

Candida Goodnough, MD, PhD

Stanford University School of Medicine, Stanford, CA

Understanding Anesthetic Mechanisms in the East Asian Population

Abstract

Alcohol use has a major impact on an individual's sensitivity to general anesthetics. However, little is known whether an intolerance to alcohol will impact general anesthesia. This is significant to understand as over half a billion people are alcohol intolerant due to a variant in the mitochondrial enzyme aldehyde dehydrogenase 2, known as ALDH2*2. The central hypothesis of this proposal is that decreased aldehyde metabolism by ALDH2*2 will cause an increase of the redox state of the brain and delay emergence from general anesthesia. In order to address this hypothesis, we will use cutting-edge and innovative techniques including in vivo metabolic imaging, bioenergetics, and rodent behavioral assays to determine the impact of aldehyde metabolism on the redox state of the brain during general anesthesia. Aim 1 will define the observed phenotype of delayed emergence from anesthesia in mice with the ALDH2*2 variant with behavioral assays. An activator of ALDH2 will be used to rescue the phenotype. Aim 2 will describe the metabolic consequences of altered aldehyde metabolism in isolated cerebellar astrocytes with mitochondrial function assays and in vivo whole brain with ³¹P magnetic resonance spectroscopy imaging. To address this question and to provide career development, I recruited a multidisciplinary mentorship team that provides expertise in aldehyde metabolism, mitochondrial bioenergetics, anesthesiology, and neuroscience. The career development portion of this grant will enable Dr. Goodnough to gain new experimental skills that will complement prior training in small animal imaging in addition to preparing her for a long-term, independent career as a leader in personalized anesthesia. In summary, Dr. Goodnough's proposal promises to offer mechanistic insights into the altered sensitivity to general anesthesia with ALDH2*2 while also preparing her for a career as an academic anesthesiologist.