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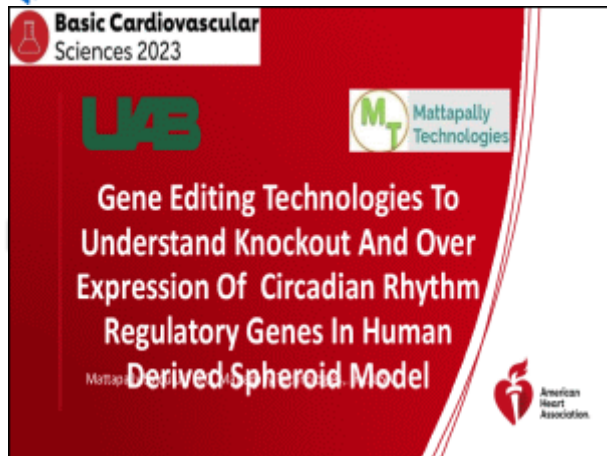


Posters

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BCVS

Gene Editing Technologies To Understand Knockout And Over Expression Of Circadian Rhythm Regulatory Genes In Human Derived Spheroid Model.



Cardiac Regeneration, Stem Cells and Tissue Engineering

APS.01 | Poster Session 1

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Author(s): Saidulu Mattapally, Mattapally Technologies, Birmingham, AL; Wesley C Labarge, Gregory Walcott, Univ of Alabama at Birmingham, Birmingham, AL; Chandrakala Mattapally, Mattapally Technologies, Birmingham, AL; Jianyi J Zhang, UNIVERSITY OF ALABAMA AT BIRMINGHAM, Birmingham, AL

Introduction: Human induced pluripotent stem cells (hiPSCs) have the ability to produce a huge variety of terminally differentiated cell types that can be used for tissue engineering, drug research, and cell therapy. Using CRISPR/Cas9 gene-editing technologies, hiPSCs with knockout mutations for Per1, Per2, CIITA, B2M, N-Cadherin, Connexin43 and over expression of Connexin43 were created. Cardiomyocytes (CM) were created from hiPSCs, and spheroid culture was carried out as previously described. The molecular basis of circadian regulation of human induced pluripotent stem cells (hiPSCs) is still under investigation. **Methods:** From hiPSCCMs, we created and described a 3D spheroid culture. We assessed the effectiveness of spheroid transplantation for cardiac healing in immunocompromised mice and pigs. We investigated border zone macrophage markers, border zone vascular density, and cell proliferation in myocardial infarction after spheroid transplantation. We used pedigree analysis and 20 years of family health diagnostics data to analyze the clinical consequences of type 2 diabetes medications among metformin combo patients in big extended family (N=30).. **Results:** TNF-Alpha, IL1-beta, NOS2, and IL-6 relative expression were shown to be lower in the KO group than in the WT group. Significant engraftment of hiPSC-derived cardiac spheroids was seen up to 4 weeks after transplantation, according to histological examination. Arrhythmogenicity is significantly altered by the spheroid therapy. Ventricular tachycardia may be related to macrophage immunological regulation. To further understand, we looked at the effects of a medication combination of dapagliflozin and metformin in a large extended family, where 5 out of 30 members had type 2 diabetes. One patient experienced mildly tachycardic heart issues over the course of a 20-year medication treatment. **Conclusion:** Our study established the promising therapeutic potential of spheroids model from hiPSCdifferentiated CMs to understand Circadian rhythm gene regulation.

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