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# Suppressing Cardiac Activity with Light Using Combined Cell and Gene Therapy

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**Background:**
The use of light sensitive proteins for controlling excitable tissues is known as optogenetics.
This method has revolutionized neuroscience since it enables a precise control of neural excitation with high temporal and spatial precision both in-vitro and in-vivo. In this study we attempted to evaluate the ability of this technology to modulate cardiac excitability as a novel anti-arrhythmic strategy. Specifically, our aim was to evaluate whether cell grafts, genetically engineered to express hyperpolarizing light sensitive proteins, could be used to suppress cardiac excitability.

**Methods and Results:**
HEK 293 cells were transfected to express the light-sensitive proton pump Archaerhodopsin-3 (Arch). The HEK-Arch cells were co-cultured with either neonatal rat cardiomyocytes (NRCM) or human embryonic stem cell-derived cardiomyocytes (hESC-CMs), and plated on 252 or 60 electrodes multielectrode array (MEA). Conduction maps and beating frequencies were calculated prior, during, and following illumination (590nm LED).
Illumination of the grafted area in the co-culture resulted in:
1) Significant suppression of the hESC-CMs beating rate (from 85.8±45.8 to 28.0±22.6 beats/min, $p<0.001$);
2) Localized termination of the electrical activity in all the NRCM co-culture studies;
3) Generation of localized conduction blocks (leading to dyssynchrony in the electrical activity) in some of the NRCM co-culture studies following focused illumination. All changes were found to be dependent on the LED output currents and the distance from the light source, and were reversible upon termination of illumination.

**Conclusions:**
A combined gene and cell therapy approach, using cells engineered to express light-sensitive hyperpolarizing proteins, could be used to modulate cardiac excitability. This novel approach could be used to suppress cardiac excitation, and could be potentially used in the future for the treatment of different tachyarrhythmia.