Prostate 'organoid' hints at how early BPA exposure may increase cancer risk

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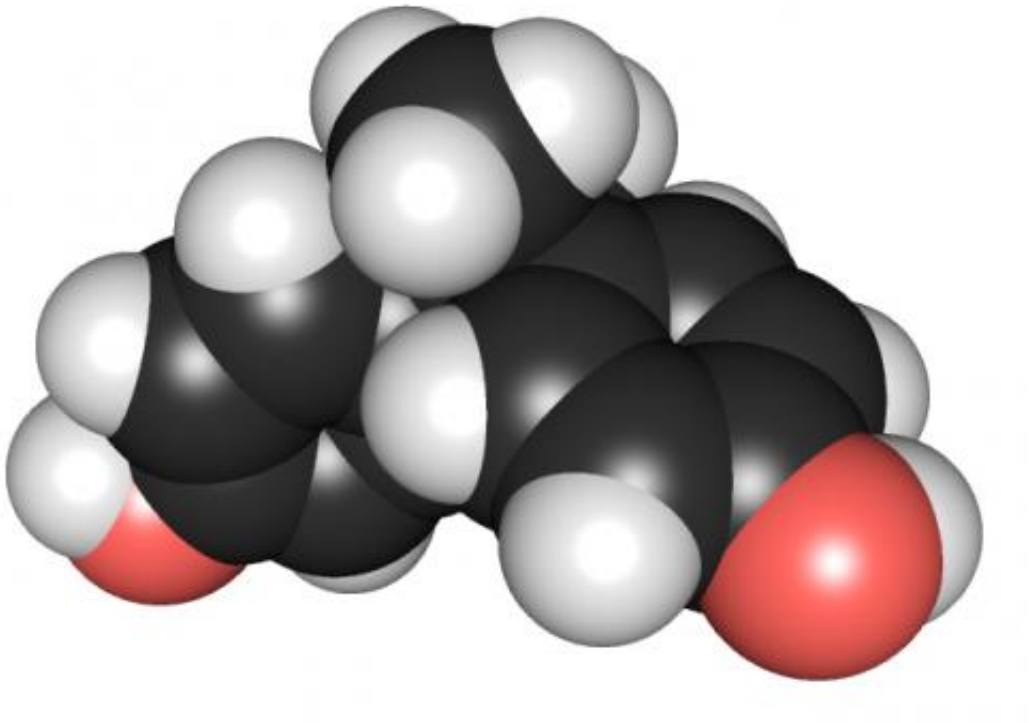

3D chemical structure of bisphenol A. Credit: Edgar181 via Wikimedia Commons

A first-of-its kind prostate 'organoid' grown from human embryonic stem cells has enabled researchers to show that exposure to bisphenol A, a chemical in many plastics, can cause overproduction of prostate stem cells in the developing organ—and thus may increase men's risk of

prostate cancer.

The research, by andrologists at the University of Illinois at Chicago, is published online in the journal *PLOS ONE*.

About a millimeter in size, the prostate organoid is coaxed into being from cultured human embryonic stem cells. Its 3-D structure resembles a prostate in miniature, and it has all the biomarkers found in the actual adult organ.

When researchers exposed the developing organoid to BPA, an additive used to soften plastic and found in everything from water bottles to carbonless receipts, the organoid grew an overabundance of prostate stem cells in 'nests' throughout the tissue.

"The higher number of stem cells we saw in developing organoids given very low doses of BPA may be the underlying mechanism by which BPA increases the risk for prostate cancer," said Gail Prins, professor of physiology in the UIC College of Medicine and director of UIC's andrology laboratory, who led the study.

A normal prostate gland, Prins said, has just a few stem cells dispersed throughout, which give rise to new prostate tissue over the course of a man's life.

In any tissue or organ, an abnormally high number of stem cells could be a risk factor for developing cancer, Prins said. Stem cells divide infrequently, but they may last a lifetime, carrying forward any abnormalities to all the tissues they give rise to. In theory, the more stem cells an organ has, the greater the risk of mutations that could cause the tissue to turn cancerous.

In previous research, using either an animal model of prostate cancer or

adult human prostate stem cells, Prins and colleagues showed that prostate stem cells exposed to BPA were more likely to give rise to tissues that showed signs of cancer. The new study confirms these findings in human tissue that is embryonic.

Using a cocktail of hormones and other factors associated with the developing embryonic prostate, Prins and co-author Esther Calderon-Gierszal, a UIC graduate student in urology, were able to coax human embryonic stem cells to differentiate into various mature cells and form a prostate organoid—a process known as directed differentiation. Other laboratories have used directed differentiation to create intestinal, thyroid and pancreas organoids.

The new findings support Prins' previous research. BPA is a known endocrine disrupter that mimics estrogen, she says, and the new study shows how that might be responsible for driving prostate cancer. If the developing prostate is exposed to BPA early in life, its stem cells may be more sensitive to the naturally rising levels of estrogen that men produce as they age.

"This is as definitive as it gets, when it comes to the effect of BPA on the developing prostate," she said. "It produces an abnormally high number of prostate stem cells in the tissue, and these nests are a strong candidate for why exposure to BPA during development has been linked to prostate cancer later in life."

Provided by University of Illinois at Chicago