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Anesthetic effects on mitochondrial localization during neural development in zebrafish

Abstract

Anesthetic drugs are small molecules that bind specifically to many proteins. The interactions are low affinity and, following removal of the drug, generally reversible. Rapid, transient binding to target proteins makes large transcriptional changes unlikely and discovery of the important molecular targets difficult. Nevertheless, defining the targets that contribute to anesthetic-induced responses is crucial to improving our understanding of the unconscious state and discovering new drugs. In this proposal, we aim to establish the validity of a new experimental model, the zebrafish. Next, we will assess the anesthetic sensitivity to a family of anterograde motor proteins, the kinesins, which are bound and functionally inhibited by propofol. We hypothesize that loss of specific kinesins will alter the animal's response to specific anesthetics. Finally, to explore the mechanistic link between loss of kinesin function and anesthesia, we hypothesize that mistargeting and maldistribution of neuronal mitochondria, an important kinesin cargo, is responsible. Therefore, we will measure mitochondrial motility and location in both WT and kinesin knock-out fish in vivo, with and without anesthetics. Together, these studies will establish the zebrafish as a new model for anesthetic mechanism studies, and further define the role of molecular motors and mitochondria in anesthetic action.