Preventing Breast Cancer in Our Daughters

A Community-Based Participatory Research Study of the Effect of Changing Personal Care Products on Healthy Human Breast Cells

Funded by the California Breast Cancer Research Program

BCERP Annual Meeting November 16, 2017

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Dedication



Luisa Preciutti Tumini



Luisa's daughter

Breast Cancer Over Time



Created and controlled by breast cancer survivors to support and assist scientific research on the PREVENTION of breast cancer



BCOT Steering Committee 2015



Our Research Team



Dr. William Goodson, M.D. Breast Surgeon California Pacific Medical Center



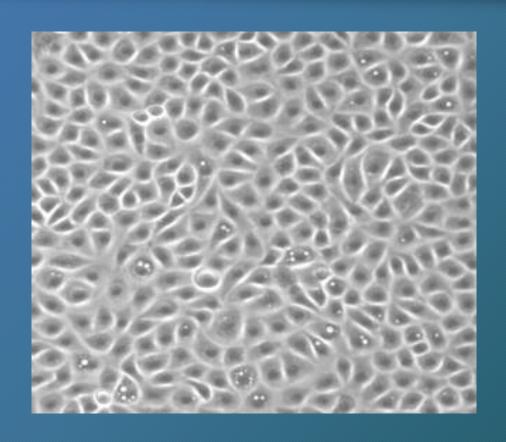
Polly Marshall , J.D. Executive Director Breast Cancer Over Time



Dr. Shanaz Dairkee, PhD
Senior Scientist
California Pacific Medical Center
Research Institute



normal human breast cells



Healthy Breast Cell Donors



Our Research Question

Does reduced exposure to common chemicals, known as xenoestrogens (XEs), in personal care products curb estrogenic hyper-signaling and its adverse effects on normal cell function within the healthy breast tissue of women volunteers participating in the XE-Low (XEL) intervention?



Preceding studies

HERMOSA study - 2016

- -community-based participatory
- -measured phthalate, paraben, and phenol levels in urine of adolescent girls
- -significant drop after 3 day intervention
- -also funded by CBCRP



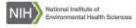
Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study

Kim G. Harley, Katherine Kogut, Daniel S. Madrigal, Maritza Cardenas, Irene A. Vera, Gonzalo Meza-Alfaro, Jianwen She, Qi Gavin, Rana Zahedi, Asa Bradman, Brenda Eskenazi, and Kimberly L. Parra

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Wonder what *causes* Breast Cancer? Help us try to find out.

BREAST CANCER PREVENTION STUDY SEEKS WOMEN AGES 18-40

For Study of Impact of Reduced Chemical Exposure on the Human Breast

Volunteers who:

- (1) Are over age 18
- (2) Are using the Mirena IUD <u>or</u> have a very regular 28 day cycle without the use of oral contraceptives
- (3) Have not had any kind of cancer (except basal cell skin cancer), and
- (4) Use self-care products such as shampoo, moisturizer, sunscreen, etc.

Are being recruited to participate in a healthy intervention in which they use paraben- and phthalate-free self-care products provided by the study, and donate samples of blood, urine and breast cells (by needle sample through anesthetized skin) in medical office in San Francisco. Volunteers receive over \$250 worth of locally-made healthy cosmetics and \$40 in Peet's cards.

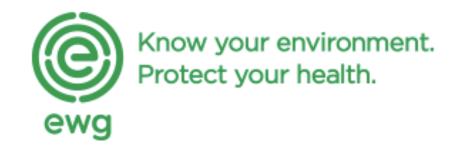
Contact Polly Marshall: 415.608.8845 polly@breastcancerovertime.org

sponsored by CPMC Research Institute and Breast Cancer Over Time

BREAST CANCER
OVER TIME



What xenoestrogens are in the products we use?

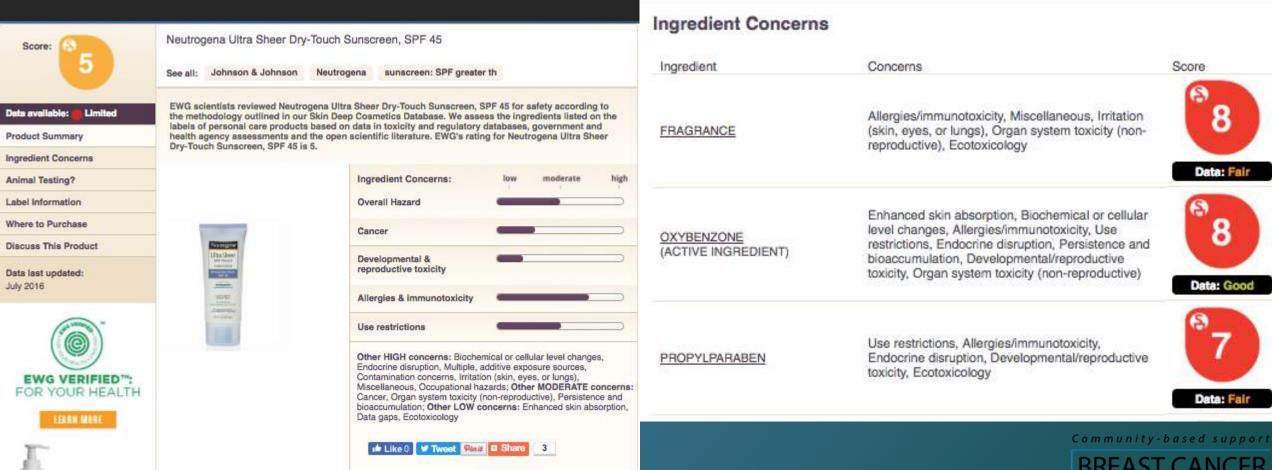


ENVIRONMENTAL WORKING GROUP





Neutrogena Ultra Sheer Dry-Touch Sunscreen, SPF 45



RETINYL PALMITATE (VITAMIN A PALMITATE)

Use restrictions, Developmental/reproductive toxicity, Biochemical or cellular level changes, Cancer, Organ system toxicity (non-reproductive)



Data: Fair

OXYBENZONE

Enhanced skin absorption, Biochemical or cellular level changes, Allergies/immunotoxicity, Use restrictions, Endocrine disruption, Persistence and bioaccumulation, Developmental/reproductive toxicity, Organ system toxicity (non-reproductive)



Enhanced skin absorption, Biochemical or cellular level changes, Endocrine disruption,

Allergies/immunotoxicity, Persistence and bioaccumulation, Developmental/reproductive toxicity, Organ system toxicity (non-reproductive)



Data: Fair

HOMOSALATE

OCTINOXATE

Enhanced skin absorption, Use restrictions, Organ system toxicity (non-reproductive), Endocrine disruption, Ecotoxicology, Contamination concerns (SALICYLIC ACID, TRIMETHYLCYCLOHEXANOL)

Data Sources

Boehnlein J, Sakr A, Lichtin JL, Bronaugh RL. 1994. Characterization of esterase and alcohol dehydrogenase activity in skin. Metabolism of retinyl palmitate to retinol (vitamin A) during percutaneous absorption. Pharm Res 11(8): 1155-9.

CIR (Cosmetic Ingredient Review). 2006. CIR Compendium, containing abstracts, discussions, and conclusions of CIR cosmetic ingredient safety assessments. Washington DC.

Cherng SH, Xia Q, Blankenship LR, Freeman JP, Wamer WG, Howard PC, et al. 2005. Photodecomposition of retinyl palmitate in ethanol by UVA light-formation of photodecomposition products, reactive oxygen species, and lipid peroxides. Chem Res Toxicol 18(2): 129-38

Duell EA, Kang S, Voorhees JJ. 1997. Unoccluded retinol penetrates human skin in vivo more effectively than unoccluded retinyl palmitate or retinoic acid. J Invest Dermatol 109(3): 301-5.

EC (Environment Canada). 2008. Domestic Substances List Categorization. Canadian Environmental Protection Act (CEPA) Environmental Registry.

FDA (U.S. Food and Drug Administration) 2006. Food Additive Status List. Downloaded from http://www.cfsan.fda.gov/%7Edms/opa-appa.html, Oct 16, 2006.

Common Endocrine Disruptors in Cosmetics

- Propylparaben
- Butylparaben
- Isobutylparaben
- Methylparaben
- Ethylparaben
- Benzyl Salicylate
- Triclosan

- Oxybenzone
- Oxtinoxate
- Homosalate
- Cyclopentasiloxone
- BHT
- Lillial butylphenyl methylpropional



Other hazardous chemicals in cosmetics

- DMDM Hydantoin (formadehyde releaser)
- 2-Bromo-2-Nitropropane-1,3 Diol (formadehyde releaser)
- Retinyl palmitate (biochemical and cellular level changes)
- Methylisothiazolinone (human immune toxicant banned in Europe, Germany; restricted in Japan and Canada)
- Cocamide DEA (possible carcinogen, nitrosamine contamination)
- Octisalate (enhanced skin absorption)



Fragrance

?

- "Trade secret" Ingredients not disclosed
- Very likely to include phthalates, per EWG



Our Study Protocol

- 1. Obtain blood, urine, and breast cell samples before and after 28 day XE-low healthy intervention.
- 2. Test blood for levels of natural hormones
- 3. Test urine for paraben and phthalate levels
- 4. Propagate live breast cells and perform assays to measure ERα activation, cell proliferation, and apoptosis signaling



Our Healthy Intervention

- Participants used only XE-low personal care products provided by Breast Cancer Over Time for 28 days between cell donations
- Participants kept logs of all products used for 28 days between cell donations



Analysis and Comparison of Samples

- Blood: analyzed for levels of natural hormones (estradiol, progesterone, sex hormone-binding globulin)
- Urine: analyzed for paraben and phthalate levels
- Breast cells cultured and assays performed for functional differences in live cells

Results

- Participants: no attrition and positive reviews
- Blood: hormone levels not significantly different
- **Urine**: significant drops in paraben and phthalate levels after healthy intervention
- **Cells**: differences on functional tests on live cells measuring estrogen receptor isoform levels, cell proliferation, and cell death

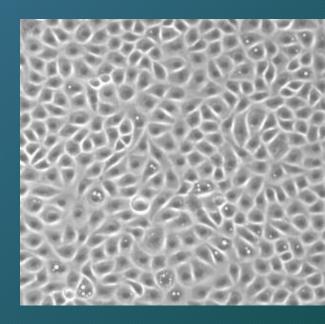


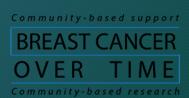
Exit Surveys

- Very positive experience
- Liked the "healthy" personal care products
- Liked having breast cancer survivor buddies
- Reported starting to read ingredient labels in cosmetics
- Gratified and proud to have donated breast cells for a scientific study
- Felt they were making a difference
- FNAs "not a big deal" they would do it again

Study Conclusions

- Women will donate normal breast cells for research
- Volunteers will comply with study protocol
- Positive changes to human breast cells <u>are</u> observable after both 14 and 28 day interventions
- Study of responses of HEALTHY LIVING HUMAN BREAST CELLS to environmental exposures is feasible and can provide important information on human breast carcinogenesis





Additional Community Conclusions

- Women want to help in scientific research
- Their participation is meaningful and educational
- Survivors are fantastic recruiters and supporters
- Studying changes in <u>healthy human breast cells</u> can provide important prevention information QUICKLY
- We need more funding!
- More stringent government regulation of environmental chemicals, including cosmetic products, is essential to public health and must be demanded by all of us!



Acknowledgements

- California Breast Cancer Research Program
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- CPMC Research Institute
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- San Francisco Public Health Foundation



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