

Press Release

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Killing the Good Guys: How Selective Elimination of Normal Human Breast Cells by Radiation can Promote Growth of Pre-Malignant Cells

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A new study by the Bay Area Breast Cancer and the Environment Research Center (BABCERC) has found that one way radiation contributes to cancer is by making the tissue that surrounds pre-cancerous cells more hospitable to tumor growth.

In this study, the researchers showed that radiation could indirectly promote the growth of cancer cells by speeding up the aging process of normal cells. By getting normal cells to prematurely age and stop dividing, radiation exposure can create a space for pre-cancerous cells to fill the void the normal cells would have normally filled.

The study¹, led by Rituparna Mukhopadhyay and Sylvain Costes of the Lawrence Berkeley National Laboratory (Berkeley Lab), was performed using breast epithelial cells that had been taken from normal breast tissue. Epithelial cells are the cells that line breast ducts, which are where most breast cancers begin.

When placed into a laboratory dish, cells from a normal human breast consist of two types: the vast majority that divide just a short time before they are unable to divide any longer, and a rare type that can divide many times longer and accumulate mutations. It is not known why variations in cell type are present in normal breast, but it is thought that the long-lived cells have a greater potential to turn into cancer cells because they lack a protein called p16 that suppresses tumor formation. The space available for expansion is another constraint that affects cell growth. Normally, because cells only grow if there is room for the daughter cells to spread out, when the dish is full, the cells stop growing.

The researchers exposed some sets of cells grown in laboratory dishes to a single low-to-moderate dose of radiation, and also grew sets of non-irradiated breast cells, which allowed them to compare differences between exposed and unexposed cells. The research team then evaluated whether radiation affected the growth of cells.

Four to six weeks after sets of cells received a moderate dose of radiation exposure, most of the cells in both irradiated and non-irradiated sets had permanently stopped dividing. Yet the daughter cells of those exposed to radiation formed larger, and more numerous patches of small, quickly growing cells than did the daughters of the unexposed cells.

Computer simulations suggest that the radiation increased the rate at which short-lived cells stopped dividing. This in turn allowed more long-lived variant cells of irradiated cell sets to grow because there was more physical space in those irradiated sets.

“Exposure to radiation is the only known cause of breast cancer. Understanding the effects of radiation on cells and the microenvironment will lead to advances in prevention,” says Janice Barlow, the Executive Director of Zero Breast Cancer.

“This is a new way of looking at the effects of radiation, and carcinogens in general,” says Paul Yaswen, a cell biologist with Berkeley Lab’s Life Sciences Division and senior author of the study. “It has long been believed that radiation causes cancer by damaging a cell’s DNA to create mutations. While this is certainly true, our work shows that radiation can also promote cancer through mechanisms that don’t involve mutations. By changing the local environment that surrounds cells, radiation can alter the way cells behave.”

Other contributors to the study included Alex Bazarov, Curt Hines, and senior researcher Mary Helen Barcellos-Hoff. The work was supported by the National Institute of Environmental Health Sciences, the National Cancer Institute and a NASA Specialized Center of Research.

¹ Mukhopadhyay R, Costes S, Bazarov A, Hines WC, Barcellos-Hoff MH, and Yaswen P. Promotion of variant human mammary epithelial cell outgrowth on ionizing radiation: an agent-based model supported by in vitro studies. *Breast Cancer Research*, 12: 2010. doi:10.1186/bcr2477

The Bay Area Breast Cancer and the Environment Research Center (BABCERC) is one of four centers nationwide funded by the National Institute of Environmental Health Sciences and National Cancer Institute that studies the environmental causes of breast cancer by focusing on mammary gland development during puberty when the breast may be especially vulnerable to environmental influences. The Center is based at the University of California, San Francisco, under the leadership of Dr. Robert A. Hiatt, Director of Population Sciences, UCSF Helen Diller Comprehensive Cancer Center. The Center includes a basic science project, an epidemiology project, and the community outreach and translation core and is a collaborative project involving University of California, San Francisco, Kaiser Permanente, Northern California, California Department of Public Health and Zero Breast Cancer. More information about the BABCERC can be found on its Web site: <http://bayarea.bcerc.org>

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To read more about this study, please visit:

<http://bayarea.bcerc.org/pubsMukhopadhyay.PromotionVariant.BCR.2010.htm>