

HCN4-GCaMP8 Mice Useful for Optically Mapping Conduction System of Heart

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Optical mapping is an incredibly valuable and widely used experimental tool in cardiac electrophysiology. It provides the unique opportunity to study monophasic action potentials of the isolated beating heart with high spatial and temporal resolution. It is made possible by the incorporation of voltage-sensitive dyes (to measure changes in the cell membrane potentials), calcium dyes (to measure the cellular activity of the myocardium), and excitation-contraction uncouplers (to remove excess motion from physical heart beats). Overall, optical mapping is a very useful tool for revealing spatial and temporal changes of cardiac action potentials in the development of heart failure, arrhythmias, metabolic diseases, and the like; however, this experimental technique relies on the injection of fluorescent dyes in ex vivo Langendorff-perfused hearts, and it is up to the researcher to manually process signals of interest. A newly developed mouse by the Cornell Heart Lung Blood Resource for Optogenetic Mouse Signaling Lab (CHROMus) uniquely expresses the genetically encoded calcium indicator GCaMP8 under control of the HCN4 promoter, directing expression to the sinoatrial (SA) node and the atrioventricular (AV) node of the heart and the nervous system. GCaMP8 responds to calcium levels in the cell, so when calcium increases, a conformation change occurs and fluorescence increases. This mouse is useful for examining calcium signaling in the conduction system of the heart. We have incorporated this mouse into our colony at GW as a new method for optically mapping calcium transients in the beating heart, without the need for injecting artificial fluorescent dyes to optically map monophasic action potentials. This mouse is the first of its kind to be proven beneficial for intrinsically mapping calcium handling of the SAN with high spatial and temporal resolution.