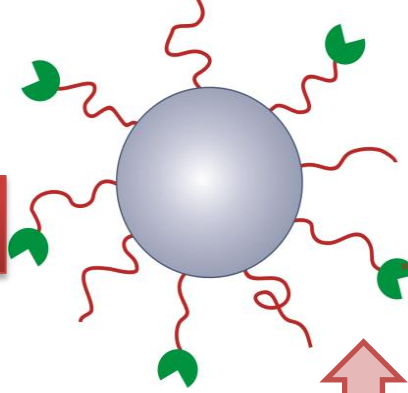
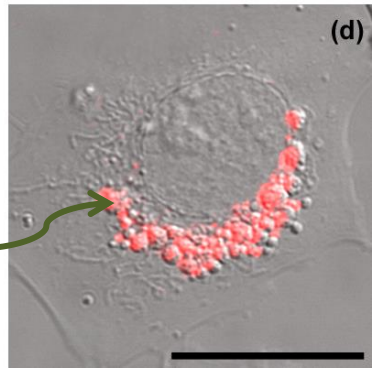
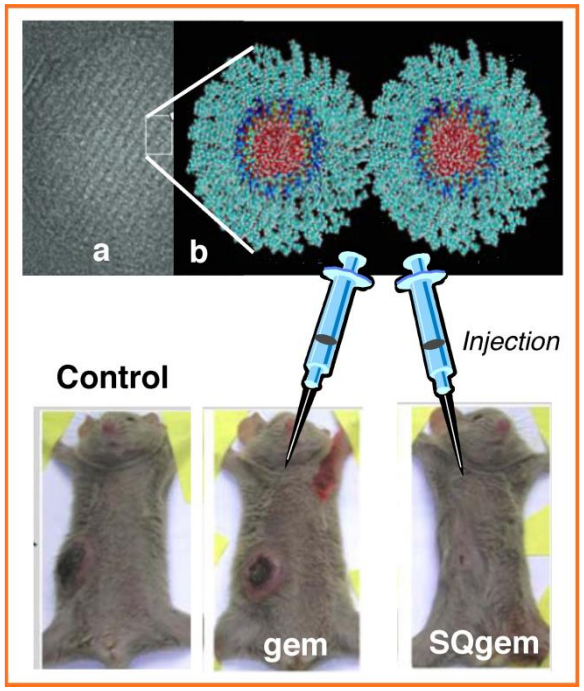
FLAGSHIP NANOMED



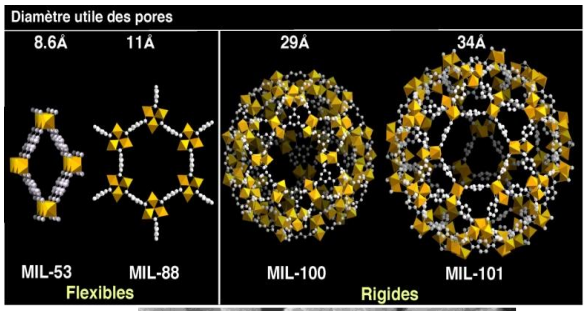


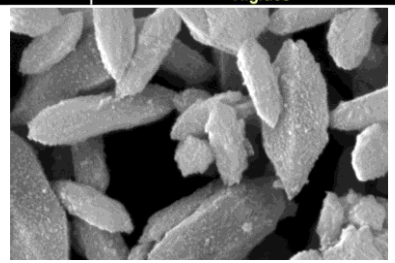
DES (NANO)THÉRAPEUTIQUES PLUS EFFICACES ET MOINS TOXIQUES CAR PLUS CIBLÉES



Squalénisation

- Caractérisation moléculaire et supramoléculaire
-Compréhension des mécanismes de formation
-Encapsulation d'anticancéreux et d'anti-infectieux
-Chimie de surface (fonctionnalisation)
-Evaluation pharmacologique et toxicologique





Nanohybrides poreux

2 technologies de rupture

LE TRAITEMENT DES MALADIES GRAVES, RESISTANTES AUX TRAITEMENTS ET INCURABLES: UN DEFI MEDICAL MAJEUR

→ NANOTECHNOLOGIES POUR LA VECTORISATION DES MEDICAMENTS

FINANCEMENTS DE POST-DOCS

Deux projets de recherche financés depuis 2012 :

1°/ Etude du mécanisme de formation de nanomédicaments squalénés (gemcitabine-squalène) (PI: O. Spalla, CEA)
2°/ Fonctionnalisation de surface par méthode Graft-Fast de nanoparticules de MOFs (PI: C. Serre, UVSQ)

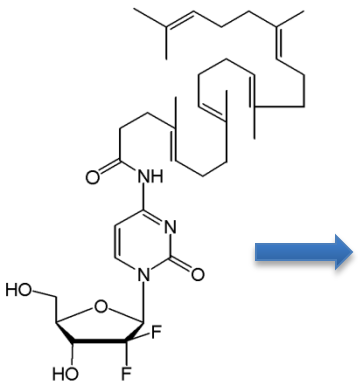
Quatre projets ont démarré en mai-juin 2015

1°/ Nanoparticules de palladium pour la manipulation intracellulaire de protéines (PI: P. Couvreur, U-PSUD
2°/ Biosenseurs luminescents pour le FRET (PI: N. Hildebrandt, U-PSUD)
3°/ Développement d'une puce pour le diagnostic de la neuropathie amyloïde (PI: A-M Haghiri, CNRS)
4°/ Nanovecteurs thérapeutiques multifonctionnels (PI: P. Horcajada, UVSQ)

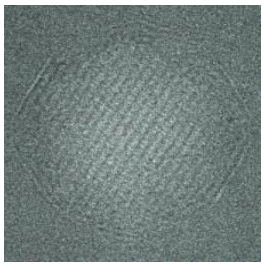
INVESTISSEMENTS EN MATÉRIELS

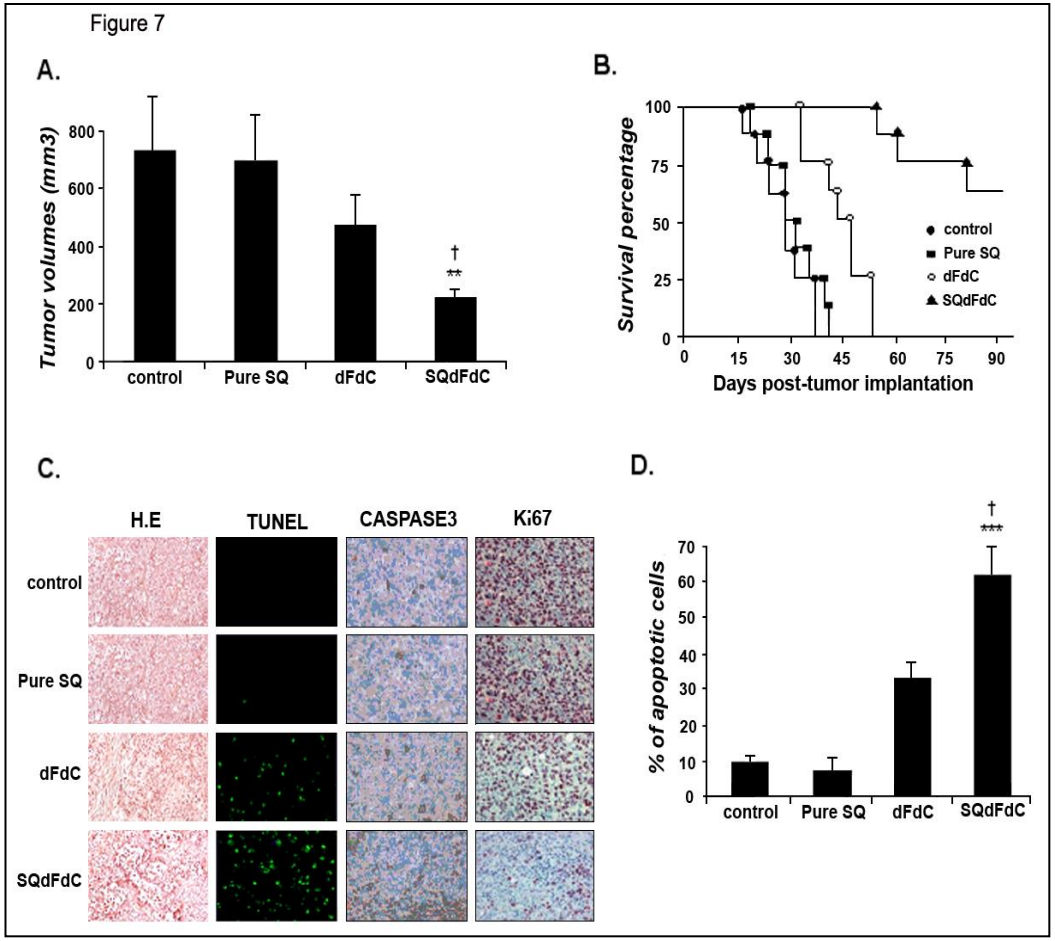
-Détecteur à bruit quasiment nul pour l'utilisation de rayons X en laboratoire (CEA, LIONS)
-Appareil d'imagerie in vivo à haute résolution IVIS Lumina LT (Univ Paris-Sud, Institut Galien)
-Incubateur de microscope (CO2 et température) pour l'imagerie des cellules vivantes (Université Paris-Sud, IEF)

LES NANOPARTICULES DE GEMCITABINE-SQUALÈNE ET CANCER DU



Sq-Gemcitabine (SQ-dFdC)

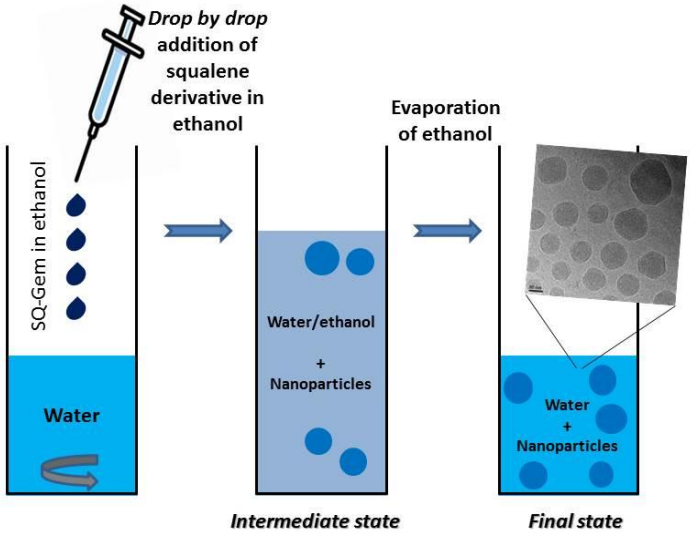


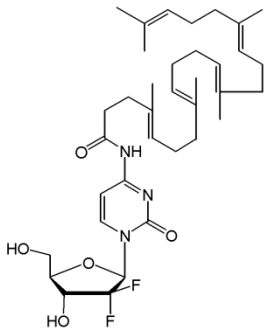


NANOPARTICULES DE GEMCITABINE-SQUALÈNE: COMPRÉHENSION DU MÉCANISME DE FORMATION

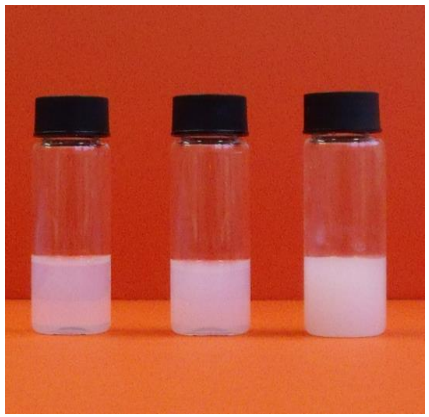
Synthèse et préparation
D. Desmaële (Institut Galien)

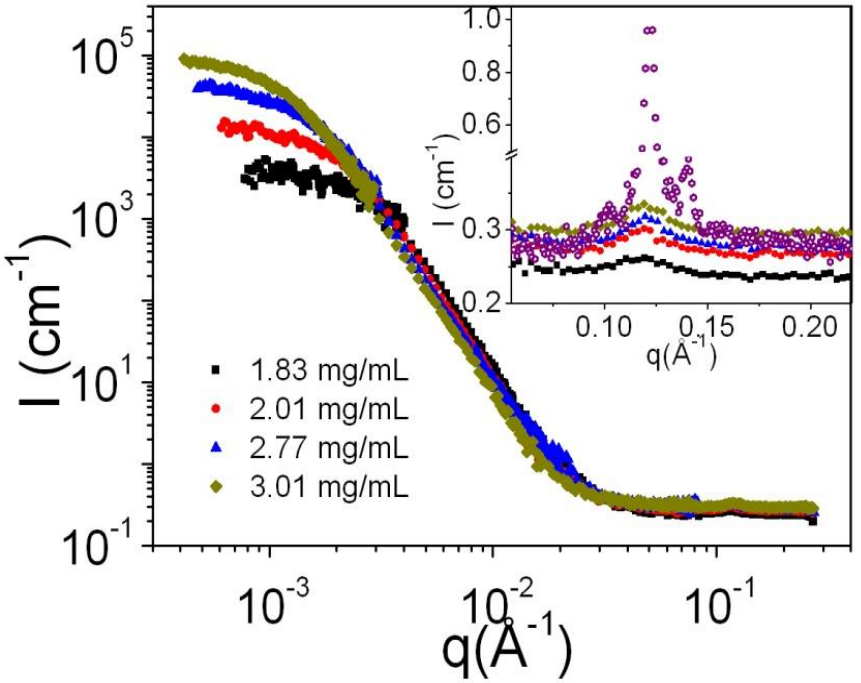
Diffusion des neutrons aux petits angles
D. Debashish et O. Spalla (CEA, LIONS)



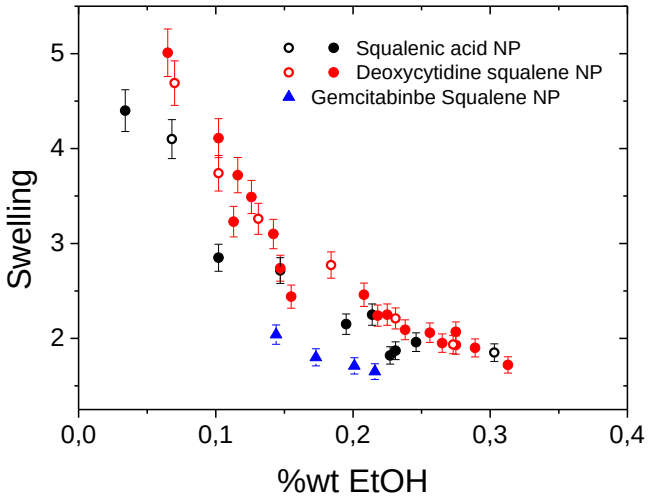


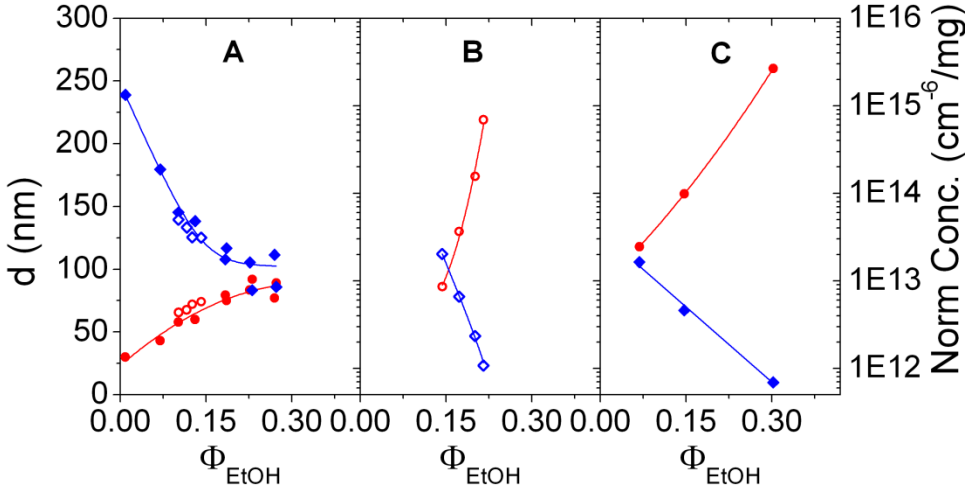
Sq-Gemcitabine (SQ-dFdC)



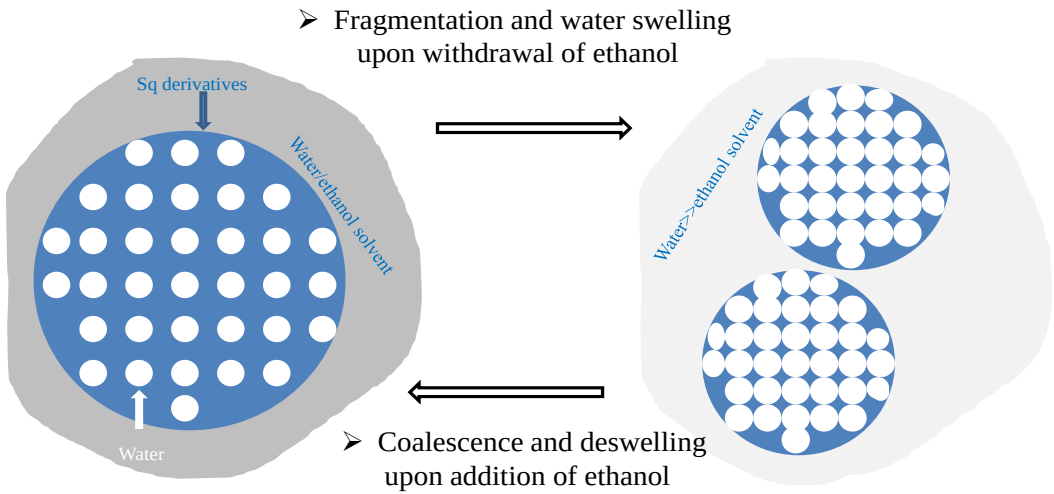


RÉSULTATS: GONFLEMENT ET FRAGMENTATION





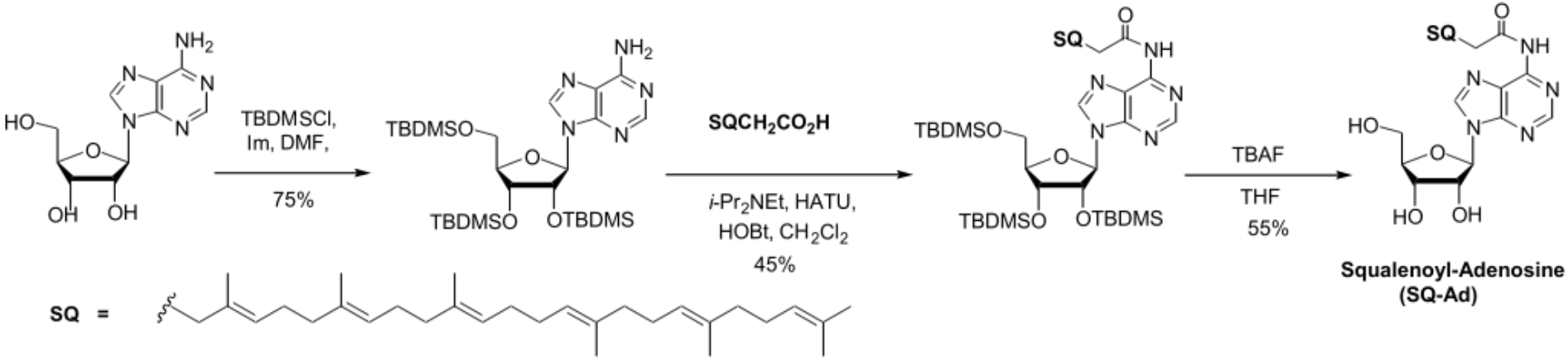
Debashish et al., Soft Matter, 11, 4173-4179 (2015)

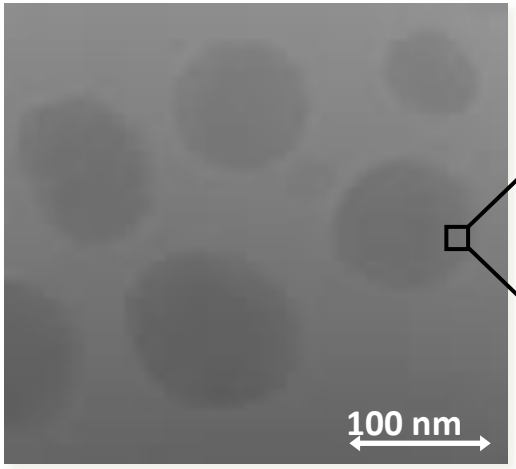


ADENOSINE-SQUALÈNE POUR LE TRAITEMENT DU TRAUMA DE LA MOËLLE ET DE L'ISCHÉMIE CÉRÉBRALE

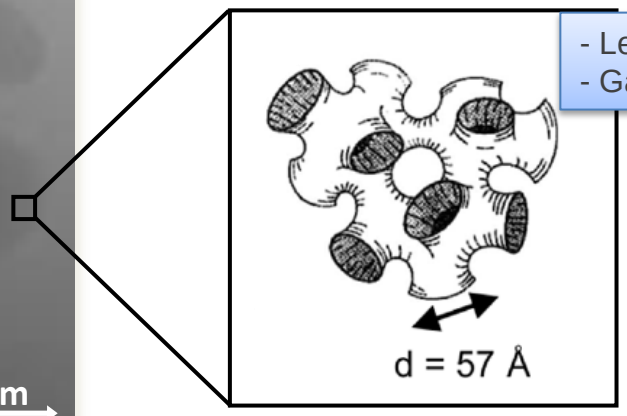
- important role in energetic metabolism (ATP) and in signal transduction (AMPc)
- neurotransmitter and neuromodulator
- pharmacological efficacy in several neurological disorders

✗ ***rapidly metabolized after intravenous injection***
✗ ***does not cross the BBB***





cryo-TEM

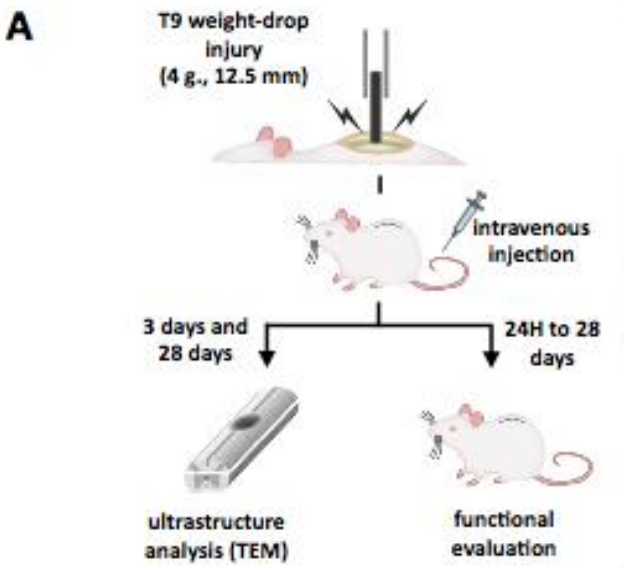


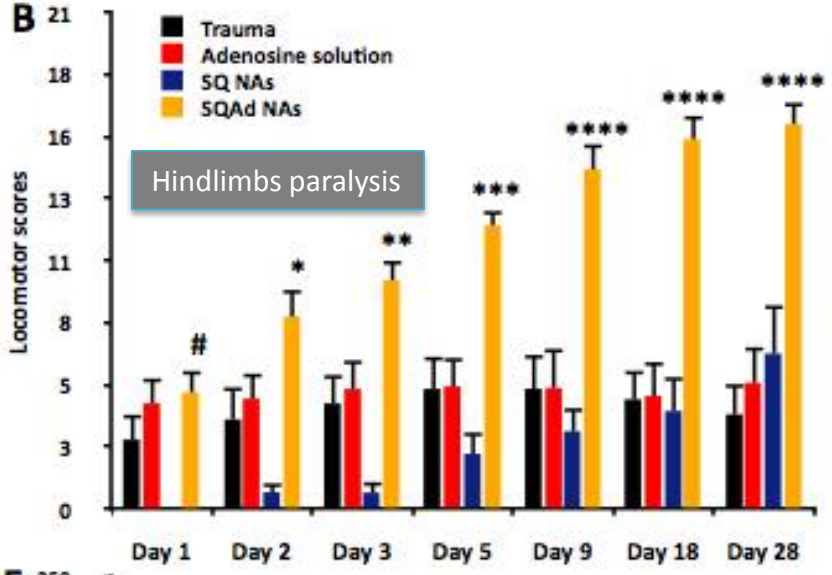
sponge-like structure

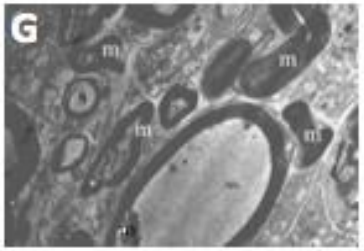
- Lepeltier et al., Langmuir, **29**, 14795−14803 (2013)
- Gaudin et al., Nature Nanotechnology, **9**, 1054 (2014)

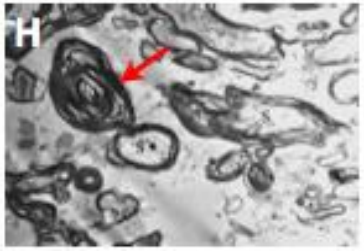
NANOPARTICULES D'ADÉNOSINE-SQUALÈNE POUR LE TRAUMA DE LA MOËLLE EPINIÈRE

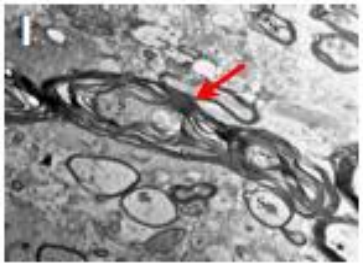
Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)

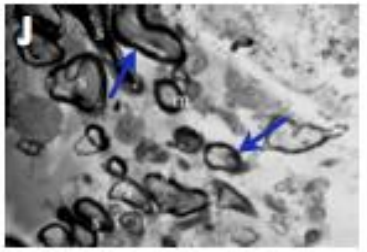


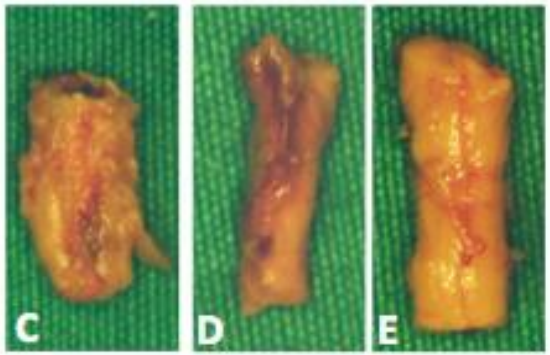


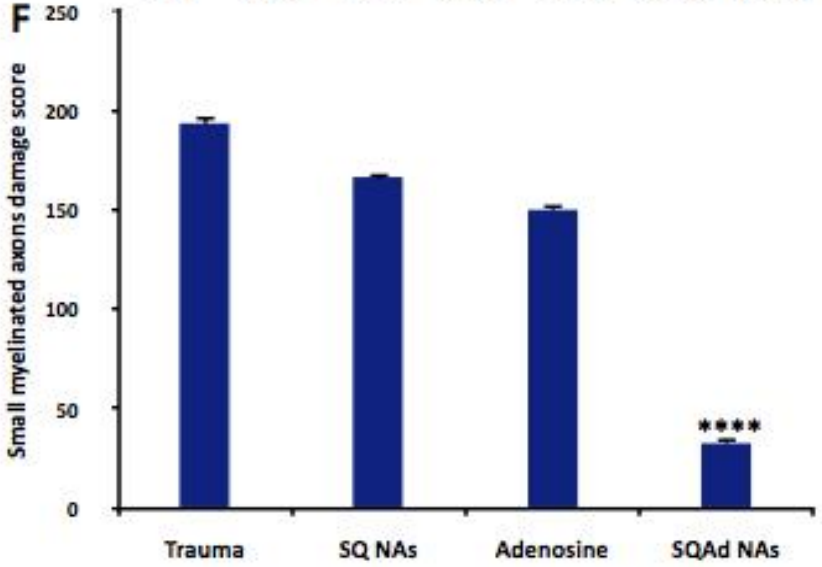








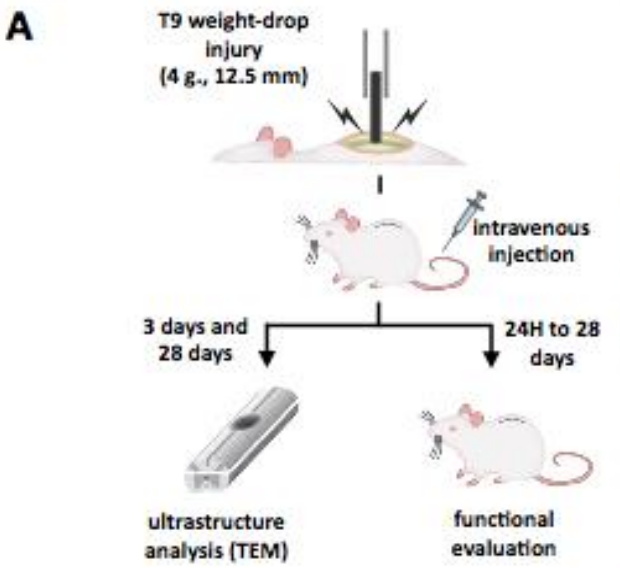


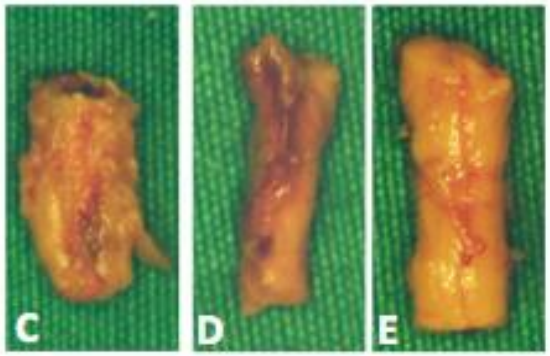


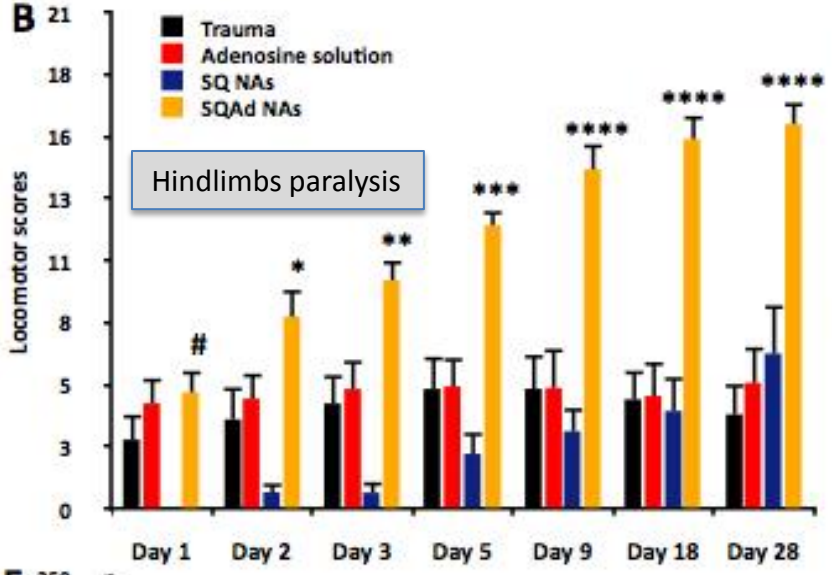
H. Eroglu, post-doc

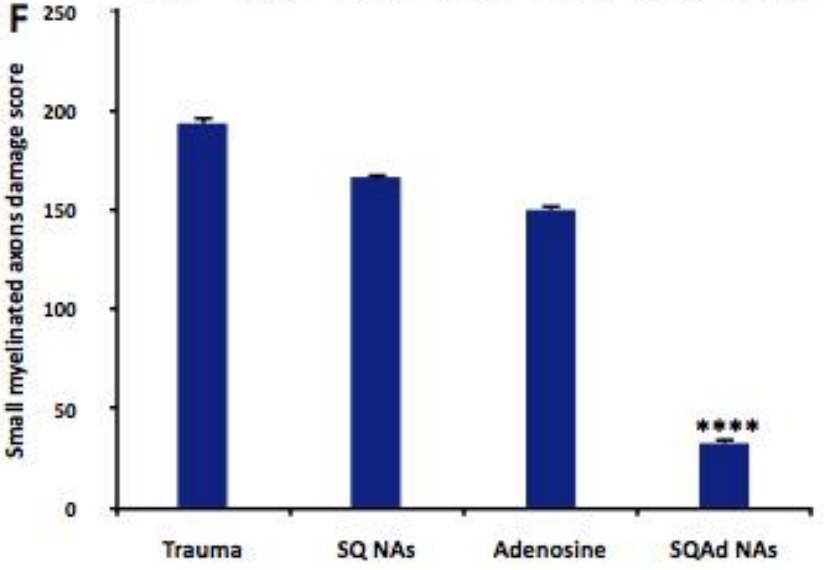
NANOPARTICULES D'ADÉNOSINE-SQUALÈNE POUR LE TRAUMA DE LA MOËLLE EPINIÈRE

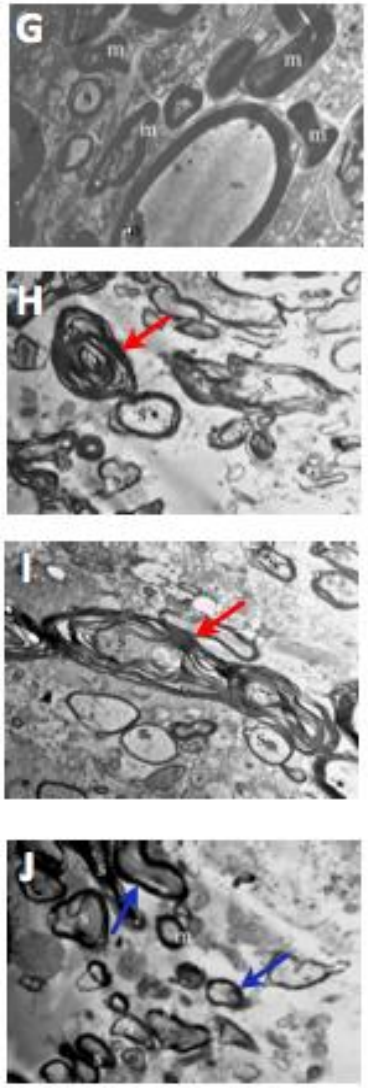
Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)







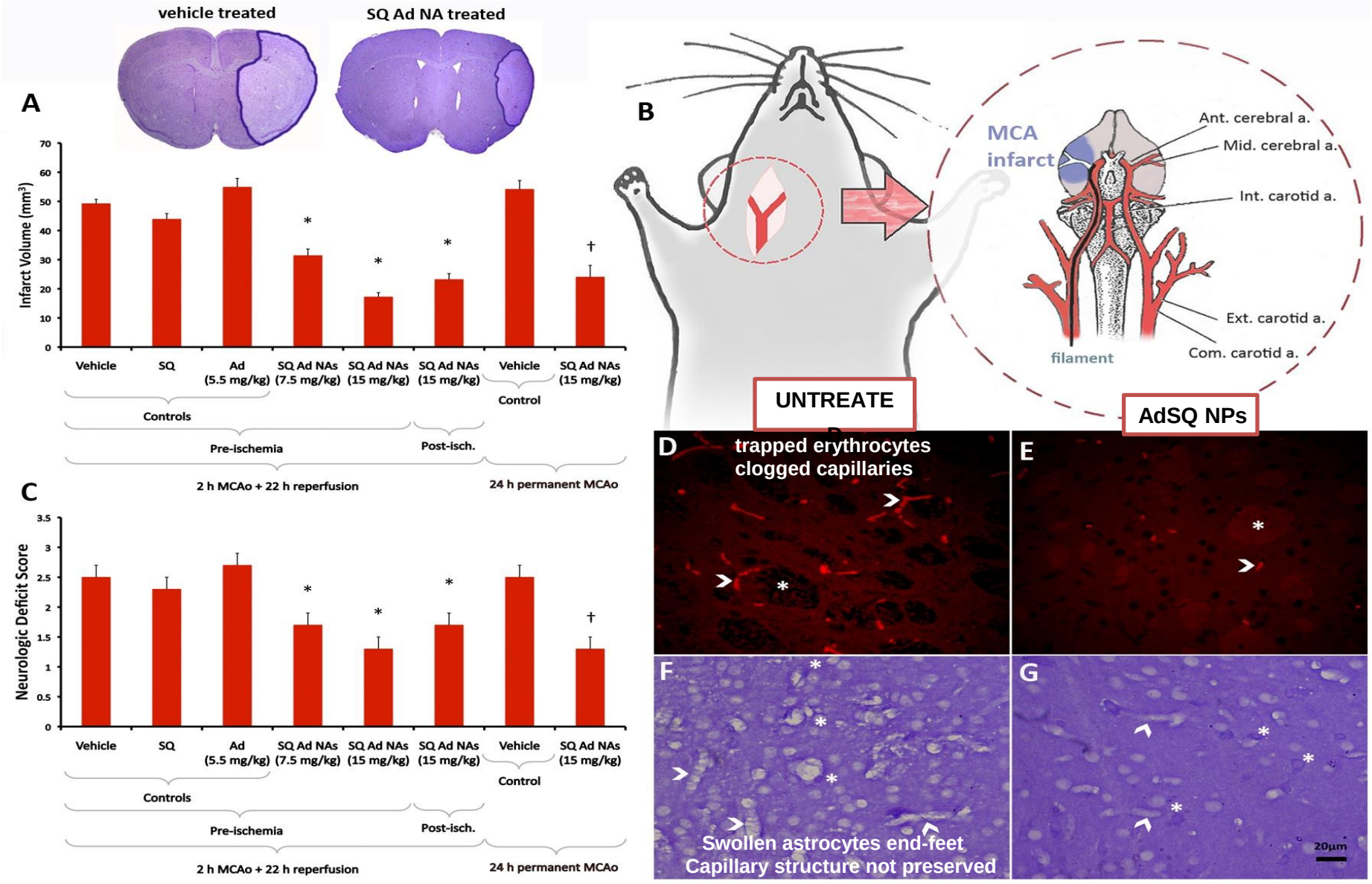




NANOPARTICULES D'ADÉNOSINE-SQUALÈNE POUR L'ISCHÉMIE CÉRÉBRALE

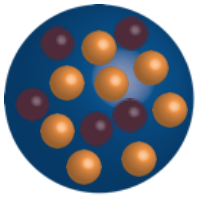
Collaboration T. Dalkara (Hacettepe Univ)

Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)

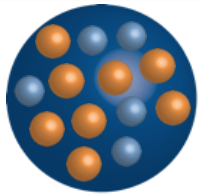


LES NANOPARTICULES D'ADÉNOSINE-SQUALÈNE PASSENT-ELLES LA BHE?

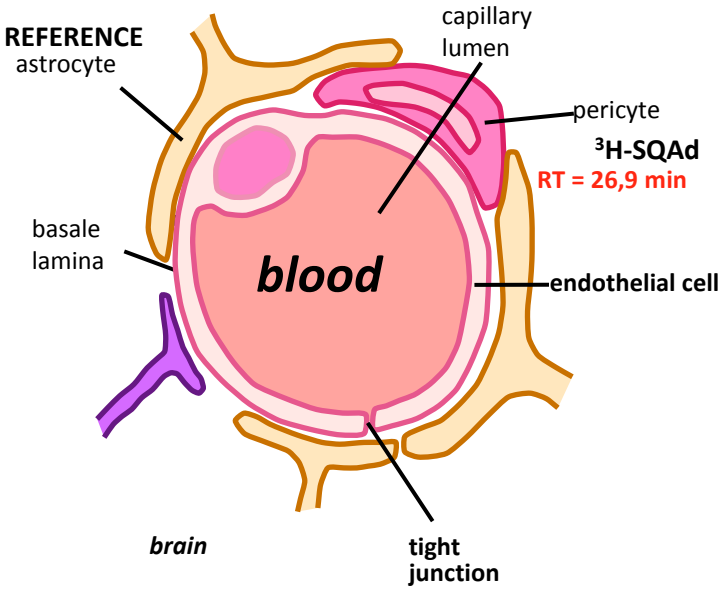
Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)
Gaudin et al., J Control Release, 10.1016/j.jconrel.2015.06.016 (2015)

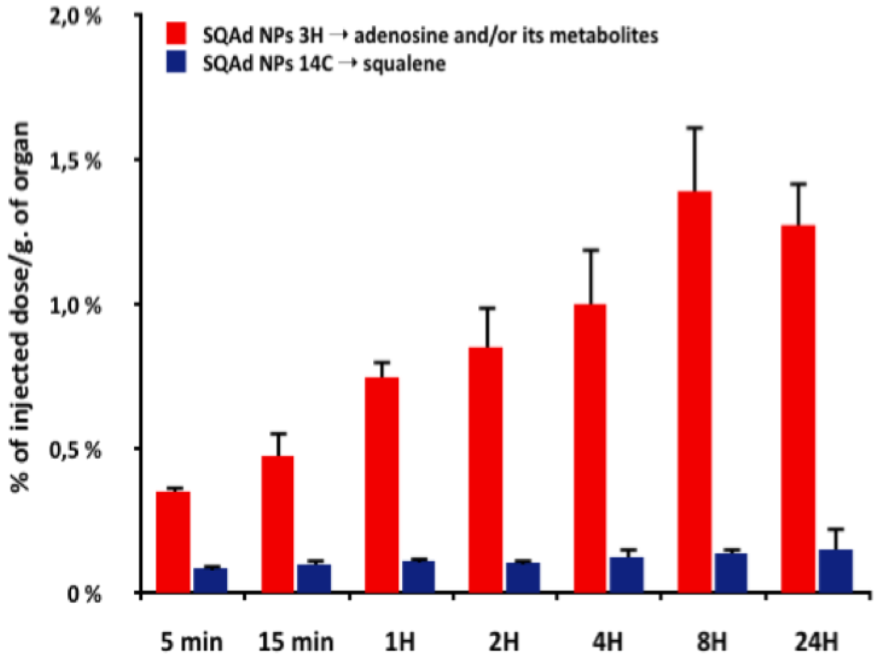


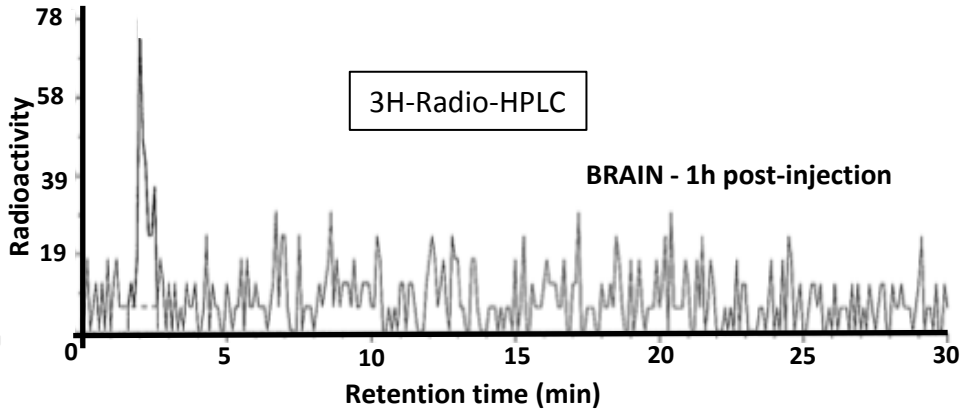
3H-Adenosine-squalene NPs
→ follow adenosine or its metabolites



Adenosine-14C-squalene NPs
→ follow the squalene

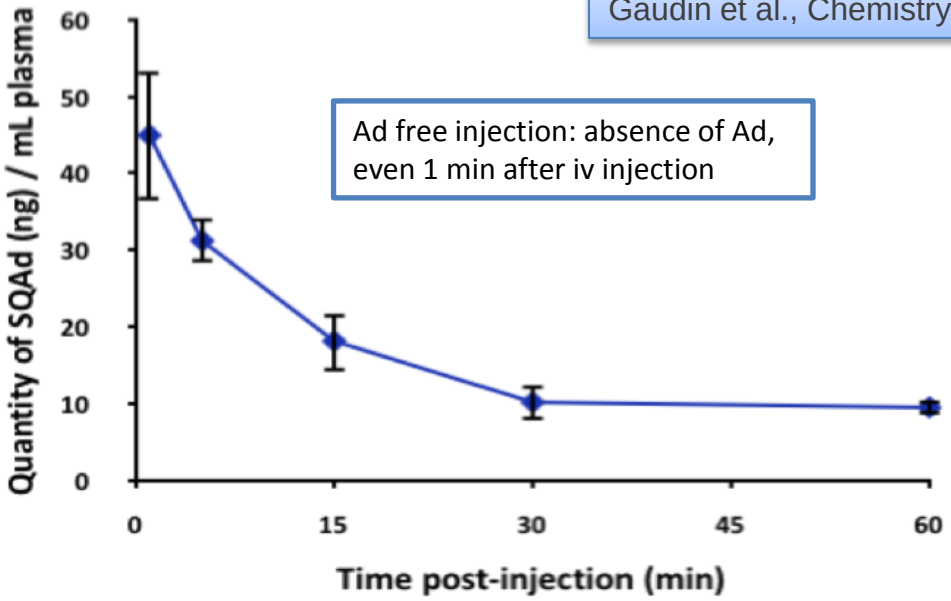




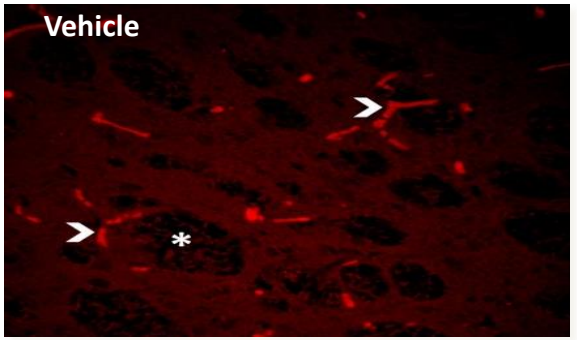


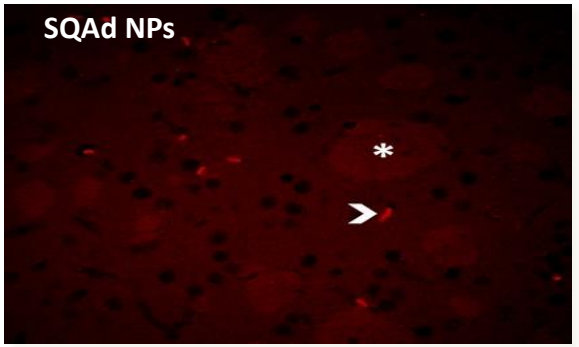
LES NANOPARTICULES D'ADÉNOSINE-SQUALÈNE ONT-ELLES UNE ACTION PÉRIPHÉRIQUE?

Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)
Gaudin et al., Chemistry of Materials, DOI: 10.1021/acs.chemmater.5b00267(2015)



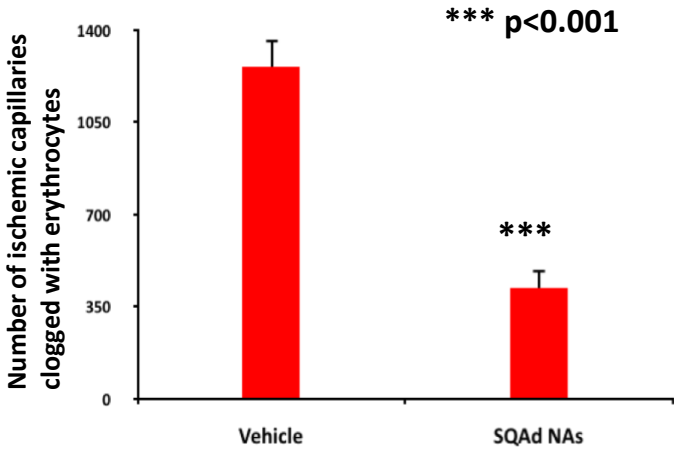
Ad free injection: absence of Ad, even 1 min after iv injection





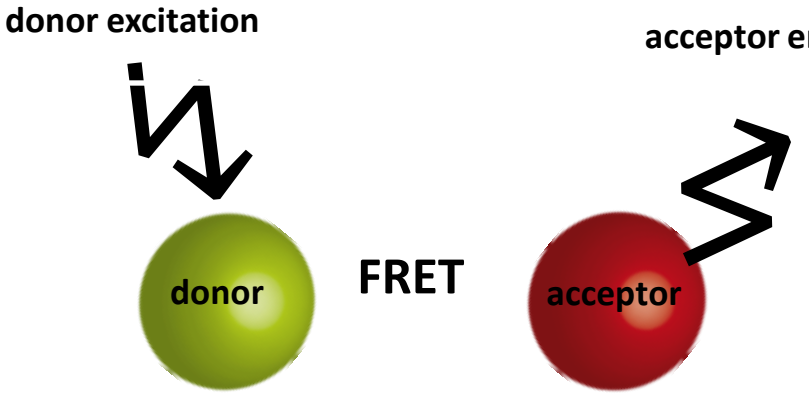
WHICH MECHANISM OF ACTION?

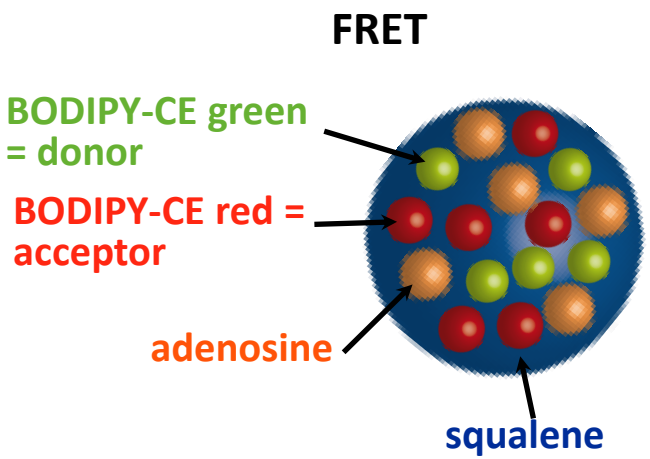
Nanoassemblies of Adenosine-Squalene extend Adenosine blood circulation and its interaction with the Neurovascular unit. This allows improving microcirculation reflow after occlusion with a cytoprotective effect on astrocytes and pericytes. Thus, the observed pharmacological activity in stroke and spinal cord injury results from rather a peripheral than a central mechanism of action.

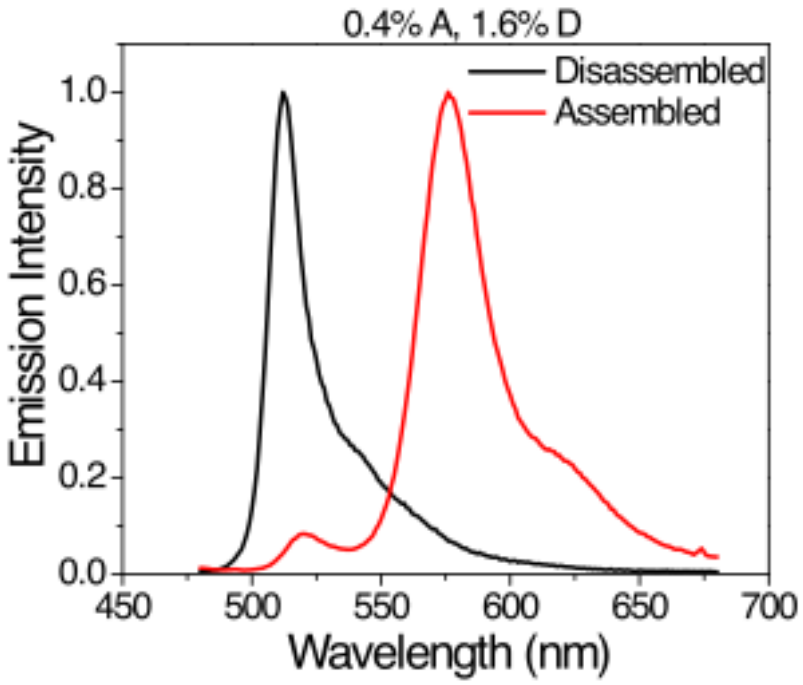


LE FRET POUR COMPRENDRE LES MÉCANISMES PHARMACOLOGIQUES

Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)
Gaudin et al., Chemistry of Materials, DOI: 10.1021/acs.chemmater.5b00267(2015)







Collaboration Dr Oya Tagit and Pr Niko Hilldebrandt – NanoBioPhotonics, IEF

LE FRET POUR COMPRENDRE LES MÉCANISMES PHARMACOLOGIQUES

Gaudin et al., Nature Nanotechnology, **9**, 1054-1063 (2014)
Gaudin et al., Chemistry of Materials, DOI: 10.1021/acs.chemmater.5b00267(2015)