Reducing Breast Cancer Risk by Eliminating Parabens and Phthalates
EDC Strategies Partnership Webinar: May 17, 2023
Q&A

The webinar audience posed a number of questions. Below are the questions the speakers did not have time to address during the webinar.

Q: How was suppression of apoptosis upon XE exposure mediated? Changes in expression of BCL-2 family proteins?

A: Dr. Goodson: First, for space reasons, this information was relegated to the supplemental material. The supplement is also open access online, under *Appendix A. Supplementary data*.

Apoptotic cells were identified by Annexin stain and counted by FACS. We previously correlated Annexin staining with changes in BCL2 for terephthalic acid. (Maria Gloria Luciani-Torres, Dan H. Moore, William H. Goodson III and Shanaz H. Dairkee. 2015. *Carcinogenesis* vol.36 no.1 pp.168–176. Exposure to the polyester PET precursor—terephthalic acid induces and perpetuates DNA damage-harboring non-malignant human breast cells)

Q: Are there similar or different implications of the study for ductal compared with lobular breast cancer? Will you repeat the study?

A: Dr. Goodson: Our endpoints were for cancer, but not specific types of cancer. As to repeating, please see the note below.

Q: Are there any plans for extending the data to larger numbers?

A: Dr. Goodson: Ideally, there would be a repeat with more participants.

More important would be that the study be done at two or more institutions with an agreed methodology. As noted in our review of studies of exposures to mixtures of chemicals (William H. Goodson*, Leroy Lowe, Michael Gilbertson and David O. Carpenter. Testing the low dose mixtures hypothesis from the Halifax project *Rev Environ Health* 2020. https://doi.org/10.1515/reveh-2020-0033. Received March 13, 2020; accepted June 2, 2020; published online August 24, 2020), the results are all over the place and thus difficult if not impossible to combine. It is important to break new ground, but the field needs repetition to confirm answers.

For example, there are several studies of differential gene expression between different types of

breast cancer, and I can find one for benign breast tissue compared to cancer (there may be ones I have not found). They are all very exciting, HOWEVER, THEY ALL REPORT DIFFERENTIAL EXPRESSION OF **DIFFERENT GENES**. This is not a race to see who can find one more new gene, especially since finding a "new" gene is meaningless if it cannot be duplicated.

We need groups to compare results, identify points of difference in methodology, and then agree on a plan that can be implemented by two or more groups collectively. Right now, there is too little funding for such a project. A lot is spent on environment, but a lot of where that goes is to persons who are doing one thing, then put a label on what they have always done to say it is environmental, and then go on doing the same thing they have always done.

A: Ms. Marshall: This study was funded as community-based participatory research by the California Breast Cancer Research Program (CBCRP), using cigarette tax monies, and is one in a series of community-based studies funded by CBCRP focused on breast cancer and the environment, including studies of chemical exposures in female firefighters, nail salon workers, and teenagers in an agricultural community. While Drs. Dairkee and Goodson have obtained funding from other sources for their previous highly innovative research studies using human breast cells (including fundraising from private individuals), it is noteworthy that the funding for this particular study was obtained because it was community-based participatory research, with people affected (in this instance, women at higher risk of breast cancer and their children) joining in the grant application, drafting study protocols, and working with volunteer participants. I believe it will be important for future funding of research of this type for people like us to continue to demand and support research that seeks to prevent the development of cancer from environmental exposures.

It is also important to note that this research was done utilizing normal human breast tissue, not rodent tissue or cancer cell lines as is more typical. There was resistance in the research and funding communities to this "invasive" sampling of healthy human subjects, but it was the insistence on meaningful research with quicker answers by the subjects themselves that helped to obtain grant funding in this instance.

Finally, we need some discussion on the application of the precautionary principle to studies like ours. Multiple levels of repeat studies at multiple institutions are necessary for more precise scientific conclusions. But how much evidence is necessary to ask industry to change their product ingredients to protect the most vulnerable while these further studies are conducted?

Q: Question for Dr. Goodson: What follow-up study do you see next to further explore your findings?

A: Dr. Goodson: I think there needs to be a meeting of all persons who have studied and ***already***

published papers on differentially expressed genes in breast tissue, either cancer or benign tissue such as ours.

They need to figure out why there is so little overlap in their answers and recommend how to resolve the methodologic differences. Then there needs to be a large multicenter study to duplicate our study.

The precedent for analyzing the differences in methods before anything else is the work of many pathologists and researchers to standardize estrogen receptor and HER2 testing in human cancers. It can be done, but it needs leadership, and the leaders need funding to get it done.

Q: I see that DEHP/MEHP was not found to be significantly reduced in this study, but MEHP is also not particularly relevant to PCPs. Do you think this REDUXE study design could be effective in studying the effect of MEHP in breast cancer by reducing something more relevant like food-packaging or medical plastics exposure?

A: Dr. Goodson: One reviewer challenged whether we could say that the subjects did not change other exposures, e.g., to food, on their own. As the person asking the question here notes, MEHP is not typically related to PCPs, so the stability of MEHP supported our conclusion that subjects did not change other things on their own initiative. I disagree that exposure from packaging would be "more relevant" than PCPs but I agree that food packaging, household dust, stain resistant materials, etc. are major sources of xenoestrogen (XE) exposure. Food exposure would be "also relevant" but logistics of replacing all food, etc. for a month are daunting. It has been tried, but that involved providing a month's worth of food. The important point is that reducing PCP exposure by itself changed genes and cell behavior. Reducing XE exposure from other sources would quite possibly help, too, but that does not negate the importance of PCP exposure.

A: Ms. Marshall: I agree with Dr. Goodson. In our study questionnaire, subjects were asked about their typical consumption of organic food and plastic-packaged food, and of beverages in plastic bottles, and we have this data, although it has not been analyzed. Study subjects were asked **not** to change other habits that might be related to their exposure to xenoestrogens. It was helpful that the intervention period only lasted 28 days, a manageable time period for subjects to continue their other daily routines, even as they were waking up to the issue of environmental exposures.

Of greater importance, perhaps, was that tests were performed on paired samples from the same individual, thereby controlling for differential environmental exposures of different subjects over their lifetimes so far.

Q: Would you predict epigenetic intergenerational transfer, given that phthalates are endocrine disrupting chemicals and some EDCs' epigenetic changes are inheritable? Phthalates can affect infertility in males up to 4 generations. What about phthalate exposures/gene expression re breast cancer? Would you predict inheritance?

A: Dr. Goodson: Valid question, but unfortunately, I do not know of data on this for phthalates.

Q: What about multi-generational effects as seen with granddaughters of women with high exposures of DDT? Is that similar to the DES story?

A: Dr. Goodson: Same answer as to the previous question. Quite possible, but I do not have data on that.

A: Ms. Marshall: For more information on studies of the multigenerational impacts of DES exposure, see descriptions and discussions of studies provided by DES Action USA (https://desaction.org/).

Q: What are the multiplier effects suspected in US and CAN expanding multiple chemical supply streams via water and food? BTEX for one example, overlapping the PFAS and Phthalates etc. in key 'hot zones.'

A: Dr. Goodson: Valid question, but I do not have an answer.

Q: Can the list of products be posted in case any participants wish to explore these products?

A: Dr. Goodson: There is a list of products in the paper that is open access online. Those products were drawn from the lists on the website of The Environmental Working Group, at www.ewg.org.

A: Ms. Marshall: The intervention products were selected by the community partners, with ingredients verified through the Environmental Working Group's SkinDeep database found on EWG's website. They are listed as an appendix in the Chemosphere paper and also on our website here: https://www.breastcancerovertime.org/research.

Q: Dr. Goodson, could you send your data to Prevent Cancer Now and spread the link for PCN to your friends?

A: Dr. Goodson: The paper is open access either through PubMed (https://pubmed.ncbi.nlm.nih.gov/36746253/) or the journal site for *Chemosphere*.

Q: Phthalates are not just in personal care products. Phthalates migrate from many plastics, including vinyl shower curtains, plastic water bottles, etc. Getting phthalates out of personal care products is a great first step. Bans need to extend to a wider variety of household products.

A: Dr. Goodson: I agree, especially for children's toys and eating utensils.

A: Ms. Marshall: There are a lot of groups working on just such legislation in several states and on the federal level. For more information on these campaigns, and how to participate in them, check out websites such as Environmental Working Group (EWG.org), Breast Cancer Prevention Partners (BCPP.org) and Breast Cancer Over Time (BreastCancerOverTime.org).