Frogs reveal clues about the effects of alcohol during development

April 6 2009

Fetal alcohol spectrum disorder (FASD) and Fetal alcohol syndrome (FAS) cause malformations in babies, including facial defects, short stature, and mental and behavioral abnormalities. The African frog, Xenopus, is a valuable tool for understanding early vertebrate development since these embryos are large, easy to work with and very responsive to environmental cues. New research uses this system to address the mechanism underlying the characteristics associated with maternal consumption of alcohol in early pregnancy.

Alcohol consumption prevents normal development by inhibiting the production of retinoic acid. Under normal conditions, the levels of retinoic acid made in different areas of the embryo provide cells with necessary information about their proper location and fate. Researchers now show that alcohol steals away the molecules that make retinoic acid and use them for its own process of detoxification, resulting in cellular disorientation during a critical period of development.

The new study, published in *Disease Models & Mechanisms* (DMM), provides evidence that the characteristics associated with FASD and FAS come from competition of alcohol for key molecules in a pathway that produce retinoic acid from vitamin A. Retinoic acid is needed for correct positioning of cells in developing embryos and by preventing its normal production, alcohol keeps cells from migrating to their correct positions and maturing properly. The researchers, at the Hebrew University in Israel, found that shutting down a molecule needed to produce retinoic acid, called retinaldehyde dehydrogenase or RALDH2,

increased sensitivity of developing embryos to low doses of alcohol. Conversely, more of the molecule RALDH2 protected embryos from the negative effects of alcohol. This provides evidence that alcohol 'hijacks' RALDH2 molecules for its own breakdown process and steals it away from its important role in synthesizing positional and maturation cues during development.

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More information: The report, titled: Ethanol induces embryonic malformations by competing for the retinaldehyde dehydrogenase activity during vertebrate gastrulation is published in the May/June 2009 issue of the research journal, *Disease Models & Mechanisms* (DMM), dmm.biologists.org.

Source: The Company of Biologists