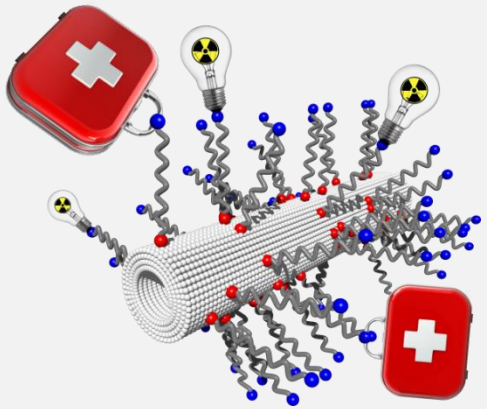
Élaboration de nanohybrides multifonctionnels à destination de la santé et étude de leur comportement *in vitro* et *in vivo*

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

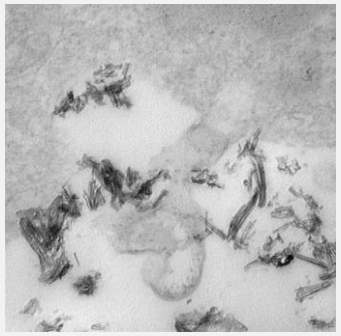


GDR B2i Groupement de recherche Bio-ingénierie des interfaces

7ème Journée thématique du GDR B2i
mardi 23 mars 2021 – E-meeting

Julien Boudon, Nadine Millot

Laboratoire Interdisciplinaire Carnot de Bourgogne
Axe Nanosciences
UMR 6303 CNRS/Université Bourgogne Franche-Comté,
BP 47 870, 21 078 DIJON cedex, France
nmillot@u-bourgogne.fr



BH2N

icb Laboratoire Interdisciplinaire Carnot de Bourgogne

UBFC UNIVERSITÉ BOURGOGNE FRANCHE-COMTÉ

cnrs

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Human resources

1 PR, 3 MCF (2 Faculty of Pharmacy), 1 DR, 1 CR, 1 AI

Nadine MILLOT

Lucien SAVIOT

Frédéric BOUYER

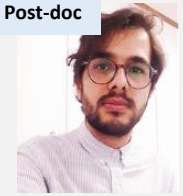
Julien BOUDON

Véronique BERARD

Lionel MAURIZI

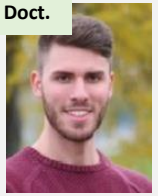
Michaële HERBST

1 post-doc, 5 on-going PhD, 2 Masters (M2)/year



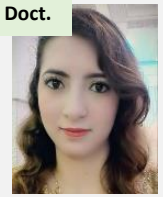
Post-doc

Laroussi CHAABANE



Doct.

Eduardo HERNANDO ABAD



Doct.

Amira MAHMOUD

Doct.

Célia MARETS

Doct.

Mélanie ROMAIN

Doct.

Alan ZERROUKI

M2R

Sullivan GUY

M2R

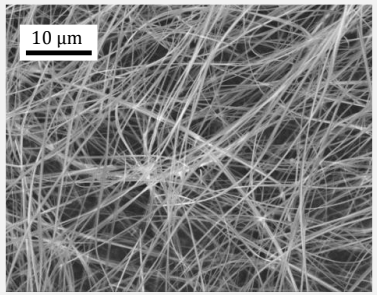
Léa PAGEARD

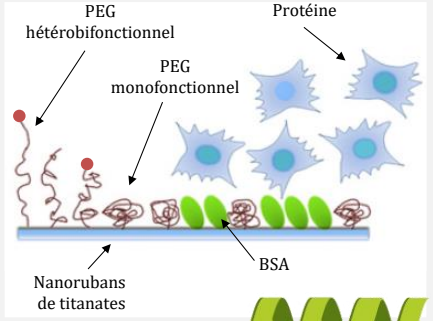
BH2N

https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Titanate nanoribbons: TiONrs

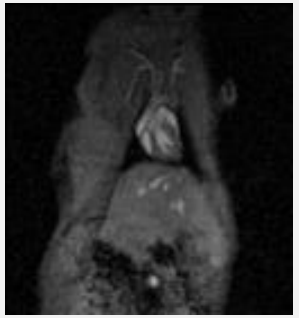




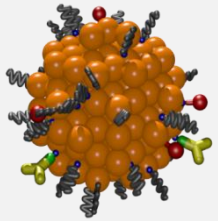
Regenerative Medicine

NVH Medicinal
BIOTECHNOLOGY

SuperParamagnetic Iron Oxide Nanoparticles (SPIONs)



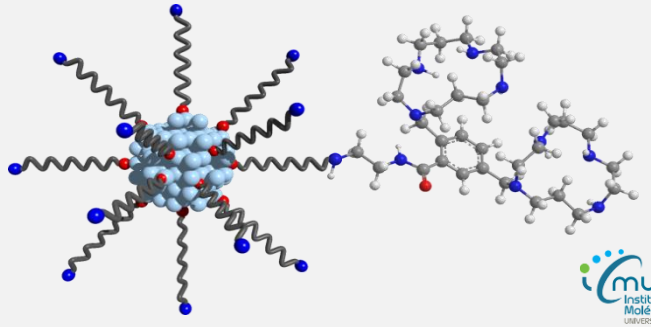
Mouse (heart)



SPIONs as new multimodal imaging probes

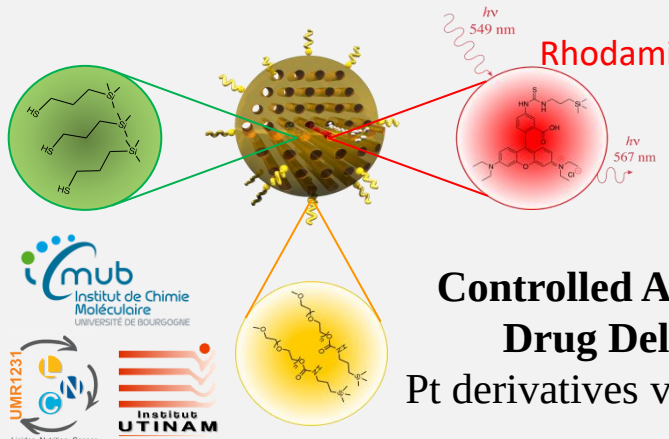
Bimodal contrast agent
Biodistribution

Tantalum Oxide Nanoparticles



- **Theranostic agent :** CT contrast agent
- Nanovectorization of AMD3100 (CXCR4+)

Mesoporous Silica Nanoparticles (MSNs)



Controlled Anticancer Drug Delivery:
Pt derivatives vectorization

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

PHARM*IMAGE*® - Consortium (GIE)
http://www.pharmimage.fr

Equipex IMAPPI: Integrated Magnetic resonance And Positron emission tomography in Preclinical Imaging

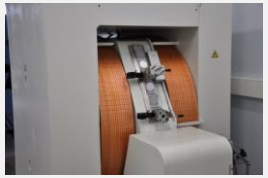
PHARM'IMAGE
Platforms and competences for pharmacology

Imagerie couplée TEP/IRM

MR SOLUTIONS

Cyclotron

CYCLOPHARMA



Onco design BIOTECHNOLOGY
CheMatech macrocycle design technologies
CCITI KNOWLEDGE & E-PATHOLOGY
NVH Medicinal BIOTECHNOLOGY
CYCLOPHARMA
Welience Innover, c'est notre métier
CHU Centre Hospitalier Universitaire Dijon
CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer
CENTRE hospitalier Nevers Agglomération de Nevers

cnrs
uB UNIVERSITÉ DE BOURGOGNE
cmub Institut de Chimie Moléculaire UNIVERSITÉ DE BOURGOGNE
L2i
Laboratoire Interdisciplinaire Carnot de Bourgogne
icb

Recherche Académique
Project 3MIM (accord trilatéral UB/CNRS/CRBFC)

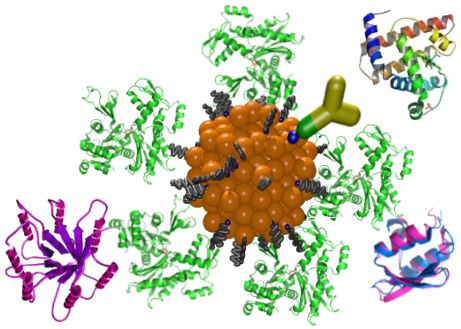
RÉGION BOURGOGNE FRANCHE COMTE

Développement de nouveaux traceurs et de nouveaux thérapeutiques (théranostiques)

BH2N
https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Study, understanding and control the protein/nanomaterials interactions

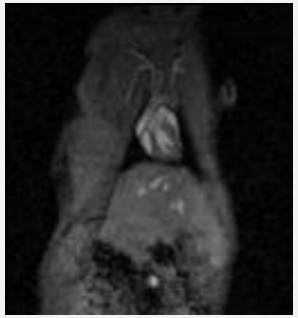


Controlled → specific uptake

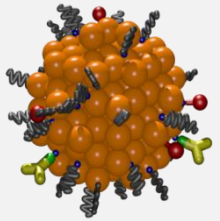
More circulating and more specific nanodrugs

Clipp Plate-forme Protéomique l'innovation en recherche clinique

SuperParamagnetic Iron Oxide Nanoparticles (SPIONs)



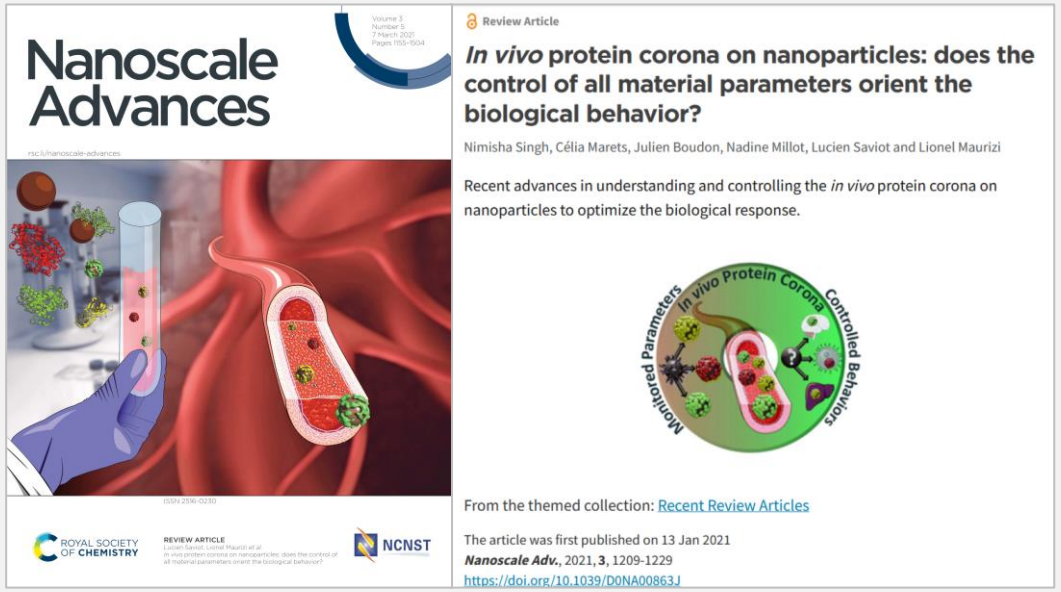
Mouse (heart)



SPIONs as new multimodal imaging probes

CHU Centre Hospitalier Universitaire Dijon

Bimodal contrast agent
Biodistribution



Nanoscale Advances

rsc.li/nanoscale-advances

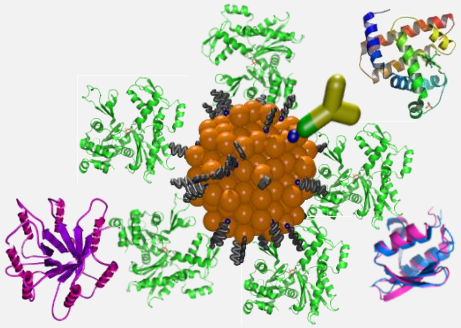
doi:10.1039/D0NA00863J

BH2N

https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Study, understanding and control the protein/nanomaterials interactions

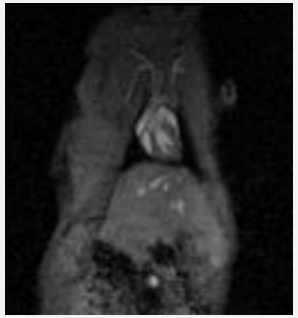


Controlled → specific uptake

More circulating and more specific nanodrugs

Clipp Plate-forme Protéomique

SuperParamagnetic Iron Oxide Nanoparticles (SPIONs)



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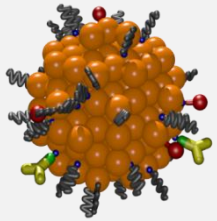
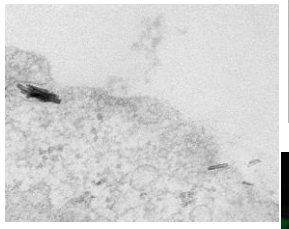


SPIONs as new multimodal imaging probes

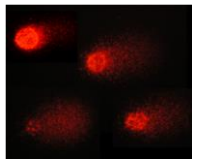
CHU Centre Hospitalier Universitaire Dijon

Bimodal contrast agent
Biodistribution

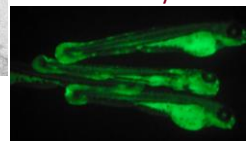
Original evaluation of the toxicity/safety of nanoparticles



Internalization (TEM)



Genotoxicity



Zebrafish embryo

- Cytotoxicity
- Genotoxicity
- Carcinogenicity
- Ecotoxicity…

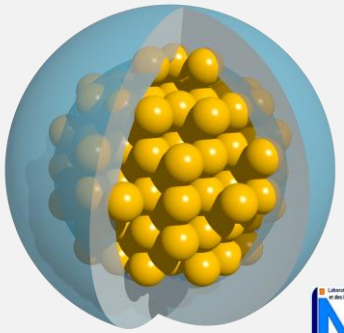
Bio-peroxIL

Physiologie de la Nutrition & Toxicologie NUTox UMR1231 Inserm

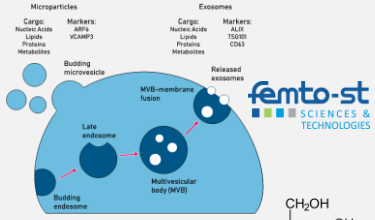
UMR1231 Lipides, Nutrition, Cancer

Nanocare platform

New developments of gold nanoparticles for targeting and sensing

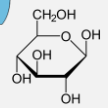


Extracellular vesicles targeting



femto-st SCIENCES & TECHNOLOGIES

Glucose sensing



BH2N
https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Plateforme NanoCare uB

Compétences et savoir-faire

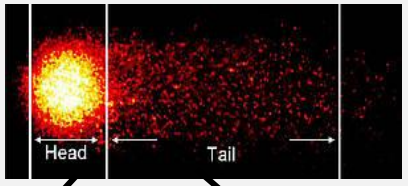
❶ **Offre de formation (nanomatériaux, risques, réglementation)**

❷ **Caractérisations fines et complètes de vos nanomatériaux** :

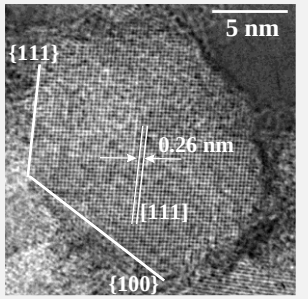
- Taille, forme, surface, charges, chimie, pollutions, structure etc.

❸ **Tests de toxicité, écotoxicité, biodistribution** :

- Cytotoxicité : *Test Alamar Blue, Test de cinétique de synthèse des ARNs totaux, Test MTT*
- Génotoxicité : *Test des comètes-fpg, Test des micronoyaux, Test d'Ames*
- Cancérogénicité : *Test de transformation cellulaire*
- Stress oxydant : *Tests de cytométrie en flux, H2DCFDA, DHE, DHR123 etc.*
- Ecotoxicité (Zebrafish)
- Biodistribution (petit animal) : *SPECT, TEP, IRM et imagerie optique*



ADN non altéré *ADN fragmenté*



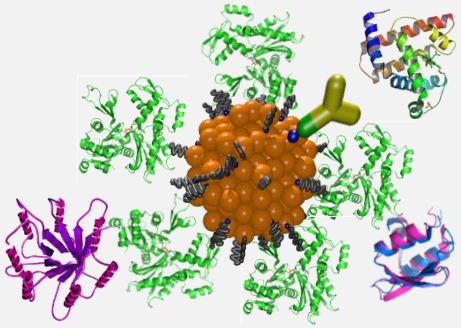
❹ **Accompagnement dans la mise en sécurité**

BH2N

https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Study, understanding and control the protein/nanomaterials interactions



More circulating and more specific nanodrugs

Controlled → specific uptake

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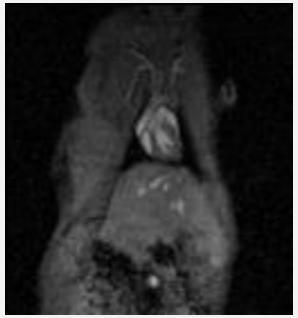

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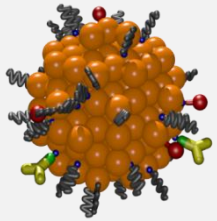

SPIONs as new multimodal imaging probes

Bimodal contrast agent
Biodistribution

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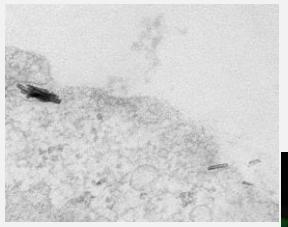

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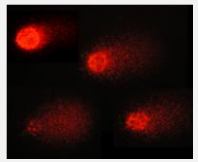
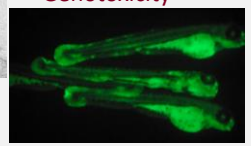


Genotoxicity

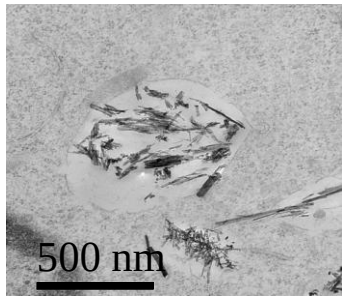


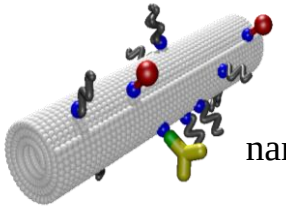
Zebrafish embryo

- Cytotoxicity
- Genotoxicity
- Carcinogenicity
- Ecotoxicity…

Nanocare platform

Titanate nanotubes: TiONts





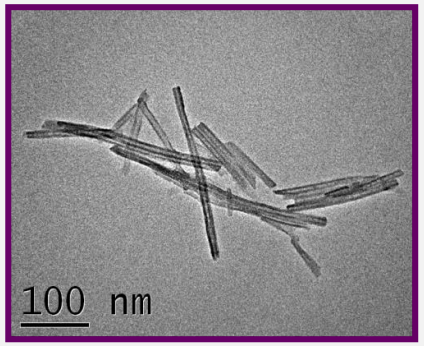
TiONts for nanovectorization

Transfecting DNA in cardiomyocytes cells

Radiosensitizing of tumors

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

A new nanomedicine for cancer treatment



Nanotubes = nano-needles:
To focus the radiosensitizer in the tumor by taking advantage of their morphology

+ intrinsic radiosensitizing effect

Radiotherapy and Oncology 108 (2013) 136–142

Contents lists available at SciVerse ScienceDirect

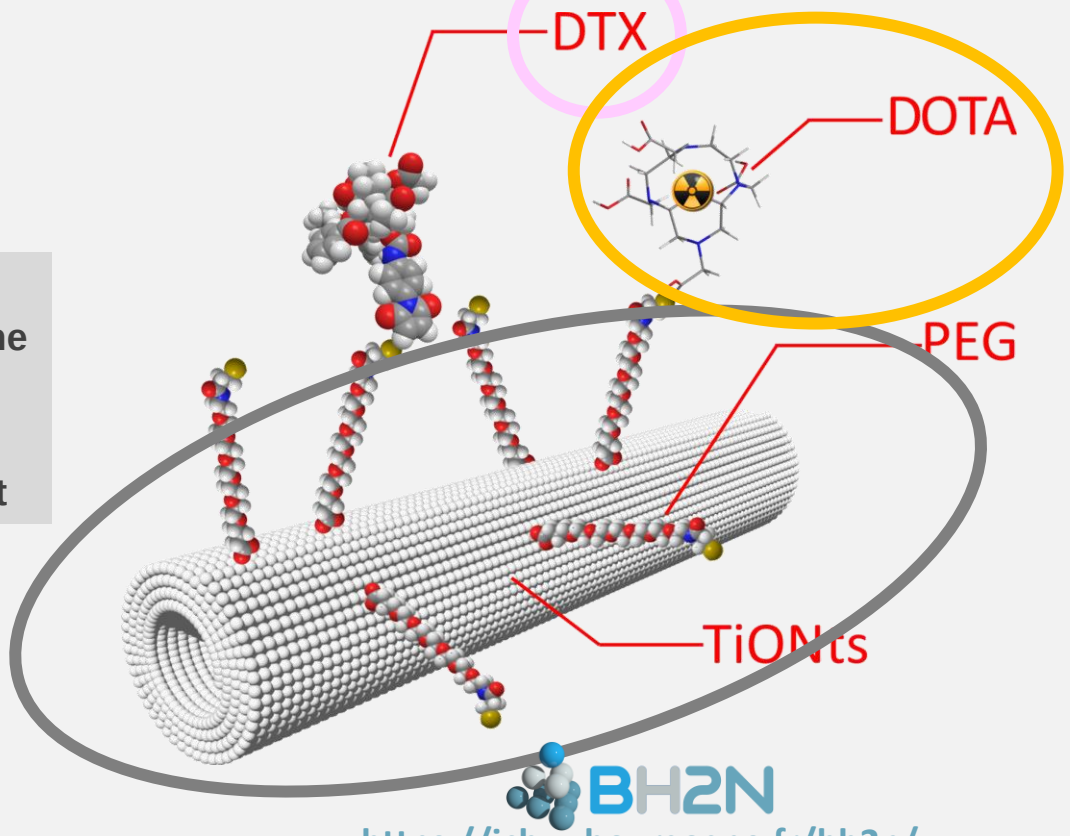
Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Radiobiology of glioblastoma

The radiosensitization effect of titanate nanotubes as a new tool in radiation therapy for glioblastoma: A proof-of-concept ☆

C. Mirjolet [a,1], A.L. Papa [b,1], G. Créhange [a], O. Raguin [c], C. Seignez [d], C. Paul [d], G. Truc [a], P. Maingon [a,*], N. Millot [b,*]



Docetaxel (taxane):
Radiosensitizer focused and maintained in the tumor

Radioelement	Half time (h)
^{99m}Tc	6
^{123}I	13
^{111}In	**67**

Chelating agent
SPECT/CT *via* ^{111}In labelling

A. Loiseau, J. Boudon, C. Mirjolet, G. Créhange, N. Millot, *Adv. Healthcare Mater.* 2017, *6*, 1700245. doi: 10.1002/adhm.201700245

C. Mirjolet, J. Boudon, A. Loiseau, S. Chevrier, R. Boidot, A. Oudot, B. Collin, E. Martin, P. A. Joy, N. Millot, G. Créhange, *Int. J. Nanomed.* 2017, 6357-6364. doi: 10.2147/IJN.S139167

BH2N
https://icb.u-bourgogne.fr/bh2n/

Titanate nanotubes = TiONts;
Docetaxel = DTX; DOTA = macrocycle

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Nos moyens d'élaboration

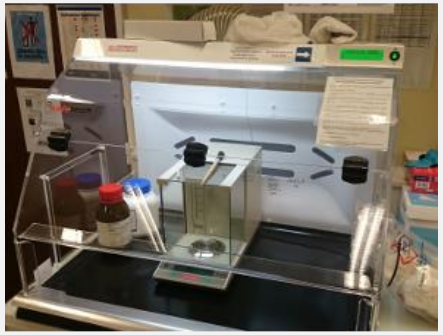
Synthesis with a Schlenk line

Batch reactor

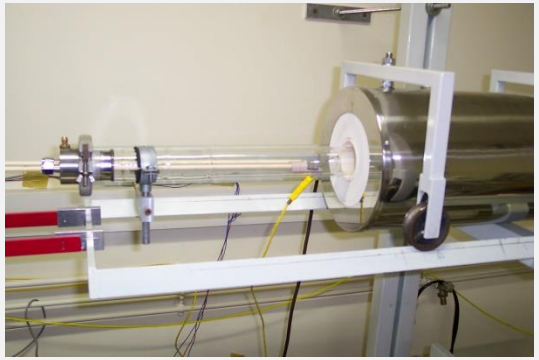
Batch reactor

Planetary grinding

Continuous flow synthesis
With Sub- or supercritical water



Safe handling/weighing of nanopowders



tube furnace for calcination

Metal oxide synthesis by coprecipitation

Autotitrator

BH2N

https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

Nos moyens de purification

Ultrafiltration

Dialysis

Cross-flow filtration

Lyophilization

Rotary evaporator

Cross-flow filtration

Ultrapure water

pH measurements

Sonication station

Centrifugation

BH2N

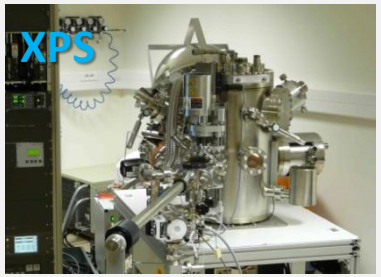
https://icb.u-bourgogne.fr/bh2n/

Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

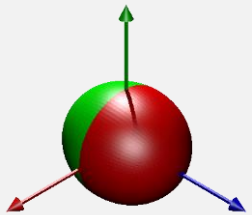
La caractérisation des nanoparticules

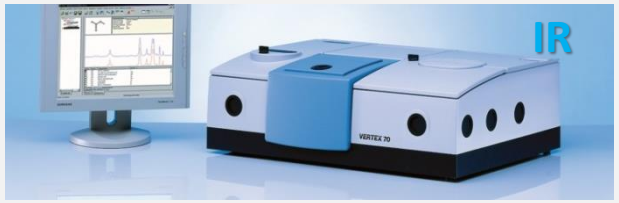
Morphologie
(taille, forme, agrégation, stabilité ?)

Surface
(développée, chimie de surface, charge de surface)



Structure





Composition chimique
(pollution)

XPS, EDX (MET/MEB), EELS

BH2N

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Équipe (Bio-)hybrid nanoparticles & nanostructures (BH2N)

cnrs GDR Groupement de recherche
B2i
Bio-ingénierie des interfaces

Recherche de nouvelles collaborations pour relever de nouveaux défis

- Biocapteurs
- Maîtrise de la couronne protéique
- Biomimétisme
- Etc.

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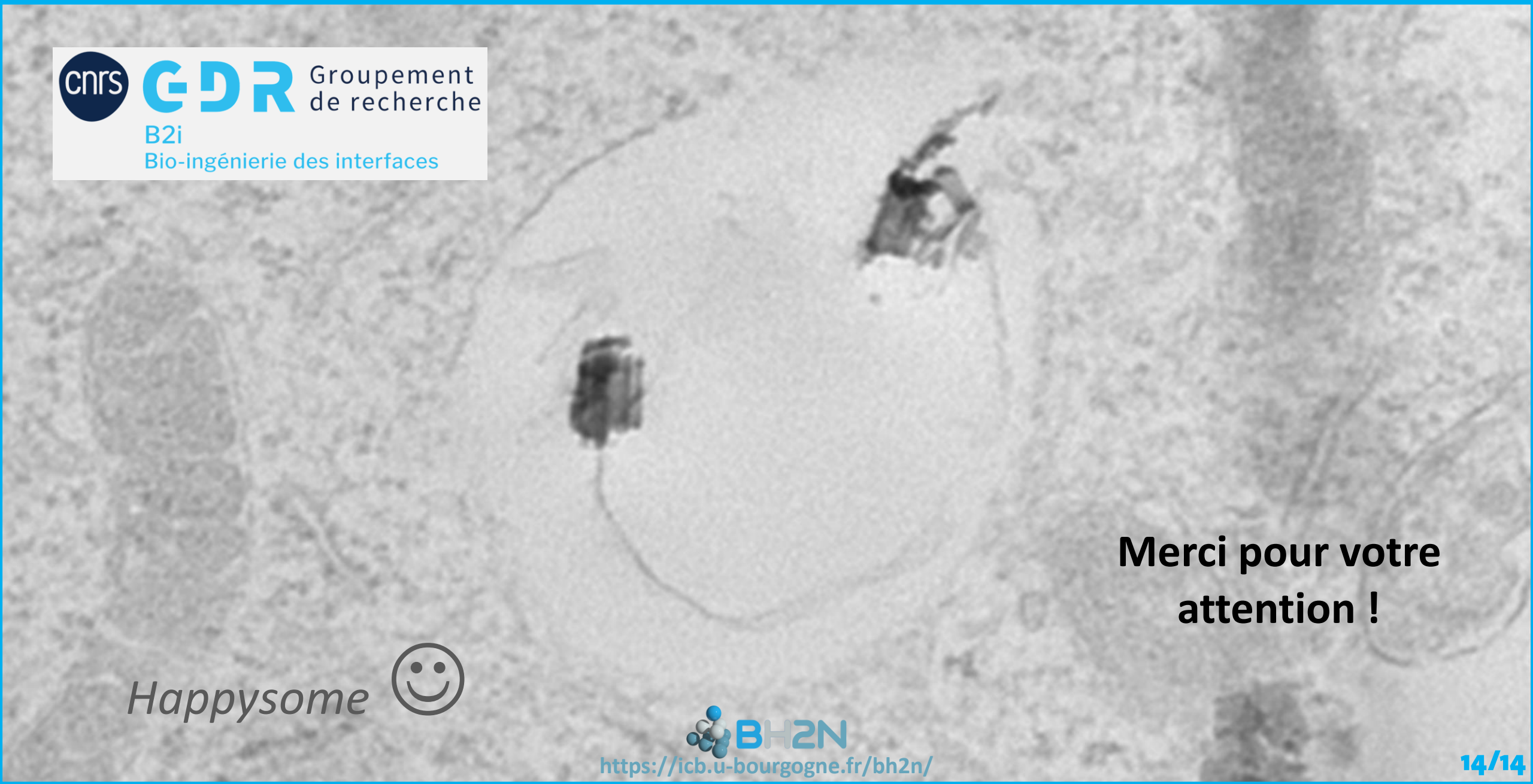

Merci pour votre attention !

Happysome ☺

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