

Circular RNA

Enhanced circular RNA translation for therapeutic and immunogenic protein production

Invention

Scientists of the University of Bonn and Stanford University have discovered that mammalian IRES-like sequences can overcome the efficiency limitations of eukaryotic translation initiation in circular RNA therapeutics. This breakthrough technology could transform RNA-based therapeutics by allowing sustained protein expression from stable circular RNA, with applications ranging from cancer treatment to enzyme replacement therapy and RNA-based vaccines. IRES (Internal Ribosome Entry Site) sequences are crucial for initiating protein translation in circular RNA, but current solutions rely heavily on viral sequences which pose significant limitations for therapeutic applications. While eukaryotic IRES-like sequences offer a safer alternative, their efficiency has traditionally been much lower than their viral counterparts. Particularly interesting are the IRES-like sequences found in Hox genes, which play critical roles in tissue development through their precise spatiotemporal expression patterns. The development of effective non-viral IRES sequences for circular RNA could provide a new path forward for long-term protein delivery in diseases requiring sustained therapeutic protein expression. IRES-like sequences from mouse Hox genes enabled highly efficient cap-independent translation in circular RNA constructs. These sequences demonstrated superior translation efficiency compared to other eukaryotic IRES sequences, while maintaining the safety advantages of non-viral elements. Importantly, the system allows for fine-tuned protein expression through targeted 2-4 nucleotide mutations in the IRES-like sequences, enabling precise control over generated therapeutic protein levels.

Commercial Opportunities

This technology has broad potential applications and could significantly advance the field of RNA therapeutics by enabling sustained protein expression with lower dosing requirements.

Applications include

- Production of therapeutic proteins for sustained expression
- Development of RNA-based vaccines with enhanced stability
- Generation of enzymes for metabolic disorders
- Expression of tumor-suppressing proteins for cancer treatment

Current Status

The technology is available for licensing e.g. for in house use in biotech-/pharmaceutical companies as well as for commercialization as a research tool/device. A US provisional patent application has been filed.

An invention from the Rheinische Friedrich-Wilhelms-University Bonn and Stanford University (Docket S24-141).

Advantages

- Higher translation efficiency
- Lower dosing
- Tunable protein expression
- Avoids safety concerns associated with viral IRES elements

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Technology validated in lab

Sector(s)

- Pharmaceutical industry
- Biotechnology industry

Ref.-No.

7067



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