
the
BREAST
BIOLOGUES
a biology dialogue about breast cancer & the environment

Introduction

The Breast Biologues video and comic book were developed by the Bay Area Breast Cancer and the Environment Research Center (BABCERC) to explain how the breast develops and how exposures to potential cancer-causing chemicals at specific times during development might influence future breast cancer risk. The Breast Biologues video, narrated by Peter Coyote, and the comic book highlight some of the fascinating genetic and cellular insights we have learned about normal breast development and its relationship to breast cancer risk.

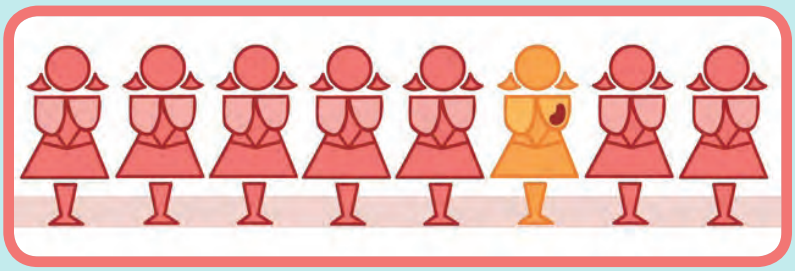
The Breast Biologues is a result of the collaboration between **Lori Schkufza**, an animation consultant; the BABCERC basic science researchers: **Dr. Zena Werb** at University of California San Francisco, **Dr. Paul Yaswen** at Lawrence Berkeley National Laboratory, and **Dr. Mary Helen Barcellos-Hoff** at New York University Langone School of Medicine; **Casandra Aldsworth** and **Janice Barlow** at Zero Breast Cancer, the BABCERC Community Outreach and Translation Core; and **Kim Huff** at Kimber Communications.

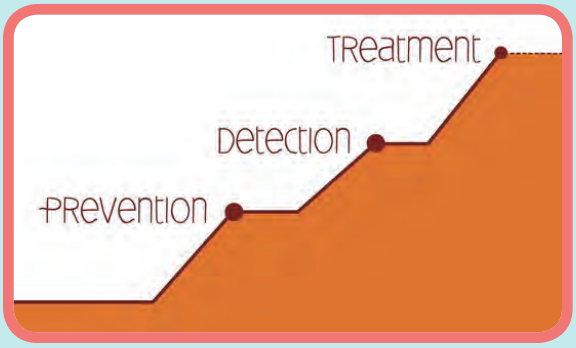
The goal of the video and comic book is to serve as an educational tool for high school and college instructors and community members to facilitate a greater understanding of the biology of the breast and how specific exposures at certain times in development might affect future breast cancer risk.

Background

Aside from non-melanoma skin cancer, breast cancer is the most common form of cancer in women. One in eight women is at risk for developing breast cancer during their lifetime.

Breast cancer is important to study and understand because it strikes women during their most productive years and can be fatal.

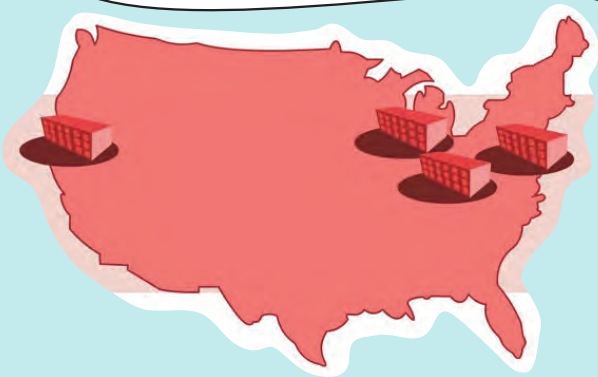


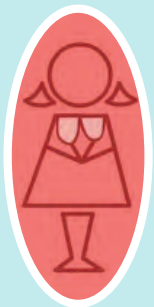


Research thus far has advanced our knowledge in prevention, detection and treatment; however, more research is still needed.

The Bay Area Breast Cancer & the Environment Research Center

The Bay Area Breast Cancer and the Environment Research Center is one of four centers nationwide that studies the environmental causes of breast cancer by focusing on breast development during puberty when the breast may be especially sensitive to environmental influences.

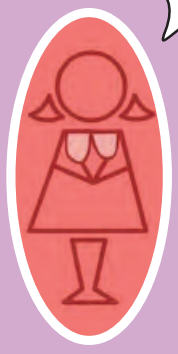


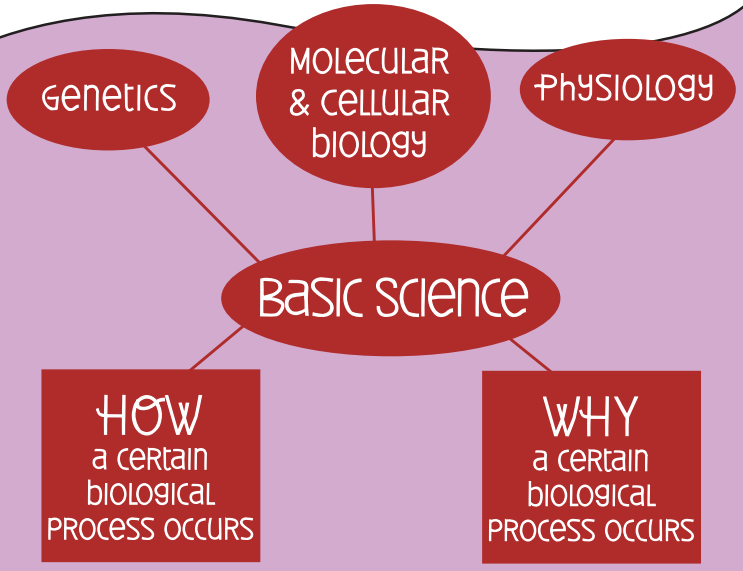


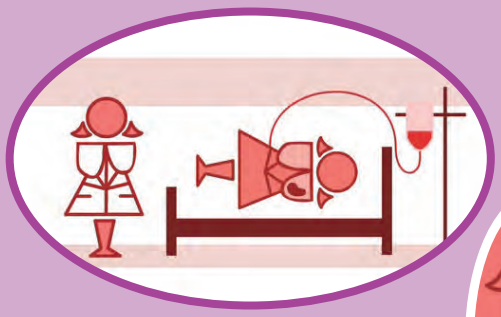
The Center includes a basic science project at the University of California San Francisco and

The Lawrence Berkeley National Laboratory that studies breast cells in normal and cancer-prone mice.

Basic science provides a framework for thinking about how the breast develops and what triggers the changes that make it possible for a normal cell to turn into a cancer cell.

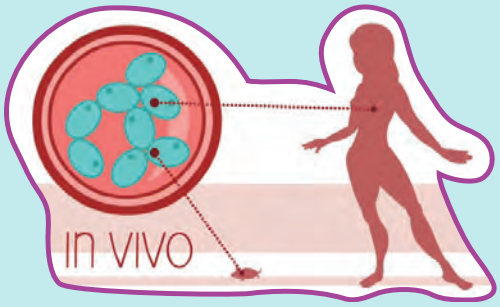




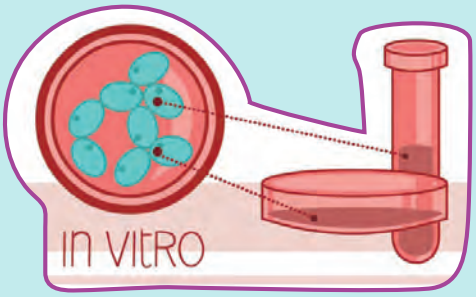


The information learned from basic science research is later applied to research aimed at developing new ways of preventing cancer as well as new therapies for treating patients.

Basic Science Research is conducted in two ways.

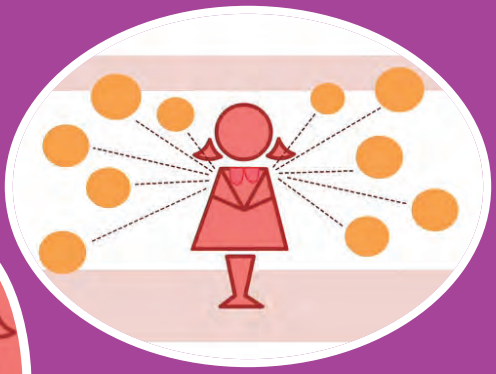


1. One way, called *in vivo*, is done using cells in a living organism.



2. The other way is called *in vitro* and is done in a laboratory dish or test tube.

The Basic Science researchers in The Bay Area Breast Cancer and the Environment Research Center are asking whether cells in the breast during puberty might be especially sensitive to environmental toxins.

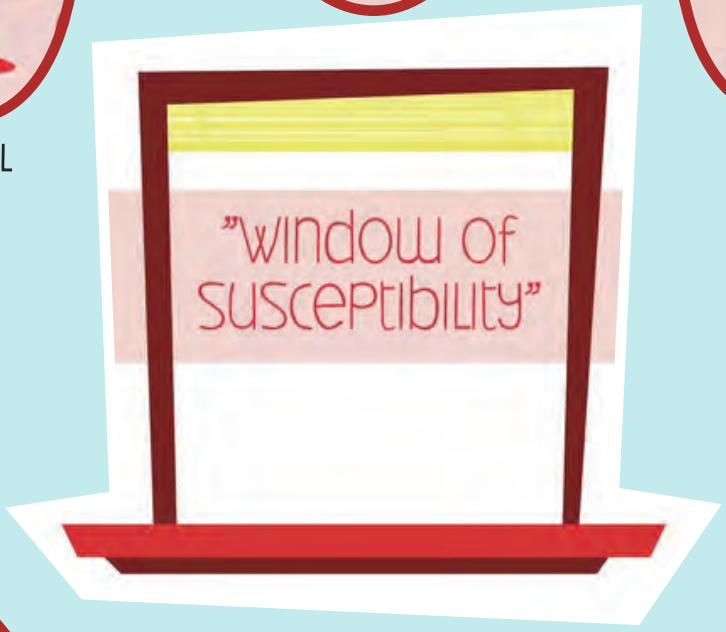


Puberty is a time in a young girl's life when a series of biological, cognitive and emotional changes occur and the breast, specifically, undergoes rapid growth.

EMOTIONAL

COGNITIVE

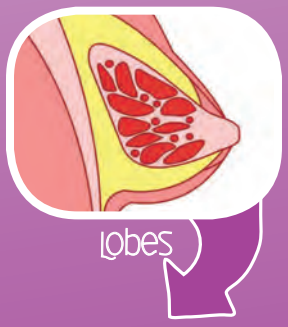
BIOLOGICAL



Exposure to potential carcinogens at this stage may affect the risk of breast cancer in later life. We call this sensitivity during a stage of growth a "window of susceptibility."

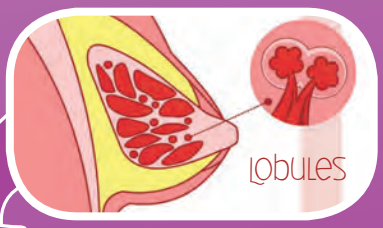
How does the breast develop?

The breast is made up of glands that make milk, as well as supporting structures and fat.



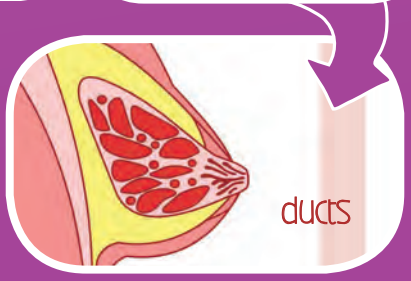
It is divided into 15 to 20 sections called lobes.

The lobes consist of smaller sections called lobules.

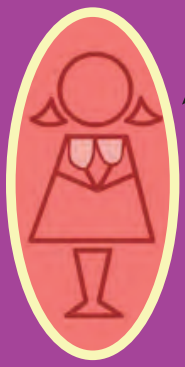


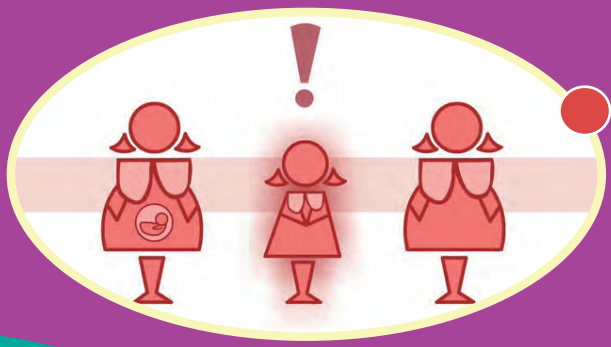
During pregnancy, structures called acini at the end of the lobular ducts increase dramatically in number.

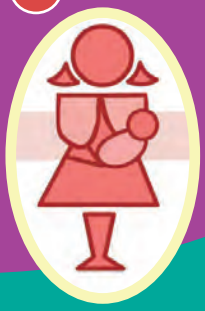
During breastfeeding, these tiny parts of the glands produce breast milk, which travels through tubes called ducts to the nipple.



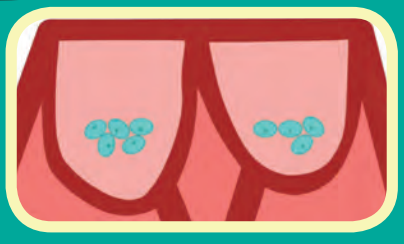
At birth, the breast is not fully developed. It grows a little in the womb, but grows a lot during puberty and again during pregnancy. The breast is sensitive during these stages, but especially during puberty which is when it develops the most.

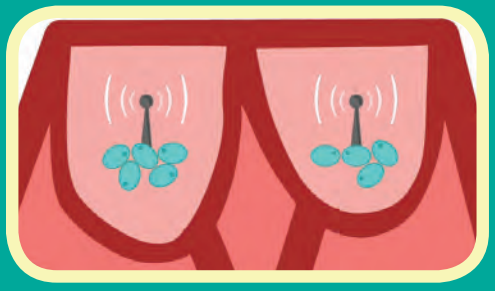


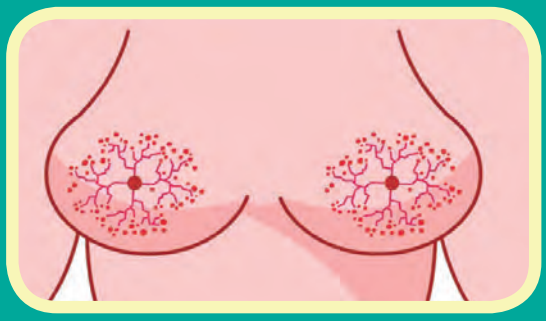




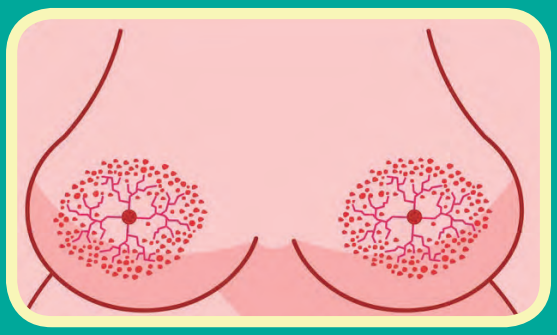
During puberty, the breast begins to develop when cells that have been sitting quietly in the breast receive hormonal messages that tell them it is now time to get to work. As a result, these cells begin to grow and divide rapidly. Their mission: to form the ductal tree that characterizes an adult breast.

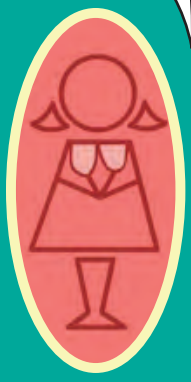




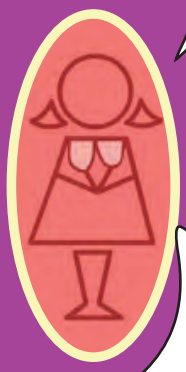


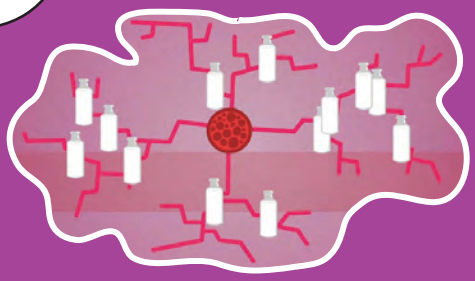
When a pregnancy occurs, the breast will go through another transformation. Only then will it be fully formed and able to make milk in lobules and then transport milk through the ducts to the nipple.



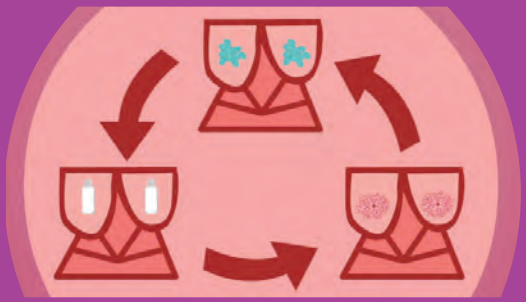


After lactation, the breast undergoes more changes called involution, which is when the breast shrinks.

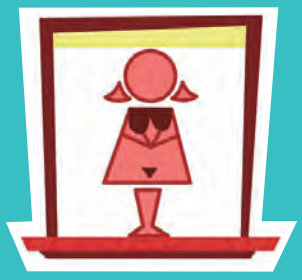


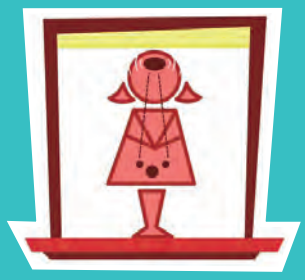


This cycle of proliferation, milk production and involution occurs with each pregnancy and is one of the more remarkable features of the organ.

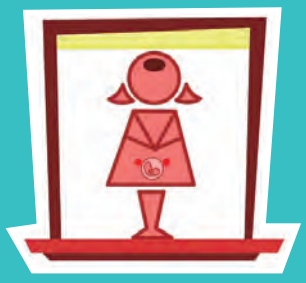


Puberty as a "Window of Susceptibility"

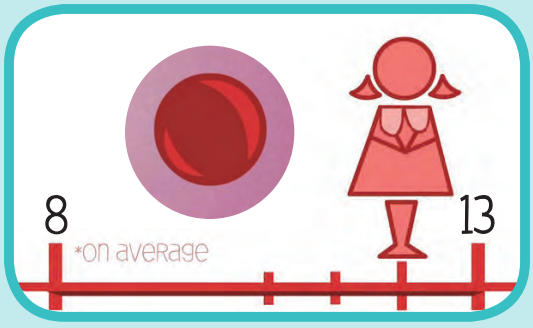


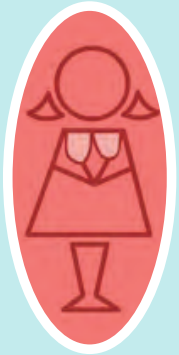


Puberty is a time in a young girl's life when a series of hormonal, physiological, cognitive and socio-emotional changes occur. These changes get underway when an area of the brain sends chemical signals to the ovaries that trigger the hormonal and physical processes that tell the body it is now time to develop the ability to reproduce. The physical changes that occur include the appearance of breast "buds" and pubic hair.

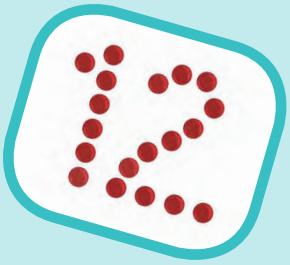


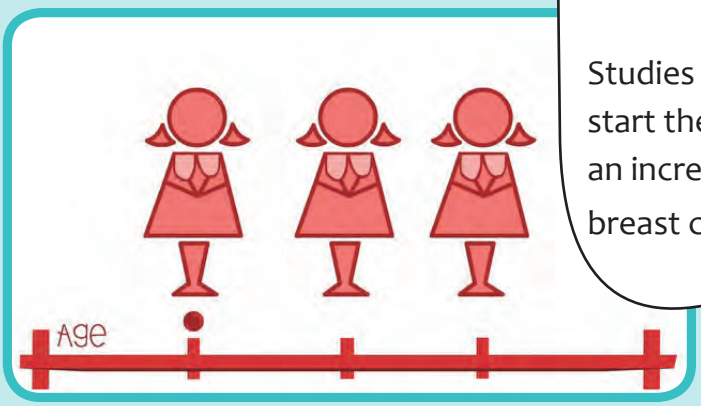
Puberty normally begins between the ages of 8 and 13. On average, two years after the development of breast buds, a girl's first period occurs.



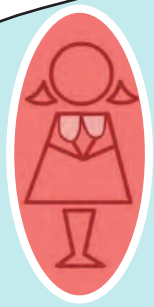


In the United States, the average age for a girl's first period is 12. Puberty is a developmental period when breast cells may be more sensitive to environmental toxins which can affect the risk of developing breast cancer.

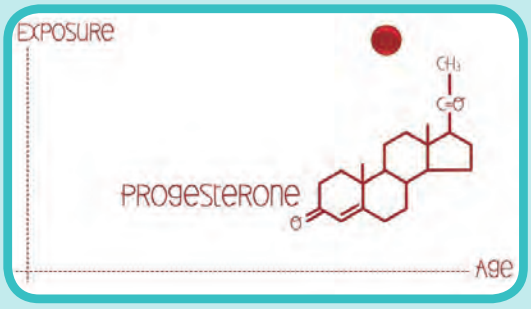


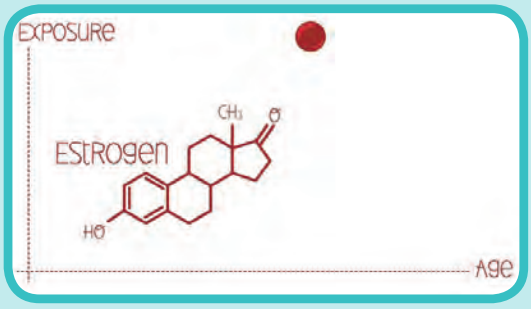


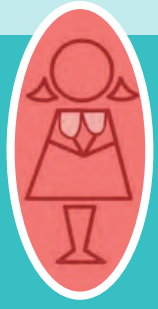
Studies have shown that women who start their period at an early age have an increased risk for developing breast cancer as an adult.



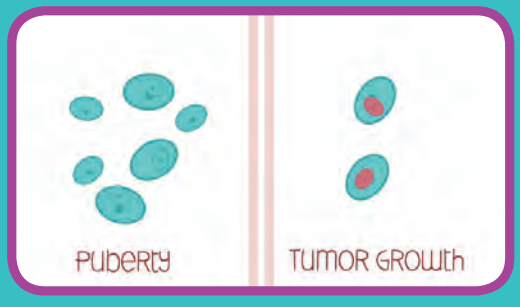
Early age of a women's first period increases a women's lifetime exposure to hormones such as estrogen and progesterone.

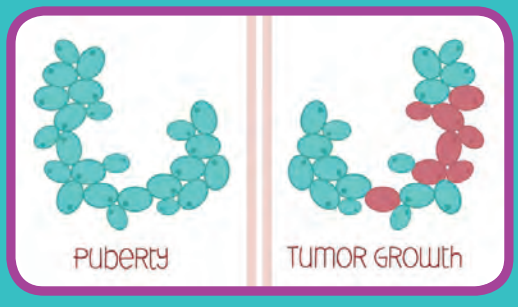


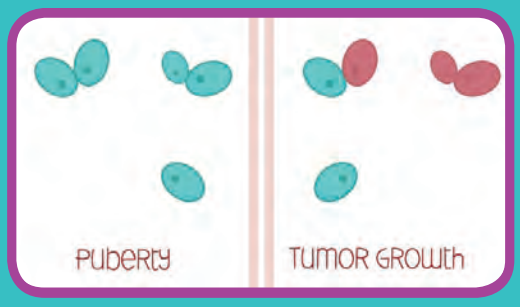


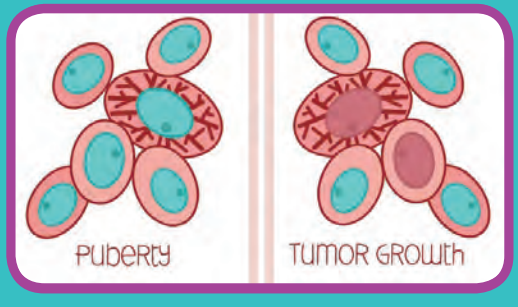


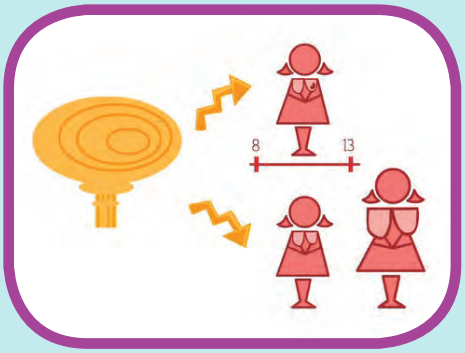
During puberty, as the breast develops normally, it displays many of the properties associated with tumor growth, such as invasion, cell growth, resistance to cell death and the formation of new blood vessels.





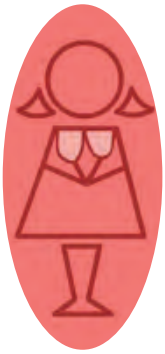




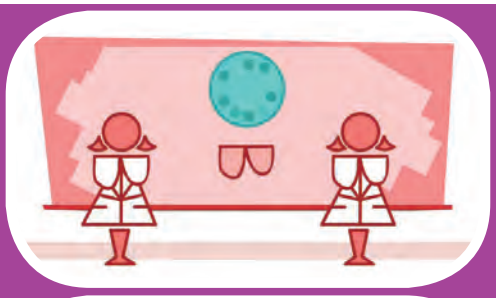


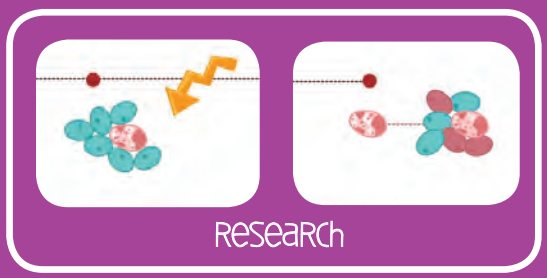
Based on research on atomic bomb survivors after World War II, young girls in the age range when puberty occurs who were exposed to radiation from the atomic bombs in Hiroshima and Nagasaki were much more likely to develop breast cancer than were exposed older girls or adult women.

While research has advanced our knowledge of breast cancer, more research is still needed to uncover how cancer corrupts normal development processes and how exposure to environmental toxins affects breast cancer risk.

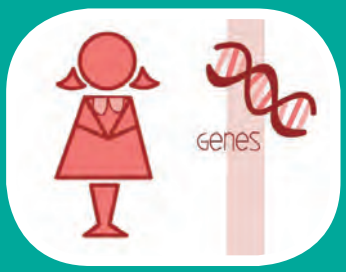


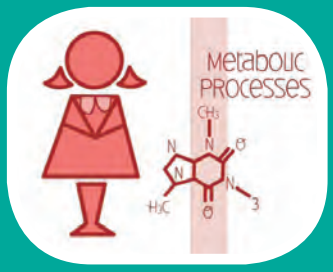
Researchers at the Bay Area Breast Cancer and the Environment Research Center focus on the processes that control normal development of the breast to understand how cancer corrupts these same processes.

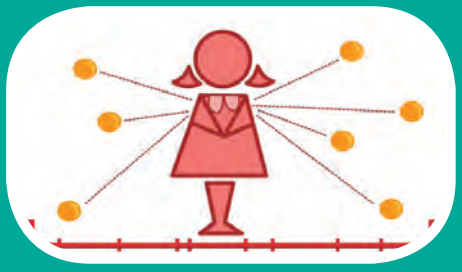




Genes, proteins, and metabolic processes are analyzed to learn what effects chemicals or other environmental exposures have on the breast at specific points in a person's life span. Since during puberty, as the breast develops normally, it displays many of the properties associated with tumor growth, this suggests that tumors hijack processes that are used normally for breast growth.

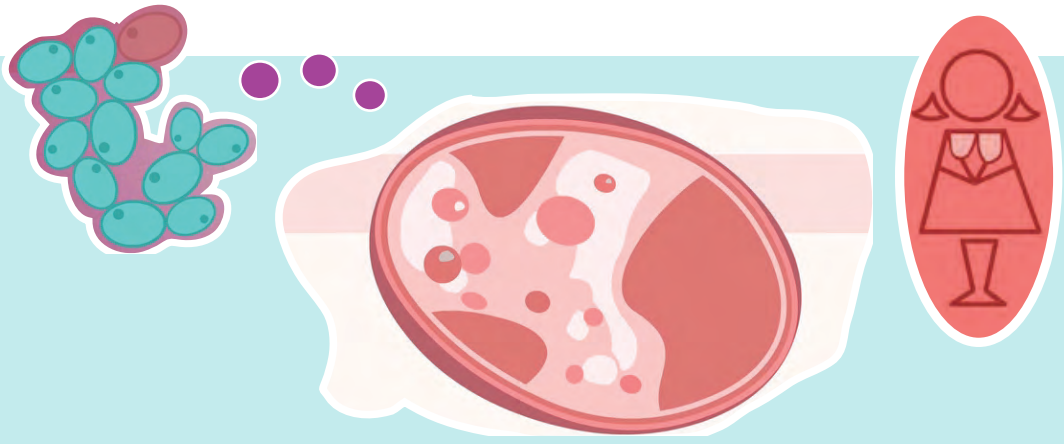




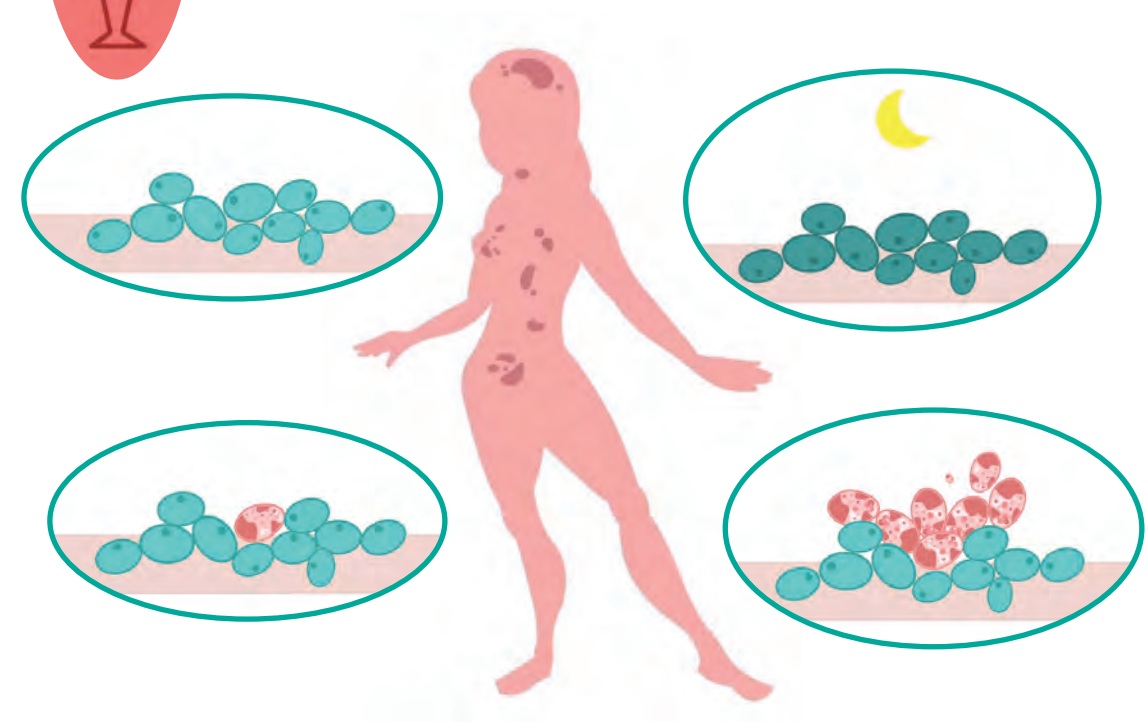


What causes a normal breast cell to turn into a cancer cell?

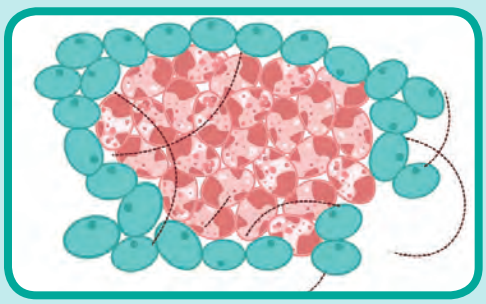
Despite decades of breast cancer research, it is still not clear how a normal cell turns into a cancer cell. We know that cancer cells are normal cells gone astray, and that it is damage to the cell's genetic structure that causes it to take on this bad behavior.



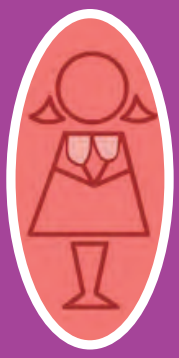
We also know that a normal cell doesn't just turn into a cancer cell overnight. It typically takes decades for a series of genetic mistakes to transform a cell into a full-fledged cancer cell that has the capacity to grow uncontrollably, invade nearby areas, and spread to other parts of the body.



Cancer is not a disease of individual cells. Instead, cancer involves changes in how cells communicate with each other. To further investigate these processes, researchers are looking at how breast ducts develop.

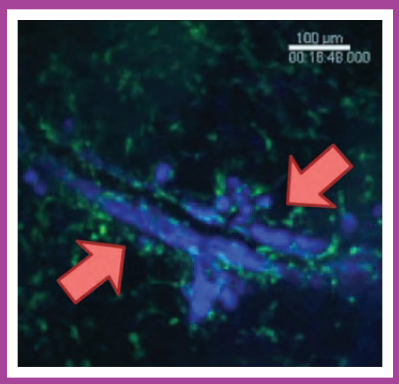


Breast Ductal Morphogenesis Videos



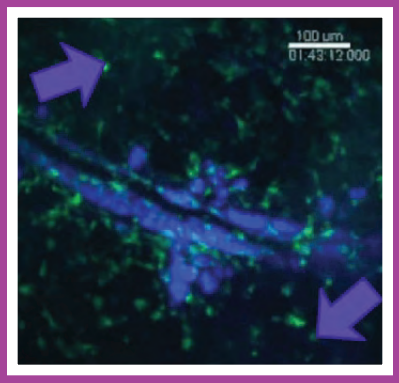
These images of breast cells show you what cellular processes that go awry in breast cancers look like and how normal cells in the breast look.

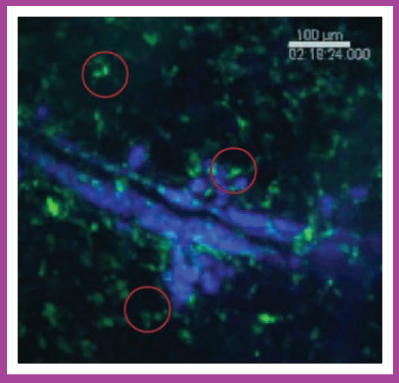
This image shows a normal breast duct in the middle of the field, blood vessels and inflammatory cells which move around in the blood vessels, and the fat of the breast.



The normal duct and its beginning branches are in blue. On top of the duct is a dark strip that is a blood vessel.

The dark areas around the duct are fat cells that make up much of the breast tissue.





The green cells that are around the duct and around the blood vessel are inflammatory cells that don't move. There are more of these cells of different sizes in the fat. You can also see round inflammatory cells in the blood stream. So this shows how dynamic some of the inflammatory cells are even in normal breast tissue.

Even in the normal breast, not everything is still.

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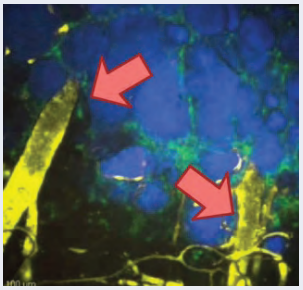
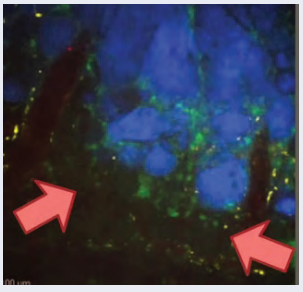
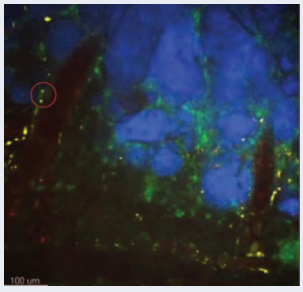
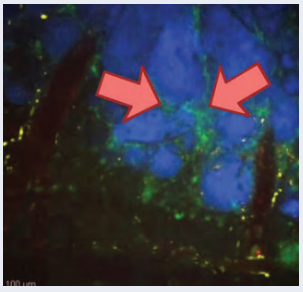
Reference: Egeblad, M., A. J. Ewald, H. A. Askautrud, B. E. Welm, M. Truitt, E. Bainbridge, G. Peeters, M. Krummell & Z. Werb (2008). Visualizing stromal cell dynamics in different tumor microenvironments by spinning disk confocal microscopy. Disease Models and Mechanisms. 1:155-167. PMCID: PMC2562195 http://dx.doi.org/10.1242/dmm.000596









This image shows tumor cells in the breast. You can see the much increased area of blue, which is the breast cancer.

The blood vessels are marked with a yellow dye. You can see that there are many blood vessels and they are rather large and tortuous, a characteristic of blood vessels recruited to tumors in a process called angiogenesis, which is new blood vessel growth.

You can see the blue tumor cells and the green and red inflammatory cells interacting with the tumor and blood vessels. Some cells turn yellow as the dye leaks from the leaky tumor blood vessels. The cells that take up the dye are tumor associated inflammatory cells.

This image shows how the tumor cells interact with blood vessels and inflammatory cells in the breast. It is also evident that there are many more inflammatory cells. Some are inside the tumor, but most are at the tumor margin, where some of them move rapidly.

What is striking is how active the inflammatory response is, while the tumor cells seem to sit doing little except growing slowly.

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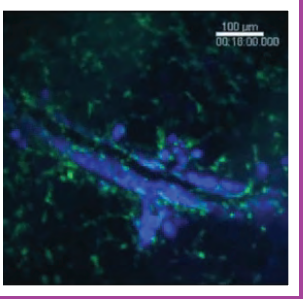
Although normal breast development and cancer are similar, there are a few important differences. Both involve invasion, cell growth, resistance to cell death and the formation of new blood vessels. As you noticed in the images, however, with cancer, the processes are more disrupted and frenetic.



NORMAL

TUMOR

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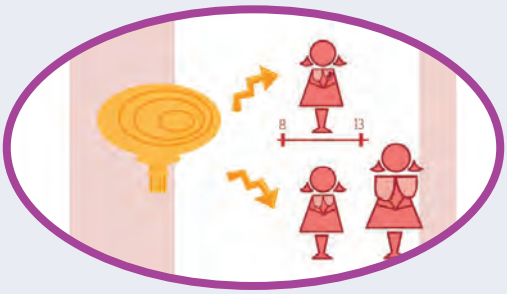
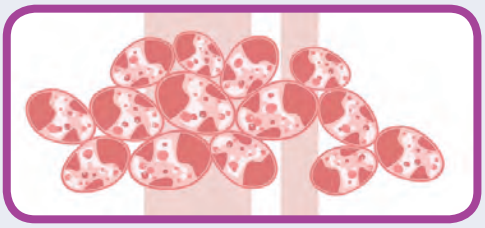
Radiation

Many chemicals and environmental exposures may affect breast cancer risk. The best documented environmental exposure known to cause cancer is high-dose radiation.



Epidemiological studies have shown that girls at puberty who were exposed to radiation from atomic bombs were much more likely to develop breast cancer than were other similarly exposed older girls or adult women.



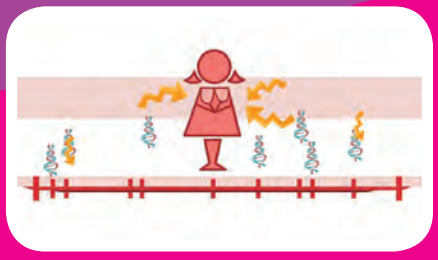
TUMOR INITIATION

TUMOR PROMOTION

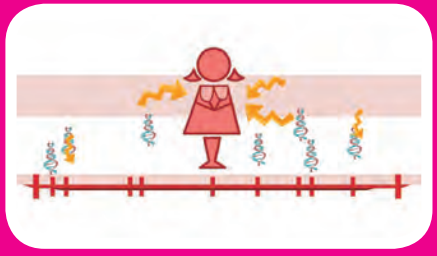
Radiation is considered a complete cancer causing agent because it affects both tumor initiation, which is a single event where a change in the genetic sequence of DNA gives a cell a potential for becoming a breast cancer, and tumor promotion- a multi-event process where the changed cell reproduces many, many times.

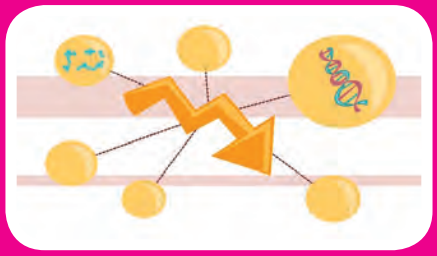
People can be exposed to radiation in many ways. Individuals exposed to atomic bombs were exposed to up to 4 Sieverts (a Sievert is a unit of radiation dose). The lowest dose at which cancer was increased was about 0.5 Sievert or 500 millisieverts (a millisievert is a thousandth of a Sievert).

According to the United States Department of Energy, natural background radiation from the sun and soil accounts for about 3 millisieverts per year. A mammogram is 2.5 millisieverts and is judged to be safe.



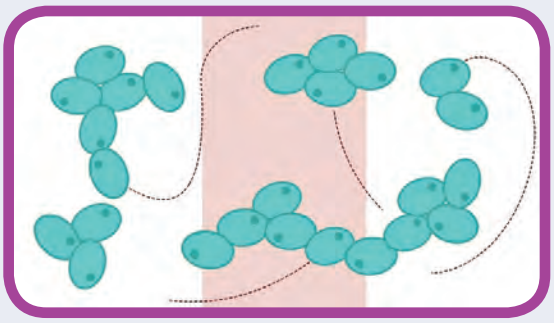
Scientists study how high dose radiation disrupts normal development, including how cells communicate during puberty. At high doses, radiation is known to cause DNA damage that leads to genetic mutations that can result in breast cancer; however, DNA mutations are only one of the ways radiation changes cells.

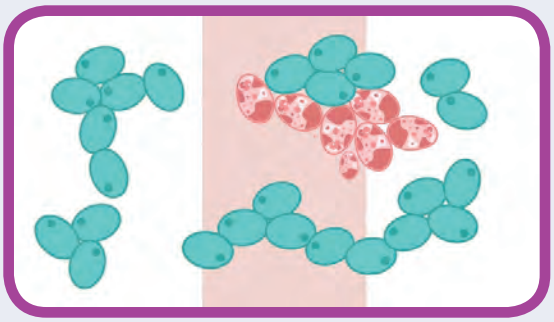




University of California San Francisco and The Lawrence Berkeley National Lab researchers have found that radiation also changes the communication that occurs between cells and allows some precancerous cells to grow and develop. This, in turn, can affect both how cells behave and the cellular neighborhood that surrounds them.

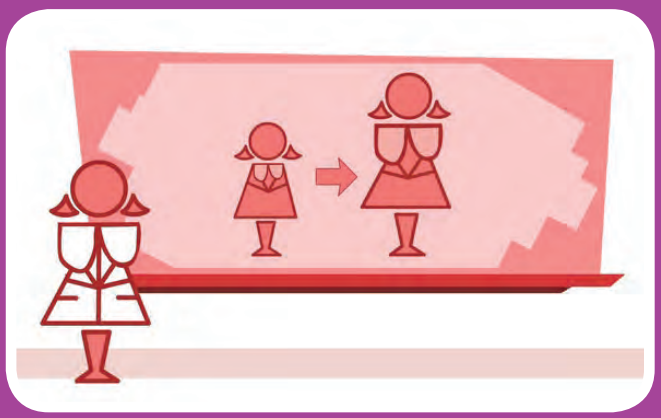
By studying mechanisms affected by radiation, we can expand our understanding of how other environmental toxins may change normal cells to cancer cells.



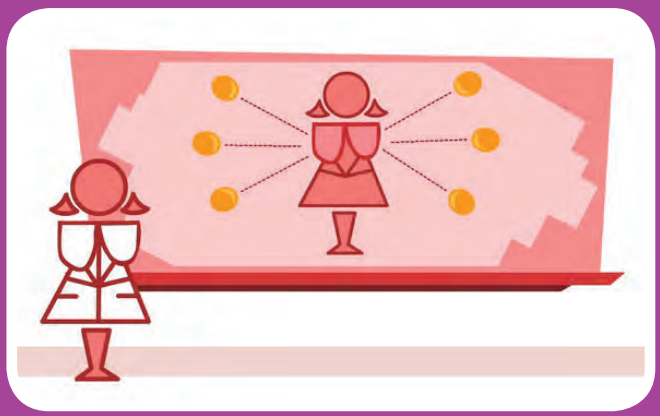


Conclusion

Basic Science researchers at the Bay Area Breast Cancer and the Environment Research Center study normal breast development and how it responds to environmental exposures.



The information learned from basic science research is later applied to research aimed at developing new ways of preventing breast cancer as well as new therapies for treating patients.

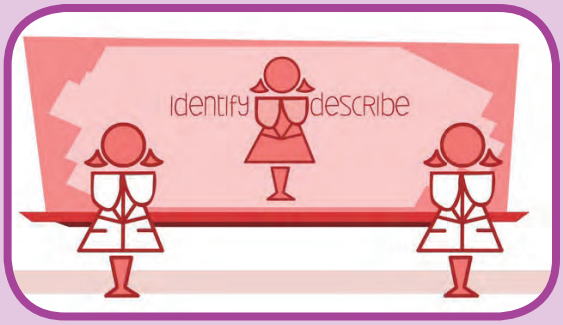


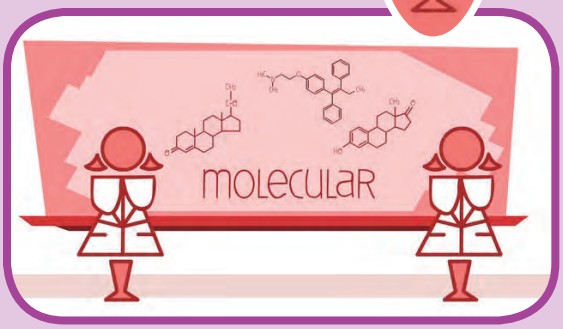
To achieve these goals, we need to understand the basic normal and abnormal processes in the body.

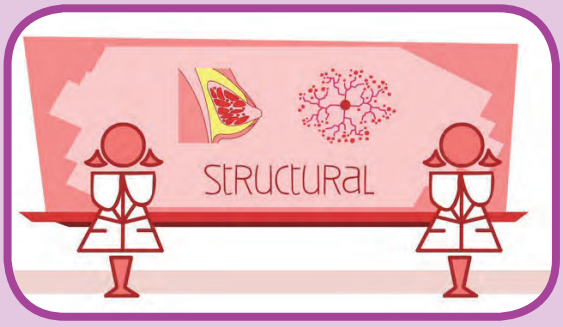
1.

The researchers are working hard to identify and describe the molecular and structural changes that occur in the breast over its lifespan.

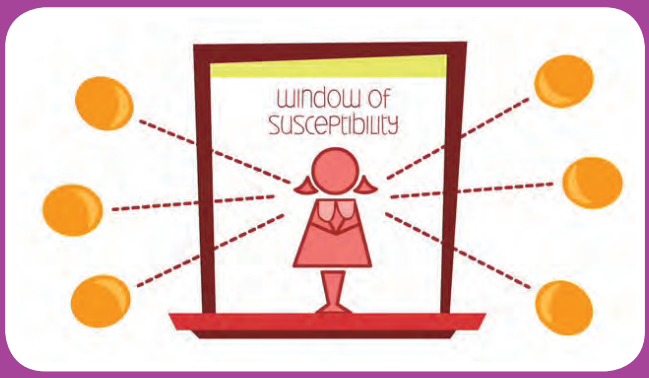
2.



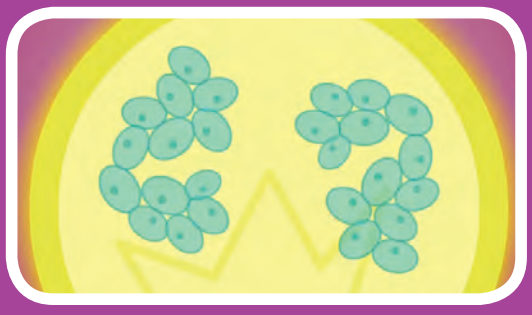


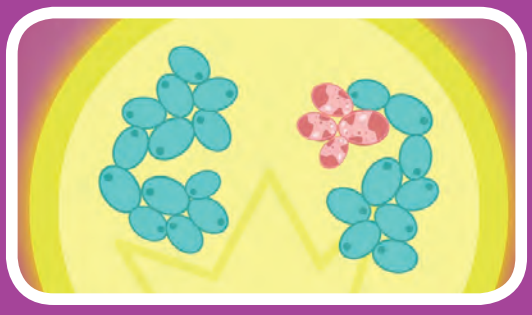


The researchers are also learning about how exposures to potential cancer causing substances during a window of susceptibility, such as puberty, influence future breast cancer risk.

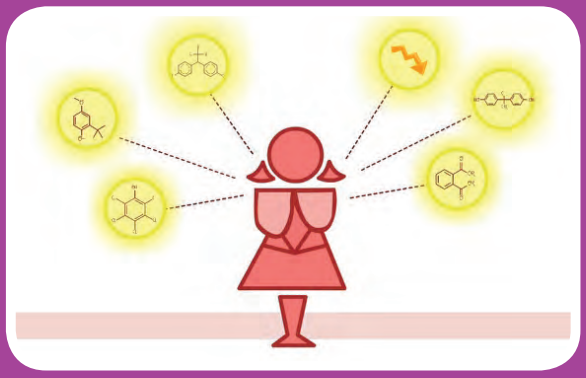


Together with Zero Breast Cancer, the Community Outreach and Translation Core of the Center, the researchers translate the scientific work through projects like this.





Through this comic book we hope you have learned new insight into how normal and cancer cells behave in the breast and how environmental exposures like radiation can affect breast cells.



The Breast Biologues

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