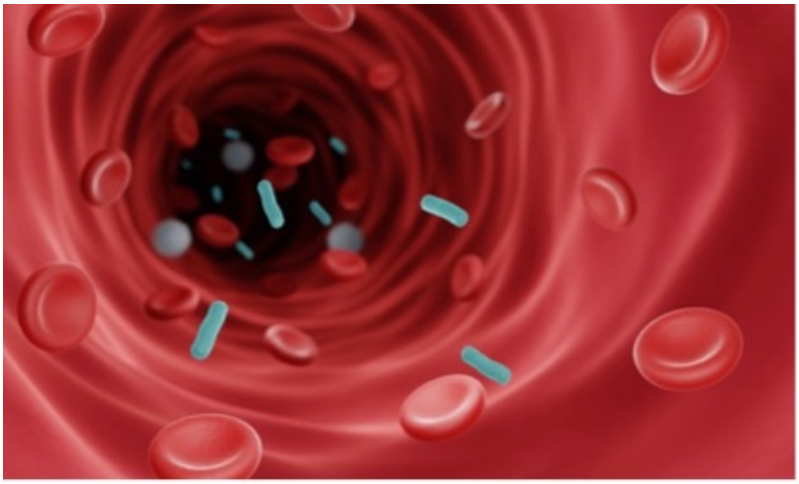
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Splice-Switching Antisense Oligonucleotides for Treating NLRP3-mediated Inflammatory Disease

TECHNOLOGY NUMBER: 2024-540



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Category
Therapeutics and Vaccines
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OVERVIEW

Antisense oligonucleotide technology to reduce pathogenic inflammation

- Targets RNA splicing to degrade harmful NLRP3 protein production
- May treat autoimmune diseases, sepsis, chronic inflammatory conditions

MODALITY

Injectable antisense oligonucleotide (ASO) therapy

INDICATION

Treatment of NLRP3-mediated inflammatory and autoimmune diseases, including CAPS (Cryopyrin-Associated Periodic Syndromes), sepsis, and other related chronic inflammatory disorders

PUBLICATIONS

"Modulating NLRP3 splicing with antisense oligonucleotides to control pathological inflammation"

INTELLECTUAL PROPERTY

Patent pending

BACKGROUND

Chronic inflammatory diseases, such as CAPS (Cryopyrin-Associated Periodic Syndromes), are often driven by gain-of-function mutations in the NLRP3 gene that result in excessive inflammation. Historically, treatments aim to manage symptoms rather than targeting the underlying cause. Traditional anti-inflammatory drugs can have broad systemic effects and may not adequately address the dysregulated protein production. With no cure available for CAPS and similar inflammatory conditions, the need for a targeted, efficient therapeutic approach to directly reduce the production of the harmful NLRP3 protein is urgent. Antisense oligonucleotides (ASOs) provide a promising strategy by specifically targeting RNA transcripts to prevent the synthesis of dysfunctional proteins.

INNOVATION

Researchers have developed a modified antisense oligonucleotide (ASO) designed to induce aberrant splicing of exon 2 of the NLRP3 RNA transcript. This intervention disrupts the open reading frame, introducing a premature termination codon, leading to the production of an unstable, non-functional mRNA. Consequently, the amount of functional NLRP3 protein is significantly reduced. In mouse models of CAPS disease, this ASO approach has shown therapeutic efficacy in reducing disease severity. Furthermore, it has demonstrated the potential to decrease inflammatory responses in sepsis models. Real-world applications include the treatment of autoimmune diseases like CAPS, sepsis, and other conditions characterized by chronic inflammation, offering a targeted solution to mitigating excessive inflammatory responses.