RNA Interference (RNAi) and the Future of Drug Development

The History of RNAi

- Alnylam is leading the translation of RNA interference (RNAi) as a potential new class of innovative medicines. The science of RNAi is widely considered one of the most promising and rapidly-advancing frontiers in biology and drug development today.[1]
- Historically, the role of RNA was only thought to be involved in protein synthesis. However, in recent years RNAs have been identified to also play significant roles in regulatory functions within the cell.[1]
- A specific class of RNA, called small-interfering RNA (siRNA), appeared to exert cellular control resulting in gene silencing. This mechanism of interference might work not only in worms, but has been also shown to occur in plants, invertebrates, and mammals.[2]
- In 2001, researchers confirmed that siRNA-mediated gene silencing did, indeed, occur in human cells.[3] This form of gene silencing has since become widely known as RNA interference, or RNAi for short. In 2006, Andrew Z. Fire, Ph.D., and Craig C. Mello, Ph.D., were awarded the Nobel Prize in Medicine, honoring their discovery of a fundamental RNA-based mechanism controlling the flow of genetic information.[4] Today, after years of research, investigational therapies based on this discovery are in late-stage clinical development.

A Potential New Approach to Human Therapeutics

- At the heart of the RNAi mechanism is a protein complex known as RISC (the RNA-induced silencing complex), a key component of the RNAi pathway. Researchers have found that RISC can bind to siRNAs that have been designed to be a complementary match for strands of the target mRNA. Once bound to the siRNA, RISC prowls the cell, searching for a lock-and-key match to the siRNA strand it carries. When it finds a matching mRNA, it degrades it. This cleavage disrupts synthesis of the protein.[5]
- Drugs based upon RNAi are a potential new class of human therapeutics. Traditionally, drugs have been developed to stop the activity of disease-causing proteins directly, but do not get to the root cause. Potential RNAi therapeutics are designed to "turn off" or silence unwanted or harmful proteins at their source.
- Because siRNAs can be designed to target essentially any protein-coding mRNA, this opens up possibilities for addressing a variety of genetically-validated targets.[5] siRNAs can also be designed to exhibit great specificity and can enter into the cell to silence the expression of intracellular proteins. Clinical trials are currently being conducted to evaluate the safety and efficacy of using this promising approach for a number of human diseases.
- Alnylam is leading the translation of RNAi into a potential new class of innovative medicines with the possibility to transform the lives of patients who have limited treatment options.
- Alnylam is advancing its proprietary RNAi delivery technology known as the Enhanced Stabilization Chemistry (ESC)-GalNAc-conjugate delivery platform to enable subcutaneous administration.

RNAi Fast Facts

- Alnylam, founded in 2002, is focused on advancing RNAi therapeutics as the next potential class of innovative medicines.
- Andrew Z. Fire, Ph.D., and Craig C. Mellow, Ph.D., were awarded the Nobel Prize for Medicine in 2006 for their groundbreaking work that revealed a novel RNA-based mechanism for gene silencing – RNAi.
- siRNAs activate RISC, then silence gene expression by targeting specific messenger RNAs (mRNA) and inhibiting synthesis of the targeted protein.
- As of April 2017, the company has eight clinical programs.

For more information, please contact media@alnylam.com or visit alnylam.com.

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