

## Designer antisense-circular RNAs (AS circRNAs) for the inhibition of pre-mRNA splicing and mRNA translation

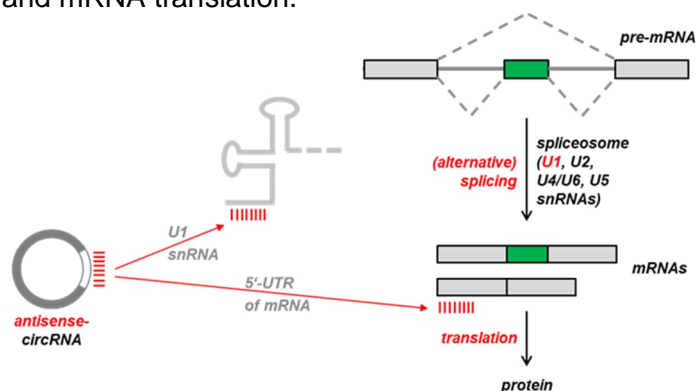
molecular medicine, antisense circRNAs, genetic disease, cancer, RNA therapeutics

### DESCRIPTION OF TECHNOLOGY

Antisense approaches are an innovative and growing field of gene therapies. Best known are therapies based on linear antisense oligonucleotides (ASOs), but they show deficits in efficiency, stability, and off-target effects.

Circular RNAs (circRNAs), which are generated from pre-mRNAs by an alternative splicing mechanism called back-splicing, show higher stability than their linear counterparts. This and other emerging features like miRNA sponging, protein sponging, and protein translation, make them attractive for novel RNA therapeutics.

We present two new lines of designer antisense-circRNAs (AS-circRNAs), which are capable of influencing pre-mRNA splicing and mRNA translation.



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AS-circRNAs targeting U1 snRNA can inhibit pre-mRNA splicing and modulate alternative splicing patterns.

AS-circRNAs targeting the 5'-untranslated region (5'-UTR) can inhibit mRNA translation.

### APPLICATION FIELDS

- Novel designer RNA therapeutics to be applied in molecular medicine, targeting multiple stages of gene expression.
- As pharmaceutical composite for treatment or prevention of proliferating diseases such as cancer.
- Possible use for treatment of humans and animals

### AT A GLANCE ...

#### Application Fields

- RNA therapeutics
- Cancer treatment/therapy
- Pharmaceutical compositions
- Molecular applications

#### Business

- Pharmaceutical industry
- Molecular biology
- Molecular medicine

#### USP

- More stable than linear RNA
- Inhibition and modulation of (alternative) pre-mRNA splicing and mRNA translation

#### Development Status

- successful proof-of-principle study

#### Patent Status

Priority application filed on 05.05.2023 with the European Patent Office. International PCT patent application is planned.

## ADVANTAGES OVER THE PRIOR ART

CircRNAs show following advantages:

- much more stable than corresponding linear RNA
- high binding specificity
- highly flexible in sequence design and target specificity

## STATE OF PRODUCT DEVELOPMENT

Proof-of-principle study was successful in assessing *in vivo* functionality of designer circRNAs.

Study showed that AS-U1 circRNA can be applied to modulate alternative splicing patterns (target: U1 snRNA) or protein translation (target: 5'-UTR) *in vivo*.

Designer circRNAs appear to be superior to standard antisense oligonucleotides (ASOs) and can be produced in preparative quantities by *in vitro* transcription and circularization.

## MARKET POTENTIAL

Increasing investments in R&D and a growing number of approved drugs for a wide range of applications, including orphan drugs and personalised medicine, make RNA-based therapeutics a highly attractive and innovative market.<sup>1</sup>

Recent research papers predict that circRNAs, due to their high metabolic stability and specificity, will open up new perspectives in molecular medicine and disease treatment.<sup>2</sup>

## COOPERATION OPPORTUNITIES

On behalf of Justus-Liebig-University Giessen, TransMIT GmbH is looking for cooperation partners or licensees worldwide.

<sup>1</sup>Winkle, El-Daly, Fabbri, Calin (2021). Noncoding RNA therapeutics - challenges and potential solutions. *Nat Rev Drug Discov.* Aug;20(8):629-651. doi: 10.1038/s41573-021-00219-z.

<sup>2</sup>Liu, Chen (2022). Circular RNAs: Characterization, cellular roles, and applications. *Cell.* Jun 9;185(12):2016-2034. doi: 10.1016/j.cell.2022.04.021.

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