23 de octubre de 2024

NanoTarget, a technological proprietary polymeric library for the encapsulation of nucleic acids through electrostatic interactions

Cristina Fornaguera, PhD

MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
AGENCIA ESTATAL DE INVESTIGACIÓN
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Content

1. The Institution
2. The Product
   a) Target Indications
   b) Innovative mechanisms of action
   c) Differential features facing the market
   d) Current status of development
   e) IPR protection
   f) Pitfalls & Risks to be considered
3. Partnering Opportunities

Content

IQS, from chemistry to multidisciplinarity

Biongineering department → NANO THERAPIES LAB → Biomaterials engineering
Nanoformulation
Gene and drug delivery systems
Immunotherapeutics

The NanoTher Lab, approaching nanoformulations from bench to the market

Stability enhancement of detergents

Encapsulation of cosmetic products

Allowing alternative administration routes

Controlled delivery of nucleic acids

Improved small drugs pharmacokinetics

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Content

The Product: a technological platform of polymers for RNA encapsulation

Proprietary polymers, experts on biomaterials engineering

pBAEs
Poly (beta aminoester polymers)

Useful to generate **polymeric nanocarriers**

Useful for many **unmet medical needs**

pBAE = modular delivery platform enabling rapid and reproducible path to clinical development

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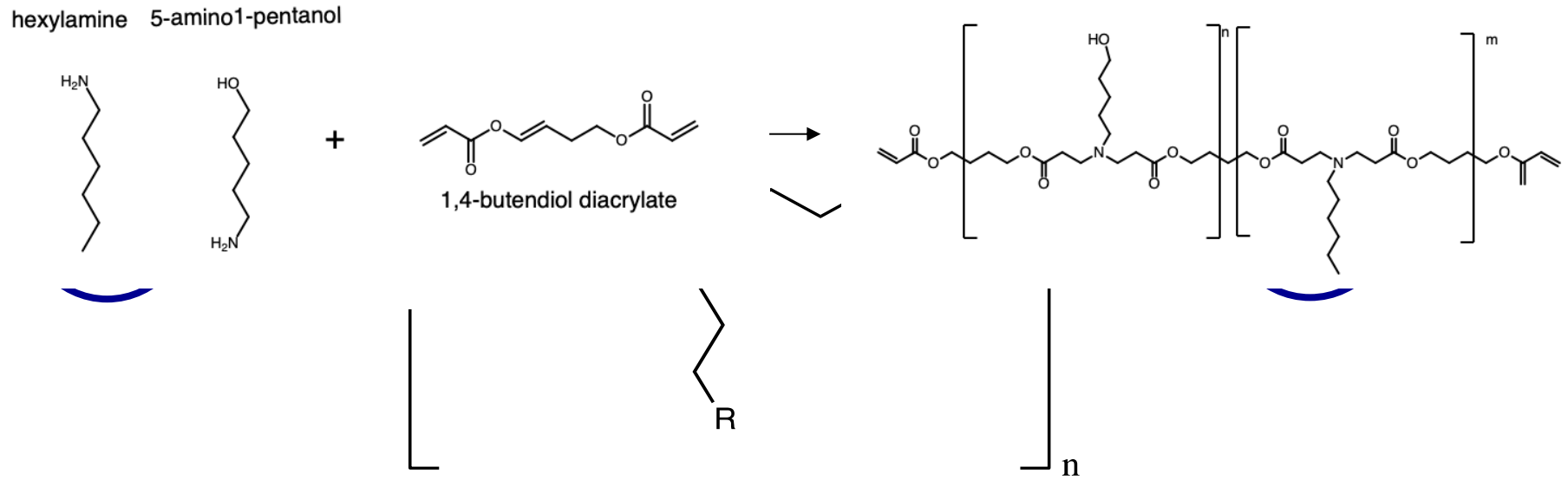
The Product: a technological platform of polymers for RNA encapsulation

Proprietary mRNA-loaded Polymeric nanoparticles

Poly (β-aminoester)



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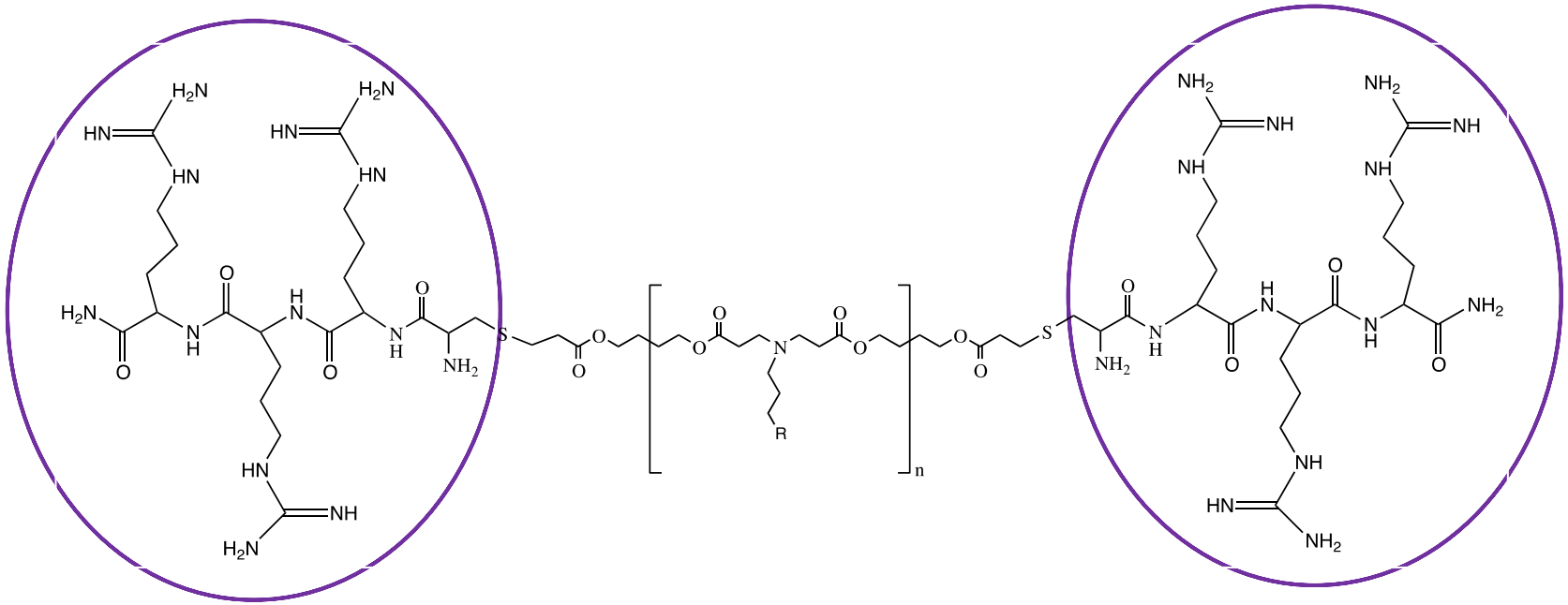
Proprietary mRNA-loaded Polymeric nanoparticles

OM- Poly (β-aminoester)



R = lateral chains for functionalization

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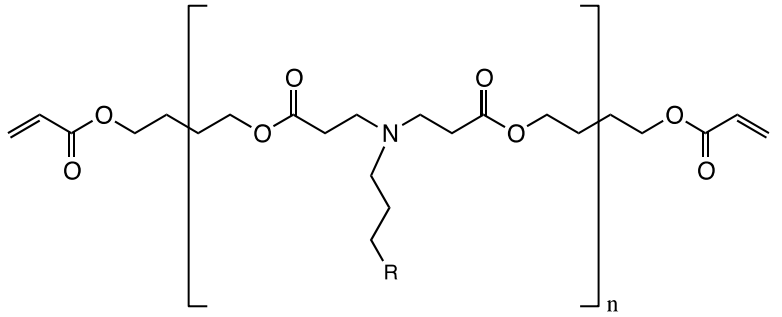
Proprietary mRNA-loaded Polymeric nanoparticles

Poly (β-aminoester) lateral chains



1) Hydrophobicity modulation
2) Addition of targeting moieties
3) Inclusion of stimulus sensitive groups
4) Functionalization with zwitterionic moieties

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The Product: a technological platform of polymers for RNA encapsulation

pBAE: advantageous candidates

- *Biocompatible and biodegradable*
- *Easy manufactured and lyophilized*
- *Easy and scalable synthesis*
- *Protein corona modulation*
- *End oligopeptides → endosome scape*
- *No immune recognition*
- *Cationic charges*
- *Selectivity to specific cell types*

Robustness and versatility for many applications

Polymeric nanoparticles loaded with nucleic acids

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The Product: a technological platform of polymers for RNA encapsulation

Placenta crossing control: Treatment of oncological pregnant patients

Crossing the lung mucosa: Lung cancer, gene therapy of lung diseases, vaccination

Metabolism modulation: Cardiovascular diseases therapies

Viruses coating: Oncolytic virotherapy, rare diseases treatment

Crossing the BBB: Neural diseases gene therapy and neural tumors treatment

Microneedles design: Gene therapy of skin diseases, vaccination, melanoma treatment

Immune modulation: Infectious diseases profilaxis and tumor therapeutic vaccination

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TARGET INDICATION: Use of our pBAE polymer platform for the formulation of stealth targeted mRNA-loaded vaccines

aim:

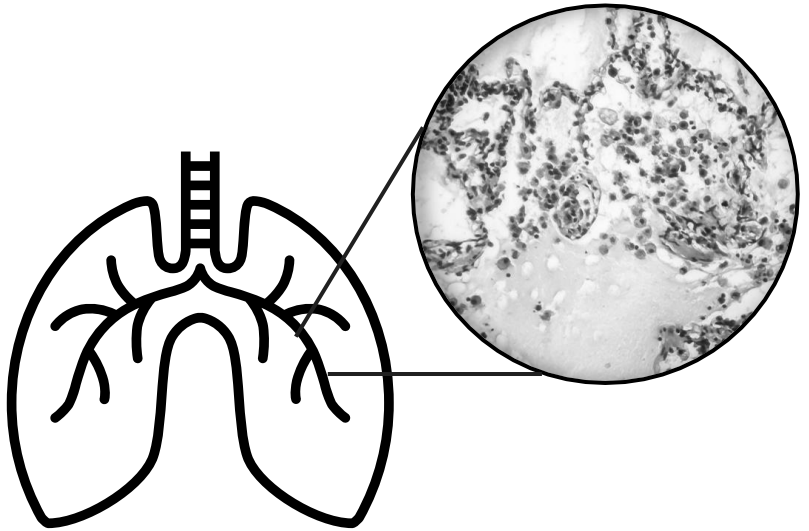
*Developing a **vaccination platform** by using **mRNA-loaded pBAE polymeric nanoparticles** for the prophylaxis and treatment of current medical urgent unmet needs in oncology that, in addition to the vaccine as the main component, can include **adjuvant therapies** based also on polymeric nanoparticles.*

Vaccines, beyond infectious diseases prophylaxis

Use of **therapeutic vaccination** for immune system activation.

Cancers cause high economic impact globally; only lung cancer aroused to **$188 billion**

Immune system supression in tumor microenvironment as the **trigger** for cancer development



NEED OF INNOVATIVE VACCINES FOR THERAPEUTIC USE

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Vaccines, need of innovative design

Use of **mRNA** as the active principle

- *Highly antigenic*
- *Encoding any gene*
- *Easy and scalable synthesis*

but

- *Compromised stability*
- *RNAses in biological media*
- *Need for extreme cold storage*

Need of a **carrier system**

NANOMEDICINE

POLYMERIC NANOPARTICLES

EXTRACELLULAR VESICLES

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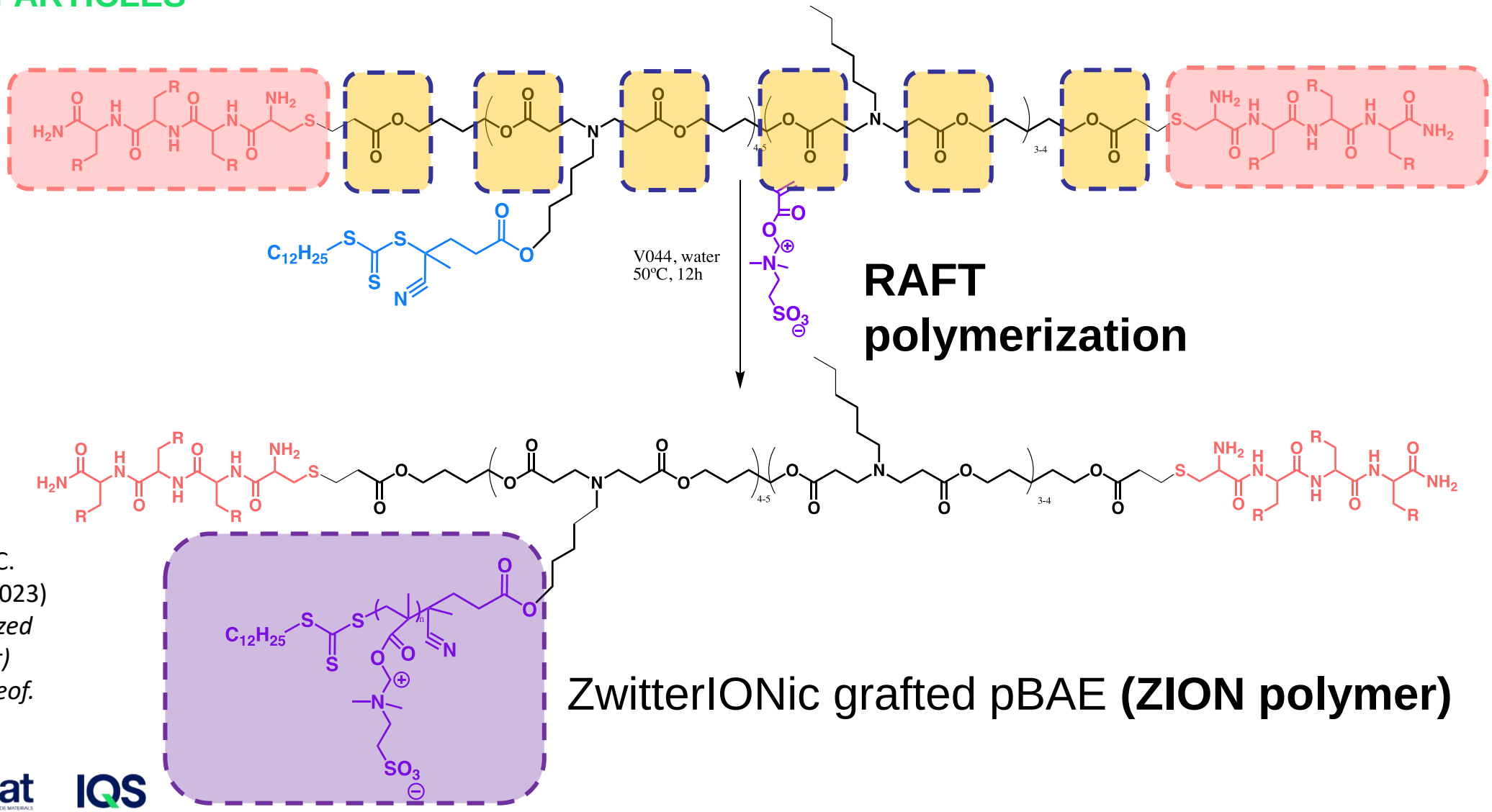
ZION, an innovative mechanism of action

STEALTH NANOPARTICLES



ZwitterIONic grafted pBAE **(ZION polymer)**

C. Garcia-Fernandez, C. Fornaguera, S. Borrós. (2023) *Zwitterionic functionalized poly(beta-aminoester) polymers and uses thereof.* EP21382923.7

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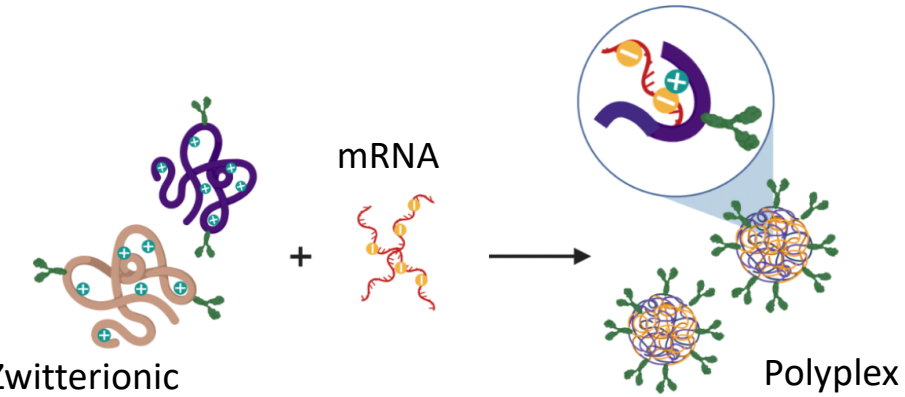
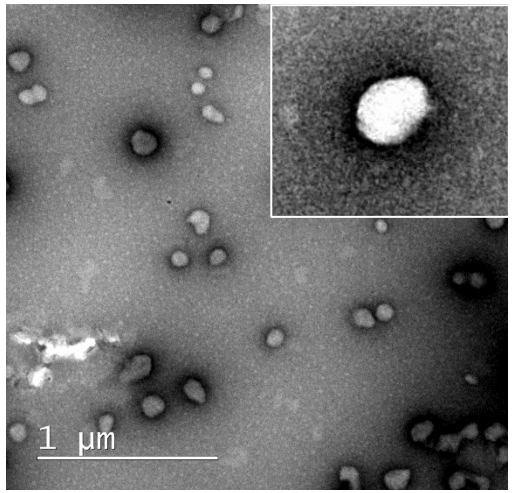


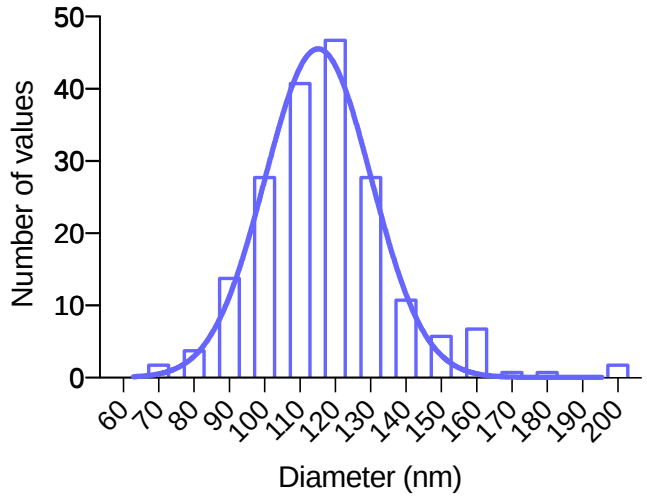
Polyplex formulation scheme for nucleic acid encapsulation

DLS and EMSA assay

NPs	Size (nm)	Z-pot (mV)	Encaps. eff. pDNA (%)
pBAE	198.2±15.3	32.2±4.5	89.2±2.5
ZION	201.5±9.2	18.4±2.1	87.3±3.1

TEM





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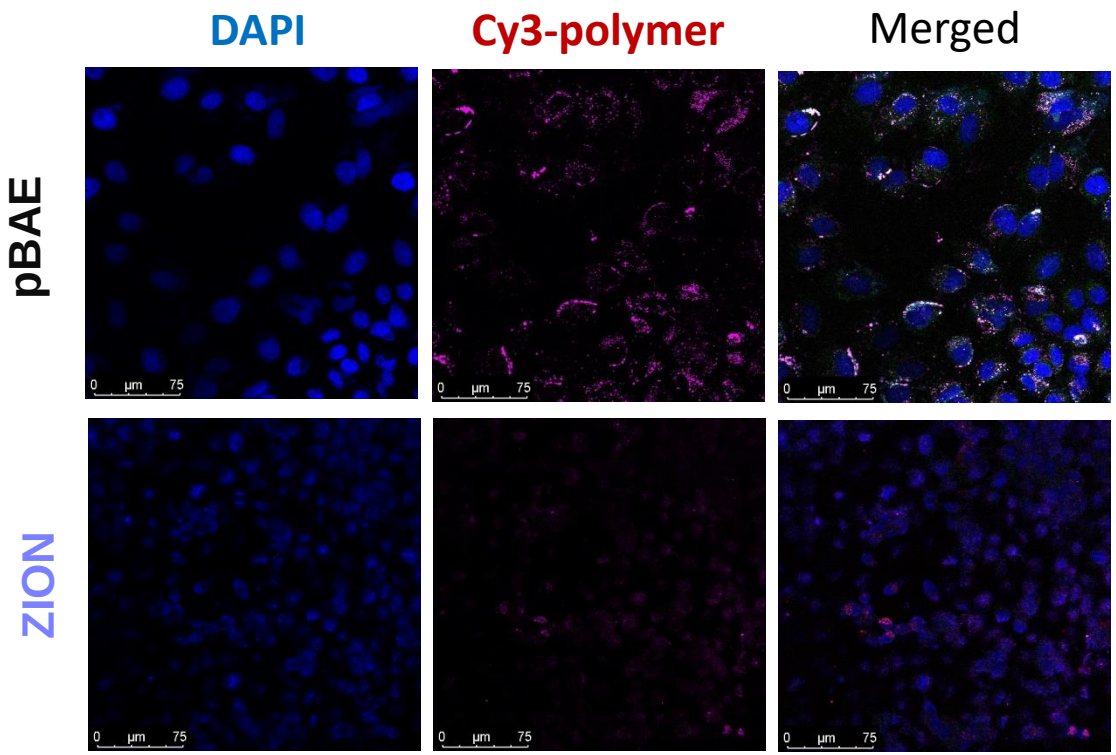

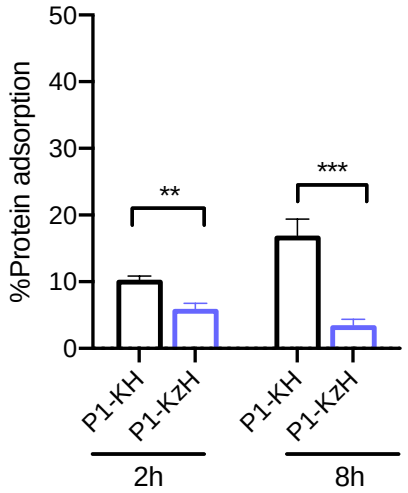

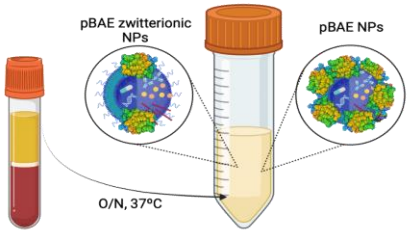

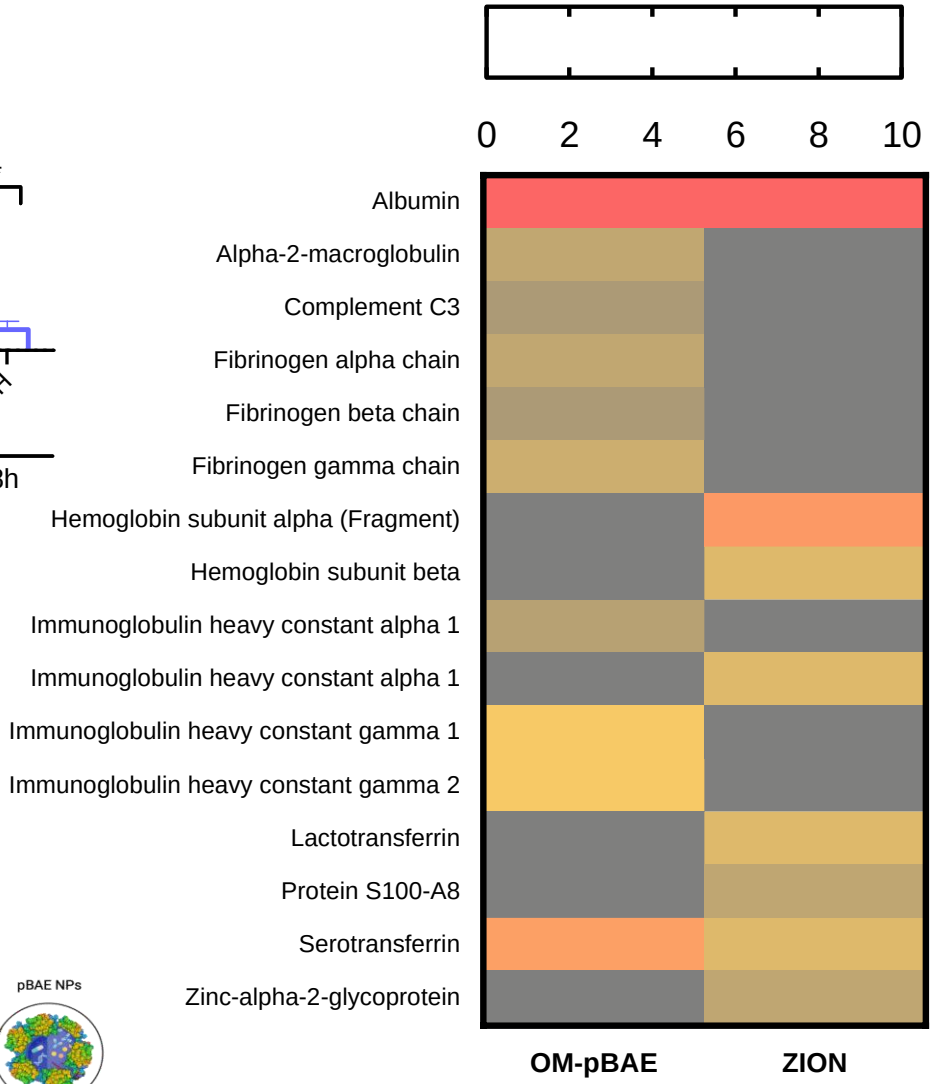

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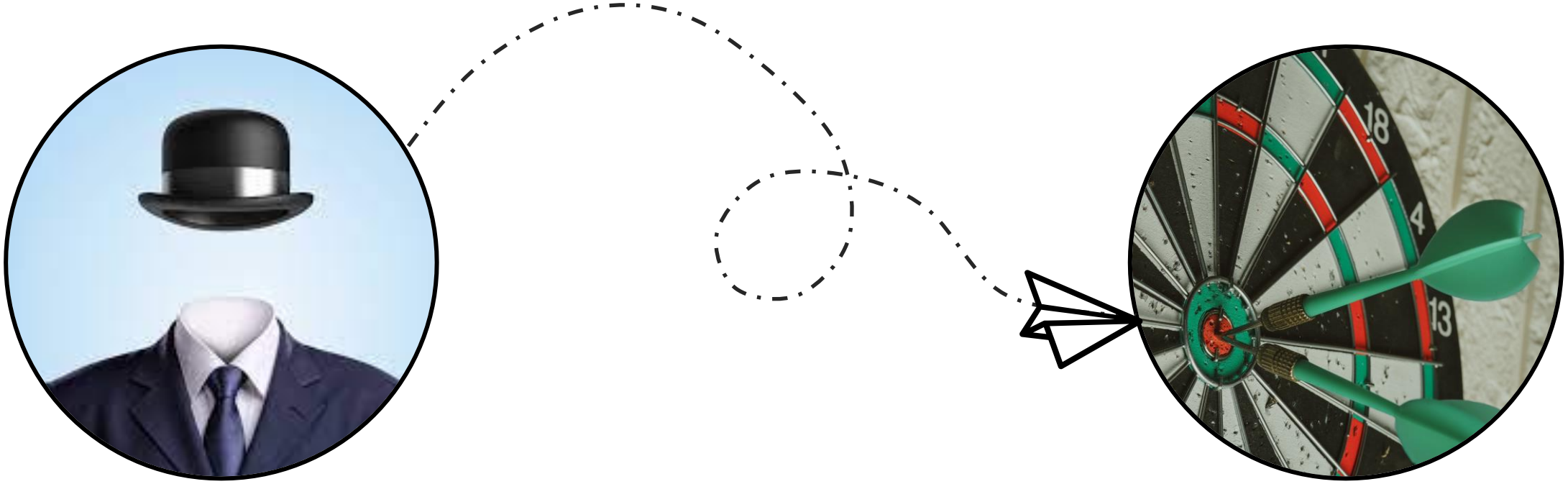
ZION, differential features facing the market

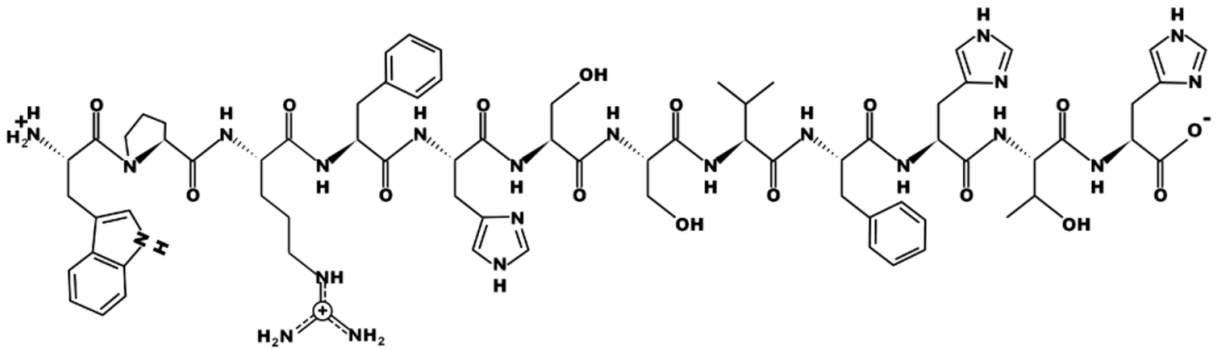
FROM STEALTH…

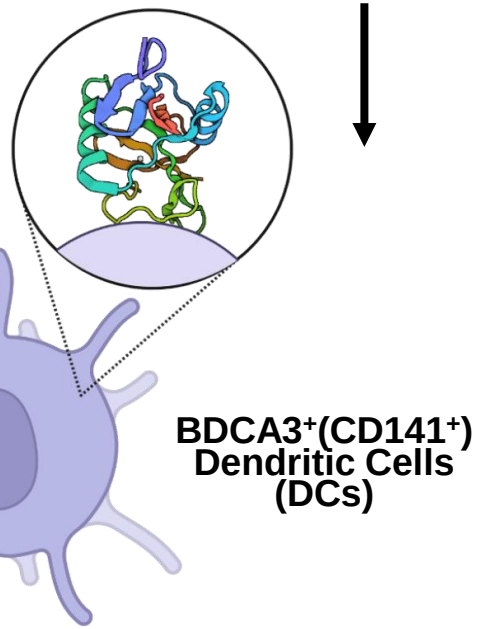
…TO TARGETING



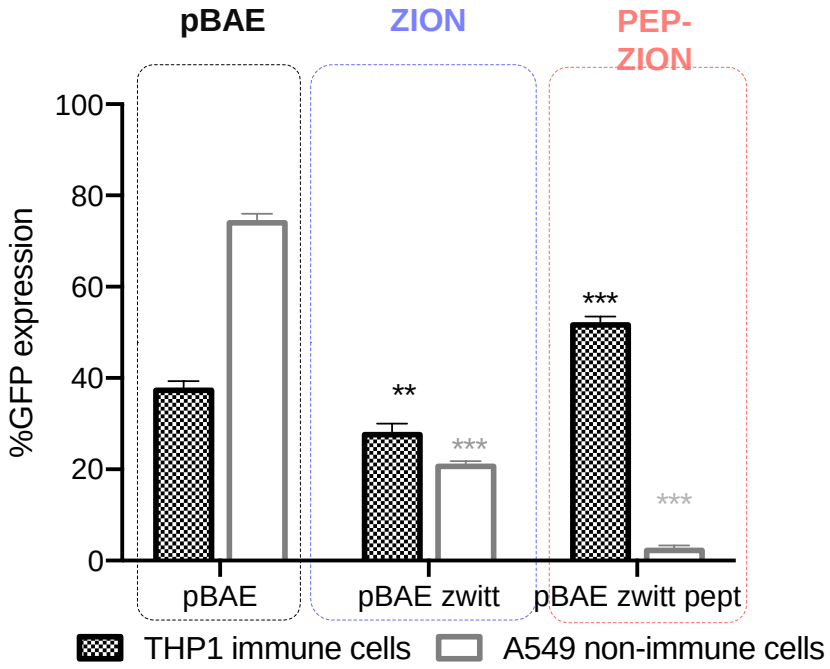
ZION, differential features facing the market

DENDRITIC CELLS-TARGETED NANOPARTICLES





DCs overexpress a family of lectin receptors, CELC9A, which are able to recognise f-actin.



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Coral García et al. *J Control Release, 2024*

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ZION, differential features facing the market

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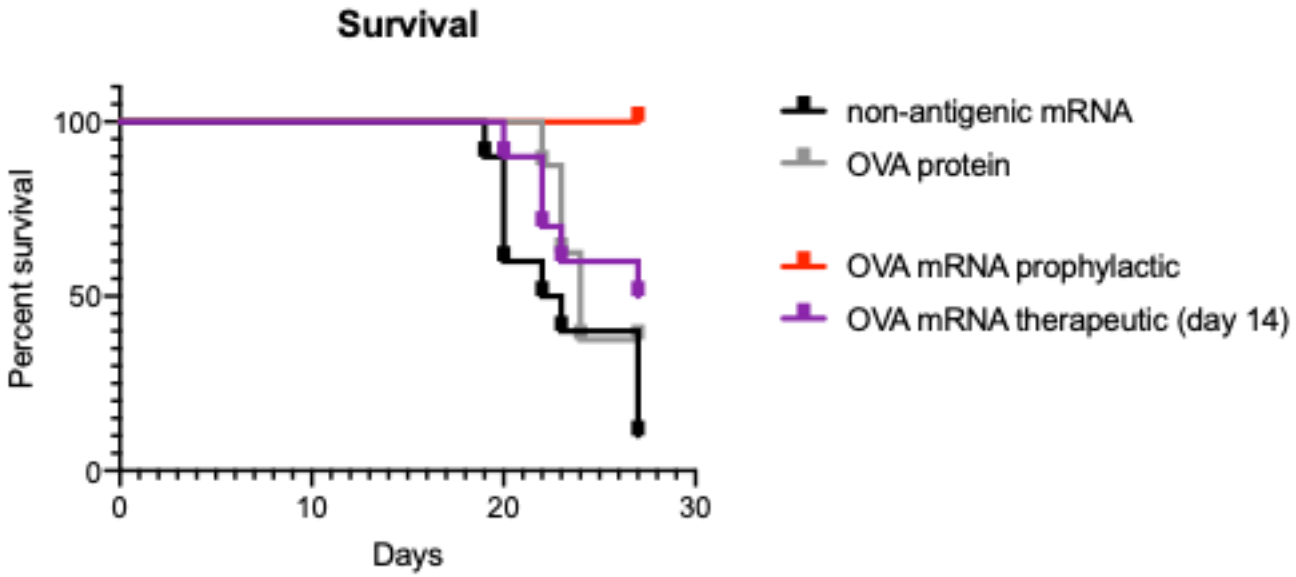

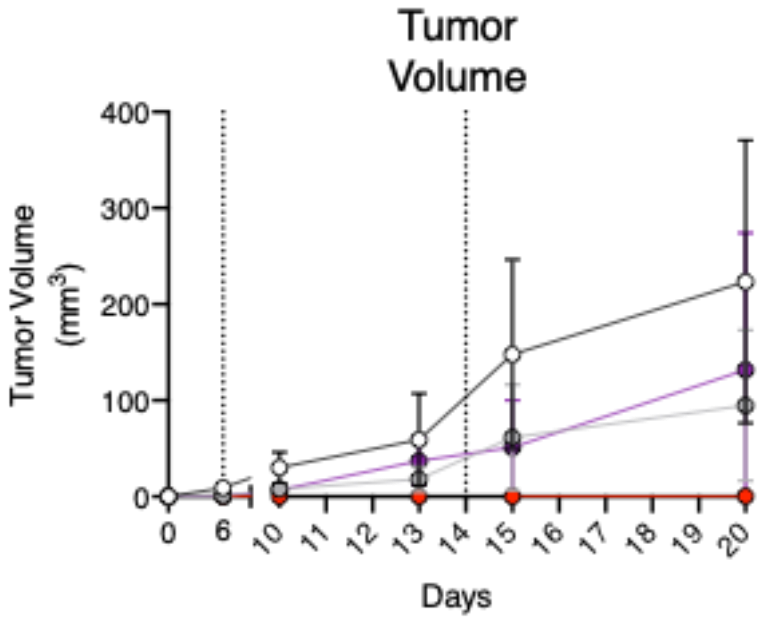

Prophylactic mRNA vaccination enables 100% survival

Prophylactic mRNA vaccination avoids tumor implementation.

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ZION, a really advantageous product

A PERSONALIZED mRNA VACCINE FOR THE TREATMENT OF SOLID TUMORS

Who are the competitors?

- Lipid nanoparticles from Moderna and BioNTech
- Already in clinicla trials for lung cancer and melanoma

Technical / market advantages from competitors:

- pBAEs not yet in the market --> first clinical trial starting on 2025-26 (CHIMERNA Project)
- No use of patented / already licences biomaterials
- No use of PEG → less immune reactivity
- No use of cationic lipids → cationic oligopeptides are protonable and more natural
- First targeted system proposed → higher therapeutic window

ZION, a really advantageous product

A PERSONALIZED mRNA VACCINE FOR THE TREATMENT OF SOLID TUMORS

Current status of development:

- PoC validated for melanoma in mice models
- Validated method of Production at industrial GMP scale
- PoC for lung cancer under development
- Adapting the technology for the inhaled administration

IPR protection:

- Patent in national phases since 2023

Pitfalls & Risks to be considered:

- Need to determine the antigenic cocktail → medical oncologists involved
- Personalized therapies → contact with producers

Content

Partnering opportunities: we can adapt to your needs

- ✓ Licencing out our proprietary technology for specific indications
- ✓ Developing new products as subcontracted partners of companies
- ✓ Applying to competitive calls with companies
- ✓ Preparing new Patents / products for companies

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Acknowledgements

Our team

Thank you for your attention!

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