Cationic polymers as non-viral vectors

Symposium: Vaccine Delivery and Immune Response
Antwerp, September 17, 2024

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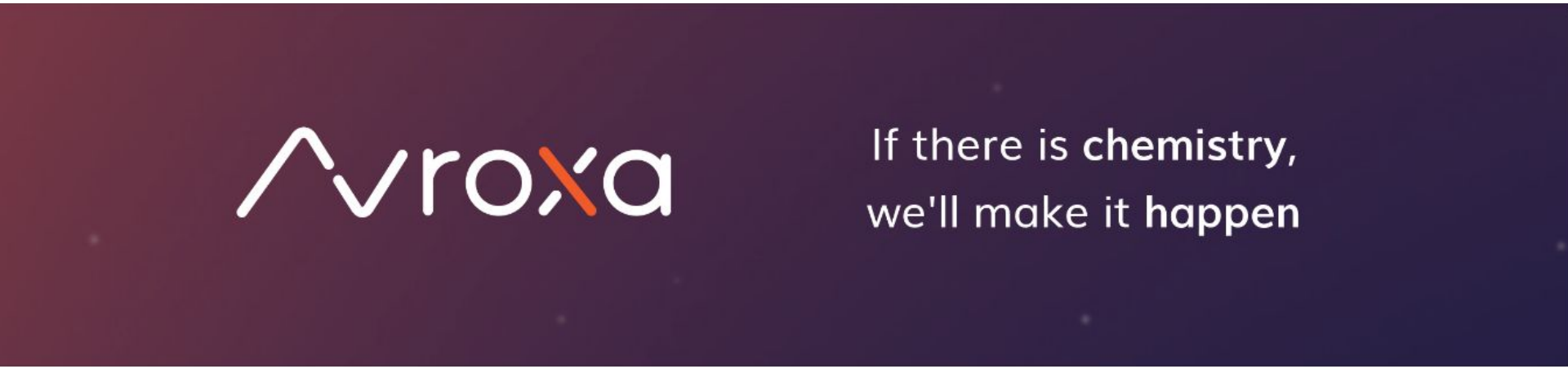
Disclaimer: Founder of Avroxa BVBA



Experts in the design and production of high-quality, well-defined, ultra-pure poly(2-oxazoline)s and derivatives such as polyalkylene imines under the ULTROXA® and UltraPEI® brand names.

Ultroxa®

UltraPEI®

Today's menu:

- Intro to poly(2-oxazoline)s
- Polymers for gene delivery

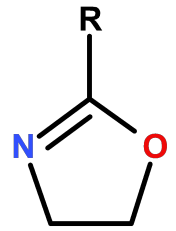
Today's menu:

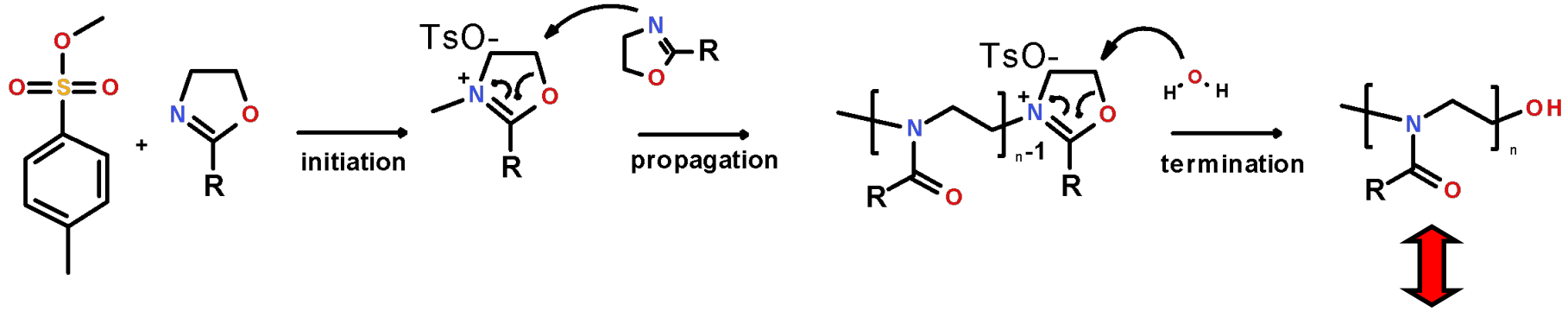
- *Intro to poly(2-oxazoline)s*
- Polymers for gene delivery

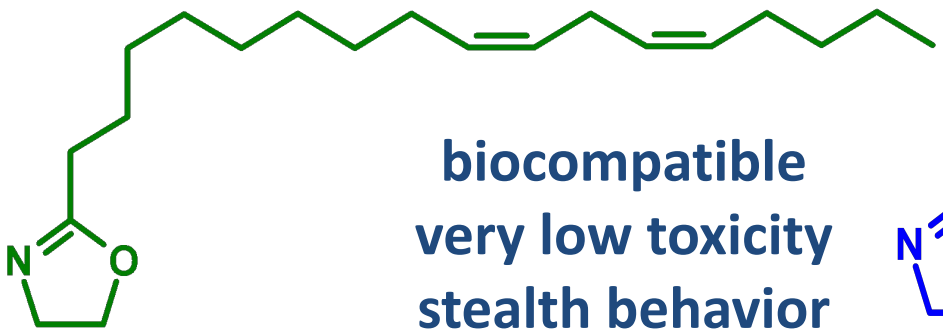
Poly(2-oxazoline)s I

The cationic ring-opening polymerization of 2-oxazolines was first reported in 1966 by 4 independent groups:

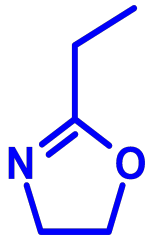
[1] D. A. Tomalia, D. P. Sheetz, *J. Polym. Sci.: Part A* **1966**, *4*, 2253-2265.
[2] W. Seeliger, W. Thier, et al., *Angew. Chem.* **1966**, *20*, 913-927.
[3] T. Kagiya, S. Narisawa, T. Maeda, K. Fukui, *Polym. Lett.* **1966**, *4*, 441-445.
[4] A. Levy, M. Litt, *Polym. Lett.* **1967**, *5*, 871-879.

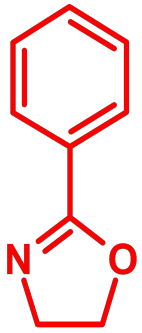


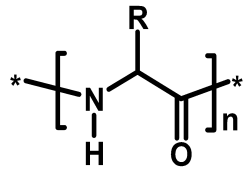




biocompatible
very low toxicity
stealth behavior



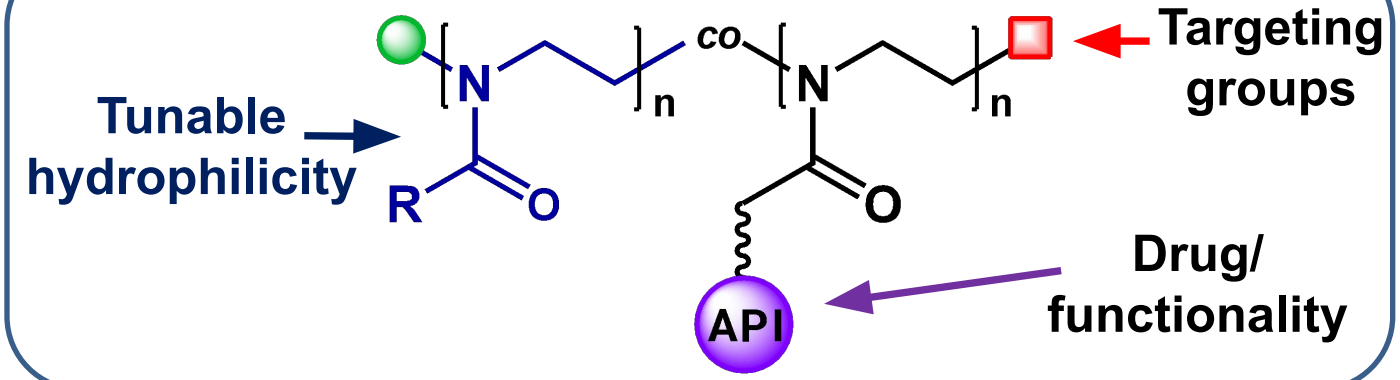


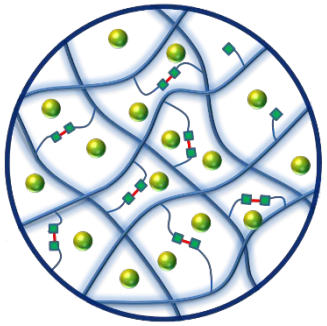


pseudo-polypeptide

Review: *Eur. Polym. J.* **2017**, *88*, 451-469

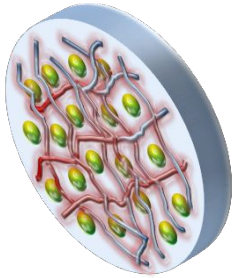
PAOx biomaterials



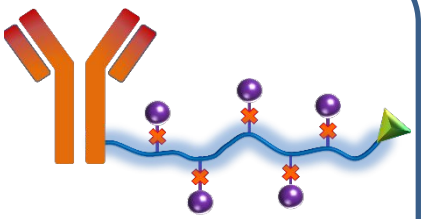


Hydrogels

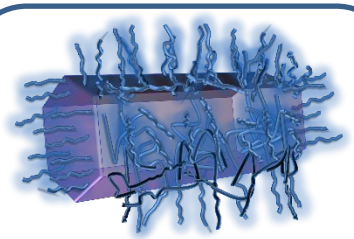
High biocompatibility, non-fouling, renal excretion limit ~ 40 kg/mol



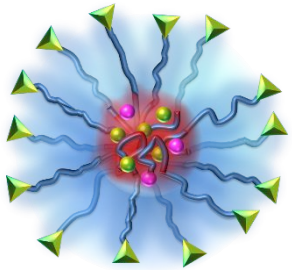
Formulation



Therapeutics



NPs and surfaces

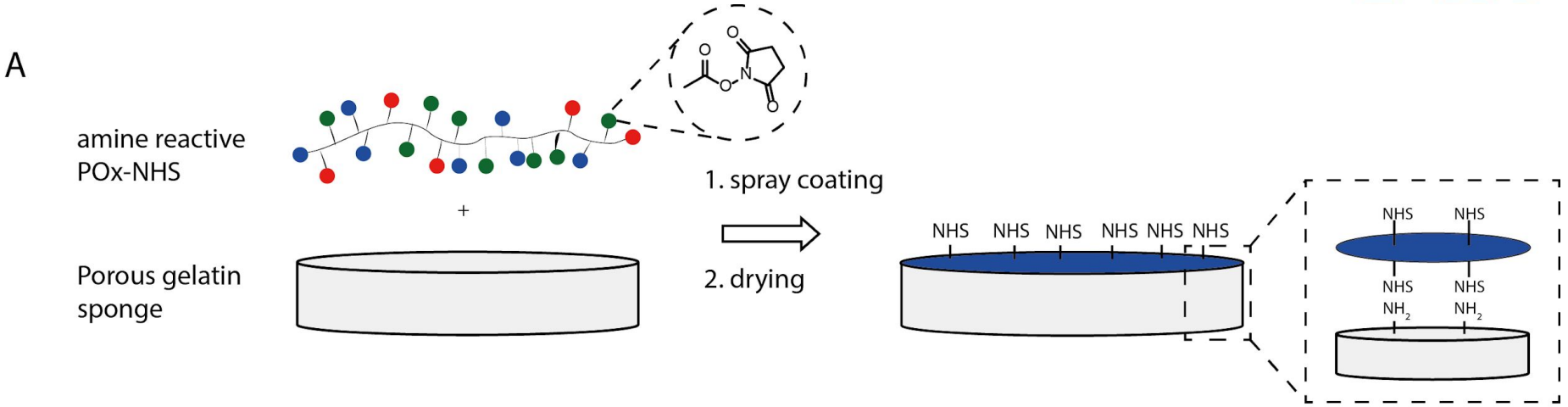


Micelles

Promising alternatives to replace and outperform PEG

Poly(2-oxazoline) hemostatic patch I

Collaboration with Prof. Jan van Hest, Nijmegen



Poly(2-oxazoline) hemostatic patch II

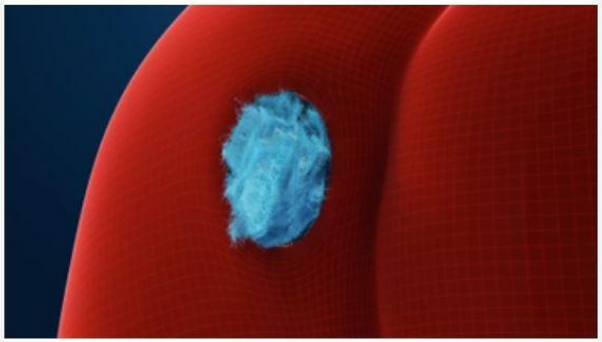
Collaboration with Prof. Jan van Hest, Nijmegen

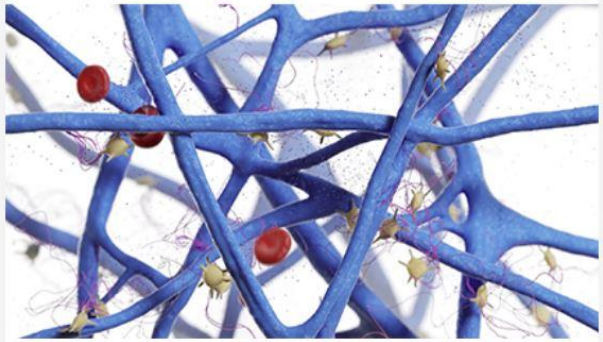
ETHICON
a Johnson & Johnson company

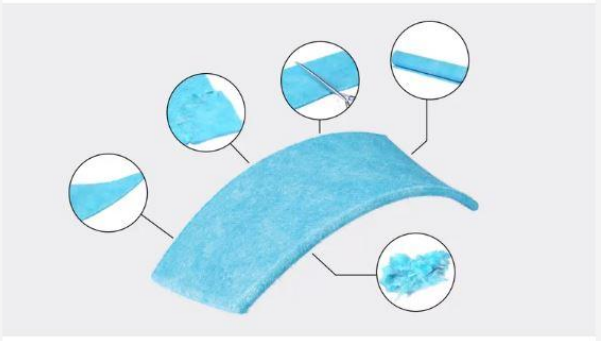
Innovation that surprises

As the blood flows into ETHIZIA™, the gelatin matrix with the embedded POx polymer system dehydrates the blood and accelerates the coagulation cascade to occur in seconds, forming a tight yet flexible physical seal that maintains a barrier to bleeding.[B,1,12]

See It in Action →







Recently approved in EU for hemostasis of difficult to control bleedings
Ethizia™ – marketed by Ethicon

Today's menu:

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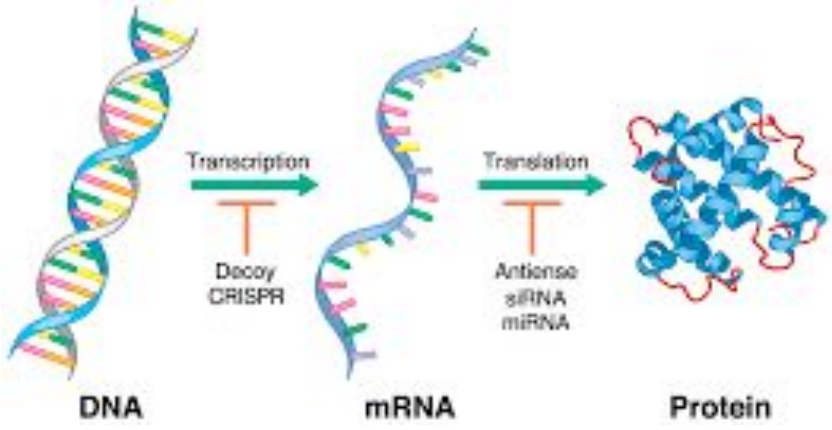
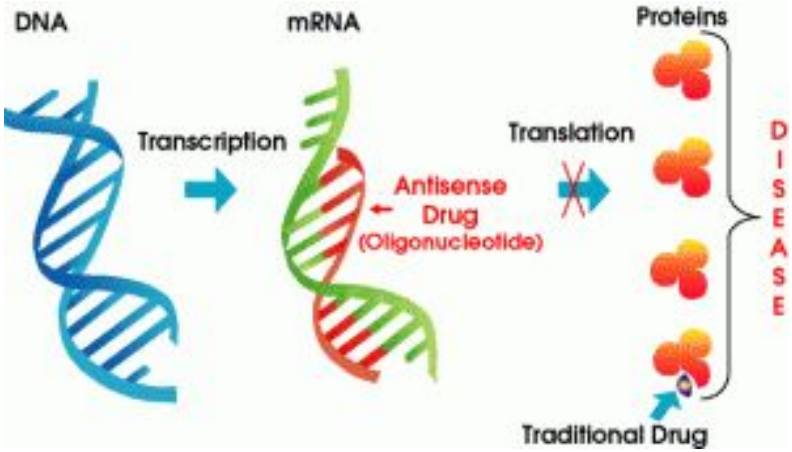
- *Polymers for gene delivery*

Gene delivery





Gene delivery based therapies and vaccinations are gaining momentum

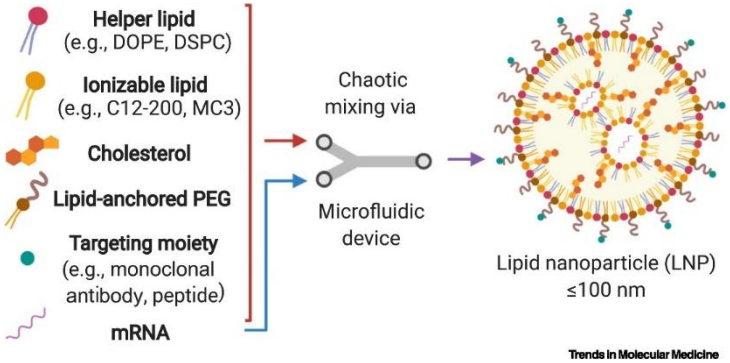
- **> 60 approved products, mostly based on viral vectors;**
  - ***Production of viral vectors requires in vitro transfection***
- **mRNA-based vaccines for COVID-19 based on LNPs**
- **CRISPR-CAS requires transfection**

Very high commercial potential and interest in non-viral vectors

Non-viral vectors

Lipid nanoparticles

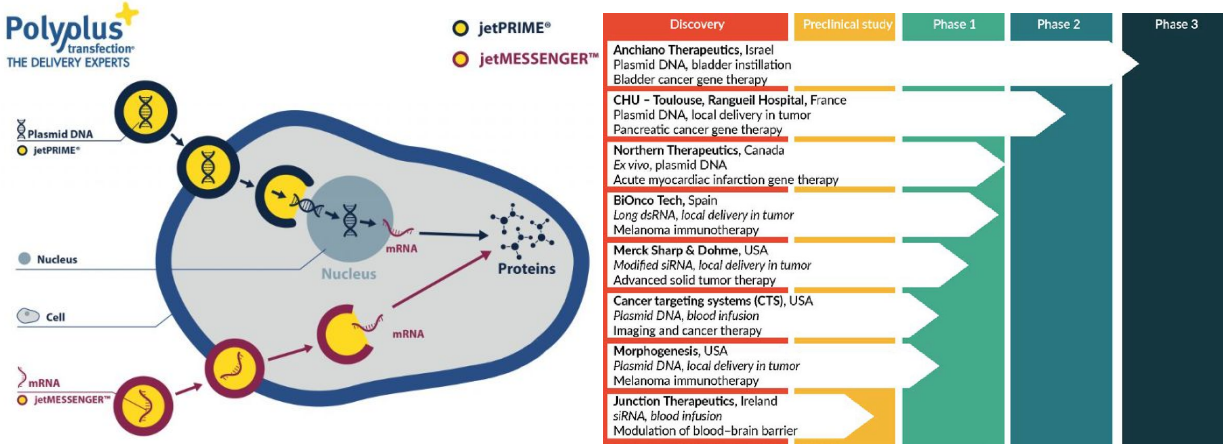
Used in current mRNA vaccines (Spikevax and Comirnatry)



Lipid anchored PAOx as non-immunogenic alternative for PEG

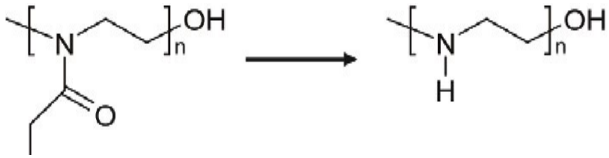
Cationic polymers – polyplexes

Clinical pipeline jetPEI (L-PEI)



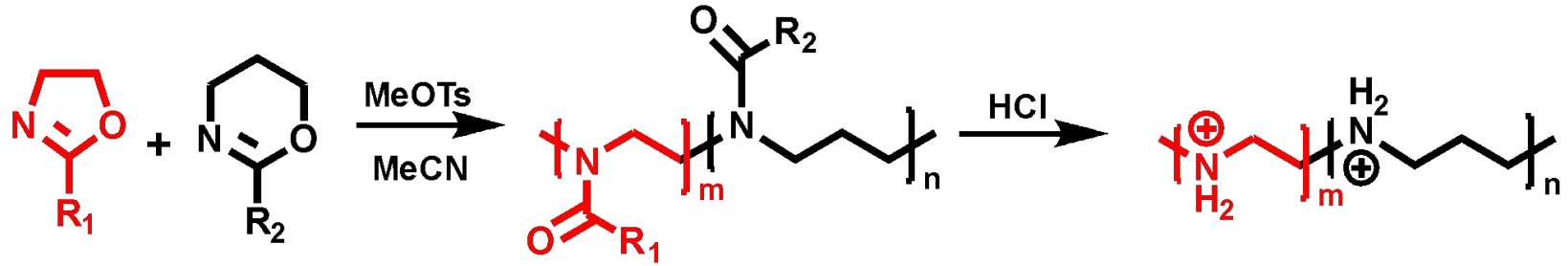
March 2023: Sartorius acquired PolyPlus for 2.4 billion EUR

Polyplus - jetPEI (L-PEI)

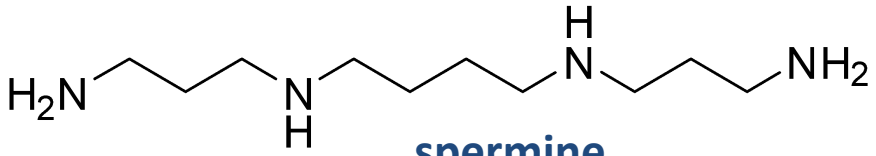


lipid-based!

Random copolymers for gene delivery?



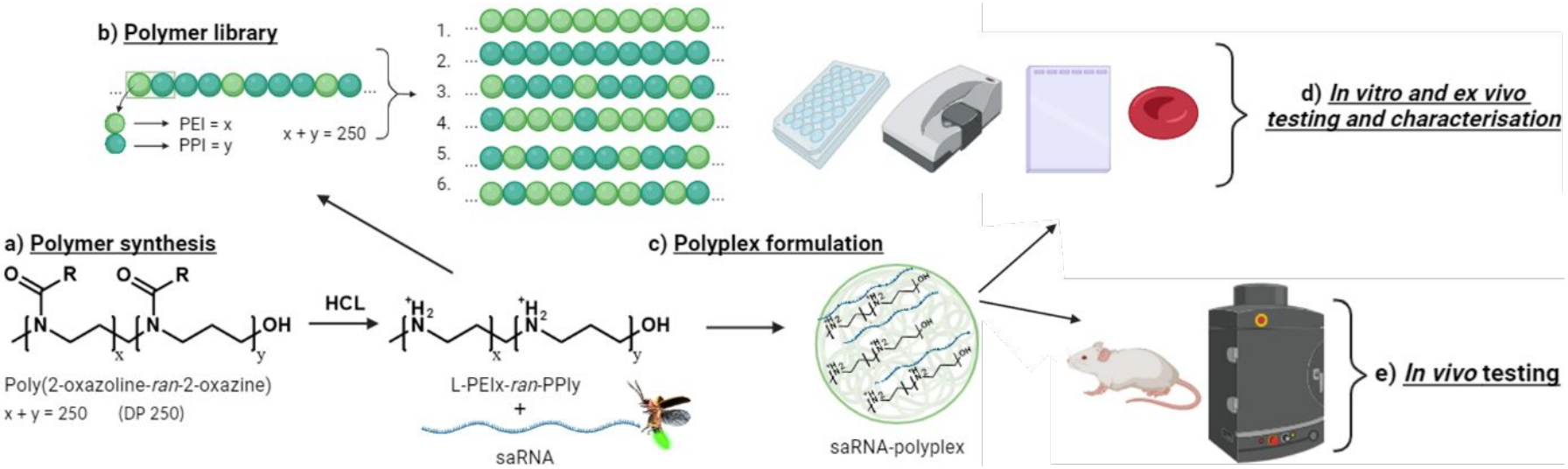
- More hydrophobic than L-PEI
- Altered charge density
- Oligoamines known in biological systems
- Large scale synthesis (10 g to kg's)
- Simple formulation



patent filed; Biomacromolecules **2022, *23*, 2459**

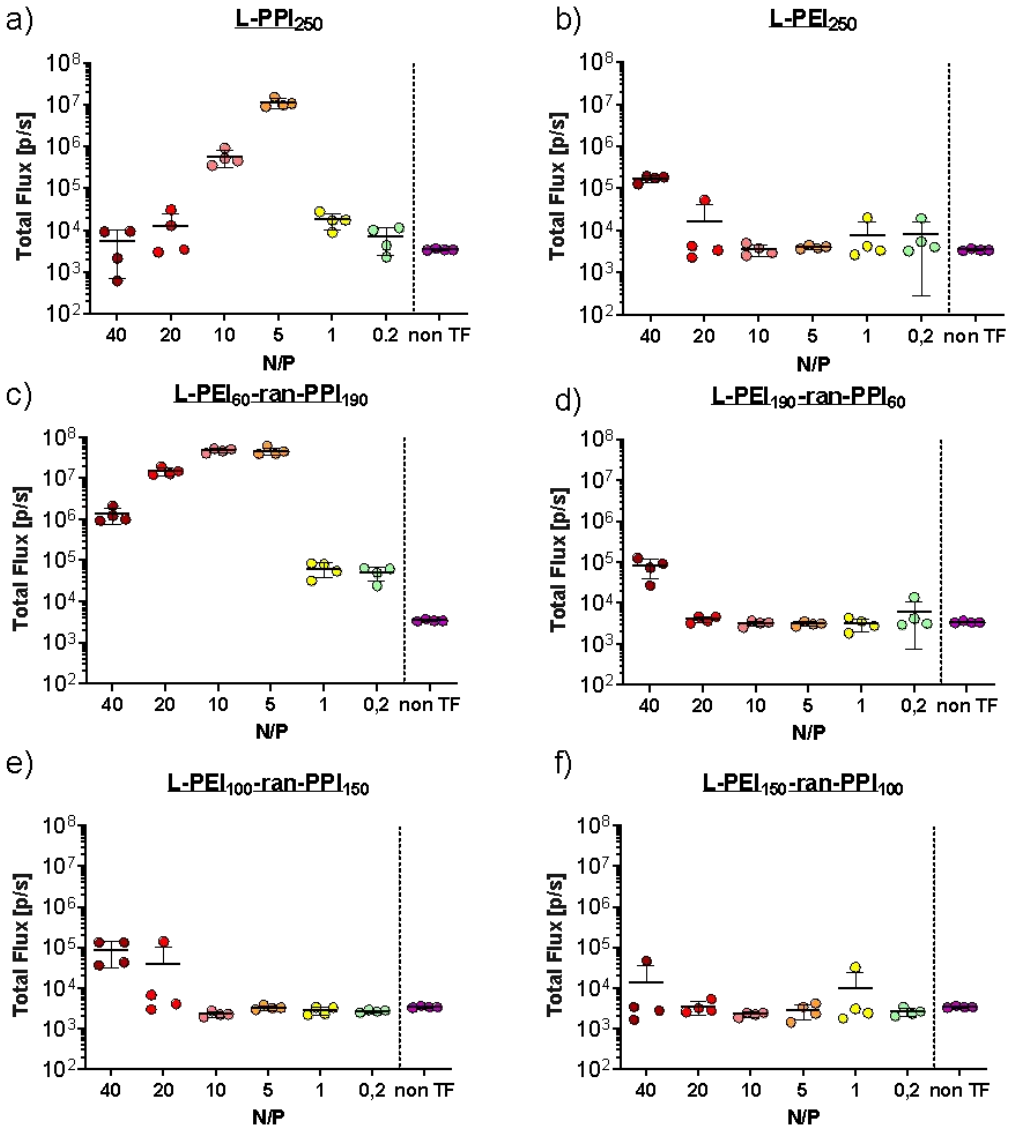
Transfection of sa-mRNA

Collaboration with Prof. Niek Sanders, UGent



In vitro transfection of sa-mRNA

Collaboration with Prof. Niek Sanders, UGent

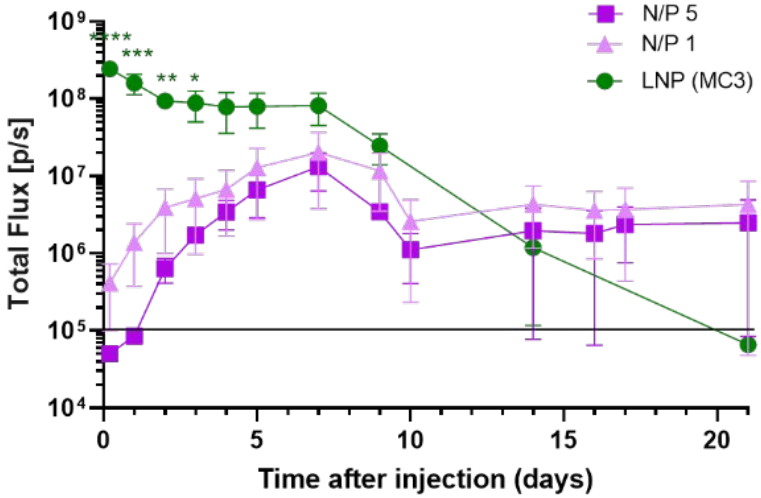


patent filed; J. Mater. Chem. B 2024, 12, 3927

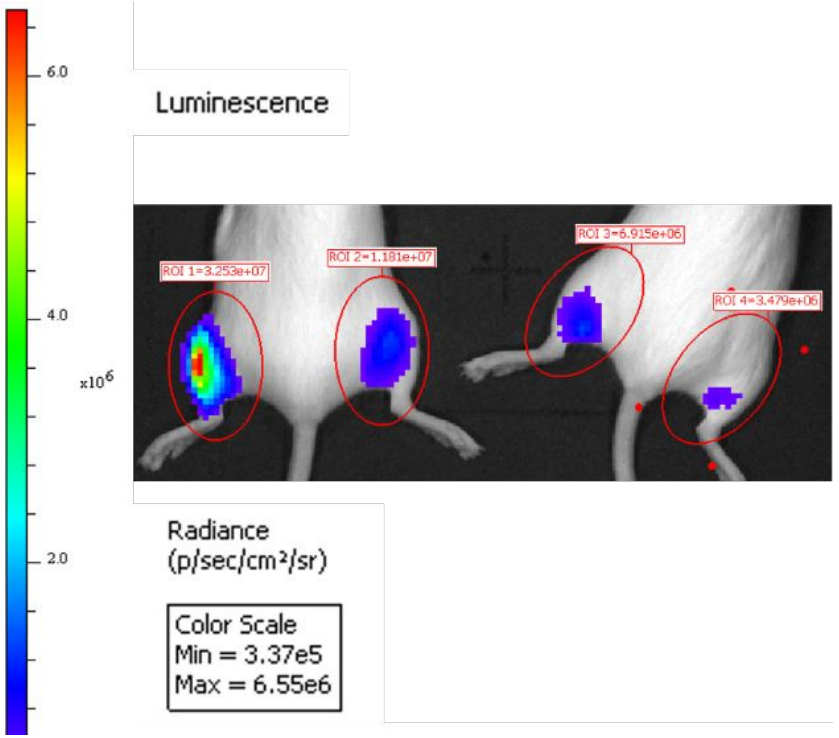
In vivo transfection of sa-mRNA

Collaboration with Prof. Niek Sanders, UGent

a)



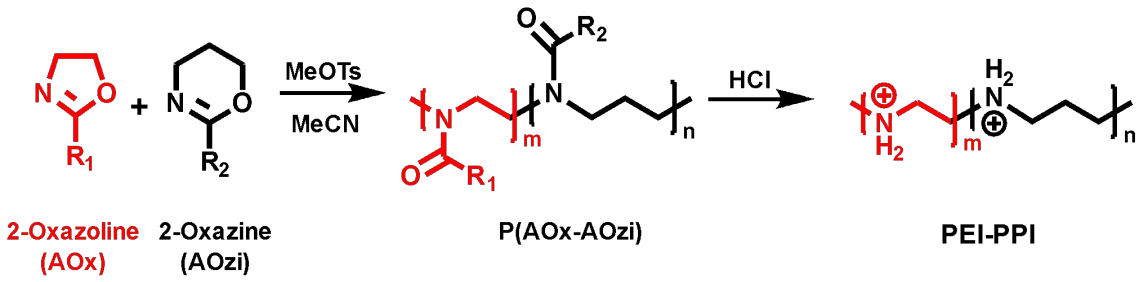
b)

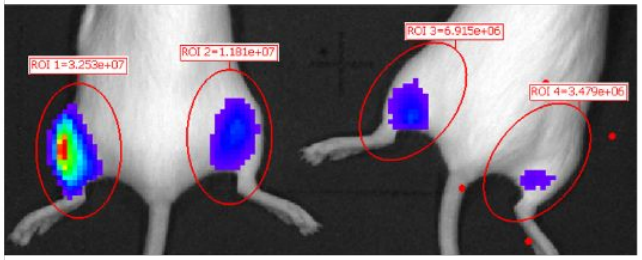


patent filed; J. Mater. Chem. B 2024, 12, 3927

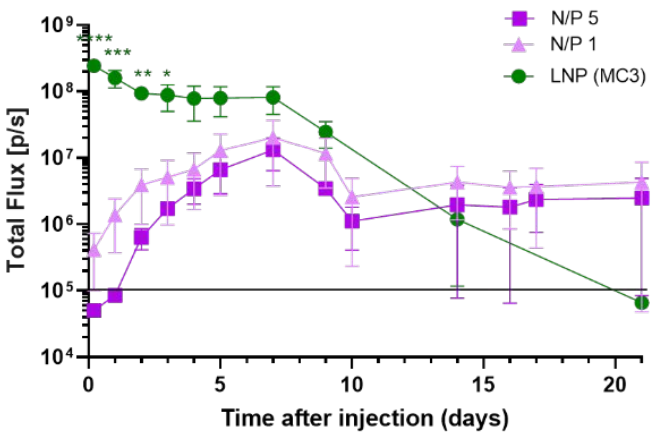
Summary

Cationic polymers for gene delivery





a)



Higher transfection efficacy than L-PEI for both pDNA and mRNA!

Further developments PEI-PPI

- Proof of concept for vaccination (mice)
- Proof of concept for protein replacement therapy (cats)
- New method developed for preparing PAOx-*block*-PEI-PPI (patent filed)

Acknowledgement

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