



HAL
open science

PEG length of PLA-PEG nanoparticles modulates nanoparticle interactions with brain endothelial cells

Soudeh Tehrani, Guillaume Bastiat, Florian Bernard, Patrice Hildgen, Patrick Saulnier, Valérie-Gaëlle Roullin

► To cite this version:

Soudeh Tehrani, Guillaume Bastiat, Florian Bernard, Patrice Hildgen, Patrick Saulnier, et al.. PEG length of PLA-PEG nanoparticles modulates nanoparticle interactions with brain endothelial cells. 4th Annual Meeting SFNano2017, 2017, Bordeaux, France. , 2017. hal-02616002

HAL Id: hal-02616002

<https://univ-angers.hal.science/hal-02616002>

Submitted on 26 May 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

PEG length of PLA-PEG nanoparticles modulates nanoparticle interactions with brain endothelial cells

Soudeh F. Tehrani^{1*}, Guillaume Bastiat², Florian Bernard¹, Patrice Hildgen¹, Patrick Saulnier², V. Gaëlle Roullin¹

1. Axe Analyse et Formulation du Médicament, Faculté de pharmacie, Université de Montréal, Canada

2. MINT, UNIV Angers, INSERM 1066, CNRS 6021, Université Bretagne Loire; Angers – France

*corresponding authors: s.fakhani.tehrani@umontreal.ca, vg.roullin@umontreal.ca

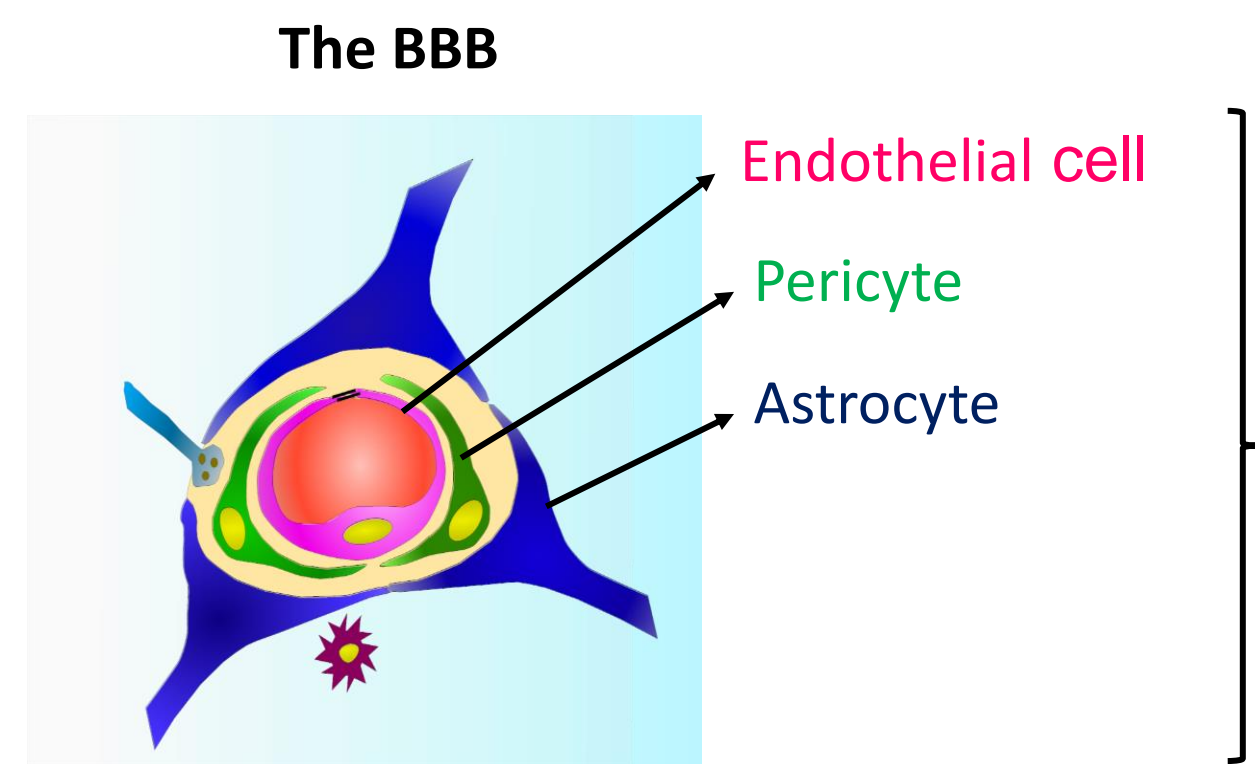
Background and Objectives

Problem

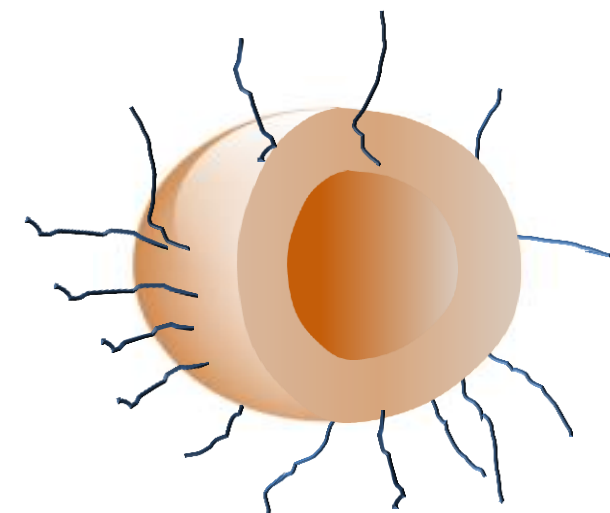
The blood-brain barrier (BBB) prevents or slows down the passage of therapeutic molecules from the blood into the central nervous system (1).

Strategy

- Vectorization of active substances via polymeric nanoparticles (NPs)
- Functionalization of NPs with polyethylene glycol (PEG) :
 - PEG chains are known to extend circulation times of NPs in blood(2).
 - PEG chains on NP surface promote penetration into the brain (3,4)



Complex multilayer barrier



PLA-PEG NPs: Hydrophobic PLA core with hydrophilic PEG corona

Hypothesis

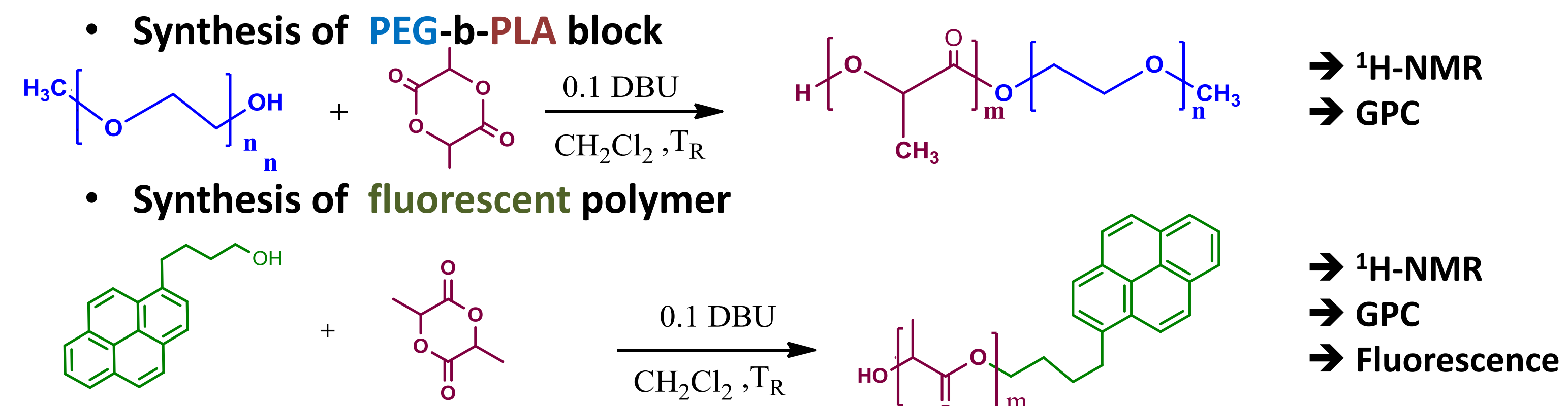
Increasing the PEG chain length will modulate NPs translocation through the BBB.

Objectives

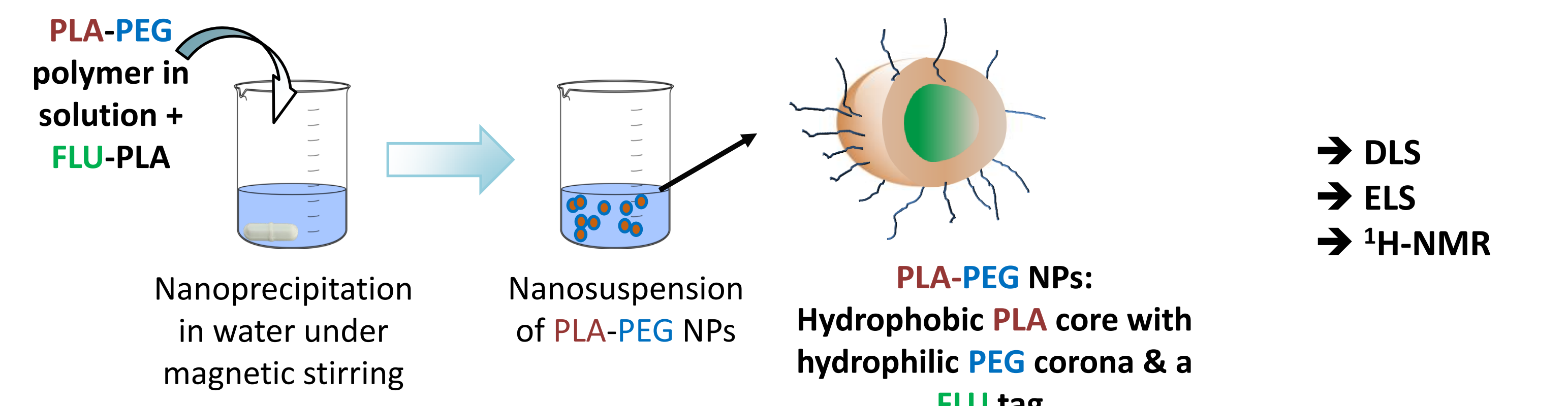
1. Synthesis and characterization of a library of PLA-PEG polymers
2. Synthesis and characterization of a library of PLA-PEG NPs
3. Investigation of endocytosis of PLA-PEG NPs in bEnd.3 monolayers
4. Investigation of the passage of the PLA-PEG NPs vs PEG chain length through bEnd.3 monolayers

Materials and Methods

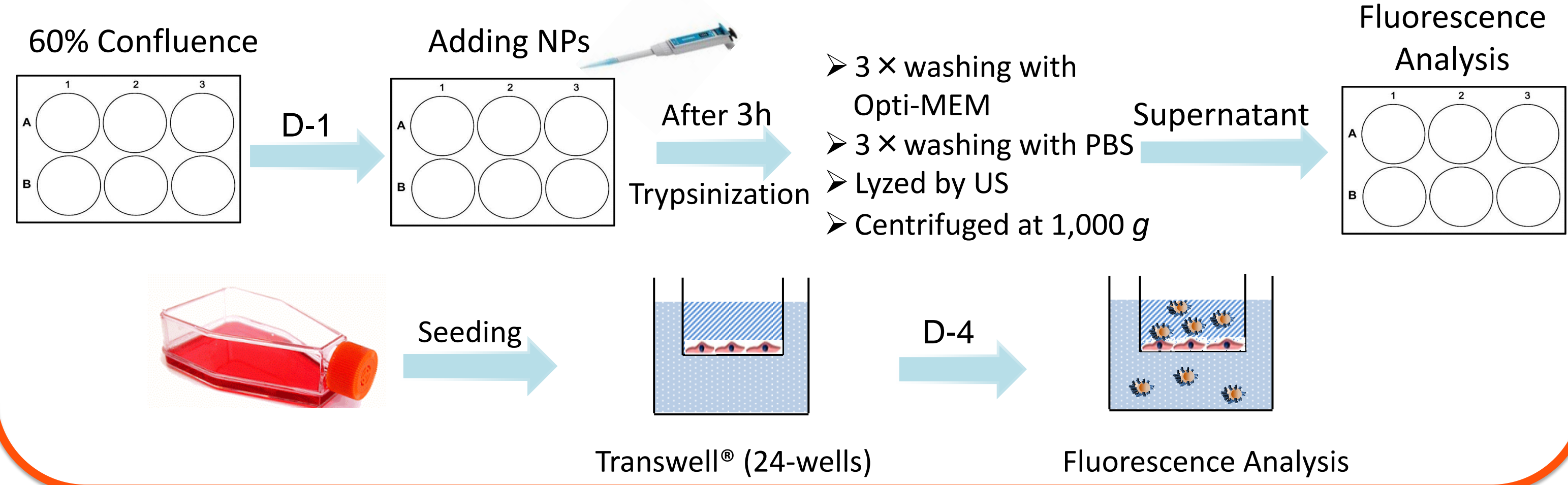
Synthesis and characterisation



Preparation of polymeric nanoparticles (10% FLU)



In vitro studies



Results: NP physicochemical characterization

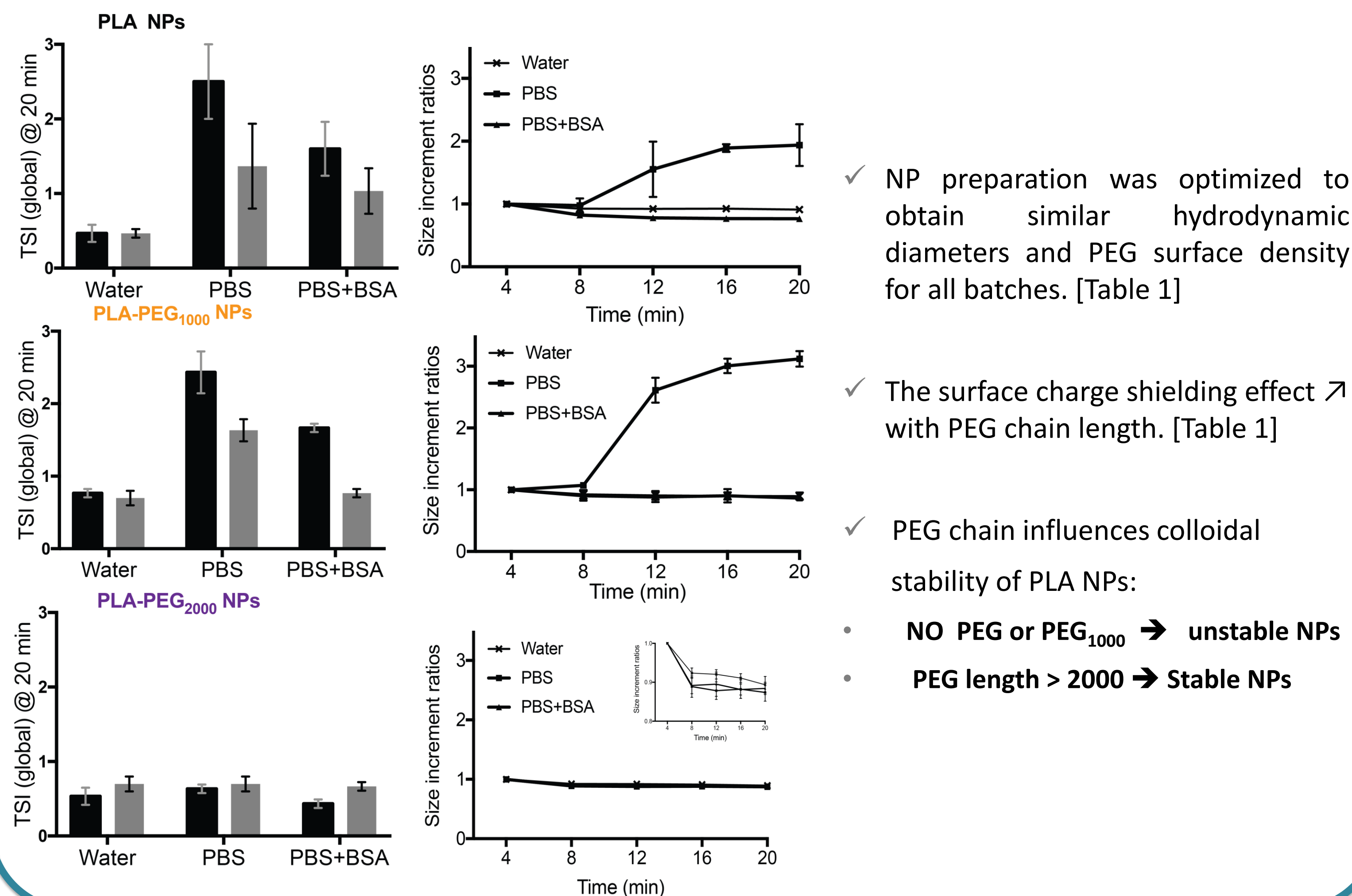
Table 1: PLA-PEG NP characteristics (n=9)

Samples	HD (nm)	PdI	ζ-potential (mV)	PEG density (N _{PEG} /nm ²)
NP-PLA	118 ± 1	0.12 ± 0.01	-32 ± 1	N/A
NP-PLA-PEG ₁₀₀₀	105 ± 1	0.14 ± 0.02	-18 ± 1	0.165 ± 0.003
NP-PLA-PEG ₂₀₀₀	107 ± 4	0.12 ± 0.03	-12 ± <1	0.170 ± 0.002
NP-PLA-PEG ₅₀₀₀	99 ± 3	0.11 ± 0.01	-11 ± <1	0.190 ± 0.001
NP-PLA-PEG ₁₀₀₀₀	98 ± 1	0.10 ± 0.02	-6 ± 1	0.175 ± 0.003

Colloidal stability results:

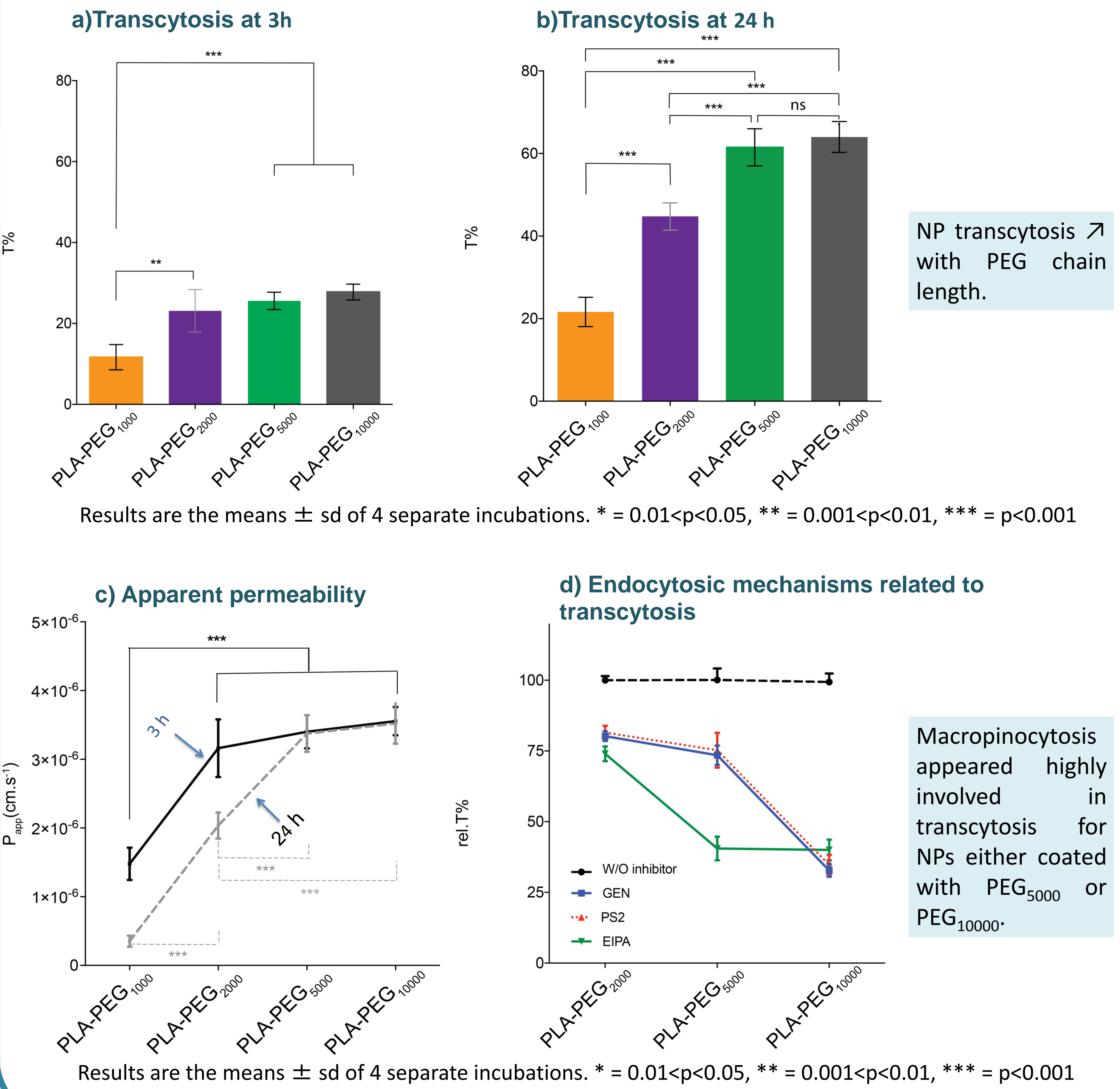
Turbidimetry (TSI)

Dynamic light scattering (DLS)



Results : Transcytosis

Figure 1: Transcytosis through the bEnd.3 monolayers



Conclusion

- ✓ For similar hydrodynamic diameters and PEG densities: NP endocytosis and transcytosis ↑ with PEG chain length: (no PEG ; PEG₁₀₀₀) < PEG₂₀₀₀ < (PEG₅₀₀₀ ; PEG₁₀₀₀₀)
- ✓ PEG chain length influences Papp of NPs across an *in vitro* model of the BBB
- ✓ PEG chain length influences NP endocytosis pathway

References

- (1). J. Stockwell, *et al.* Chem. Biol. Drug Des. 2014;83(5):507-520.
- (2). F. Alexis, *et al.* Mol Pharm. 2008;5(4):505-15.
- (3). K. Andrieux, *et al.* Nanomed Nanobiotechnol. 2009;1(5):463-74.
- (4). X-J. Du, *et al.* Biomaterials. 2015;69:1-11.

Acknowledgements

Part of this work was supported by a grant from Fonds de Recherche Nature et Technologies Québec (FRQ-NT). SFT is grateful to MITACS for her travel scholarship.