Development of a new mRNA vaccine platform for Tuberculosis

Laura Matarazzo[1,2], Laura Taina-González[3,4], Ricardo Pinheiro[2], David Pires[1,2,5], María de la Fuente[4,6,7], Paulo J. G. Bettencourt[1,2]*

[1]Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, Lisboa, Portugal [2]Universidade Católica Portuguesa, Faculty of Medicine, Rio de Mouro, Portugal
[3]Universidad de Santiago de Compostela (USC), 15782 Santiago de Compostela, Spain. [4]DIVERSA Technologies, Santiago de Compostela, Spain
[5]Host-Pathogen Interactions Unit, Research Institute for Medicines, iMed-ULisboa, Faculty of Pharmacy, Universidade de Lisboa, Lisboa, Portugal
[6]Nano-Oncology and Translational Therapeutics Group, Health Research Institute of Santiago de Compostela (IDIS), SERGAS, Santiago de Compostela, Spain.
[7]Cancer Network Research (CIBERONC), Madrid, Spain * Correspondence: pbettencourt@ucp.pt

Introduction

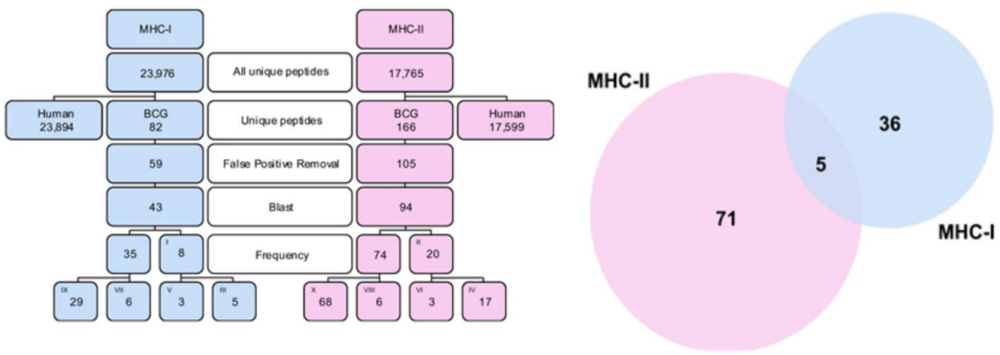
- Tuberculosis (TB) is the first cause of death by an infectious disease worldwide, killed 1.6 million people in 2021.
- Bacillus Calmette-Guerin (BCG), the only approved vaccine for TB, has inconsistent efficacy and does not prevent transmission, highlighting the need for new vaccine development.
- mRNA vaccine technology have been demonstrated as effective, safe and relatively easy and fast to produce in recent COVID-19 pandemic.
- This project aims to develop a new mRNA vaccine platform for TB, based on mRNA coding for antigenic peptides from BCG and *M.tb* identified by immunopeptidomics, and a new patented technology of lipid nanoemulsions (NE) as a carrier.

mRNA vaccine production

Antigen selection

Infection of macrophages with M. bovis BCG → **Immunoprecipitation and purification of HLA-bound peptides**

Mass spectrometry and peptide identification (LC/MS - MS, Peaks 8)



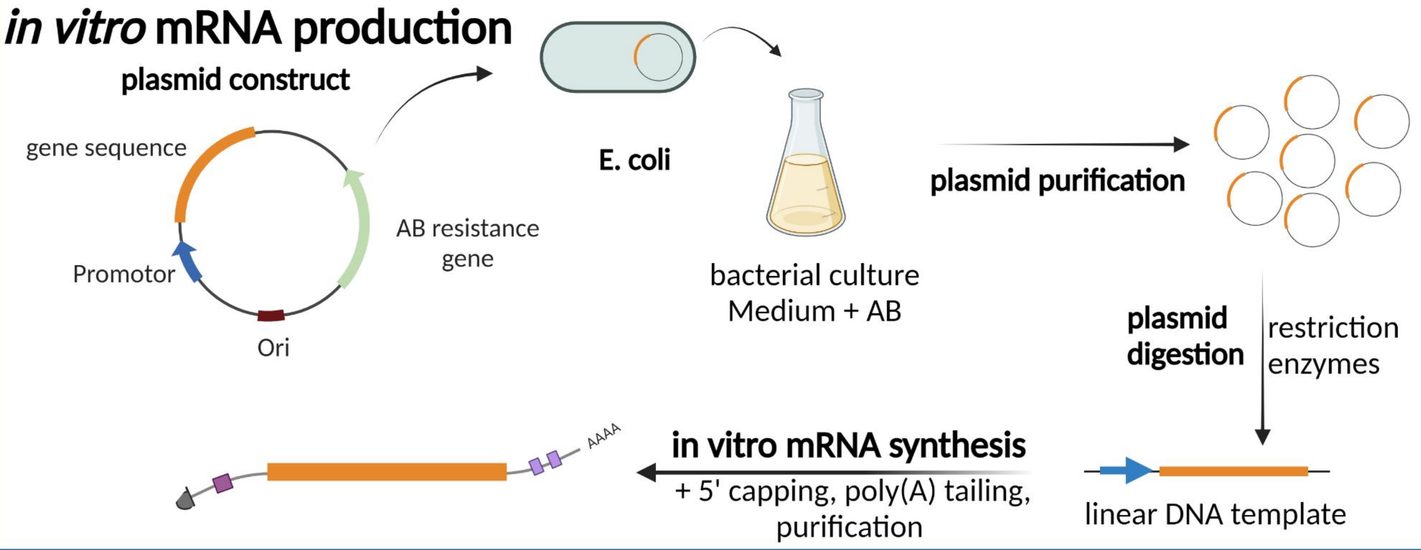
Antigen selection

Antigens selected		Identification		
Symbol	**Name**	**Exp.**	**Presented**	**Refs.**
BCG_3870c (glfT2)	Galactofuranosyl transferase	1	MHC-I	This study and Flyer et al (2002)
fas	Probable fatty acid synthase fas	2, 3	MHC-I and -II	This study
iniB	Isoniazid inductible gene protein iniB	N/I	N/A	Flyer et al (2002) McMurtrey et al (2017)
PPE15	PPE family protein PPE15	N/I	N/A	Stylianou et al (2018)
fbpA (Ag85A)	Diacylglycerol acyltransferase/ mycolyltransferase Ag85A	3, 4	MHC-I	This study and Stylianou et al (2015)

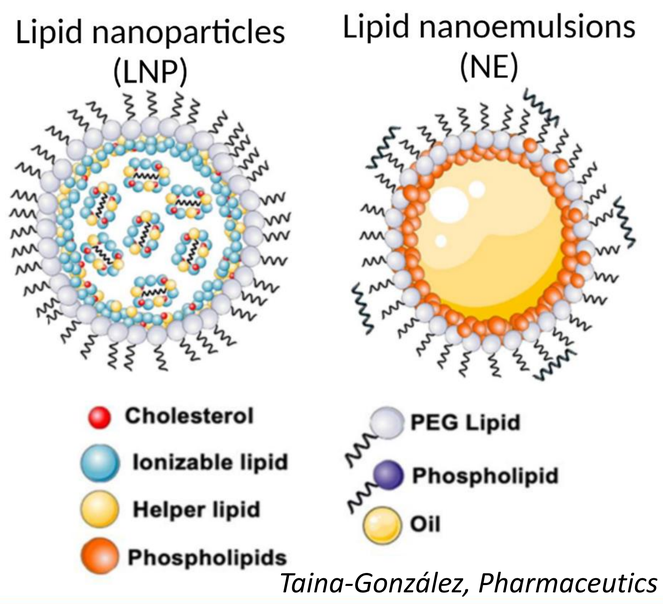
N/I – Not identified in this study.
N/A – Not available.

Bettencourt, NPJ vacines 2020

in vitro mRNA production

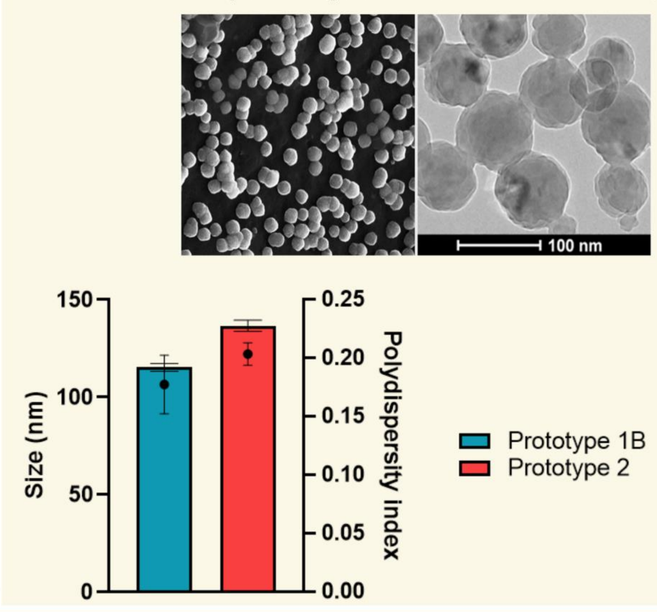


Lipid nanocarriers for mRNA delivery



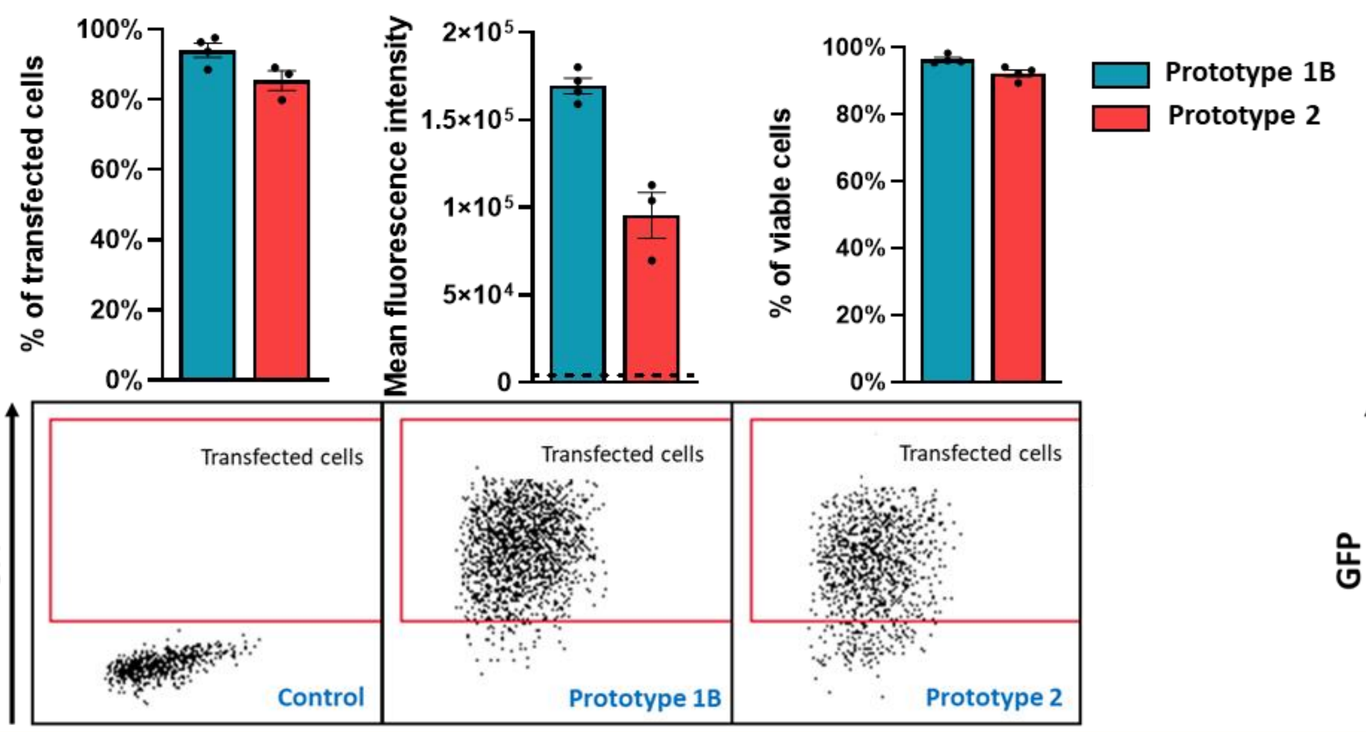
Taina-González, Pharmaceutics 2022

Characteristics of lipid NEs (patent WO 2019/138139 A1)

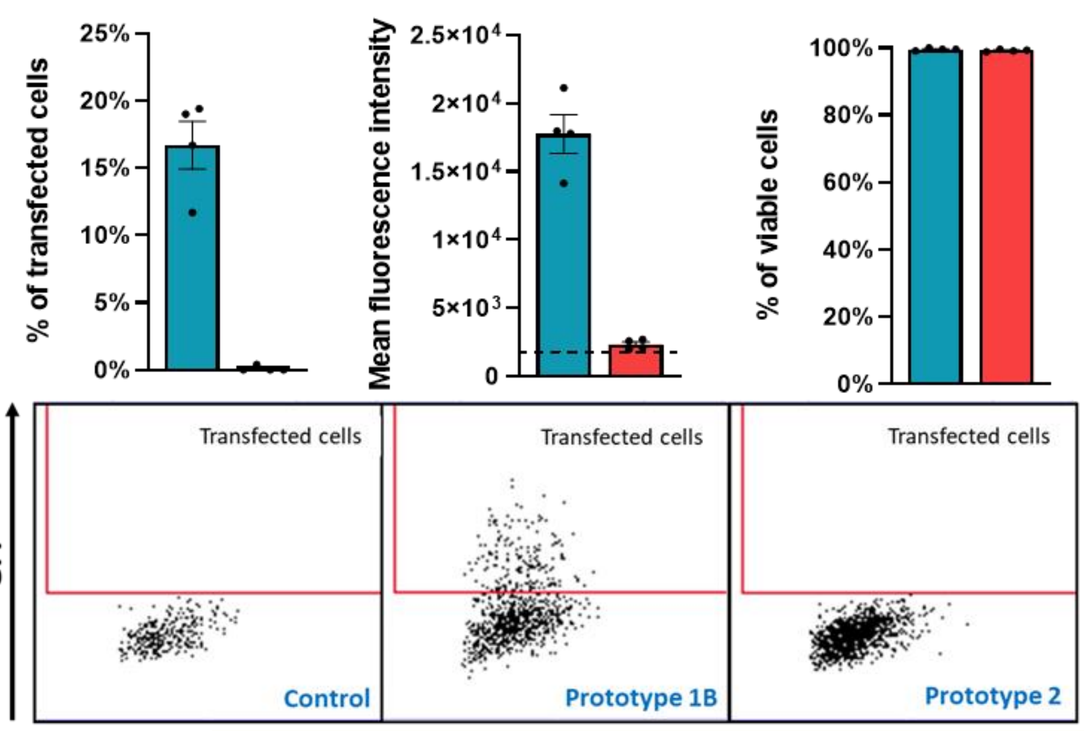


Transfection efficiency of NE – mRNA (GFP) formulations

A549 cells (human alveolar basal epithelial cells)



Human primary macrophages



Discussion

- The NE technology presented here is safe, stable, and can efficiently deliver mRNA to different cell types
- The lipid NE prototype 1B demonstrates greater transfection efficiency *in vitro*
- Selected NE formulations will be used as a carrier for a new vaccine candidate against TB, based on mRNA encoding relevant antigenic peptides
- The candidate vaccines will be tested in mice for safety, immunogenicity and efficacy against TB

References

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