CAMB - UMR 7199

Laboratory of Functional Chemo-Systems

L'équipe aujourd'hui

3 Permanents (1DR, 1CR, 1TCN)
7 Doctorants & Post-Doctorants
3 Doctorants en cotutelle
2 ANR; 1 ITN Marie Curie; 1 BDI;
2 Bourses Région; 1 Bourse FRC

Période 08-2007 / 2011

Médaille de Bronze CNRS
Lauréat INPI et CETI
Accréditation du Labex MEDALIS
Création de 2 start-up; Phytodia - eNovalys
2 Brevets en exploitation
21 Thèses soutenues
79 (64) Publications

UNIVERSITÉ DE STRASBOURG

FRC
International Center for Frontier Research in Chemistry

medalis

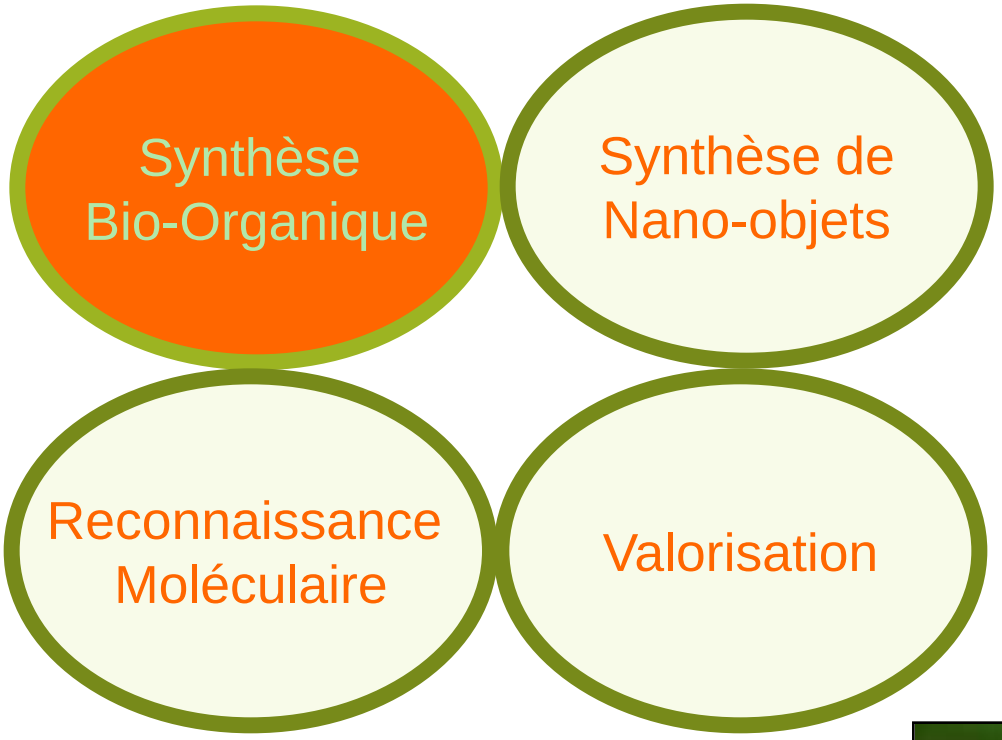
cnrs

Le Laboratoire de Synthèse Bioorganique en 2007

Une expertise en synthèse organique
Des compétences transverses

Synthèse totale
Méthodologie
Catalyse / Organo-catalyse

Nanobagues
Nanotubes



Empreintes moléculaires
Sondes réactives

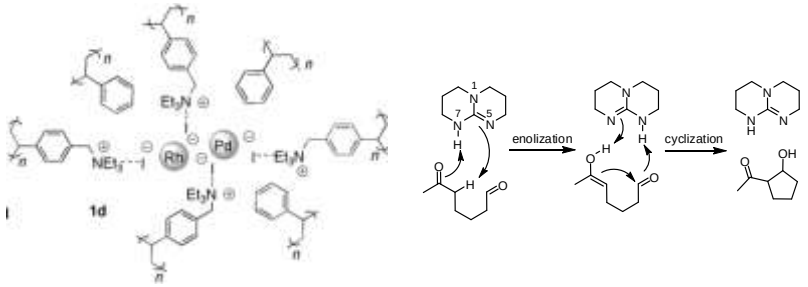
Novalyst DISCOVERY
A ChemoTechnology Compagnie

PHYTODIA

La nutraceutique au service des maladies métaboliques

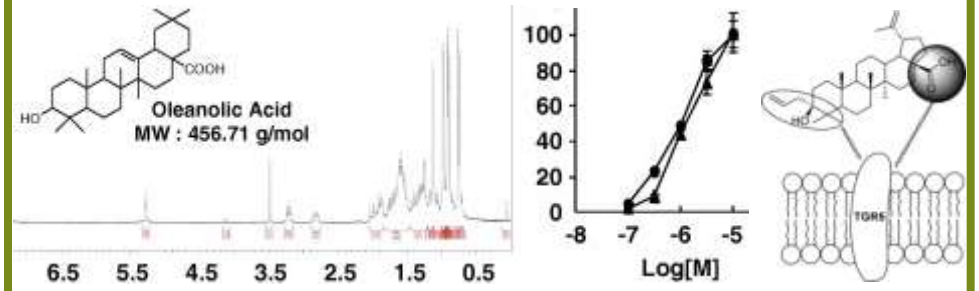
Key results: Organic & Medicinal Chemistry

Catalysis and Organocatalysis



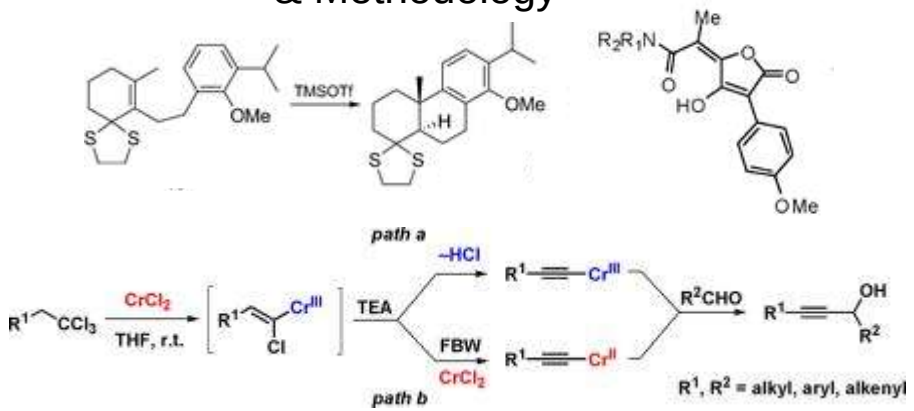
ChemEurJ**2008;** EurJOrgChem **2009;** EurJOrgChem **2010;** JOrgChem **2010;** ChemCatChem **2 010;** ChemComm **2011**

Anti-hyperglycemic activity of TGR5 agonist



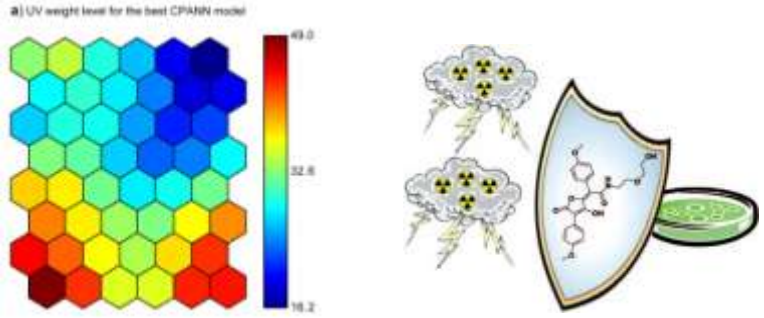
BiochemBiophysResComm **2007**; JMedChem**2010** ChemMedChem **2010**

Total Synthesis of Natural Compounds & Methodology



ChemComm **2009;** EurJOrgChem **2010;** EurJOrgChem **2010;** ChemComm **2010;** JOrgChem **2011;** IntJArt Intel **2011**

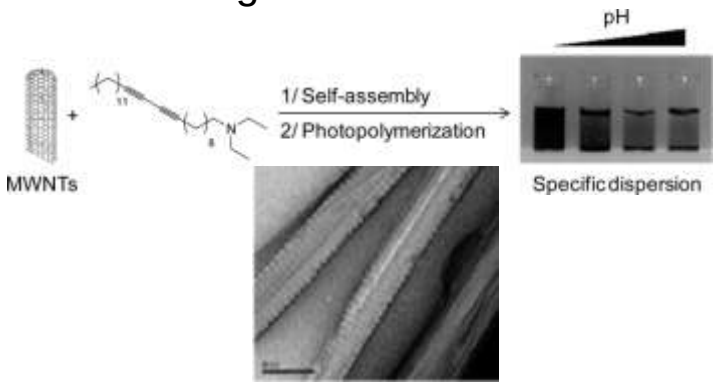
Anti-oxidant & radio-protective properties of small molecules



JOrgChem **2008;** JMedChem **2009;** BioorgMed Chem 2**010** ChemMedChem **2011; J**ChemInfo&Model **2011**

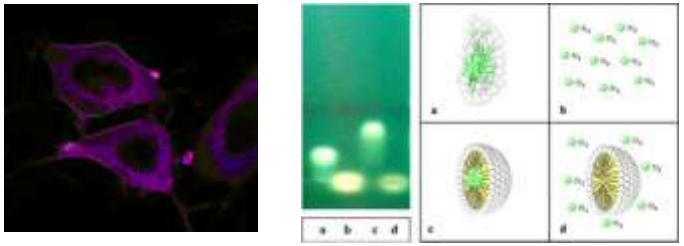
Key results: Nano-constructs

Auto-arrangement on CNT surface



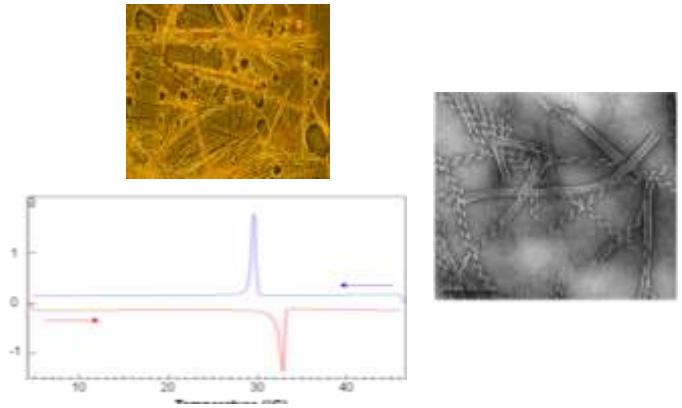
NanoLett **2008**; ChemEurJ**2009;** SoftMater **2009;** **ChemComm 2009; JnanosNanotech 2009;** J PhysChem **2010** ; J Phys Chem **2011;**

« Nano-ring » and micelles



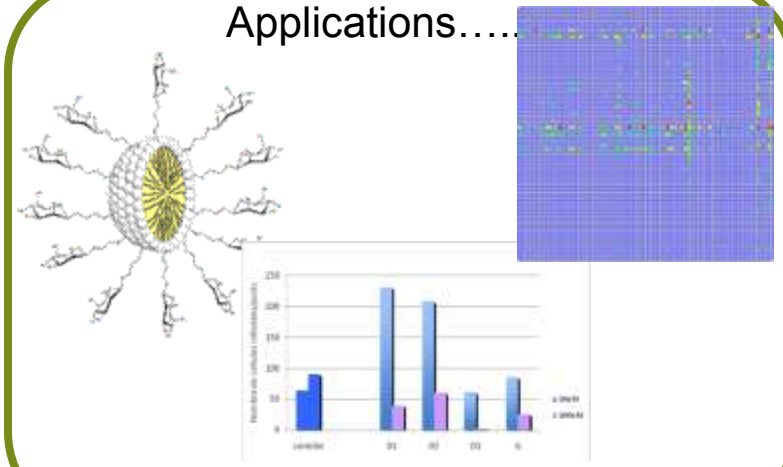
NatNanotech **2008**;SoftMat **2011**;MacroChemPhys **2011**;

Nanotube, lats and others



JPhysChem **2010**; Langmuir **2011**;

Applications…..

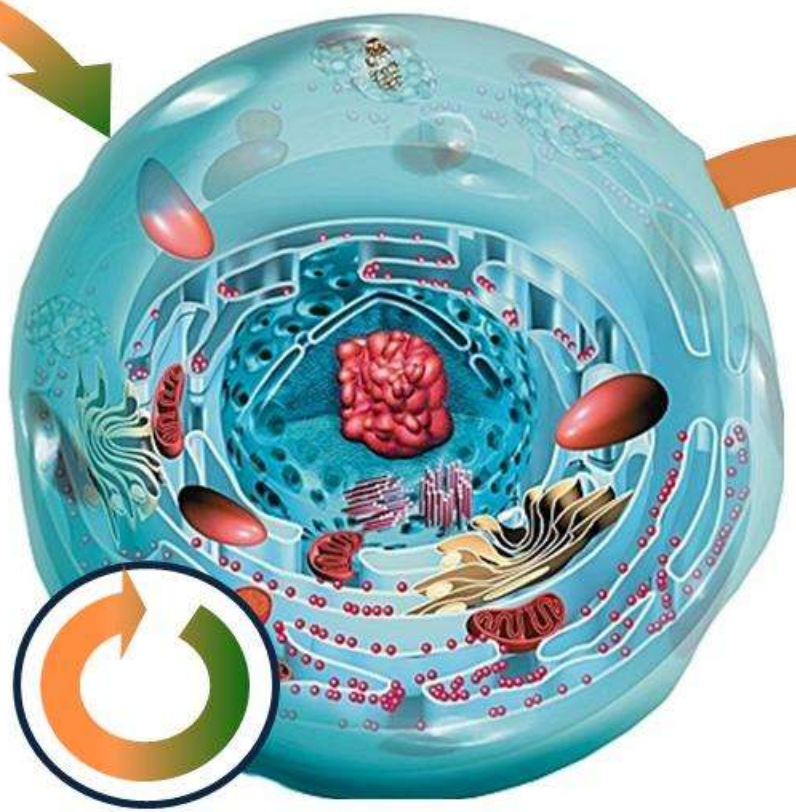


Bioconj **2011**, Patent application **2011**

A new field opens-up…

…biofunctional chemistry

Biospecific reactions
Staple peptides
Bioconjugation
Proteomic
Capture



Bioresponsive reactions
Measuring system deregulation
GSH / ROS
pH
Malondialdehyde
Normoxic / hypoxic

Bioindependant reactions
Molecular probes for activity profiling
(Topoisomerases, PARPs, PRMTs)
Catalysts and reagents for interfering
(Esterase, Phosphatase, Metabolization)

Synthetic Chemistry in Biological Media

"Synthetic" reactions ⟷ "Biological" reactions

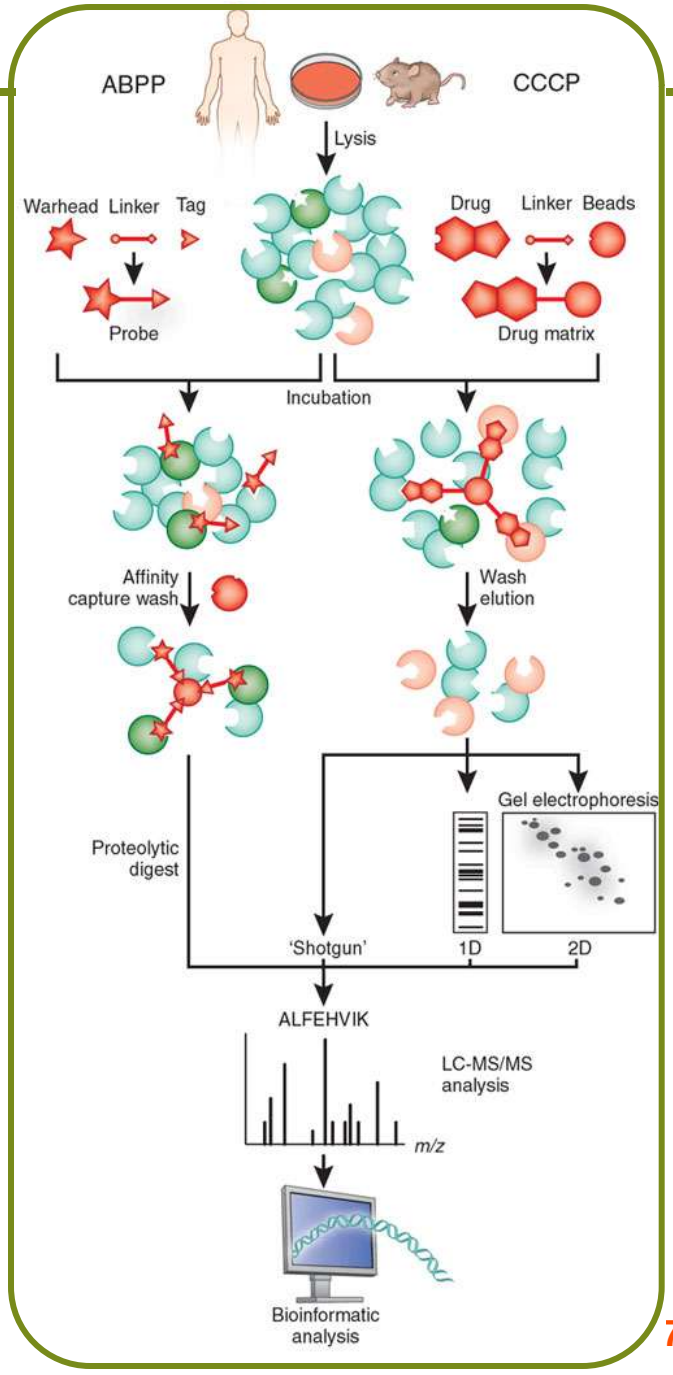
"Synthetic" reactions	"Biological" reactions
Closed and defined system	Open and evolving system
Standardized media	Complex media
High concentration	Low concentration

-	← Number of steps →	+++
+++	← Variety of reaction conditions →	+
+++	← Variety of chemical acts →	+
+++	← Variety of functional groups →	+
+++	← Variety of reagents →	-
-	← Complexity of reagents →	+++
-	← System compartmentalization →	+++

➡ Developing "chemical" reactions, reagents or catalysts to interfere with biological media require to first define new guidelines and evaluation methodologies.

Chemical Proteomic Today

As we move toward systems biology and personalized medicine, comprehensively determining small molecule–target interaction profiles and mapping these on signaling and metabolic pathways will become increasingly necessary. Chemical proteomics is a powerful mass spectrometry–based affinity chromatography approach for identifying proteome-wide small molecule–protein interactions.



Diagnostique par protéomique chimique

Les techniques de protéomiques chimiques sont adaptées à la recherche de marqueurs mais pas à leur analyse diagnostique.

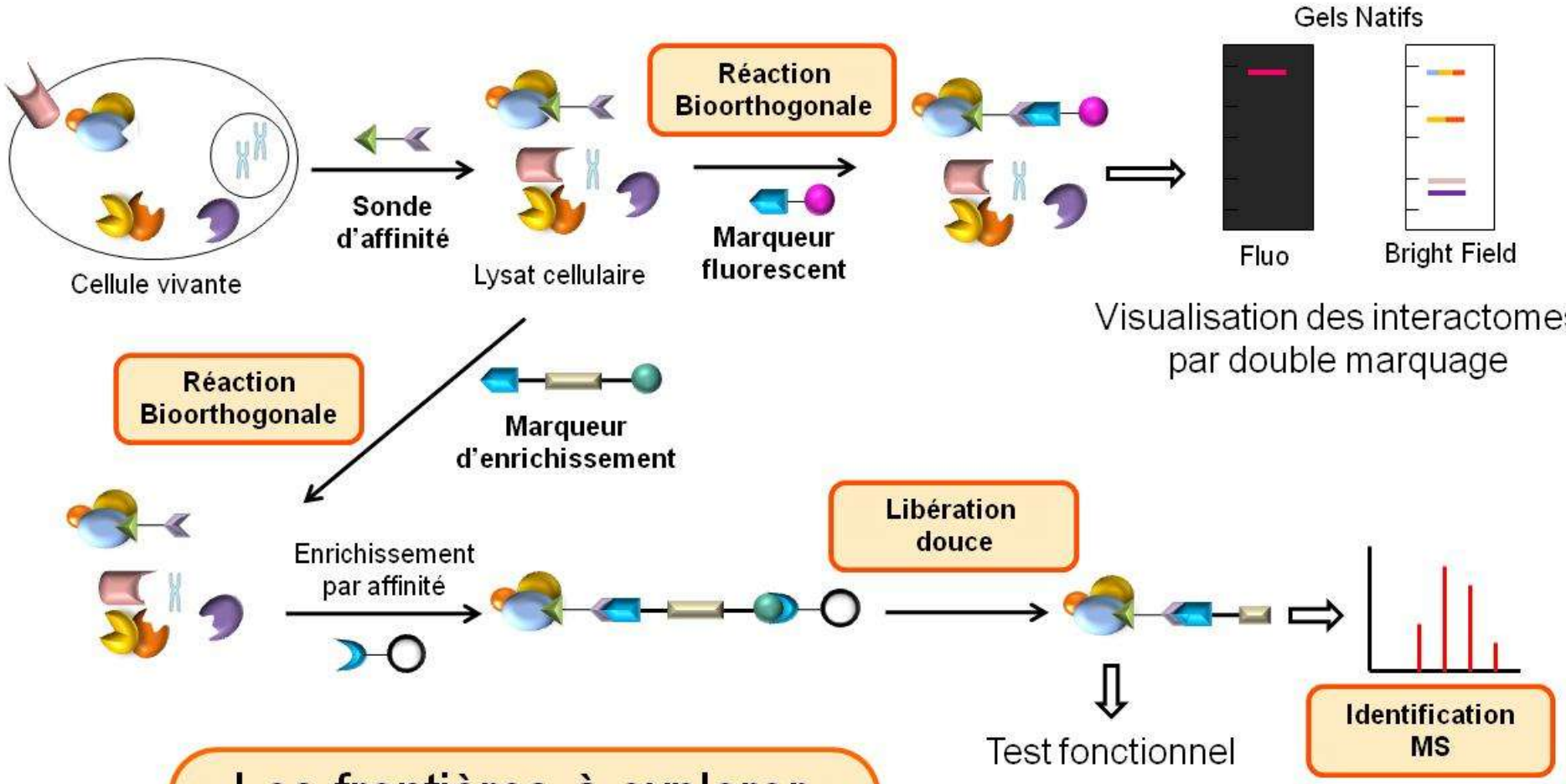
Contraintes d'une analyse diagnostique:
- Echantillon de petite taille
- Analyse rapide et fiable
- Complexité et coût maitrisée.
- Technologie de routine

Alternatives:
Culture organotypique *ex vivo*.

Example of significant issue:

Un haut niveau de protéine p21 (Cyclin-Dependent Kinase Inhibitor) est associé a une chimio résistance p.ex. dans les leucémie lymphoïdes aigues. Cette pathologie est traitée par des inhibiteurs de tyrosine kinase (TKIs), comme l'imtinibe, le dasatinibe, ou le nilotinibe. La détermination du profil des complexes p21-CDK chez les patients traités offrirait une opportunité d'envisager des traitement personnalisés.

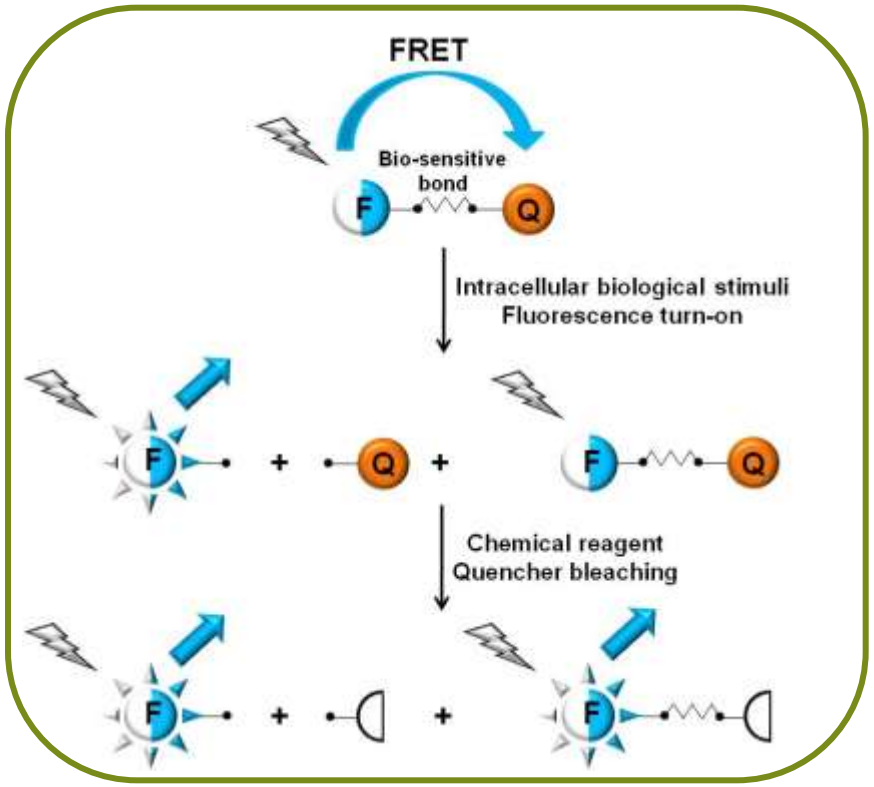
L'approche non dénaturante

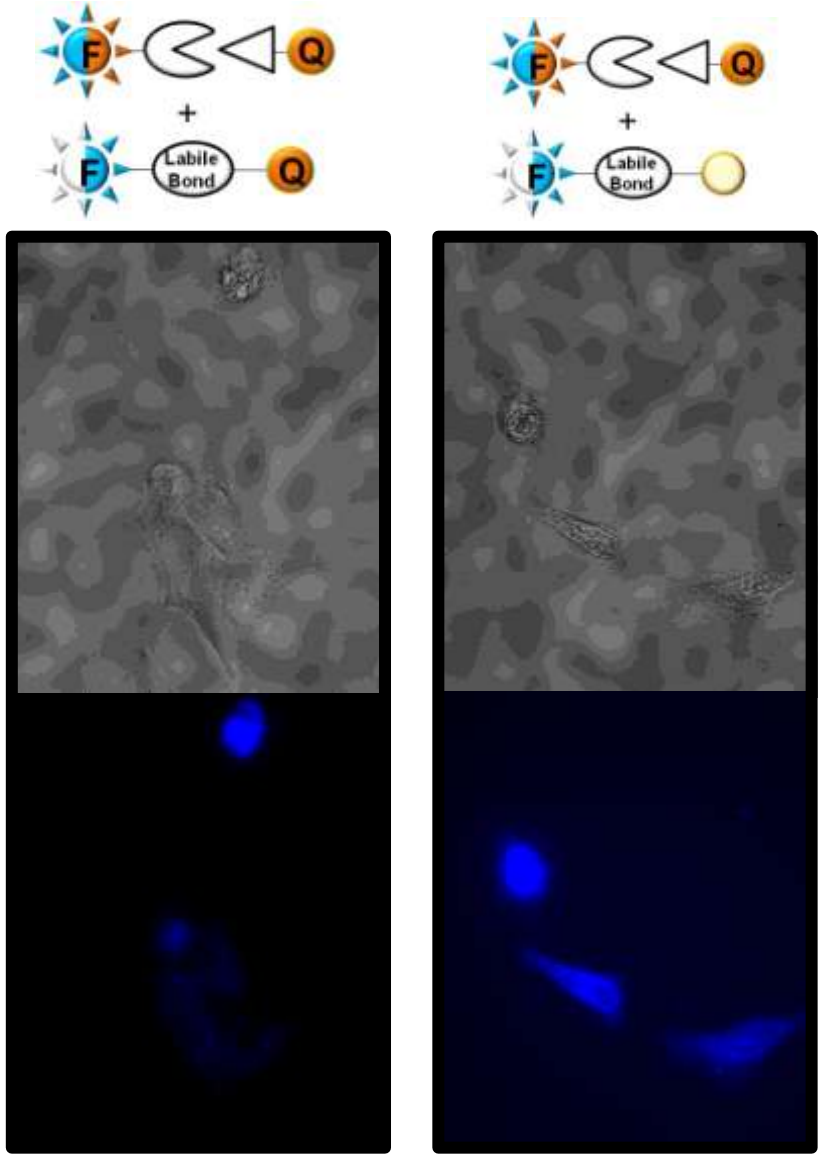


Les frontières à explorer

- Ligation intracellulaire
- Marquage sélectif *C-ter*
- Réactif MS compatibles

Réactifs chimiques biocompatibles

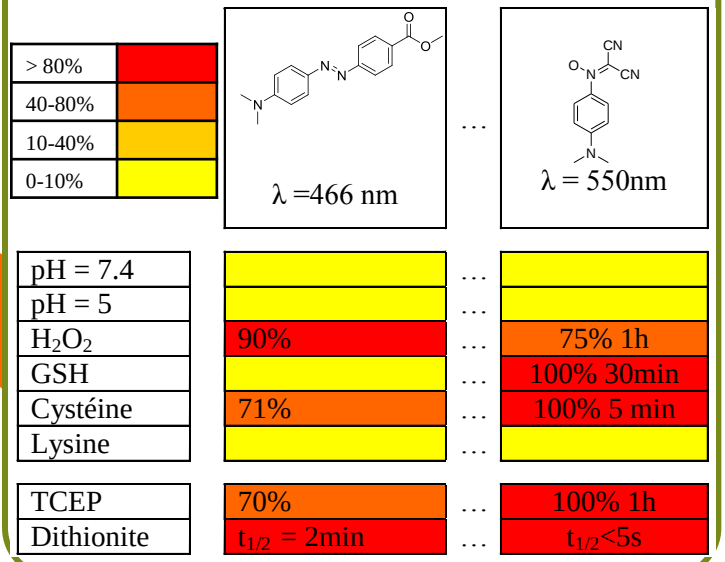




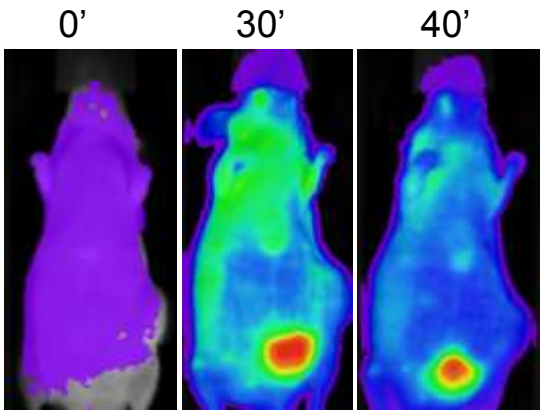
Bio-sensitive chemical bonds

Stimuli	Pathologies
Glutathione (GSH)	Brain disease (Parkinson)
Nitric oxide (NO)	Viral disease
Hydroperoxides	Aging
Reactive Oxygen Species (ROS)	Glomerular disease
pH alteration	Oncology
Free metal	Alcoholism
Malondialdehyde (MDA)	Ischemia–reperfusion injury
4 Hydroxynonenal	Cardiac conditions
Methylglyoxal	Premature birth
3-Acetyl-2,5-hexanedione	Erectile dysfunction
Phosphocholine	Cigarette smoke effect
Lactates, Créatine, Myoinositol	Cornea disease

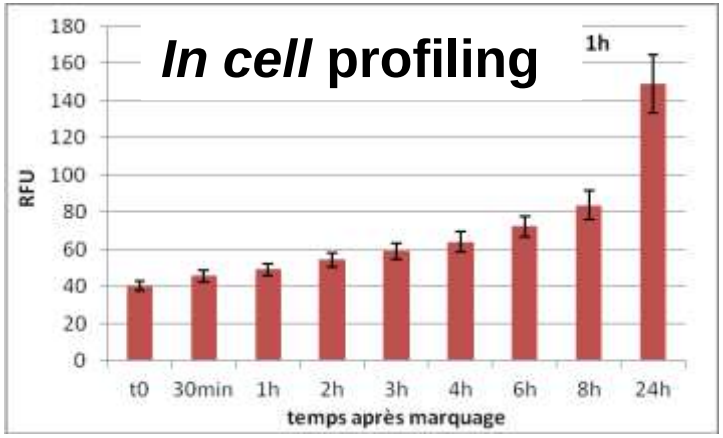
In vitro profiling



In vivo profiling



In cell profiling



Les atouts du LFCS

Une recherche originale → Chimie en milieux biologique

Une recherche fondamentale → au service de problèmes concrets
(3 starts up crées, une technologie en cours de développement)

Une équipe renforcée → Hélène Muller-Steffner et Isabelle Kuhn

Des collaborations établies →

- Alain Van Dorsselaer (Analyses protéomiques)
- Dominique Bagnard, David Brasse (Imagerie de petit animal)
- Yves Melly (Fluorescence)
- Valérie Lamour, Valérie Schreiber, Georges Noel, Jean Cavarelli et Bertrand Jean-Claude (Cibles en oncologie)
- Jean-Serge Remy, Evelyne Schaeffer, Jean-François Nierrengarten (Nano-assemblages)

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Proteomic
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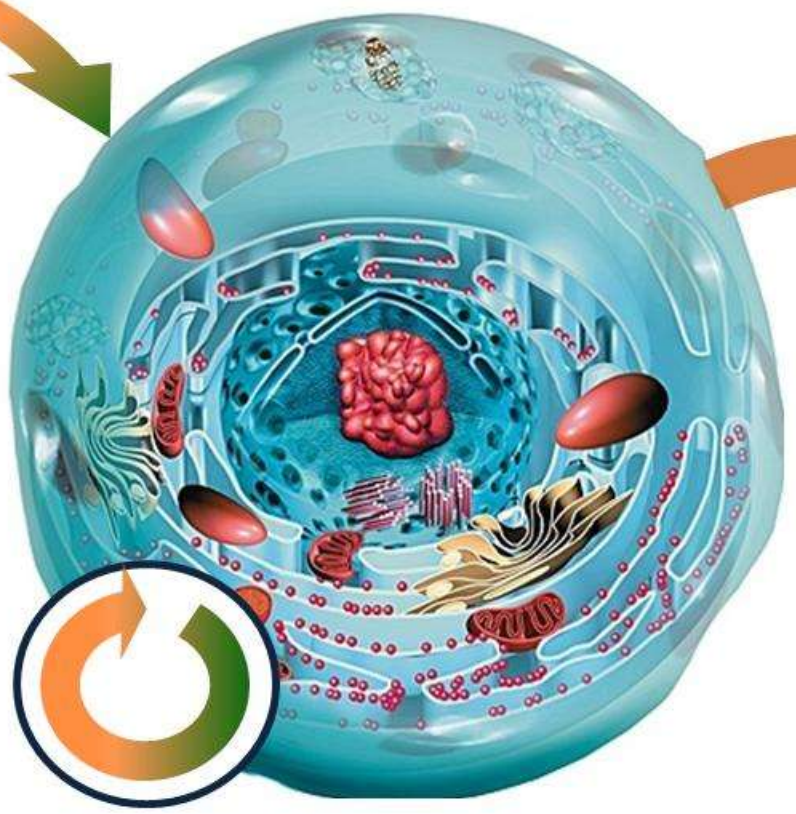

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