A Novel Fluorescent General Anesthetic Enables Imaging of Sites of Action In Vivo

Daniel J. Emerson, B.S., Zhengzheng Liao, B.S., Roderic G. Eckenhoff, M.D.,* Ivan J. Dmochowski, Ph.D.
* Department of Anesthesiology & Critical Care, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania. roderic.eckenhoff@uphs.upenn.edu

DIFFICULTY in understanding anesthetic pharmacology lies in the fleeting drug interactions with tissues and cells, which makes difficult the determination of distribution at any level. A better understanding of general anesthetic distribution is important for quantifying “off-target” and “on-target” effects and may be useful in assessing drug efficacy and safety. We have discovered a molecule with anesthetic properties\(^1\) that becomes strongly fluorescent when constrained in a hydrophobic pocket, such as a protein binding site, and are using it to define potential sites of anesthetic action.

Albino Xenopus laevis tadpoles (stage 40–47, Nasco, Fort Atkinson, WI) were incubated for 30 min in pond water containing the fluorescent general anesthetic 1-aminoanthracene (15 \(\mu\)M). Immobilized tadpoles were rinsed with fresh pond water and imaged again with an Olympus IX81 fluorescence microscope (Center Valley, PA). The tadpoles were excited with \(\sim 440\) nm light and emission collected at \(\sim 520\) nm; then, we obtained regional images that were stitched together to obtain the fluorescence micrograph shown. This image shows striking preference for labeling of neuronal tissues (brain, eyes, olfactory organs, spinal cord), which is consistent with our preconceived notion of where a general anesthetic ought to be acting. Also consistent with our current ideas of anesthetics acting on ion channels and synapses in excitable tissues is the labeling of tail muscle and gut. Aside from directly visualizing binding sites for general anesthetics in a living organism, this new tool allows the dissection and validation of molecular targets far more rapidly and inexpensively than previous methods. Using approaches such as this, it should be possible to begin a campaign of target discovery to more fully understand the cellular and molecular basis of general anesthesia.

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Reference

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