

INVITATION PUBLIC DEFENSE

Pulmonary Delivery of Self-Amplifying RNA: From Inflammation Control to Protection against Respiratory Syncytial Virus

Qing Sun

30th November 2026
15:00h at Campus Merelbeke

PROMOTORS

Prof. dr. Niek N. Sanders
Faculty of Veterinary Medicine, Ghent University

Prof. dr. Xavier Saelens
VIB -UGent Center for Medical Biotechnology
Faculty of Sciences, Ghent University

Curriculum Vitae

Qing Sun was born on 1 February 1992 in Anhui province (China). She obtained her bachelor's degree in Traditional Chinese Medicine from Anhui Medical University in 2016 and her master's degree of Industrial Pharmacy from China Pharmaceutical University in 2019. Before starting her PhD study, Qing worked for two years as a research assistant in oncology pharmacology at Innovent Biologics Co., Ltd. Since October 2021, she has been pursuing her PhD study under the supervision of Prof. dr. Niek N. Sanders at the Laboratory of Gene Therapy, Faculty of Veterinary Medicine Ghent University, and of Prof. dr. Xavier Saelens at the VIB-UGent Center for Medical Biotechnology.

Qing has authored or co-authored several scientific publications and presented her research at multiple international conferences.

Where?

The defense will take place on **Monday 30 November 2026 at 15:00h**

Auditorium D (Entrance 19)

Faculty of Veterinary Medicine
Ghent University, Campus Merelbeke
Salisburylaan 133, Merelbeke

The public defense will be followed by a reception

How to attend?

If you would like to attend, please register before 20 November 2026, by email to Qing.Sun@UGent.be

Members of the Jury

Prof. dr. Herman Favoreel

Chairman of the Jury

Department of Translational Physiology, Infectiology and Public Health, Faculty of Veterinary Medicine, Ghent University

Prof. dr. Koen Raemdonck

Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Ghent University

Dr. João Paulo Portela Catani

VIB-UGent Center for Medical Biotechnology

Department of Biochemistry and microbiology, Faculty of Sciences, Ghent University

Prof. dr. Peter Delpitte

Department of Biomedical Sciences, University of Antwerp

Prof. dr. An Garmyn

Secretary of the Jury

Department of Pathobiology, Pharmacology and Zoological Medicine, Faculty of Veterinary Medicine, Ghent University

Summary

Respiratory diseases, encompassing both infectious and non-infectious conditions, represent a broad and diverse group of conditions affecting the airways and lungs, ranging from acute infections to chronic, life-limiting illnesses. Acute respiratory infections caused by pathogens such as *Mycobacterium tuberculosis*, influenza virus, SARS-CoV-2 and respiratory syncytial virus (RSV) continue to rank among the foremost causes of hospitalization and mortality globally. Recent innovations in structural biology, computational immunology, and high-throughput screening have transformed infectious disease research. Technologies such as peptide-major histocompatibility complex (pMHC) yeast display and artificial intelligence platforms, including immuScope and P-TEAM, have rapidly advanced the efficient identification of protective epitopes, thereby accelerating vaccine development. Self-amplifying RNA offers a key advantage as a drug payload through its intrinsic capacity for self-amplification, enabling transient yet high-level gene expression that yields potent and sustained protein production from a single, low-dose administration, all while circumventing the genotoxicity risks inherent to integrating viral vector systems. Targeted delivery of saRNA to the primary site of infection, such as the lungs in respiratory diseases, promotes localized deposition at the affected epithelial surfaces while largely circumventing systemic dissemination through the bloodstream. This localized delivery strategy not only maximizes saRNA-encoded protein production at the site of action, but also substantially reduces off-target biodistribution and accumulation in non-target organs, thereby enhancing both efficacy and safety profiles.

Chapter I provides a general introduction related to this thesis and cover four areas: (1) an overview of the most important RNA platforms, and strategies to reduce innate immunogenicity and boost protein production of synthetic mRNAs via nucleotide modifications; (2) in vivo delivery vehicles for synthetic mRNA; (3) saRNA applications and delivery barriers in respiratory diseases; (4) RSV biology, pathology, current prevention strategies, and emerging candidates.

Chapter II describes the scientific rationale and objectives of the the PhD thesis, which are: (1) optimizing LNP formulations and saRNA dose for maximal and prolonged transgene expression in mouse lungs; (2) characterizing the pulmonary inflammatory responses induced by intratracheal

saRNA-LNP delivery at the cytokine and innate 216 immune response level; (3) evaluating the feasibility of pulmonary delivery of saRNA-LNPs encoding SARS-CoV-2 nanobodies or RSV antigens.

Chapter III is the first research chapter and deals with the optimization of LNP formulations and saRNA dose to achieve maximal and prolonged transgene expression in mouse lungs, while limiting lung inflammation. Additionally, the mechanism of lung inflammation induced after pulmonary delivery saRNA-LNPs was elucidated from both cytokine and innate immune cell response perspectives. Finally, a proof-of-concept experiment involving the pulmonary delivery of saRNA-LNPs encoding nanobodies against SARS-CoV-2 is also reported.

Chapter IV describes the second research project, which focuses on the development of saRNA vaccines against RSV. In this chapter, the systemic and local adaptive immune responses were evaluated following intranasal, intratracheal, and intramuscular delivery of three doses of the saRNA^{WT-F} vaccine encoding the wild-type RSV F protein. The intratracheal route was identified as the most efficient respiratory route. Subsequently, after comparison of the saRNA^{WT-F} vaccine with a saRNA encoding a prefusion stabilized RSV F protein, the latter was selected as the better-performing vaccine candidate for subsequent RSV challenge experiments in mice immunized via intratracheal and intramuscular routes.

Chapter V provides the general discussion. It discusses the key findings and limitations of our research. It starts with a very short discussion on intratracheal administration, clinical nebulization devices and patient compliance. Subsequently, the characteristics of the self-amplifying RNA platform and its delivery systems are examined, with particular attention to the sometimes divergent requirements of saRNA vaccines and saRNA-based protein therapies. Furthermore, we highlight our observation that efficient intracellular delivery does not necessarily result in successful saRNA translation. We also demonstrate that intratracheal administration of saRNA-LNPs leads to transgene expression in multiple pulmonary cell types, a finding with important implications for the intended application of the platform, whether for vaccination or protein therapy. The discussion further addresses the use of membrane-anchored versus secreted viral antigens and their respective capacities to induce cellular and humoral immune responses. The various animal models employed in RSV vaccine development are also briefly reviewed. The chapter concludes with a discussion of the limitations of this PhD thesis and directions for future research.