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# Researchers discover novel risk factor in breast cancer protein 1 (BRCA1) for fetal alcohol spectrum disorders

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Researchers at the University of Toronto have discovered a novel function performed by the breast cancer 1 protein (BRCA1), which regulates DNA repair. Well known for the role it plays in breast and ovarian cancer, this study revealed that the BRCA1 protein actually plays a much broader biological role, particularly in protecting the developing embryo from the damaging effects of reactive oxygen species (ROS).

ROS are formed naturally from oxygen in the body and are necessary for normal cellular function. In excess, however, ROS can alter cellular signaling pathways or cause DNA damage, resulting abnormalities in embryonic development. Drugs like alcohol (ethanol) can enhance the embryonic formation of ROS, which have been implicated in fetal alcohol spectrum disorders (FASD) caused by the mother's use of ethanol during pregnancy.

Using a genetically altered mouse model with a modest BRCA1 deficiency, the study by Professor Peter Wells and PhD graduates Dr. Aaron Shapiro and Dr. Lutfiya Miller-Pinsler of the Leslie Dan Faculty of Pharmacy showed that progeny with this deficiency were susceptible to increased embryonic DNA damage and abnormalities in embryonic development caused by exposure to a low concentration of alcohol that had no effect on embryos with normal BRCA1 levels. As a result, this study published in Redox Biology revealed that the BRCA1 protein plays an important role in preventing embryonic DNA damage, and that

embryos with even mild deficiencies in BRCA1 are more susceptible to birth defects caused by drug-enhanced embryonic ROS levels.

"Effects in mice cannot be extrapolated directly to humans," cautioned Dr. Wells, "but the increased susceptibility observed with only a modest BRCA1 deficiency suggests that the level of embryonic BRCA1 could be an important and relatively common determinant of risk for birth defects in FASD, and possibly for other ROS-enhancing environmental conditions during pregnancy."

If confirmed in humans, the results from this study may help to identify unborn children at high risk for birth defects, and provide a basis for new dietary and other strategies for pregnant women carrying offspring with a BRCA1 mutation to ensure the health and safety of their unborn children.

This study was funded by the Canadian Institutes of Health Research, the Government of Canada's health research investment agency. Created in 2000, the mission of this independent agency is to create new scientific knowledge and to enable its translation into improved health, more effective health services and products, and a strengthened Canadian healthcare system.

**More information:** Aaron M. Shapiro et al. Breast cancer 1 (BRCA1)-deficient embryos develop normally but are more susceptible to ethanol-initiated DNA damage and embryopathies, *Redox Biology* (2016). DOI: 10.1016/j.redox.2015.11.005

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