Antisense Oligonucleotide Therapy for Genetic Disorders

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Advances in deciphering the complex roles RNA plays in normal health and disease have been substantial over the past decade, and RNA is becoming an increasingly important target for therapeutic intervention. Antisense oligonucleotides (ASO) are perhaps the most direct therapeutic strategy to approach RNA, and ASO technology has emerged as a powerful alternative to conventional small molecule approaches or gene replacement strategies for the treatment of genetic disorders. ASO are short, synthetic single-stranded DNA sequences designed to bind to target RNA by well-characterized Watson-Crick base pairing, and once bound to the target RNA, can modulate RNA function through a variety of post binding events. ASO-mediated gene silencing occurs either through degradative mechanisms, where the target RNA is cleaved by endogenous nucleases, or non-degradative mechanisms, where sterically bound ASO block or modulate translation, capping, or splicing. The majority of ASO drugs in development work through the RNaseH1 dependent degradation mechanism.

This presentation will cover antisense technology platform and will include new preclinical data on the characterization of mouse Gys1 ASOs, a potential novel therapy approach for APBD and Lafora disease.