Researchers make breakthrough on new anesthetics

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A novel approach may lead to the next generation of better, safer general anesthetics. Credit: American Society of Anesthesiologists

For the first time since the 1970s, researchers are on the verge of developing a new class of anesthetics. According to a study published in the February issue of *Anesthesiology*, the official medical journal of the American Society of Anesthesiologists (ASA), a new approach to identifying compounds may lead to the next generation of anesthetics.

"While physician anesthesiologists have improved the safety of anesthesia over the years, there are still many risks associated with general anesthesia. And yet, no new anesthetics have been developed for more than 40 years," said Roderic G. Eckenhoff, M.D., lead author of the study and professor of Anesthesiology and Critical Care at the Perelman School of Medicine at the University of Pennsylvania. "We are only beginning to understand the actual mechanisms that allow general anesthetics to achieve an anesthetized state, and this study is a breakthrough into that world."

According to Dr. Eckenhoff, the search for new anesthetics has historically been a mixture of empiricism and serendipity. Researchers modify existing anesthetic drugs, rather than develop an entirely new class of anesthetics. Dr. Eckenhoff and his team sought to prove that a new approach could reveal completely new anesthetic structures. Their approach, often used in drug development for therapeutics, but never before with anesthetics, identified two new anesthetic drugs that have the potential to be used on humans.

The researchers used a screening process that allowed them to test over 350,000 compounds for their potential to serve as anesthetic agents, in collaboration with the Chemical Genomics Center of the National Center for Advancing Translational Sciences (NCATS). The compounds were tested for their ability to bind a surrogate anesthetic binding protein target, apoferritin. Among the 350,000, researchers found 2,600 compounds that had strong interactions with apoferritin. A subset of the 2,600 were chosen based on structural criteria to be tested for anesthetic

activity, first on tadpoles and then on mice, an effort performed by Andrew McKinstry-Wu, M.D., an instructor in the department of Anesthesiology and Critical Care. The researchers concluded that two compounds could potentially serve as anesthetics.

"The anesthetics identified by this approach require further development before they can be considered for use in the O.R.," said Dr. Eckenhoff. "However, the study results show that novel anesthetics do exist, and that we need not restrict ourselves to small modifications of existing drugs."

Provided by American Society of Anesthesiologists