IEO
Istituto Europeo di Oncologia

NovaRNA

# 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⁺ 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⁺ T-cells, as protein abundance poorly correlates with immunogenicity. Consequently, **commonly used UTRs may induce suboptimal antigen presentation** and **limit activation of CD8⁺ 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⁺ 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⁺ T-cell activation and improved survival in a murine melanoma model**.

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## Advantages

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

- **enhanced CD8⁺ 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

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

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