Breast Cancer UK
Prevent the preventable

Animal Free Research UK and Breast Cancer UK collaboration

Effect of Endocrine Disrupting Chemicals on Breast Density

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Breast Density – what's it got to do with breast cancer?

Breast Cancer UK and Animal Free Research UK are asking people to raise money to fund research into breast density. The aim of the research is to try and identify whether different endocrine disrupting chemicals can affect breast density, which can determine breast cancer risk. But what is breast density? Which factors affect it? And how might this research help us to prevent breast cancer?

What is breast density?

Breast density or mammographic density refers to how breasts appear on a mammogram (or breast X-ray). You can't tell if you have dense breasts simply by looking at them or feeling them.

Breasts are made up of glandular tissue (milk ducts and lobules) and fat tissue, held together by connective tissue which contains cells known as fibroblasts.

High breast density means there is a greater amount of connective and glandular tissue, compared to fat tissue. Low breast density means there is more fat tissue.

Women are 4-5 times more likely to get breast cancer if they have high breast density compared to those with low breast density (1). High breast density is the most significant breast cancer risk factor for women after ageing (2).

What determines high or low breast density?

Breast density is partly inherited but is also influenced by the environment and changes over a women's lifetime (3). Breast density increases in response to hormones such as oestrogen, although how this occurs at the cellular level is not fully understood. Post-menopausal women, who have less circulating oestrogen, have lower breast density than women who have not gone through the menopause.

What factors are associated with high breast density?

Environmental factors that increase breast density include alcohol and diet (4), including consumption of sweet foods (5), and air pollution (6) - although further studies are needed to confirm this. Use of certain synthetic hormones, including combined hormone replacement therapy (HRT), increases breast density and cessation of use lowers it (7, 8).

What factors are associated with low breast density?

Certain chemotherapeutic drugs used to prevent breast cancer, such as Letrozole (9) and Tamoxifen (10), and stopping HRT use, have been shown to reduce breast density. Paradoxically, it seems that a High Body Mass Index (BMI), usually an indication of being overweight, is generally associated with low breast density (11). However, it is important to remember that being overweight with high BMI is itself a risk factor for breast cancer.

What do we know about breast density and its link to breast cancer?

Whilst scientists are agreed that high breast density is associated with an increased risk of breast cancer, it remains unclear why this is the case. It is thought that fibroblasts play an important role in the initiation and proliferation of breast tumours. In more dense breasts there are more "active" fibroblasts, which produce growth factors and other substances associated with breast cancer initiation and progression (12). But how they act at a cellular level to influence breast cancer is not fully understood.

How will the research project help prevent breast cancer?

As well as hormones produced by the body and synthetic hormones that are prescribed, we are exposed to low concentrations of numerous endocrine disrupting chemicals (EDCs) at different times throughout our lives. Some of these mimic the actions of oestrogen. Currently, it is unclear if these may contribute to changes in breast density.

The research project, led by Professor Val Speirs from the University of Aberdeen, will investigate the effects of some of these oestrogen mimics on fibroblasts from breast tissue of different breast density, in order to understand how these influence breast density and in turn drive breast cancer development. The PhD studentship was awarded to Ms Kerri Palmer.

The fibroblasts will be generated from human breast tissue and will use an innovative 3D in vitro human mammary gland model.

The long term objectives of the study are to identify biochemical pathways which mediate breast density, which could be modified to reduce the risk of breast cancer. It may also help us to determine which chemicals are the most harmful, and so allow us to recommend effective policy measures that aim to reduce exposure to certain chemicals, in a bid to reduce contributors to breast density. The ultimate goal is to identify an effective strategy for breast cancer prevention.

How are we studying breast cancer development using human-relevant animal free research?

Alongside pathologists, who concentrate on what tissues look like in order to diagnose disease, the team will build animal-free breast cancer models. These models will reflect human disease as the researchers will ensure, as far as possible, that they look and behave like human breast tissues.

Importantly, the research will not use any animals or animal-derived materials. It will be done using different types of breast cells, including fibroblasts generated from human breast tissue - from consenting patients - whose mammographic densities vary.

The team will work with clinicians to explore how human breast fibroblasts respond when exposed to EDCs. Complex 3D breast cell culture models will then be used to examine how exposure to such chemicals may contribute to breast cancer development.

The models will help understand how fibroblast cells may affect breast cancer development. This question cannot be answered successfully using mouse models because human fibroblasts are very rapidly replaced by mouse fibroblasts when transferred to mice.

What is the impact on animals used in the research?

According to Professor Speirs, over the past 5 years there were 3016 publications which used animal models (mostly mice) to study breast cancer, and over 109 of these included UK-based authors.

A typical mouse experiment includes around 40 mice. Of the publications from UK groups, a conservative estimate means more than 4000 mice would have been sacrificed, excluding any required for breeding programmes, which can often run into thousands.

Professor Speirs' research aims to replace two currently used animal models of breast cancer, by using fully humanised animal free models.

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