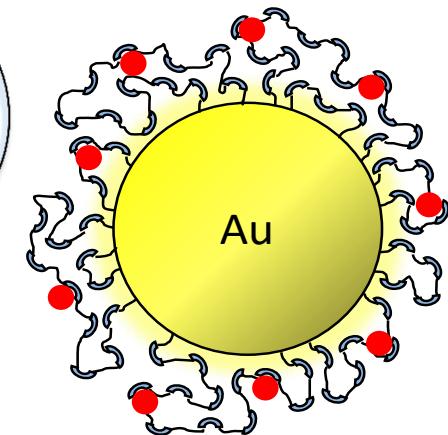
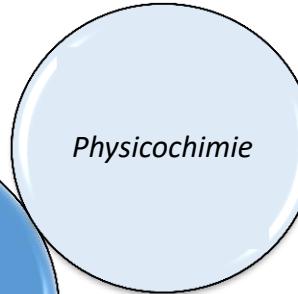


EXPERTISES, SAVOIR-FAIRE & ENJEUX



SYNTHESE & CARACTERISATION

NANOParticules
MULTI-
FONCTIONNELLES
EXCITABLES PAR
RAYONS X

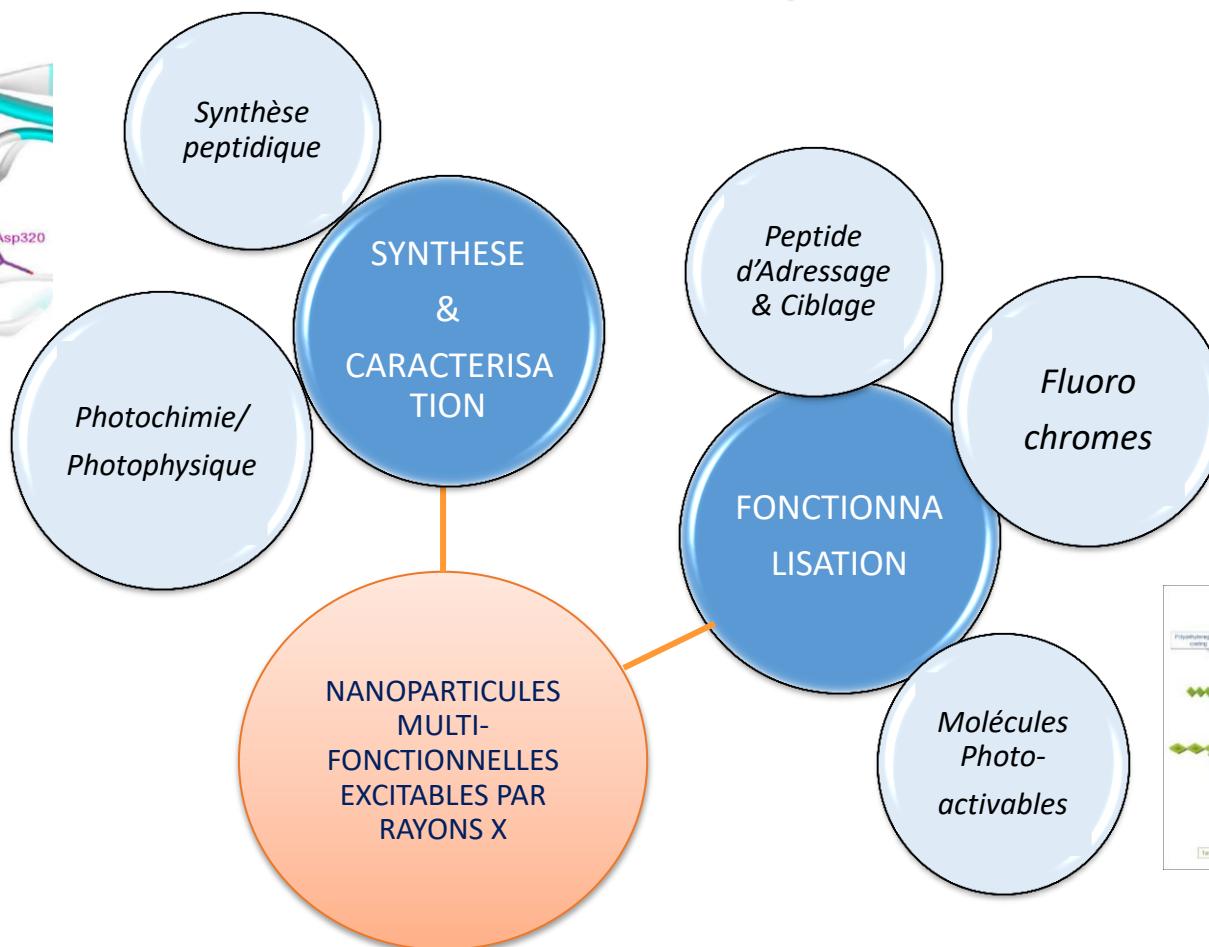
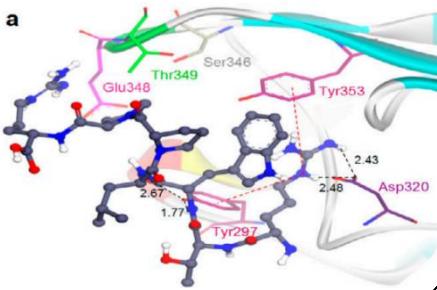


PR STEPHANE ROUX



1. Le Duc, G.; Miladi, I.; Alric, C.; Mowat, P.; Bräuer-Krisch, E.; Bouchet, A.; Khalil, E.; Billotey, C.; Janier, M.; Lux, F.; Epicier, T.; Perriat, P.; Roux, S.; Tillement, O. "Toward an Image-Guided Microbeam Radiation Therapy Using Gadolinium-Based Nanoparticles" *ACS Nano*, **2011**, 5, 9566-9574.
2. Alric, C.; Miladi, I.; Krysa, D.; Taleb, J.; Lux, F.; Bazzi, R.; Billotey, C.; Janier, M.; Perriat, P.; Roux, S.; Tillement, O. "The biodistribution of gold nanoparticles designed for renal clearance" *Nanoscale* **2013**, 5, 5930-5939.
3. Miladi, I.; Alric, C.; Dufort, S.; Mowat, P.; Dutour, A.; Mandon, C.; Laurent, G.; Bräuer-Krisch, E.; Herath, N.; Coll, J.-L.; Dutreix, M. Lux, F. Bazzi, R.; Billotey, C.; Janier, M.; Perriat, P.; Le Duc, G.; Roux, S.; Tillement O. "The In Vivo Radiosensitizing Effect of Gold Nanoparticles Based MRI Contrast Agents" *Small* **2014**, 10, 1116-1124.

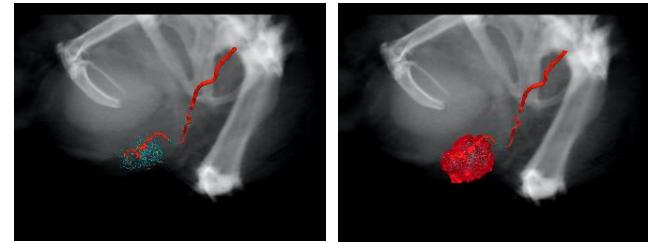
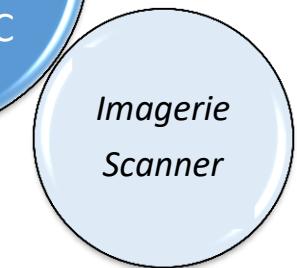
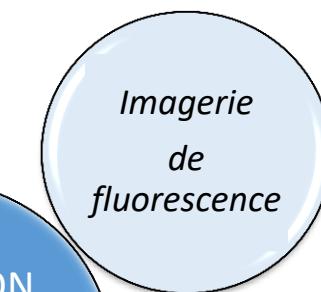
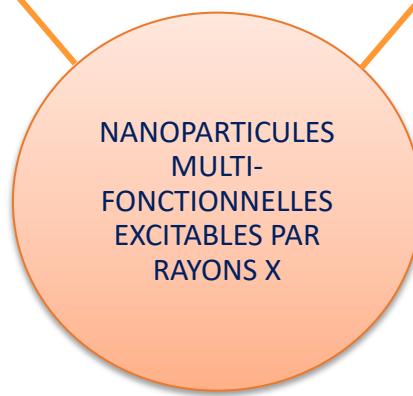
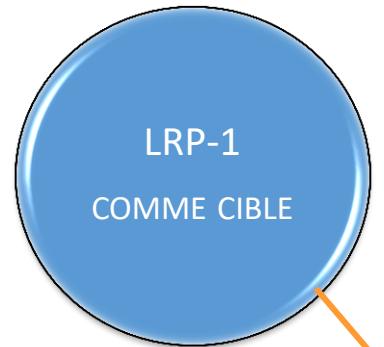
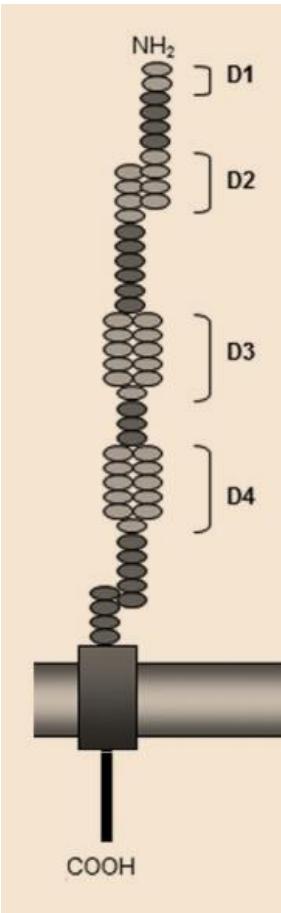
EXPERTISES, SAVOIR-FAIRE & ENJEUX



DR CÉLINE FROCHOT

- Verhille M, Benachour H, Ahmad I, Achard M, Arnoux P, Barberi-Heyob, André JC, Allonas X, Baros F, Vanderesse R, Frochot C. Photodynamic Molecular Beacons triggered by MMP-2 and MMP-9: Influence of the distance between photosensitizer and quencher onto photophysical properties and enzymatic activation. *Curr. Med. Chem.* **2012**, 19(32), 5580-5594
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EXPERTISES, SAVOIR-FAIRE & ENJEUX



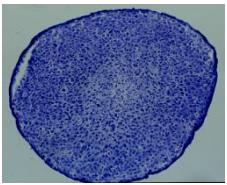
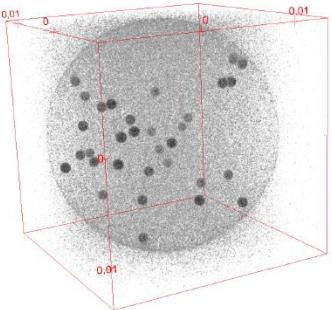
PR JÉRÔME DEVY

MEDyC UMR CNRS 7369

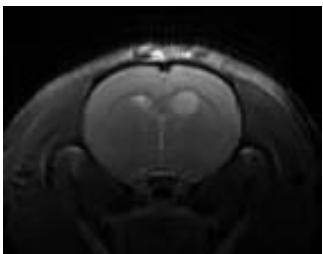
UNIVERSITÉ
DE REIMS
CHAMPAGNE-ARDENNE

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3. Thevenard J, Verzeaux L, Devy J, Etique N, Jeanne A, Schneider C, Hachet C, Ferracci G, David M, Martiny L, Charpentier E, Khrestchatsky M, Rivera S, Dedieu S, Emonard H. Low-density lipoprotein receptor-related protein-1 mediates endocytic clearance of tissue inhibitor of metalloproteinases-1 and promotes its cytokine-like activities. *PLoS One*. 2014 Jul 30;9(7):e103839.

EXPERTISES, SAVOIR-FAIRE & ENJEUX



NANOParticules
MULTI-
FONCTIONNELLES
EXCITABLES PAR
RAYONS X



VALIDATION PRE-
CLINIQUE POUR
LA THERAPIE

Etudes
in vivo

Analyses
in silico

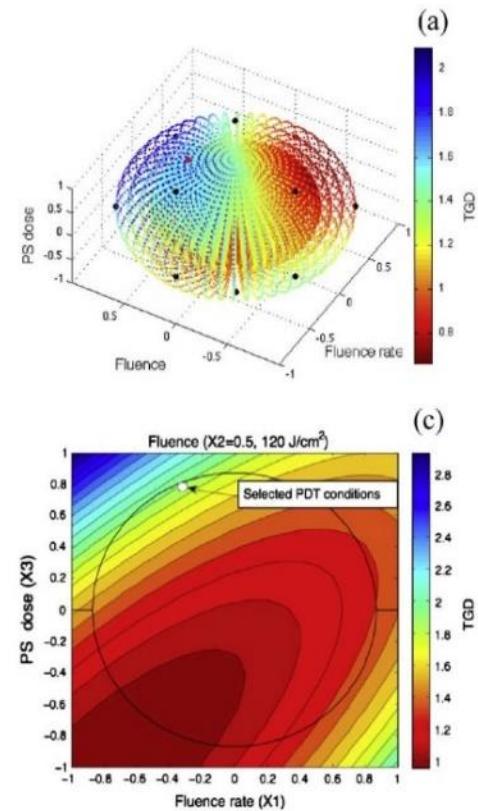
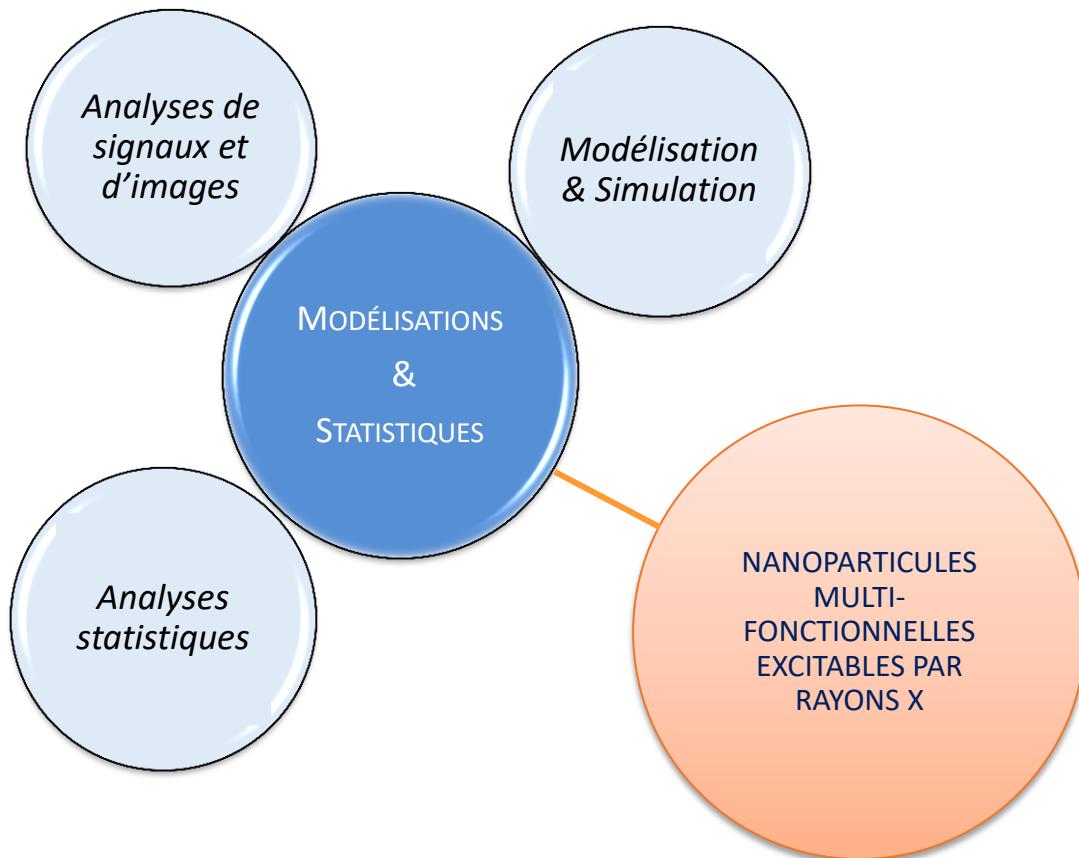
Analyses
in vitro



DR SOPHIE PINEL

1. Chastagner P, Sudour H, Mriouah J, Barberi-Heyob M, Bernier-Chastagner V, Pinel S. Preclinical studies of pegylated- and non-pegylated liposomal forms of Doxorubicin as radiosensitizer on orthotopic high-grade glioma xenografts. *Pharm Res*. 32(1):158-66, 2015.
2. Retif P, Pinel S, Toussaint M, Frochot C, Bastogne T, Barberi-Heyob M. Nanoparticles for radiation therapy enhancement: the key parameters. *Theranostics*, 5(9):1030-1044, 2015.
3. Retif P, Reinhard A, Paquot H, Jouan-Hureaux V, Chateau A, Sancey L, Barberi-Heyob M, Pinel S, Bastogne T. Monte Carlo simulations guided by imaging to predict the in vitro ranking of radiosensitizing nanoparticles. *Int J Nanomedicine*, en revision, 2016.

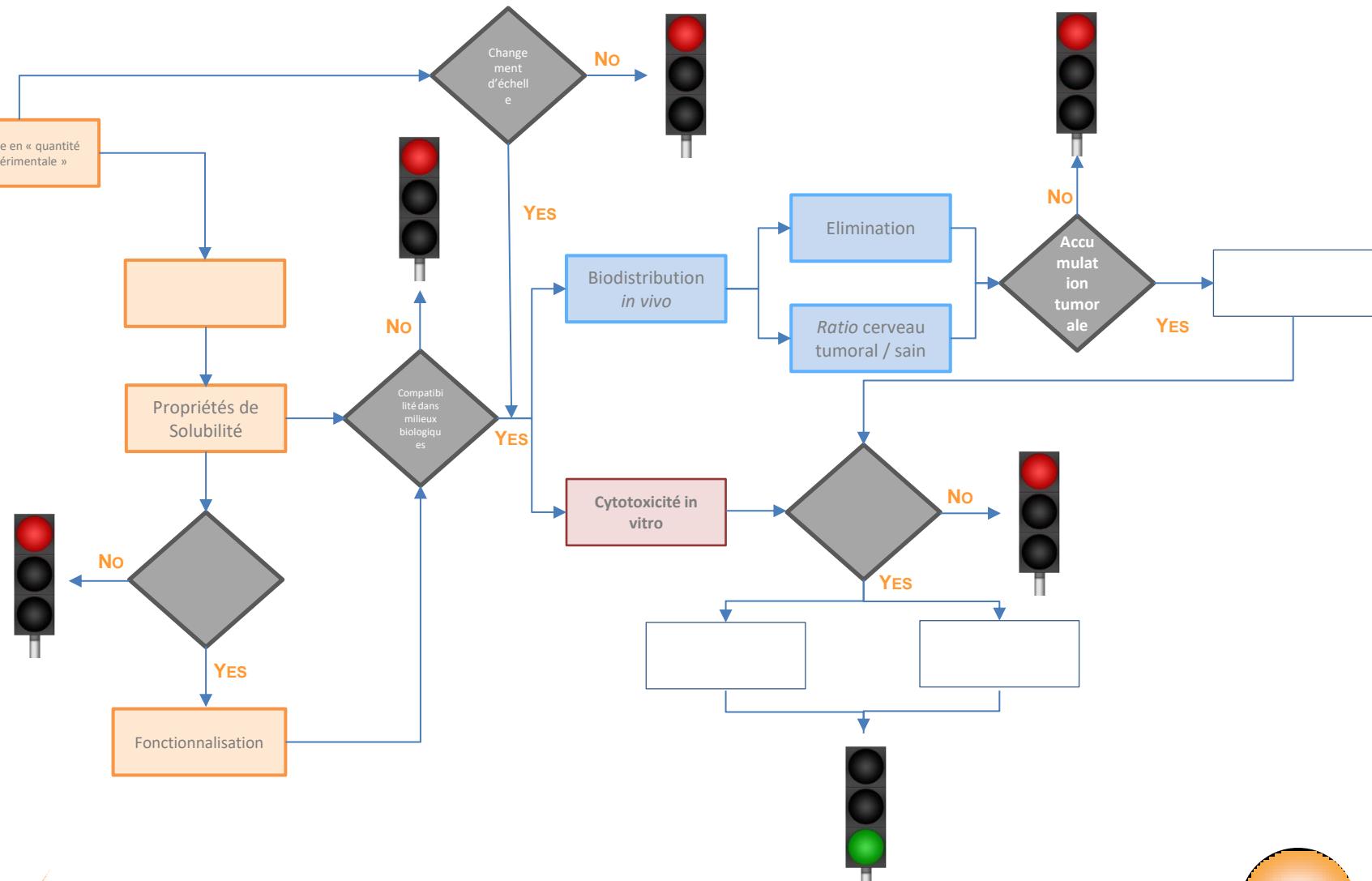
EXPERTISES, SAVOIR-FAIRE & ENJEUX



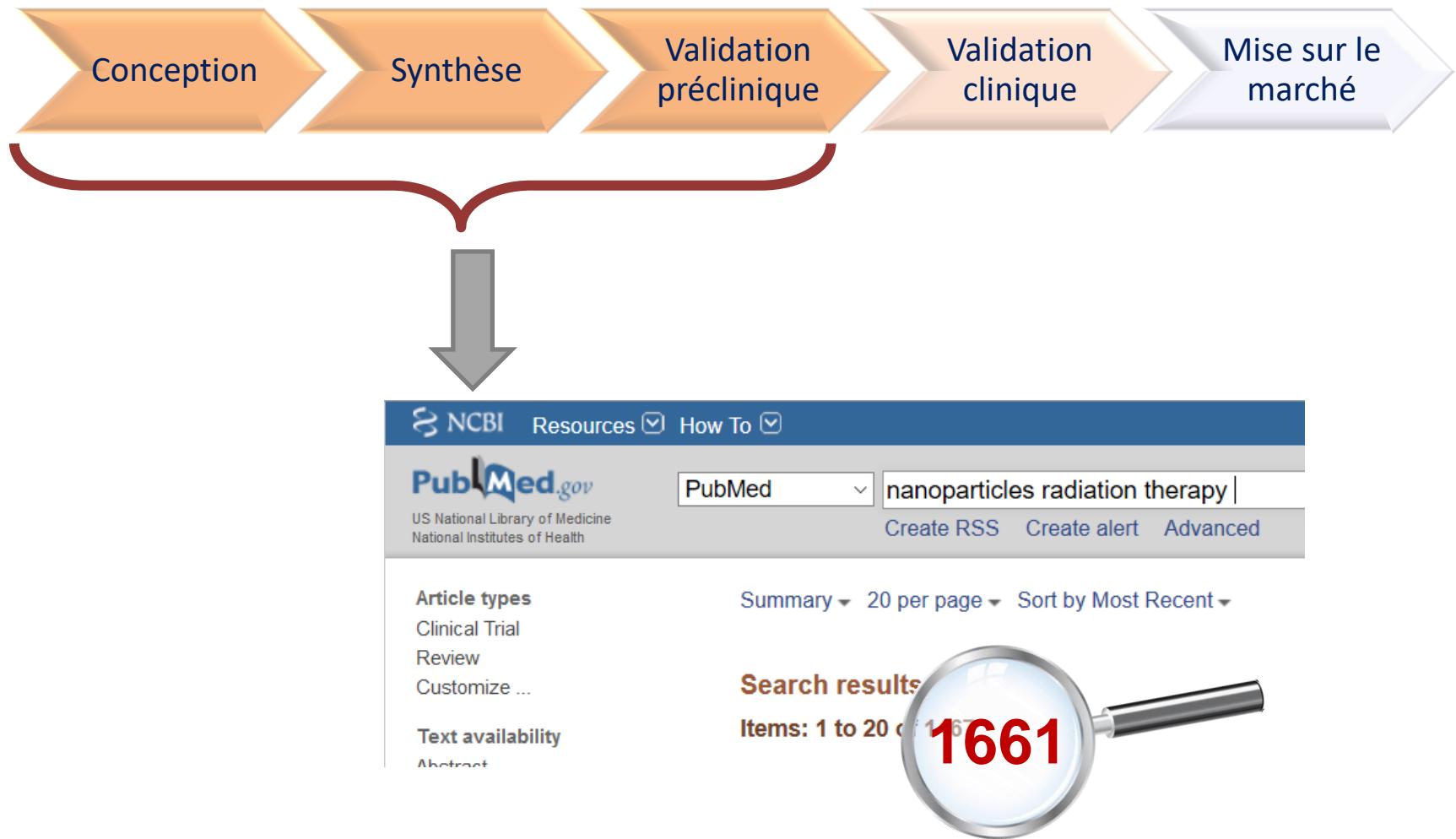
PR THIERRY BASTOGNE

1. Retif P, Pinel S, Toussaint M, Frochot C, Bastogne T, Barberi-Heyob M. Nanoparticles for radiation therapy enhancement: the key parameters. *Theranostics*, 5(9):1030-1044, **2015**.
2. Retif P, Bastogne T, Barberi-Heyob M. Robustness analysis of a Geant4-GATE simulator for nano-radiosensitizers characterization IEEE Trans Nanobioscience. **2016**
3. Retif P, Reinhard A, Paquot H, Jouan-Hureaux V, Chateau A, Sancey L, Barberi-Heyob M, Pinel S, Bastogne T. Monte Carlo simulations guided by imaging to predict the in vitro ranking of radiosensitizing nanoparticles. *Int J Nanomedicine*, en revision, **2016**.

LE LIVRABLE GÉNÉRIQUE



SITUATION ACTUELLE



SITUATION ACTUELLE



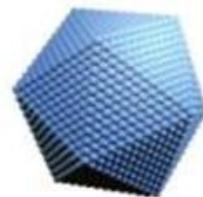
Conception

Synthèse

Validation
préclinique

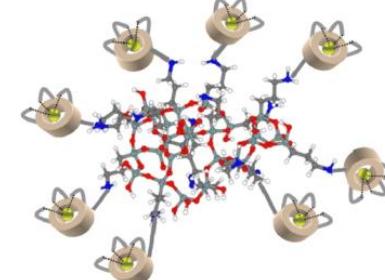
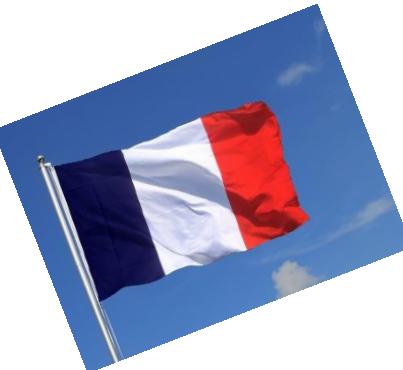
Validation
clinique

Mise sur le
marché



Hafnium
(Z=72)
Nanobiotix™

6 Essais cliniques – différents cancers



Gadolinium
(Z=64)
NH TherAguix™

Essai clinique phase 1 – métastases cérébrales

Merci pour votre attention

