



# InNOVative approach to optimize untraslated regions for next-generation mRNA vaccines.

## Introduction

Cancer represents a leading cause of mortality worldwide, with several tumors evading immune detection despite expressing recognizable antigens. **Therapeutic cancer vaccines aim to stimulate the immune system, particularly cytotoxic CD8<sup>+</sup> T cells, to recognize and eliminate tumor cells.** Among emerging strategies, mRNA-based vaccines offer a flexible platform for delivering tumor antigens.

## Unmet Medical Need

Current **mRNA-based** therapeutics, including cancer **vaccines**, typically **employ untranslated regions (UTRs)** selected for their ability to enhance mRNA stability and translation efficiency across diverse cell types. However, these UTRs are **not specifically optimized for antigen-presenting cells (APCs)**, where the primary goal is not just protein production, but effective antigen presentation, a key process to trigger a robust immune response, ensuring vaccines' efficacy. Indeed, high levels of antigen translation do not guarantee effective presentation to CD8<sup>+</sup> T-cells, as protein abundance poorly correlates with immunogenicity. Consequently, **commonly used UTRs may induce suboptimal antigen presentation and limit activation of CD8<sup>+</sup> cytotoxic T-cell responses, reducing vaccines' therapeutic efficacy.**

## Solution

NovaRNA has developed a **proprietary platform** that **redefines mRNA vaccine design** by selecting and engineering 5' and 3' UTRs from genes naturally expressed at high levels in human tissues. Using a **dual functional screening strategy**, employing either eGFP-encoding mRNA to assess translation or antigen-encoding mRNA to measure MHC-I presentation, the platform identifies **UTR pairs** that not only **boost protein expression** but also **enhance antigen presentation and downstream CD8<sup>+</sup> T-cell responses**. Furthermore, **rational UTR engineering was found to reduce innate immunogenicity**, lowering reactogenicity without relying on costly nucleoside modifications. The therapeutic relevance of these optimized UTRs was demonstrated by integrating them into an mRNA vaccine encoding a melanoma-associated antigen, which resulted in **stronger antigen-specific CD8<sup>+</sup> T-cell activation and improved survival in a murine melanoma model**. This project was supported by the Italian Ministry of University and Research through the National Recovery and Resilience Plan (PNRR) funding (CN00000041/CN3).

## Advantages

NovaRNA's platform enables **next-generation mRNA cancer vaccines** characterized by:

- **enhanced CD8<sup>+</sup> T-cells activation**
- **reduced innate reactogenicity**
- **high translation efficiency**
- simple and **affordable production**
- **broad applicability** across different antigens and disease models for prophylactic and therapeutic use.

## Opportunity

Istituto Europeo di Oncologia is seeking **industrial partners** (license or co-development opportunities) **and/or investors** interested in moving NovaRNA [TRL3] into clinical settings.

## Team



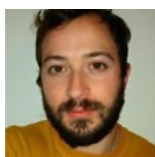
**Pier Giuseppe Pelicci, MD, PhD**

*Molecular Mechanisms of Cancer and Aging Group Leader at IEO; Advanced Molecular Diagnostic Centre Director at IEO; Professor at University of Milan; Alleanza Contro il Cancro (ACC) Scientific Coordinator.*



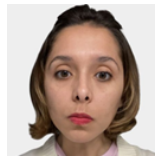
**Saverio Minucci, MD**

*Chromatin Alterations in Tumorigenesis Group Leader at IEO; New Drugs Program Director at IEO; Preclinical Drug Testing Unit Coordinator at IEO; Professor at University of Milan.*



**Stefano Persano, PhD**

*Molecular Mechanisms of Cancer and Aging Postdoctoral Researcher at IEO; Assistant Professor at University of Milan.*



**Maria Guevara, PhD**

*Molecular Mechanisms of Cancer and Aging Postdoctoral Researcher at IEO.*



**Federico Arlati, MSc**

*Chromatin Alterations in Tumorigenesis PhD Fellow at IEO and University of Milan.*

**IP asset:** Patent application IT-102025000026428; co-owned by IEO and University of Milan.

## Contact:

Marzia Fumagalli, Head of Technology Transfer Office · [marzia.fumagalli@ieo.it](mailto:marzia.fumagalli@ieo.it) ; [tto@ieo.it](mailto:tto@ieo.it) · +39 02 9437 5179