Docket #: S21-353

Small interfering RNA (siRNA) therapy PLN-R14del cardiomyopathy

Phospholamban (PLN) regulates cardiac contractility and modulates sarcoplasmic reticulum (SR) Ca2+ sequestration by inhibiting the dephosphorylated SR Ca2+-ATPase (SERCA). Arginine 14 deletion from the PLN gene (PLN p.R14del) has been linked to the pathogenesis of inherited cardiomyopathy with prominent arrhythmias. Patients with the PLN R14del mutation may develop dilated or arrhythmogenic right ventricular cardiomyopathy. Although a clear link has been established between the mutation and cardiac disease, there are currently no treatments for patients.

Stanford researchers developed an allelic-specific silencing approach by interfering with RNA (RNAi) to reduce the expression levels of the PLN R14del allele. They designed, tested, and identified RNAi oligonucleotides that specifically decrease the expression of the R14del allele by 50-70% in patient-derived induced pluripotent stem cell cardiomyocytes (iPSC-CMs) without affecting the normal wild-type allele. These data suggest that the PLN R14del allele can be selectively, specifically, and efficiently targeted by RNAi oligonucleotides.

Stage of Development
Proof of concept

Applications

- Disease-specific gene therapy for PLN R14del cardiomyopathy

Advantages

- Novel treatment for PLN R14del cardiomyopathy

Patents

- Published Application: WO2023215481

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