Finding of genetic region controlling cardiovascular sensitivity to anesthetic propofol

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Researchers at The Medical College of Wisconsin in Milwaukee have identified the genetic region in rats responsible for cardiovascular collapse during anesthesia. While it is well known that people have different cardiovascular sensitivity to anesthesia causing some to collapse even when low doses are administered, the mechanism responsible for this susceptibility is not clear.

"By identifying a genetic susceptibility for cardiovascular collapse to low dose propofol, our findings may provide a key to better understand the underlying cause of the mysterious death of Michael Jackson," says Richard Roman, Ph.D., co author, professor of physiology and director of the Kidney Disease Center at the College.

The study was published in the September 2009, issue of the *Journal of Pharmacology and Experimental Therapeutics* with an editorial commentary.

To find the genetic mechanism that causes this reaction, researchers at the Medical College led by Thomas A. Stekiel, M.D., and Anna Stadnicka, Ph.D., both associate professors of anesthesiology, administered the anesthetic propofol to a strain of rat (Dah S) that is very sensitive to anesthetics versus Brown Norway (BN) rats that are quite resistant. Through extensive genetic analysis, they were able to determine that a small region on chromosome 13 contained the genetic

switch responsible for the difference in the response of these strains to anesthesia. This region also contains the renin gene, an important blood pressure controller.

"The next step is to identify the exact gene and see if it is also responsible for cardiovascular collapse with propofol in humans," says Carol Moreno Quinn, M.D., Ph.D., co-author at the Medical College's Human and Molecular Genetics Center at the College. "We can then test which persons with this gene would be sensitive to anesthesia and prevent deaths and accidents due to cardiovascular collapse in the operating room."

The findings support earlier work by the researchers showing that propofol has greater impact on vascular smooth muscle in the hypertensive salt-sensitive Dahl rats compared to the normotensive Brown Norway rats, and that chromosome 13-associted genes are responsible for variable responses to propofol.

The Dahl salt-sensitive strain develops severe hypertension when fed a high-salt diet. This salt-sensitive characteristic is similar to what is often seen in African Americans with high blood pressure. This Dahl rat model is used to better understand the causes and mechanisms behind the development of high blood pressure and cardiovascular disease in this population.

Source: Medical College of Wisconsin (news : web)