

Faculté de pharmacie

Université 
de Montréal

Chaire en Biothérapie de l'Association Canadienne du Médicament

Générique (ACMG) et Biosimilaires Canada

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Montréal

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Biosimilars Canada
The Voice of Biosimilar Medicines in Canada



L'équipe



www.brambillaudem.com

Sam Bability: étudiant PhD
Philippe Delbreil: étudiant PhD
Fatma Moawad: étudiante PhD
Carolina Penaloza: étudiant PhD
Yasmin Ruel: étudiante PhD (ULaval, Prof. Pouillot)
Nastaran Rezaei: étudiant PhD
Naghme Rezania: étudiante Maitrise
Alfonso Nieto: étudiant PhD (McGill et INRS)
Matthias Zadory: étudiant PhD
Alessia Filippini: étudiante PhD (X. Banquy)
Rita Maria KENAAN EL RAHBANI: étudiante PhD

Stage et. internationales

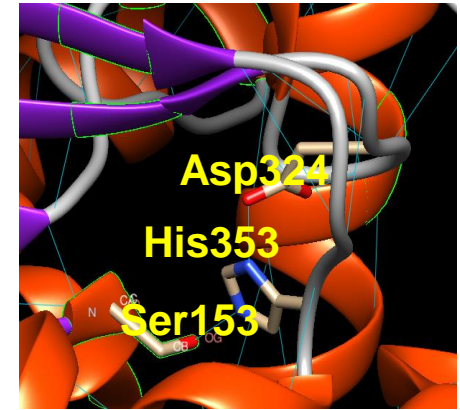
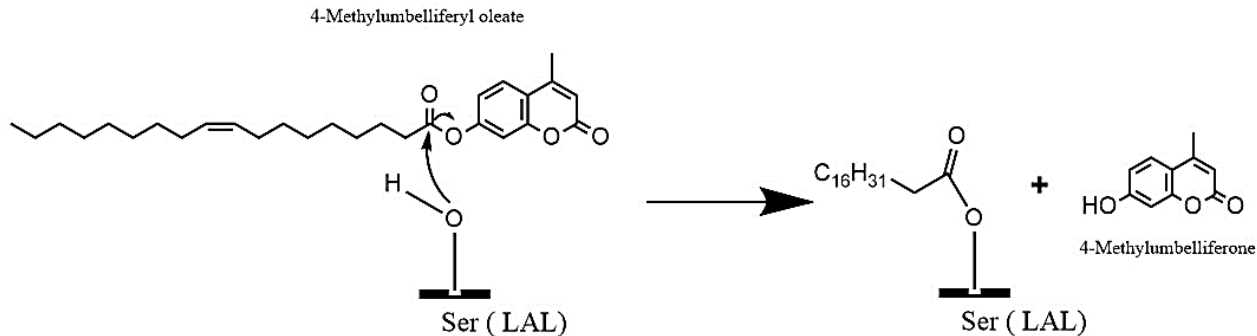
Anja Muetschard (SUI)

Lysosomal acid lipase deficiency (LAL-D)

Deficiency in the serine hydrolase lysosomal acid lipase (LAL) enzyme

Break down cholesteryl esters (Ecs) and Triglycerides

Caused by deleterious mutations in LIPA gene (mostly SNP)



LAL-D can affect infants and adults

Most progressive form: Wolman disease, mostly in infants

Hepatosplenomegaly

Growth and liver failure

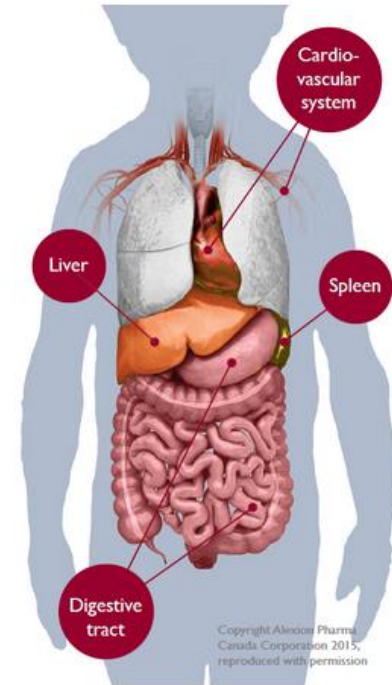
Rarely surviving beyond 6 months of age

Less progressive form: cholesteryl ester storage disease (CESD) in children and adults

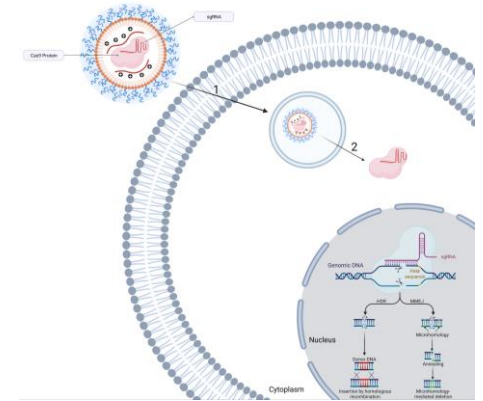
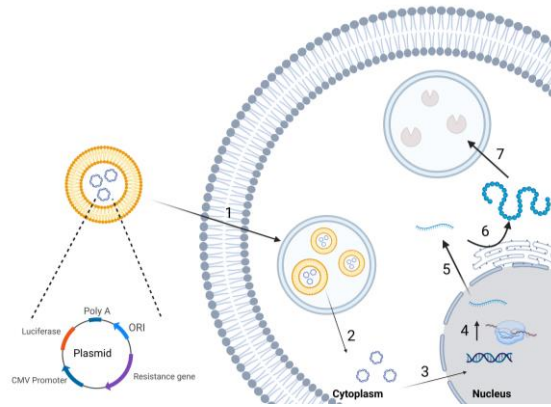
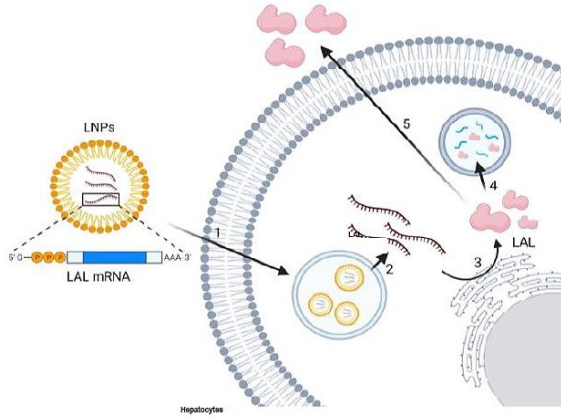
Progressive liver disease (liver fibrosis, failure)

Accelerated atherosclerosis with premature mortality

Prevalence estimated at 1:40'000



Concept

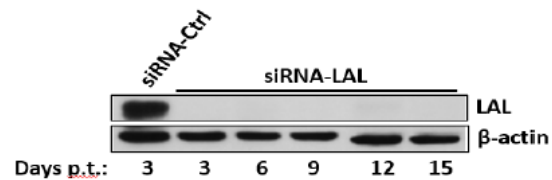
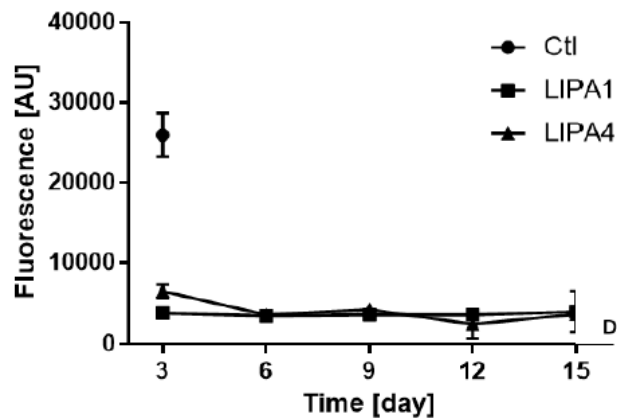
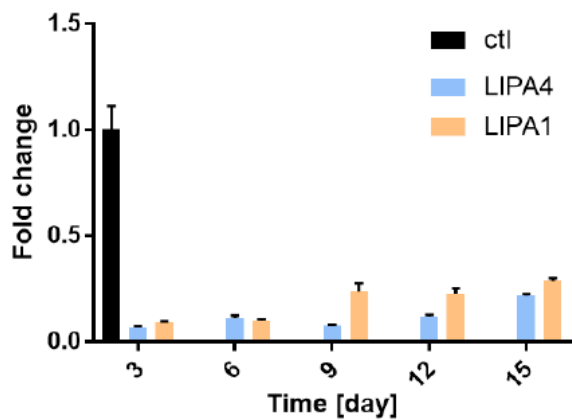


Use “Onpatro®” formulation as benchmark
Hepatocytes targeting

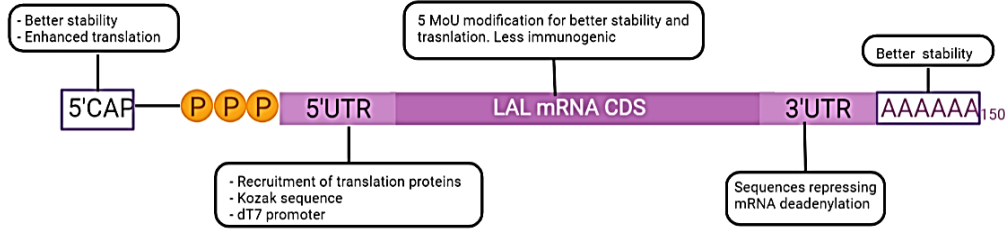
Extended expression
Intracellular expression

In vitro model

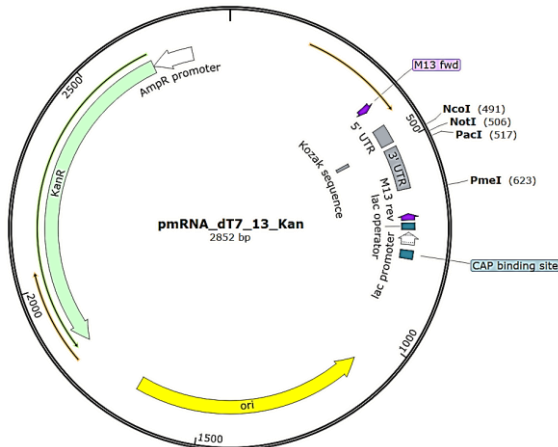
Knockdown model (siRNA), HepG2 cells



mRNA sequence



c.46A>C/p.Thr16Pro Mutant

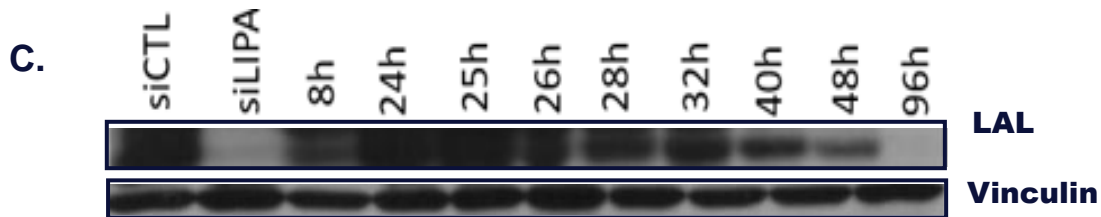
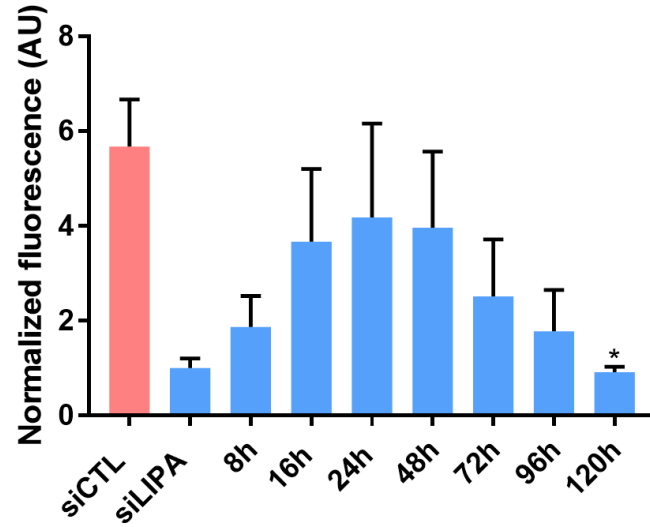
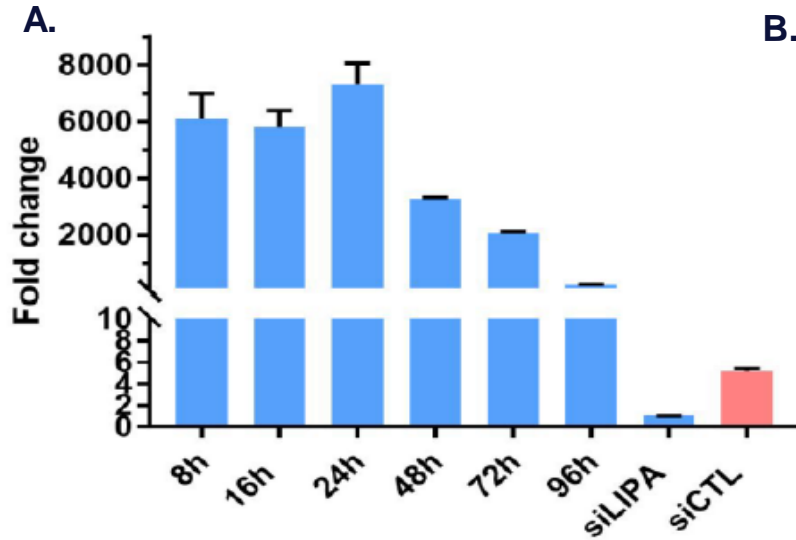


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AAG
    
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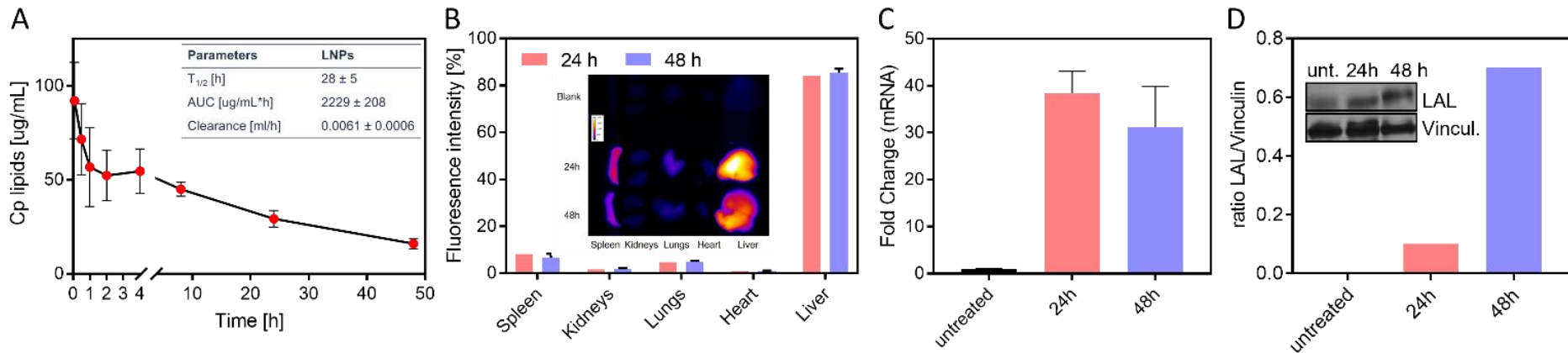
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5' UTR: GACTACAAAGACGATGACGCAAG
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START Codon: ATG
Signal peptide: AAAATGCGGTTCTTGGGGTTGGTGTCTTGGTTCTCTGGACCTGCATTCTGAGGGG
Lipa SEQUENCE
5'UTR and 3'UTR

Expression kinetics with « F1 »



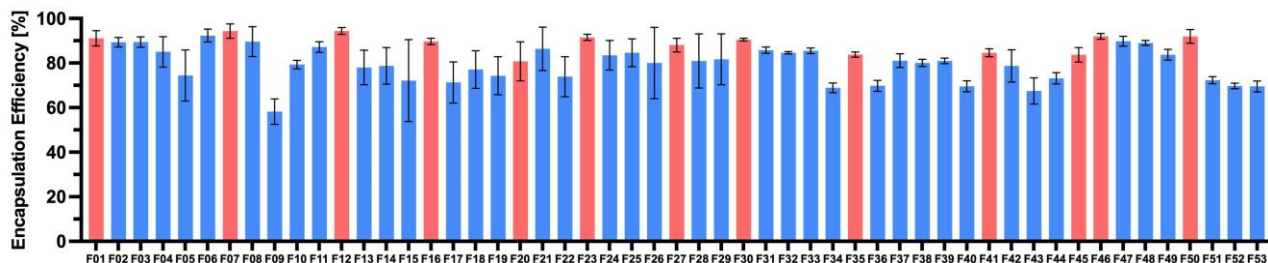
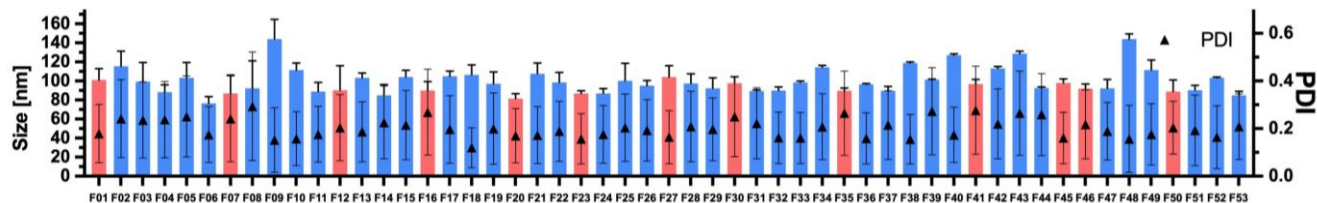
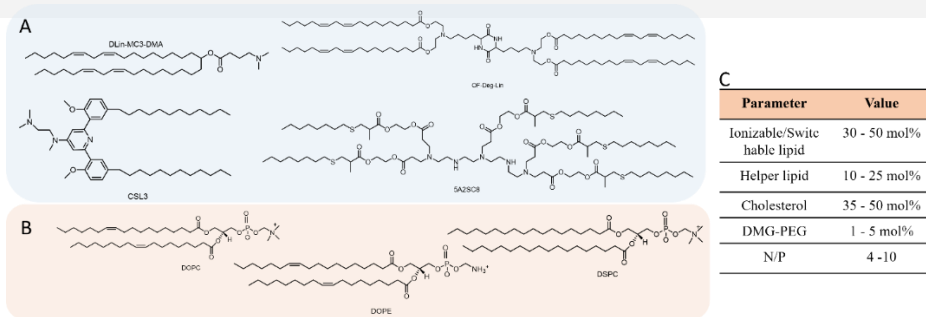
Elliot Lopez,
ENS Paris-Saclay,
Paris

In vivo protocols optimization

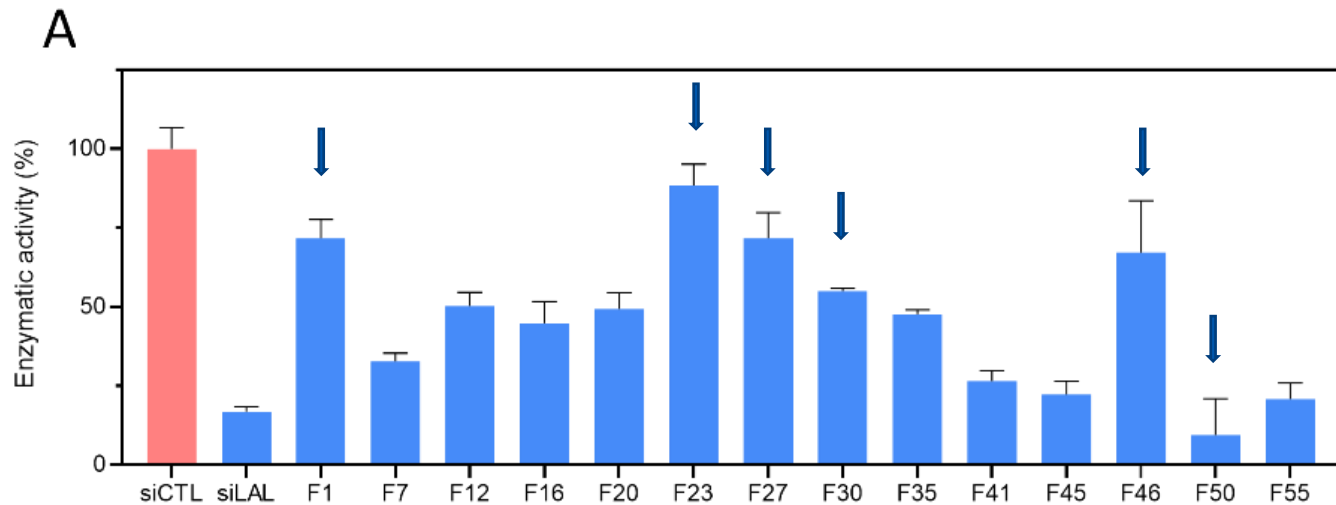


Tested 4 different Ab
Liver lobes and sections
Enzymatic activity
radioactive test (Austria)

LNPs library (Nassim)



Hits formulations activity



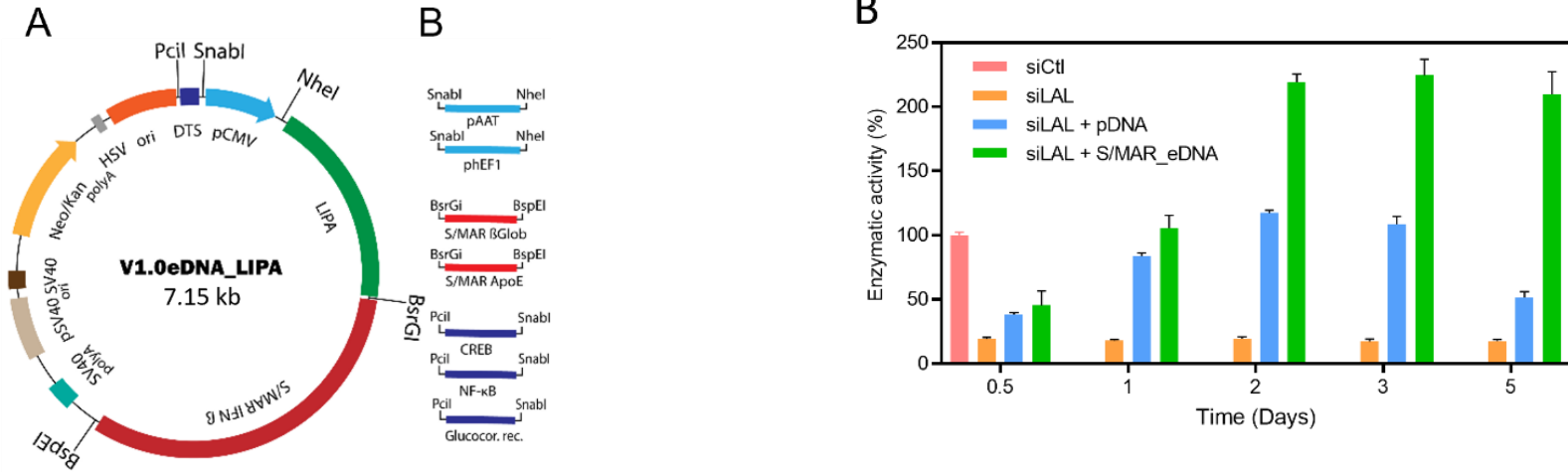
Kinetics running now

Episomal DNA

Scaffold/matrix attachment region (S/MAR)

Promoter

DNA nuclear targeting sequence (DTS)



Output

Publications

1. *Therapeutic applications of nanoparticles targeting neutrophil and extracellular traps*. N Rezaei, M Zadory, S Babity, S Marleau, D Brambilla. *Journal of Controlled Release*. 2023. Accepted
2. *In-Situ Non-Invasive Imaging of Neutrophil Myeloperoxidase and Skin Reactive Oxygen Species in Experimental Murine Atopic Dermatitis*. S Babity, S Pei, J Galimi, D Brambilla, F Couture. *Advanced Sensor Research*. 2023. Accepted
3. *Template-Based Porous Hydrogel Microparticles as Carriers for Therapeutic Proteins*. P Delbreil, X Banquy, D Brambilla *ACS Bio & Med Chem Au*. 2023
4. *Biomimetic Strategy to Enhance Epithelial Cell Viability and Spreading on PEEK Implants*. A. Saad, C. Penaloza Arias, Min Wang, Osama ElKashty, Davide Brambilla, Faleh Tamimi, Marta Cerruti. *ACS Biomaterials Science & Engineering*. 2022.
5. *Current knowledge on the tissue distribution of mRNA nanocarriers for therapeutic protein expression*. M. Zadory, E Lopez, S Babity, SP Gravel, D Brambilla. *Biomaterials Sciences*. 2022. Accepted
6. *Portable Multi-Wavelength Fluorescence Measurement Device*. R Hagen, D Fehr, F Spano, D Brambilla, M Bonmarin. *IEEE Transactions on Instrumentation and Measurement*.
7. *Transdermal Delivery of Fluoropolymer-Modified Microneedle Vaccines against Rabies Elicits Potent Humoral Immunity*. *ACSNano*. Revisions requested.

Patent

Ratiometric biosensor tattoos and use thereof for real time measurements. D Brambilla S Babity. Can. App. P68857CA00.

Awards

2023 Young Investigator Award, Association of Faculties of Pharmacy of Canada
2022 Young Investigator Award, Transdermal Focus Group, Controlled Release Society
2023 Canadian Biomaterials Society Young Investigator Award

Students' awards

Fatma Moawad, Best presentation CSPS 2023. Toronto.

Translation

mTatt.Inc funded (CSO and co-founder), 1st place Innovinc/RBC award (1rd)

Funding

Grants

1. Phosphopilid Research Center: 200k\$ (4 ans)
2. Leo fondation: 250 k\$ (3 ans)
3. Fonds de recherche du Québec – Santé, Recherches en milieu collégial (TBT Institute) 192 k\$ (totale)
4. Réseau The Cell (50 k\$)

Scholarships students

Fatma (FRQNT PhD), Alfonso (FRQNT/S PhD), Matthias (FRQNT/S PhD), Yasmine (FRQS PhD)

Submitted

1. FCI
2. Catalyst NSERC
3. CHIR
4. RQRM x 2
5. Servier x 2
6. FRBC (X 4) writing

Activities

Editorial Activity. Assistant Editor, *Journal of Controlled Release* (Elsevier, IF: 11.5)

Major Scientific Revision Committees

- a. Project Grant reviewer, Pharmaceutical Sciences, Canada Institute Health Research (CIHR), 2022-2025.
- b. Expert reviewer for Natural Sciences and Engineering Research Council of Canada (NSERC), Strategic Partnership Grants competition.
- c. Expert reviewer for Canada Foundation for Innovation, John R. Evans Leaders Funds.
- d. Expert reviewer for NSERC, Discovery grant competition.
- e. Expert reviewer, Agence Nationale de la Recherche France.
- f. Expert reviewer, Controlled Release Society annual meeting.
- g. Selection committee member MSc and PhD scholarship NSERC.
- h. Selection committee member PhD scholarship Fonds de Recherche du Quebec Nature et Technologies.
- i. Expert reviewer, CQDM.
- j. Organiser and selection committee member CC-CRS travel grants.
- l. Sainte Justine NRC

Memberships:

President of the Canada Chapter of the Controlled Release Society and Member of the International Representative Committee of the Controlled Release Society; Treasurer du Transdermal delivery Focus Group CRS

GRUM

Co-director (Prof. Helene Girouard)

Teaching