An optimal approach for optogenetic to control function of cardiac and neural cell in vitro and in vivo

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Introduction: Optogenetic, which is a novel and useful tool due to its unique ability to act on specific neuronal groups, has gained wide application in basic and clinical medical researches. It can manipulate different groups of specific neurons at the same time at the right location. Therefore, our novel objective of the study is to use optogenetics to specifically dissect the complex network of sympathetic and parasympathetic nerve functions in cardiac diseases. However, the primary goal of this study was to produce neural progenitor cells from human induced pluripotent stem cells (iPSC) with a differentiation protocol established for the co-culture system. This research project is a bold first attempt to further develop these important experimental techniques toward optogenetic applications in neurocardiology.

Methods: AAV vectors have successfully manipulated CNS function using a wide variety of approaches including expression of foreign genes, expression of endogenous genes. With the discovery and characterization of different AAV serotypes, the potential patterns of in vivo vector transduction have been expanded substantially, offering alternatives to the more studied AAV 2 serotype.

Result: Schematic depicts neural differentiation process and the conversion of I into ChR2-expressed motor neurons. Optogenetically controlled with ChR2-expressing iPSC-derived motor neurons when they were under 430 nm blue light stimulation. Following optogenetic activation of neurons, the motor neuron derived from iPSC were quickly demonstrated action potentials, while immediately down after stimulation. The ChR2-expressed neurons exposed to 430nm blue light stimulation enabled regulation of membrane voltage and depolarized the cells. The results confirm that we generated iPSC into functional neurons. The efficiency of transfection is a key point to dominated successful or fail treatment. Cardiomyocytes is non-monolayer cell type and it is connected to each layer and cells. However, it is interesting that when one of cardiomyocyte is stimulated, the neighborhood is also changed action potential at the same time. After AAV virus injection for four to six weeks, the heart is excised, perfused with Tyrode's buffer ex vivo. However, when the heart is illuminated by blue light, the heart is coordinated with stimulation.

Conclusion: We derived motor neuron form iPSC and they can from physical and functional connections with smooth muscles cells. We aimed to further probe the effect of optogenetic in iPSC-derived motor neurons, specifically determining the sufficiency of this optogene function for the development of the in vitro phenotypes. We adopted a co-culture strategy for this purpose, providing a valuable tool in the future. The potential of iPSC could be further valorized by generating other cell types that may be relevant to the pathology and more clinically relevant.