# POLYMER FOR HEALTH AND BIOMATERIALS

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[3]Department of Pharmacy, Nimes University Hospital, Nimes

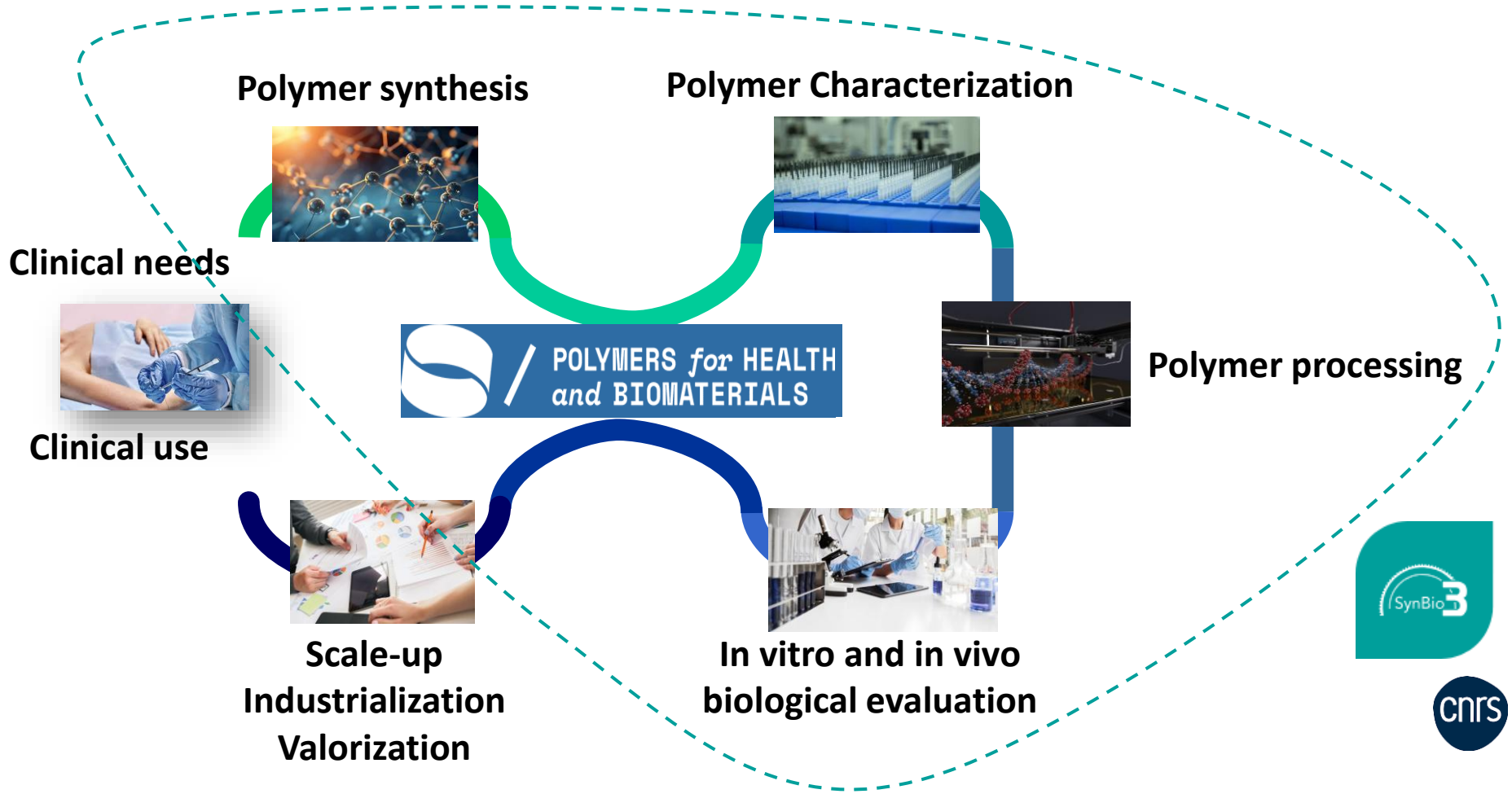
*ibmmpolymerbiomaterials.com*
*@BiopolymerTeam*




**With the support of:**

# DEPARTMENT "POLYMERS FOR HEALTH AND BIOMATERIALS"

*A multidisciplinary research group dedicated to polymers related to biomedical applications*

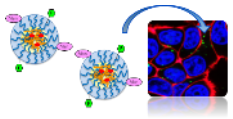


# DEPARTMENT « POLYMERS FOR HEALTH AND BIOMATERIALS »

*A multidisciplinary research group dedicated to polymers related to biomedical applications*

**Drug Delivery**

Micelles



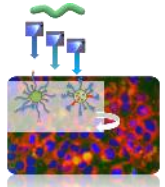
Micro & Nanoparticles



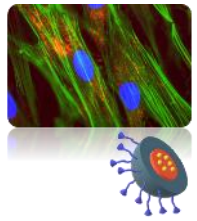
Hydrogels



Stimuli-responsiveness



Targeting



**Tissue Engineering & Medical Devices**

Advanced scaffolds for tissue engineering



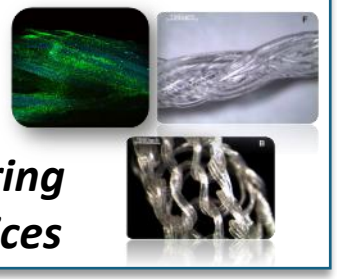
3D printing & bioprinting



Anti-adherent & self-expandable biomaterials



Temporary reinforcement

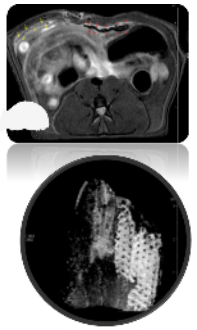


**Polymers & Diagnostic**

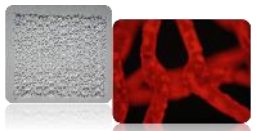
X-ray & µCT scanner



MRI

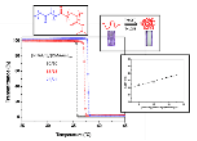


Fluorescence

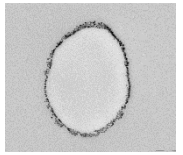


**Advanced Polymeric Biomaterials**

Stimuli-sensitive biomaterials



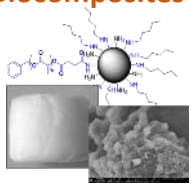
Hybrid biomaterials



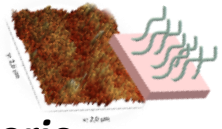
Degradable elastomers



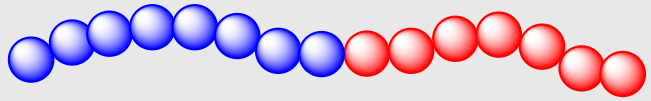
Biocomposites



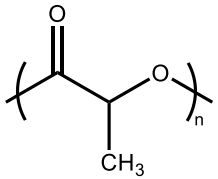
Bioactive surfaces



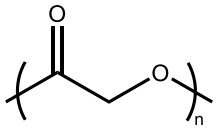
# DRUG DELIVERY



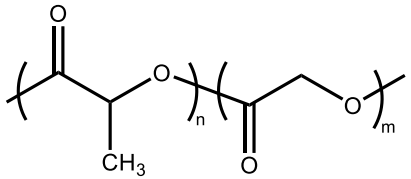
***Amphiphilic copolymers based on aliphatic polyesters such as poly(lactic acid), poly(glycolic acid), poly(ε-caprolactone) or poly(hydroxyalcanoate)***



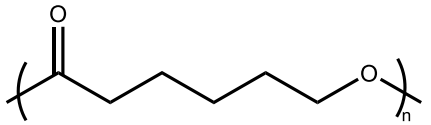
**poly(lactic acid)**
**PLA**



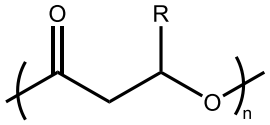
**poly(glycolic acid)**
**PGA**



**poly(lactic acid-*co*-glycolic acid)**
**PGA**

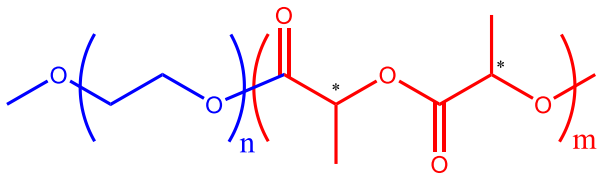


**poly(ε-caprolactone)**
**PCL**

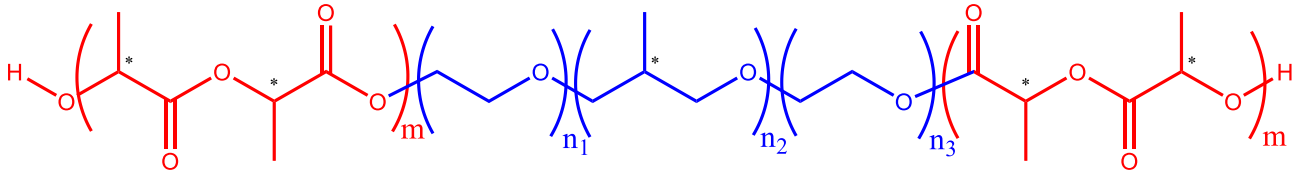


**poly(hydroxyalcanoate)**
**PHA**

***associated with an hydrophilic block such poly(ethylene glycol) or pluronic***



**poly(ethylene glycol)-*b*-**
**poly(lactic acid)**



**poly(lactic acid)-*b*-Pluronic®-**
***b*-poly(lactic acid)**

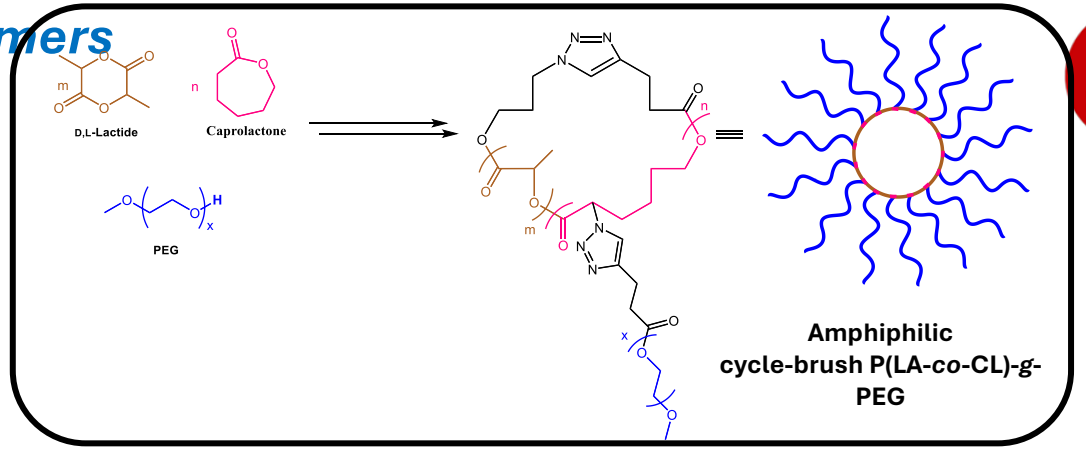
***But also polysaccharides such chitosan, dextran, alginate or hyaluronic acid***

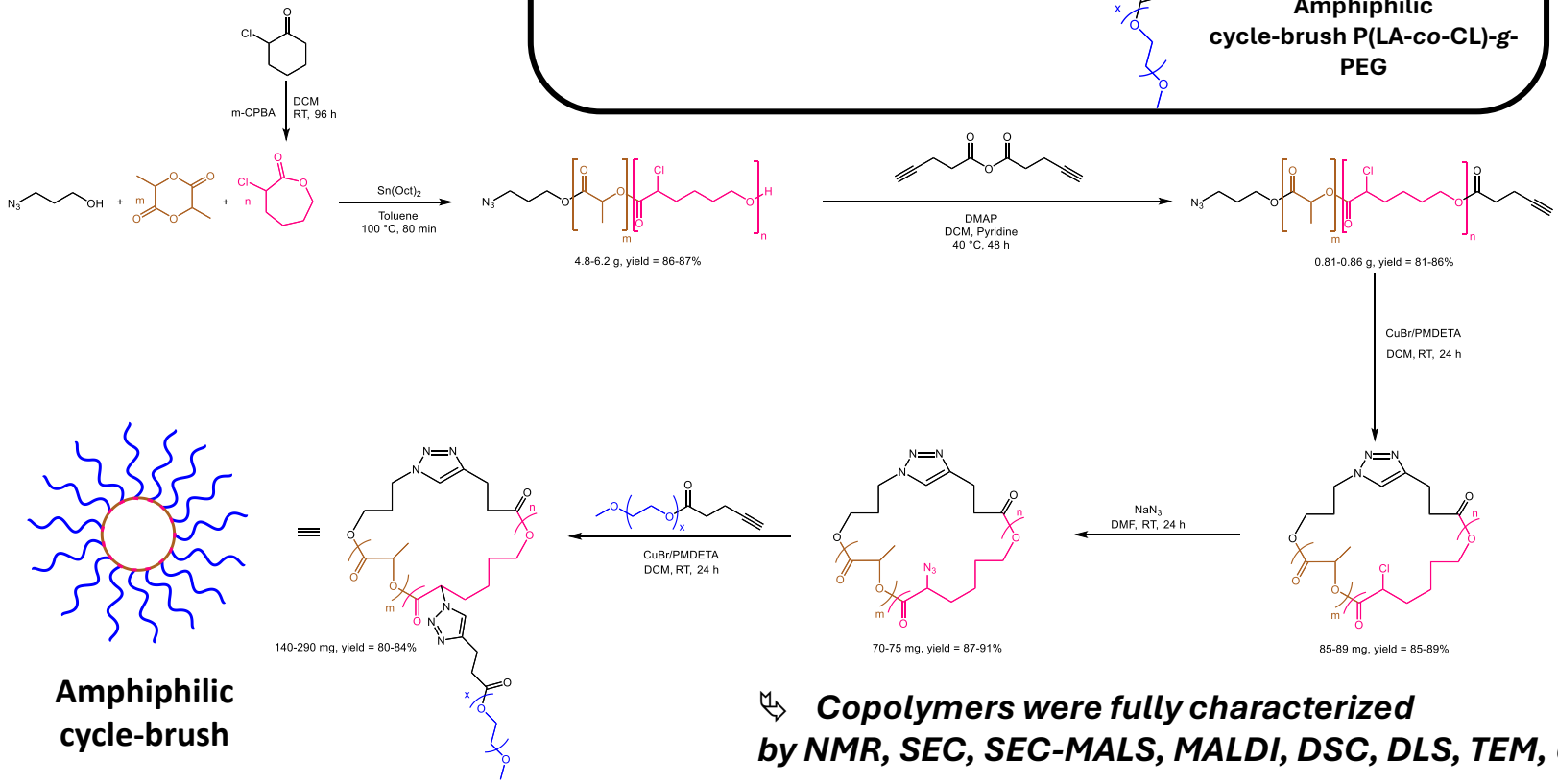
*Dr Vincent Darcos*
*Dr Minh-Thuong Khong*
*PUPH Benjamin Nottelet*

## *Amphiphilic copolymers based on cyclic polymers*

**Cyclic polymers have unique properties derived from cyclic topology and absence of chain-end terminations:**

- ✓ **Reduced hydrodynamic volume**
- ✓ **Higher glass transition temperature ($T_g$)**
- ✓ **Lower intrinsic viscosity**
- ✓ **Improved stability**
- ✓ **Slower degradation profile**



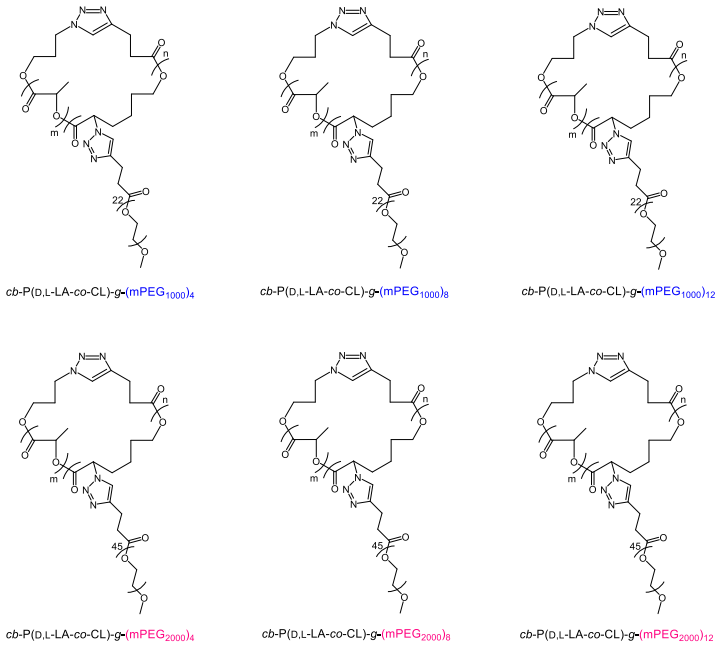

☹ **Scale-up mg / grams**



*Copolymers were fully characterized by NMR, SEC, SEC-MALS, MALDI, DSC, DLS, TEM, cryo-TEM*

# SELF-ASSEMBLY BEHAVIOR

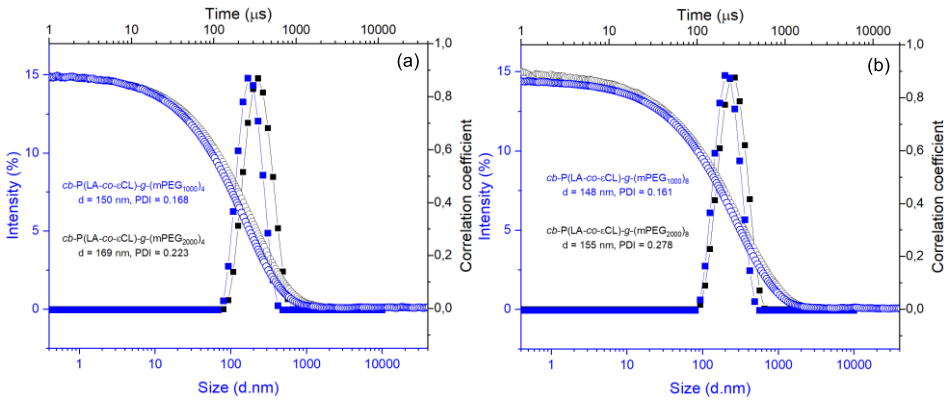
*Dr Vincent Darcos*
*Dr Minh-Thuong Khong*
*PUPH Benjamin Nottelet*



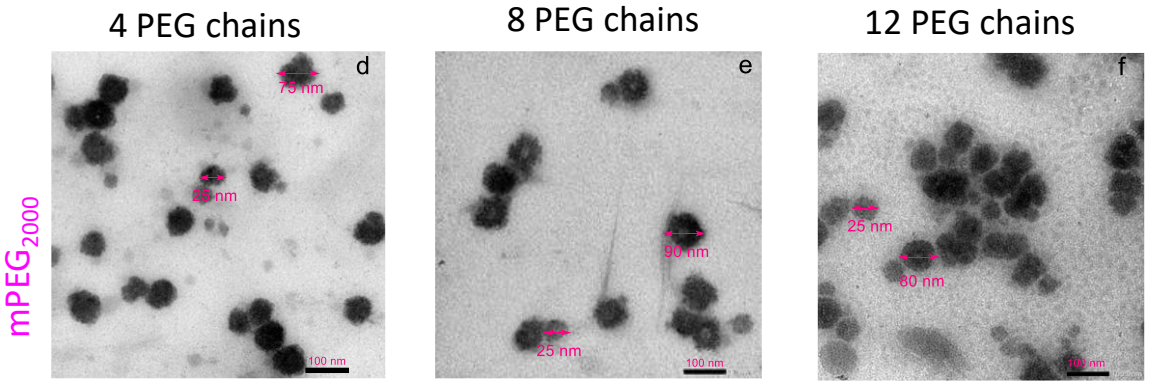

**Characteristic of micelles obtained from self-assembly of *cb*-P(D,L-LA-*co*-CL)-*g*-mPEG in water** (direct dissolution)

| Polymer | HLB[a] | CMC ($g.L^{-1}$)[b] | DLS Size (nm)[c] | DLS PDI[c] | TEM Size (nm) |
|---|---|---|---|---|---|
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{1000})_4$ | 1.20 | 0.032 | 150 | 0.168 | 20-70 |
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{2000})_4$ | 2.39 | 0.040 | 169 | 0.223 | 25-75 |
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{1000})_8$ | 2.49 | 0.058 | 148 | 0.161 | 10-70 |
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{2000})_8$ | 4.98 | 0.112 | 155 | 0.278 | 25-90 |
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{1000})_{12}$ | 4.01 | 0.083 | 155 | 0.225 | 25-85 |
| *cb*-P(D,L-LA-*co*-εCL)-*g*-$(mPEG_{2000})_{12}$ | 8.02 | 0.199 | 160 | 0.143 | 20-80 |

[a] Hydrophilic-lipophilic balance (HLB) of copolymers calculated by EO/(LA+CL), [b] Critical micellar concentration, determined with a dye solubilization method, [c] DLS in intensity mode (1g/L).




**DLS analyses of micelles obtained in aqueous media from self-assembly of different cyclic brush copolymers**

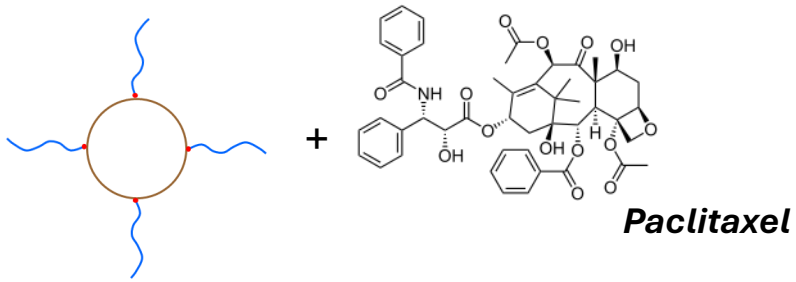



**TEM images of micelles obtained in aqueous media from self-assembly of different cyclic brush copolymers**

# ENCAPSULATION OF PACLITAXEL

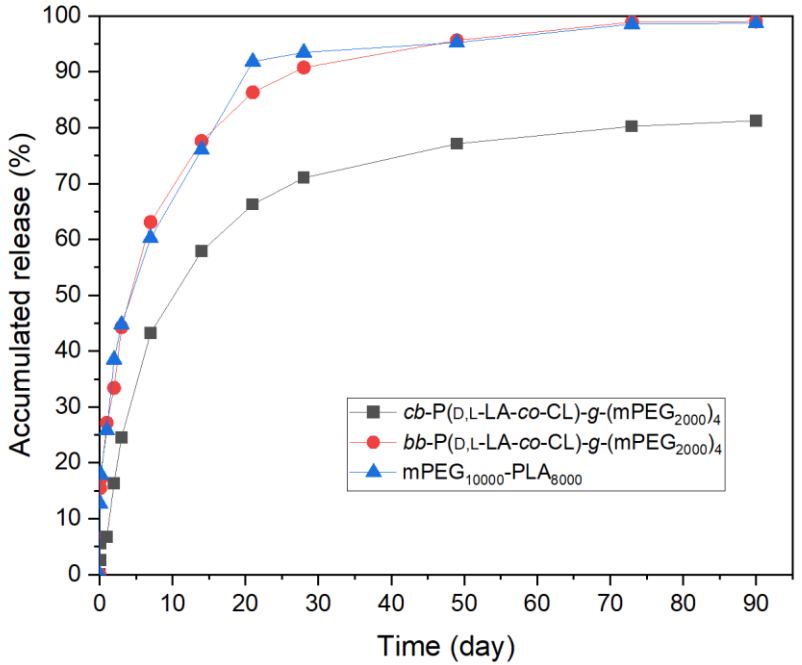
*Dr Vincent Darcos*
*Dr Minh-Thuong Khong*
*PUPH Benjamin Nottelet*

## *Paclitaxel-loaded cyclic-brush P(LA-co-εCL)-g-PEG*

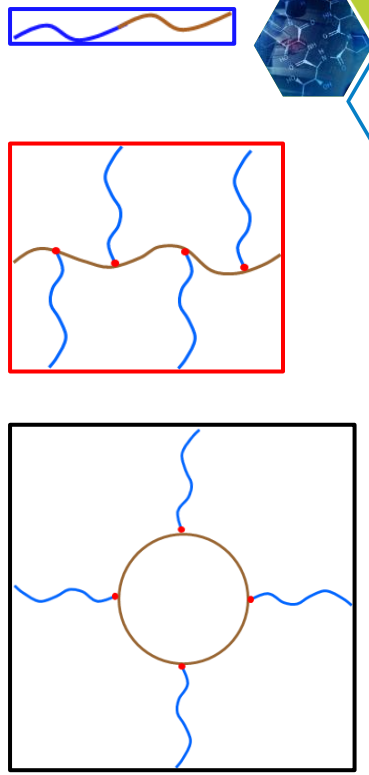



| | PTX/copolymer (w/w) | Size[a] (nm) | PDI[a] | DL (%) | EE (%) |
|---|---|---|---|---|---|
| cb-P(D,L-LA-*co*-CL)-*g*-(mPEG$_{2000}$)$_4$ | 20/8 | 191 | 0.223 | 14 | 41 |
| cb-P(D,L-LA-*co*-CL)-*g*-(mPEG$_{2000}$)$_4$ | 20/4 | 213 | 0.301 | 13 | 75 |
| cb-P(D,L-LA-*co*-CL)-*g*-(mPEG$_{2000}$)$_4$ | 0 | 169 | 0.223 | / | / |

[a] DLS in intensity mode (1g/L).




*In vitro* drug release profiles of PTX-loaded micelles of **CB**, BB, and **L** copolymers in PBS (pH 7.4) at 37 °C.



**Release impacted by topology**
**Release order : CB < BB = L**

M. T. Kong et al. *in preparation*

# DRUG DELIVERY

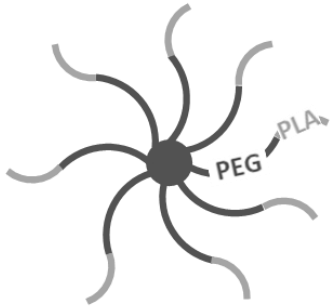
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*PUPH Xavier Garric*

## *Amphiphilic copolymers based on star polymers*

anr agence nationale de la recherche

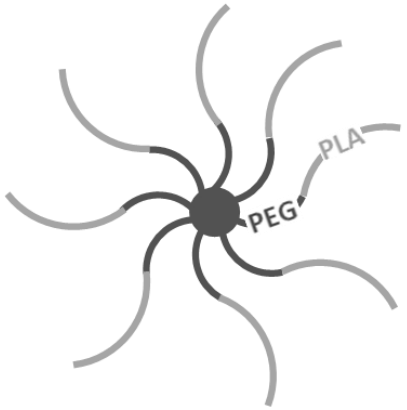
### HYDROGEL

$PEG_{8arm}20k\text{-}(PLA_{13})_8$
EG/LA = 4.4
*Mn = 27 500 g/mol*

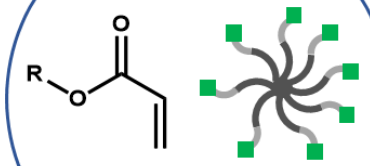



### ELASTOMER

$PEG_{8arm}10k\text{-}(PLA_{69})_8$
EG/LA = 0.4
*Mn = 50 000 g/mol*

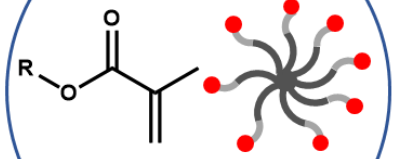



**ACRYLATE**



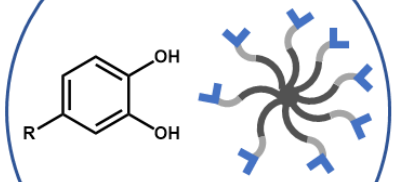

$PEG_{8arm}$-PLA-AC

**METHACRYLATE**



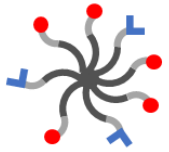

$PEG_{8arm}$-PLA-MC

**CATECHOL**



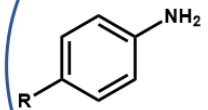

$PEG_{8arm}$-PLA-CT

**METHACRYLATE + CATECHOL**



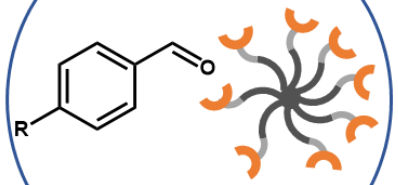
$PEG_{8arm}$-PLA-MC/CT

**PHENYLAMINE**




$PEG_{8arm}$-PLA-AM

**BENZALDEHYDE**




$PEG_{8arm}$-PLA-AL

**☺ Scale-up grams / kg**



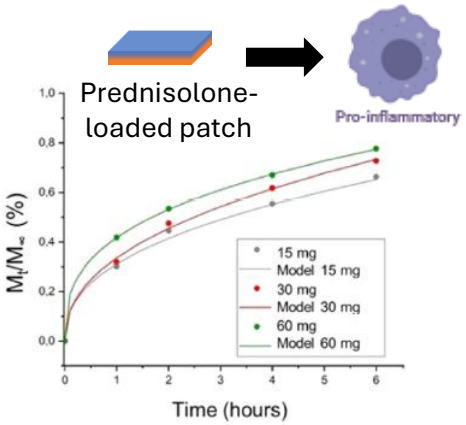
M. Grosjean et al. *Biomacromolecules* **2022**
M. Grosjean et al. *Mater. Design* **2024**
S. Ouedraogo et al. *Colloids and Surfaces B: Biointerfaces* **2024**

# STAR COPOLYMERS BASED ON PLA AND PEG

*PUPH Benjamin Nottelet*
*PUPH Xavier Garric*

## *Copolymers with the same "star" topology for various applications*

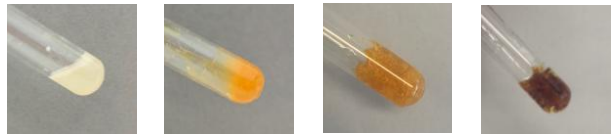
### Development of drug-loaded patches




S. Ouedraogo et al. *Colloids and Surfaces B: Biointerfaces* **2024**

### Development of degradable networks with bioadhesive properties

***Bioadhesive hydrogels***

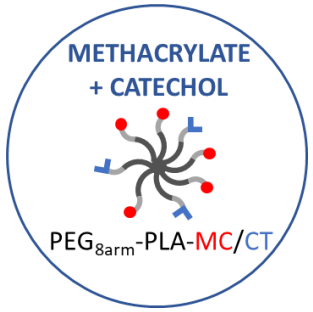


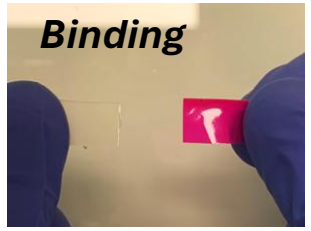


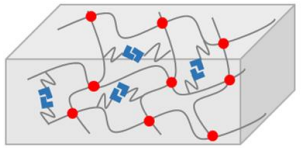

***Tested on different substrates***

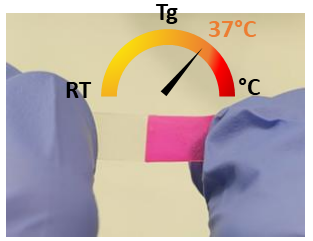
*Substrates: Gelatin, mouse skin, colon*

### Development of self-healable elastomers



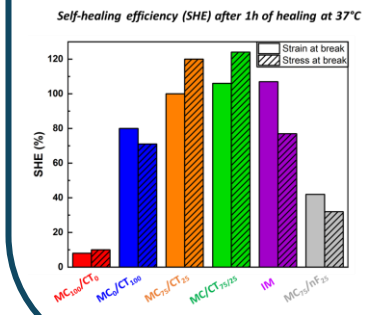



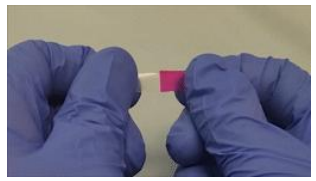






*Dual-crosslinked elastomeric network*

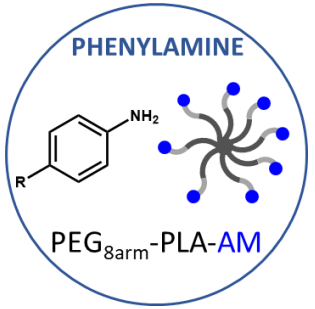


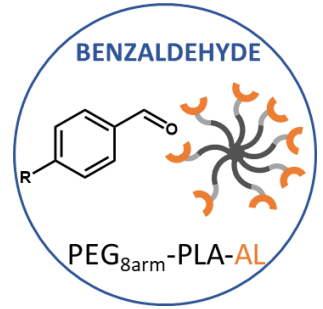



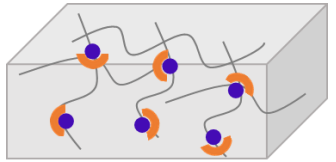



M. Grosjean et al. *ACS Appl. Mater. Interfaces* **2023**

### Development of printable self-healable medical devices

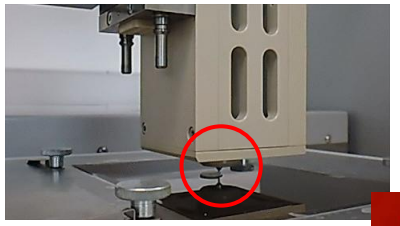


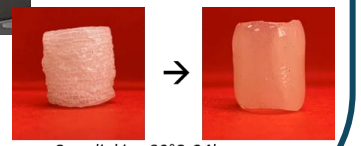



*Imine-based dynamic network*

***FDM 3D-printing of imine-based networks***





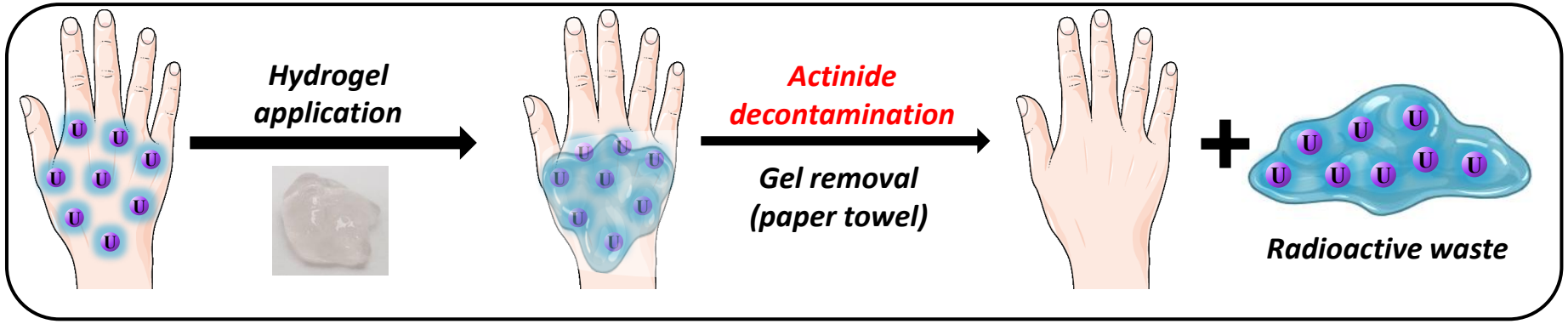
*Crosslinking 80°C, 24h, vacuum*

M. Grosjean et al., *Adv. Mater. Interf.* **2023**

# ADVANCED POLYMERIC BIOMATERIALS

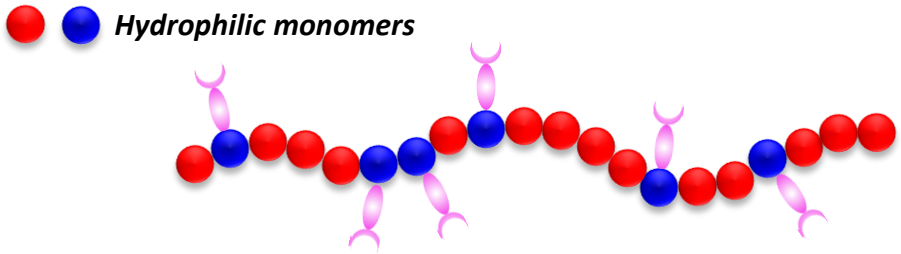
*Dr Vincent Darcos*
*Pr Sophie Monge*

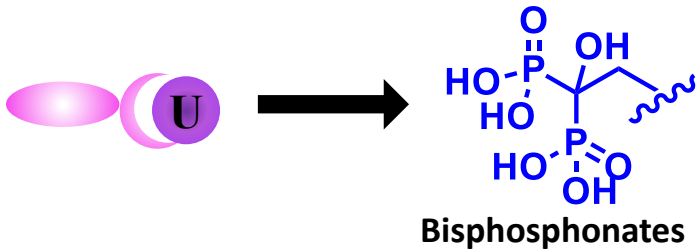
## *Innovative polymers for actinide decontamination*




AGENCE INNOVATION DÉFENSE
anr agence nationale de la recherche




**Bisphosphonates**

☺ **High affinity towards actinides (especially $U^{238}$)**

☺ **High chelating efficacy**

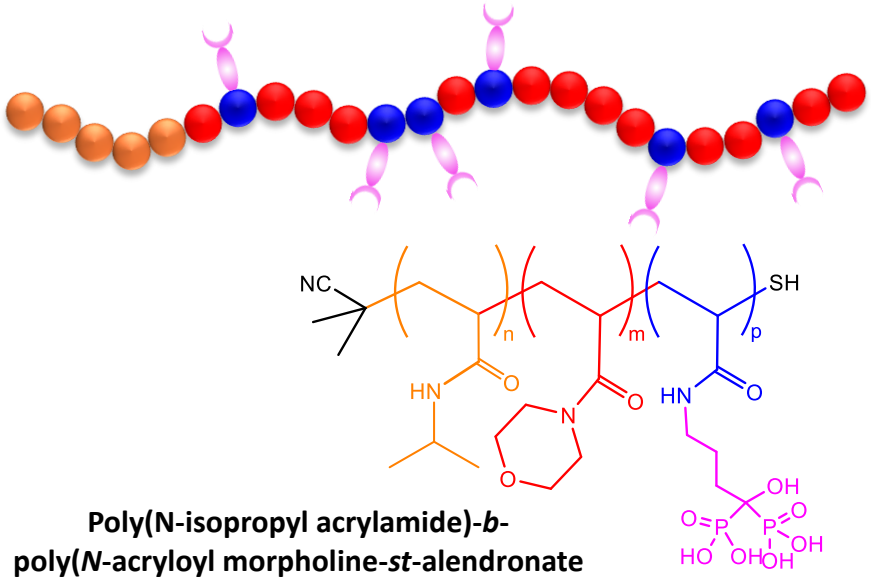
L. Ferrié et al. *React. Funct. Polym.* **2022**
C. Arrambide et al. *Biomacromolécules* **2023**
S. Monge et al. *WO2025133267* **2025**
M. Guerreiro et al. *Sep. Purif. Technol.* **2025**
V. Darcos et al. *j.Pol. Sc.* **2026**

# ADVANCED POLYMERIC BIOMATERIALS

*Dr Vincent Darcos*
*Pr Sophie Monge*

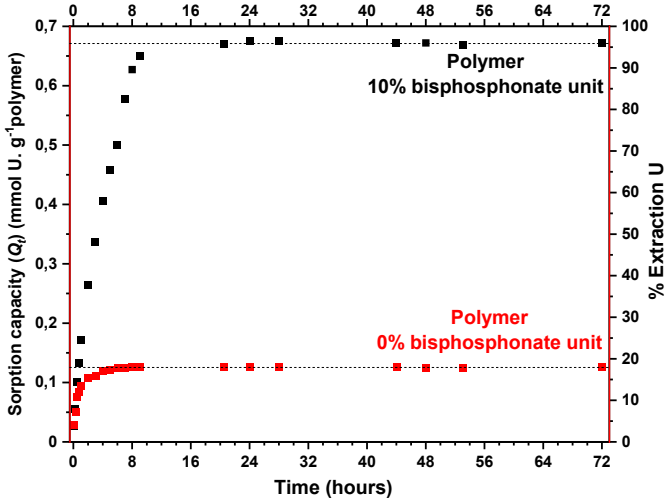
## *Innovative polymers for actinide decontamination*

- Radical polymerization
- Thermosensitive behavior P(NIPAAm)
- Poly(NAM): hydrophilic
- Poly(AleMAm): complexing agent

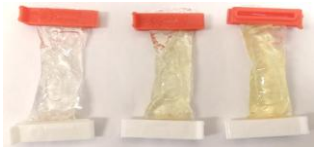



**Poly(N-isopropyl acrylamide)-*b*-poly(*N*-acryloyl morpholine-*st*-alendronate acrylamide)**
**P(NIPAAm)-*b*-(PNAM-*st*-AleMAm)**

### Study of uranium sorption



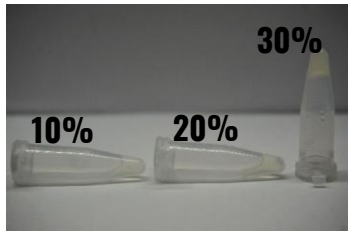


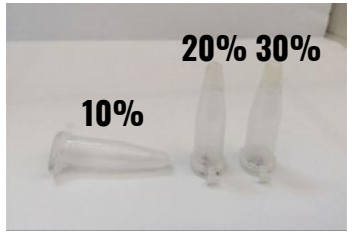

S. Monge et al. *WO2025133267* **2025**
M. Guerreiro et al. *Sep. Purif. Technol.* **2025**
V. Darcos et al. *j.Pol. Sc.* **2026**



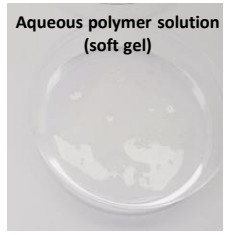
### Formulation at 10, 20 and 30 %*wt*




Hydrogel formation
T=25°C




Hydrogel formation
T=37°C



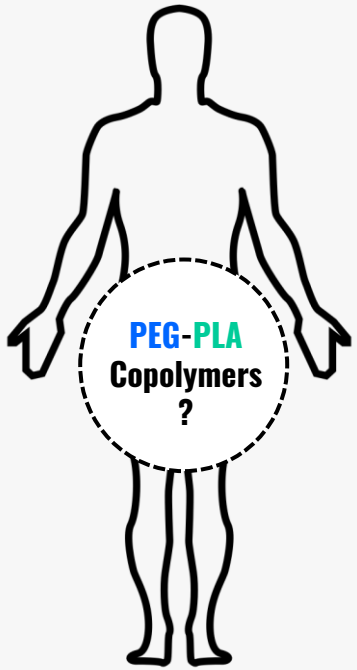

$Nd^{3+}$



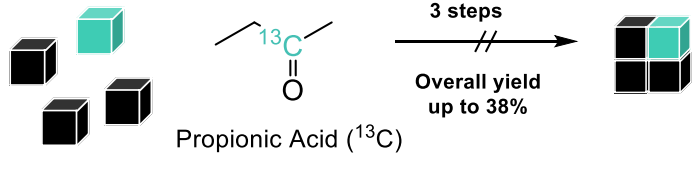
# CHARACTERIZATION / DEGRADATION FATE

*Dr Vincent Darcos*
*PUPH Xavier Garric*
*PUPH benjamin Nottelet*

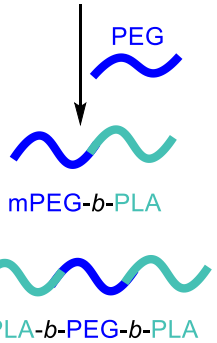
## *Determination and quantification in vivo of degradation products of injectable polymers by isotopic monitoring*



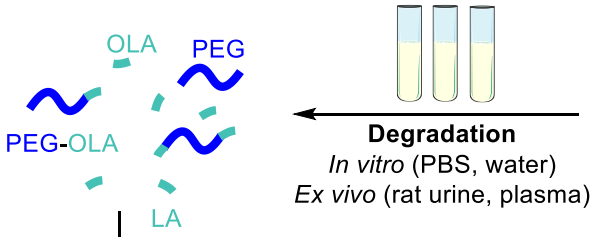

- **PEG-PLA widely used in healthcare**
- **Study of degradation is challenging**
- **Degradation fate depending of different factors**



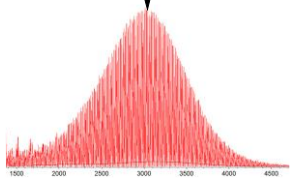

*Isotopic labeling strategy using carbon-13 labeled monomers*




**Copolymers soluble in water**

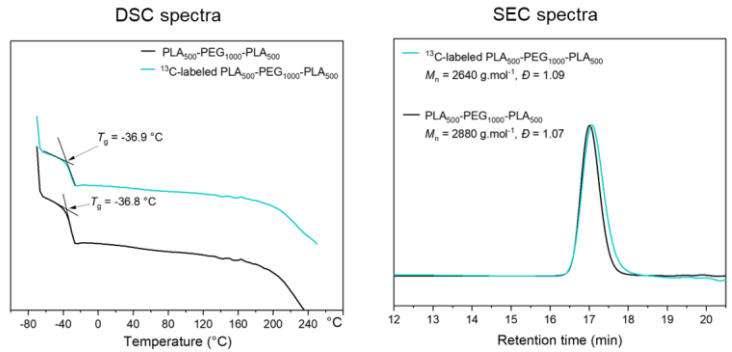



**Ultra-sensitive MALDI-TOF**
**Detection of $^{13}$C labeled species**



**High resolution**
MALDI-TOF spectra

**Characterization of labeled PLA**

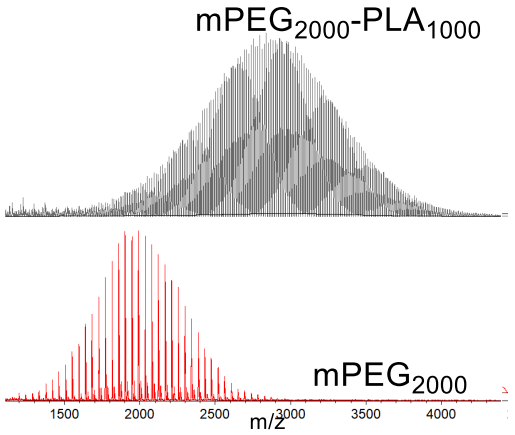


# CHARACTERIZATION / DEGRADATION FATE

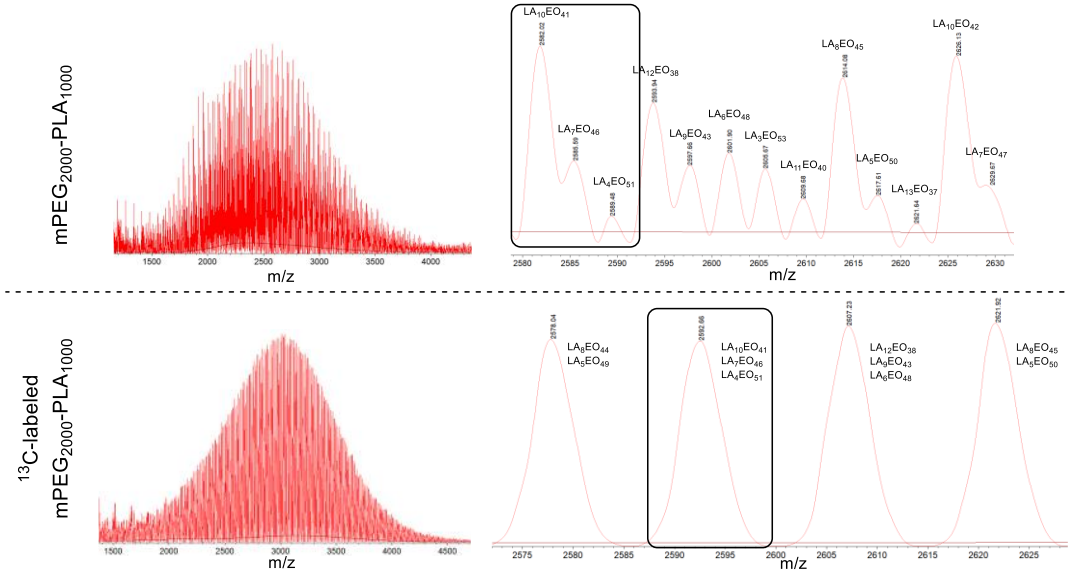
*Dr Vincent Darcos*
*PUPH Xavier Garric*
*PIPH benjamin Nottelet*

## *Determination and quantification in vivo of degradation products of injectable polymers by isotopic monitoring*

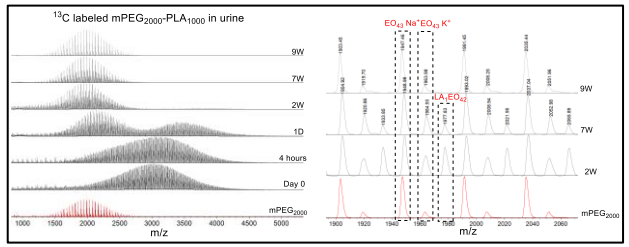
### MALDI-TOF spectra of mPEG2000 and mPEG-PLA

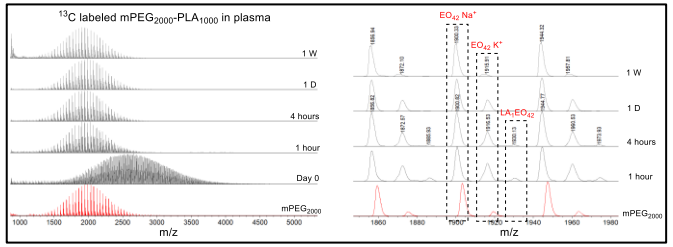



### MALDI-TOF spectra of mPEG-PLA non labeled *versus* labeled

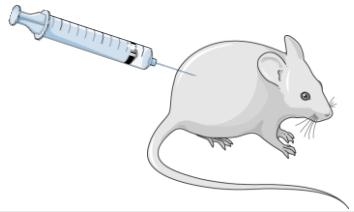



### Monitoring degradation by MALDI-TOF



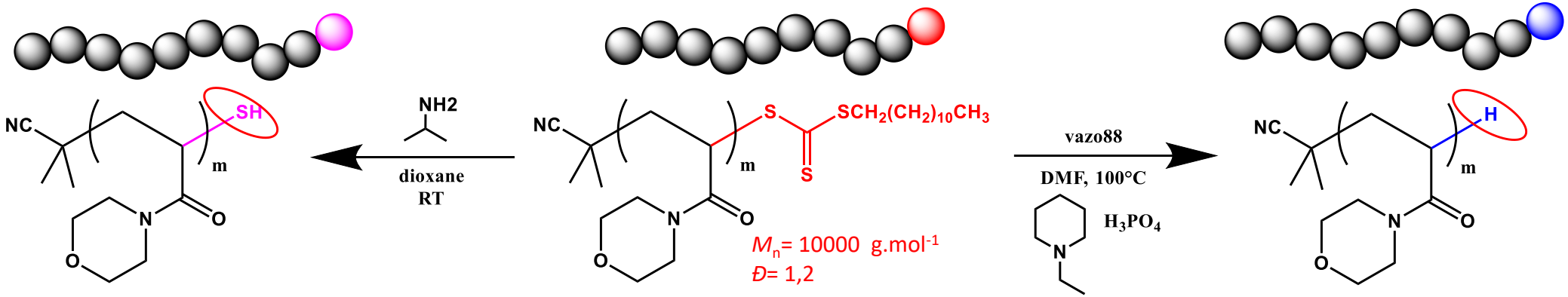

### *In vivo* monitoring in rat models *in progress*



M. T. Khong et al. *Biomacromolecules* **2024**

# CHARACTERIZATION / LIQUID CHROMATOGRAPHY (SEC, HPLC)

## Development of new chromatographic methods to characterize copolymers with complex architectures in term of molar mass and composition




SynBio3

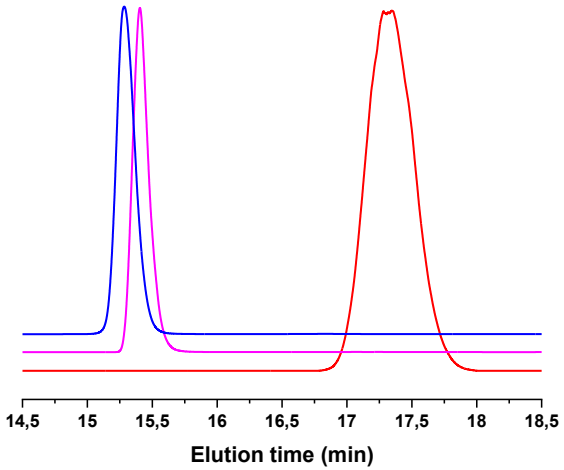
PLATEFORMES CHIMIE BALARD

Labellisée IBISA

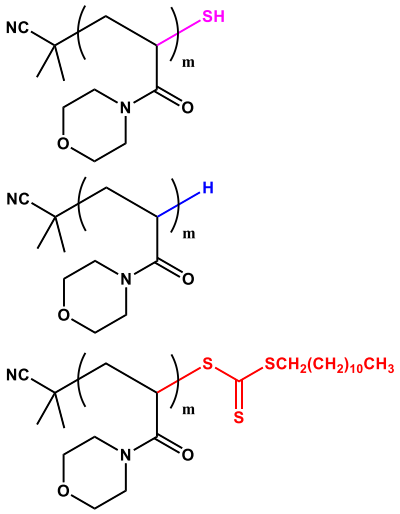
Certifiée ISO 9001:2015 AFNOR

Tarification auditable

HPLC




Système Agilent 1260, colonne C18, detection ELSD.




⇨**Separation is not controlled by molar mass but by chemical heterogeneity, notably end-group functionality**

***Our tools:***

***Analytical chromatography:*** **SECs, SECs MALS, HPLCs, LC2D (degradation fate, impurity analysis)**

***Preparative chromatography:*** **Flash chromatography & recycling preparative HPLC (deformulation, impurity analysis)**

# PHBM TO WOMED: A START-UP SUCCESS STORY

*PUPH Xavier Garric*
*Dr Coline Pinese*

## ANTISYN project: Design and Development of an Intrauterine Anti-Adhesion Device

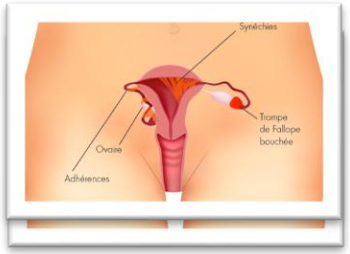
womed

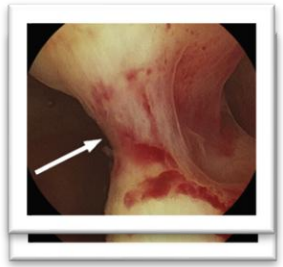
aXLR SATT

INSTITUT CARNOT Chimie Balard Cirimat

CHU NIMES

➪Intrauterine adhesions (IUA) develop after surgery due to impaired healing of the endometrium, resulting in adhesion of the uterine walls and partial or complete obliteration of the uterine cavity (formation of fibrotic tissues).

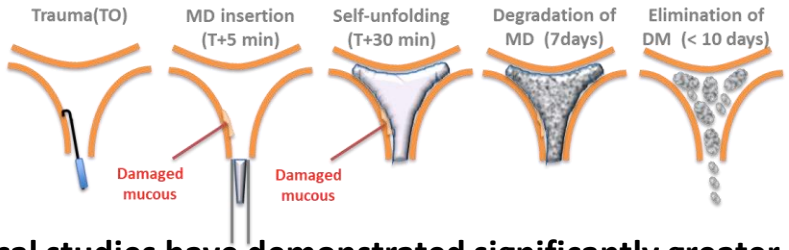


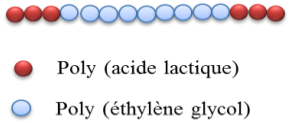


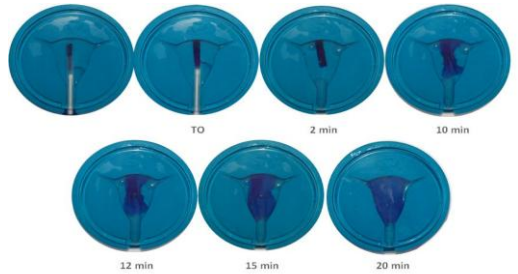

**Approximately 20% of miscarriages are linked to intrauterine adhesions.**

➪Design strategy: Biodegradable intrauterine medical device to prevent the formation and recurrence of UAI and restore uterine morphology



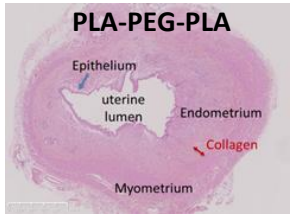

➪Synthesis and shaping of a triblock copolymer based on poly(lactic acid) (PLA) and high molecular weight poly(ethylene glycol) (PEG)




➪Preclinical studies have demonstrated significantly greater anti-adhesion efficacy in vivo compared to commercial anti-adhesion products.



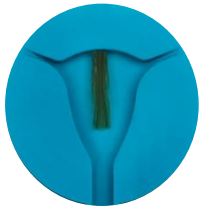

**Creation of the start-up : WOMED**
**Winner of the i-Lab 2018 competition**

i-Lab

# PHBM TO WOMED: A START-UP SUCCESS STORY

## Collaborations Womed

### Womed Leaf

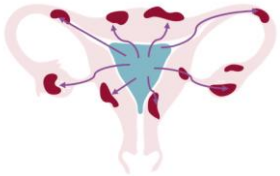





CE FDA ANVISA

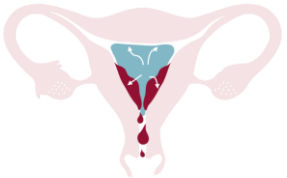
**Large randomized clinical trial: Womed Leaf demonstrates its efficacy in moderate to severe intrauterine adhesions—the first clinically significant improvement in this challenging indication**

### Treatment of fibroids and endometriosis



EIC Accelerator

### Treatment of emergency uterine bleeding



i-Nov concours d'innovation

# DEPARTMENT OF POLYMERS FOR HEALTH AND BIOMATERIALS

## *Acknowledgments*

### *THE TEAM*



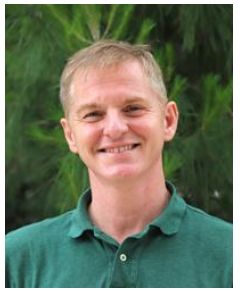
PLATEFORMES CHIMIE BALARD

***Contact: ibmm-synbio3@umontpellier.fr***

**Vincent Darcos**



**Xavier Garric**



**Benjamin Nottelet**



**Hélène Van Den Berghe**



**Coline Pinese**

