

E. Railey White, MD, PhD

University of Pennsylvania

The molecular mechanism of propofol analogues on the depression of myocardial contractility

Abstract

The mechanisms of anesthesia have been debated for decades, but anesthetics do more than sedation and hypnosis. Fropofol is a fluorinated analogue of propofol that exhibits the negative inotropy of propofol without its anesthetic endpoints. These characteristics make it a potential pharmacologic treatment of hypertrophic cardiomyopathy (HCM). Propofol binding sites in myocardial proteins have previously been identified with photoaffinity labels (PALs), and this work will use this same technique to identify binding sites for fropofol. Genetically modified zebrafish lines will be used to test the mechanistic importance of these sites and confirm their role in cardiac depression via characterization with in-vivo measurements of cardiac contractility. Pharmacologic effects of propofol will be correlated to direct measurements of contractile force in ex-vivo ventricular tissue. Together, these studies will provide further understanding of propofol and fropofol's mechanism of cardiac depression that could generate a novel pharmacologic therapy for HCM.