Docket #: S18-210

Retinoic Acid to treat RBM20-dependent dilated cardiomyopathy

Researchers at Stanford have developed a method of using retinoic acid to treat dilated cardiomyopathy (DCM). DCM, a heart disease characterized by enlargement of the left ventricle and reduced systolic function, is the leading cause of heart failure and most common indication for heart transplant. Recently, efforts have been made to identify the genetic causes of DCM. Mutations in RBM20 (a regulator of heart-specific splicing of genes for muscle function) are associated with early onset of DCM, end stage heart failure and increased incidence of sudden death. Currently, despite the genetic understanding, therapeutic strategies to treat DCM only manage the symptoms. Thus, there is a need for better methods to treat DCM. To help meet this need the inventors have taken advantage of the understanding of the genetic causes of DCM to develop a method to treat RBM20-dependent DCM. RBM20 mutations reduce the functional level of RBM20 leading to DCM. Here, the inventors provide a method of using retinoic acid to increase the RBM20 levels. This leads to reversion of the splicing defect and mitigates the cellular phenotypes of DCM. This technology offers a new therapeutic strategy to treat DCM and has the potential to improve the care of patients with RBM20-dependent DCM.

Stage of research
Using iPSC-derived cardiomyocytes, the inventors have shown that upregulation of RBM20 by retinoic acid corrects the splicing defects and ameliorates the clinically relevant phenotypes.

Applications

- Treatment of RBM20-dependent dilated cardiomyopathy

Advantages

- New therapeutic strategy to more effectively treat DCM
- Easily accessible
- Limited and easy to monitor side effects
- Treats the molecular cause of the disease rather than the symptoms

Publications

- F. Briganti et al iPSC Modeling of RBM20-Deficient DCM Identifies Upregulation of RBM20 as a Therapeutic Strategy *Cell Reports* Sept. 2020.

Patents

- Published Application: WO2020092171

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