

EFFECTS OF LOW-DOSE EDC MIXTURES

Breast Cancer UK awarded a grant to Dr Elisabete Silva, at Brunel University, to support research which examined the effects of low dose endocrine disrupting chemical (EDC) mixtures on breast morphology and carcinogenesis (cancer formation), using an in vitro 3D breast cell culture system. This system uses non-cancerous human breast cells which express oestrogen receptors and so respond to oestrogen and oestrogen mimics. Dr Sibylle Ermler, Dr Hemad Yasaei, Professor Martin Widschwendter and Ms Phoebe Maund were also involved in the research.

Summary of results

Dr Silva and colleagues showed that low concentrations of four EDCs (propylparaben, BPA, DDT and benzophenone-3) added to breast cells grown in 3D cell culture caused changes resembling early stage breast cancer. When EDC mixtures were added, changes were even more significant.

Detailed project description

Oestrogen responsive breast epithelial cells will be grown on a reconstituted basement membrane matrix, enabling cells to grow in three dimensions. This system can reproduce features of malignant changes which can be observed microscopically. Changes in gene expression and gene methylation patterns will be assessed using molecular biology techniques. The cell culture system uses non-cancerous breast cells which express oestrogen receptors and are responsive to oestrogen and oestrogen mimics.

The EDC mixtures include bisphenol A (BPA), the (banned) pesticide DDT, the preservative propylparaben and the UV filter,

benzophenone-3. All of these have been detected in human breast tissue, can act as oestrogen mimics, and, with the exception of DDT (which is now banned in Europe although still used elsewhere in the world), are used in numerous everyday products.

The use of oestrogen responsive breast cells grown in 3D is an original and potentially effective means to test oestrogenicity of environmentally relevant concentrations of EDC mixtures. In addition, this type of research is a good example of an alternative method of testing EDCs which does not involve animal experimentation. As such, we are very proud to be supporting such an approach in scientific testing. The results of this research will demonstrate whether the EDCs tested in combination are able to induce changes in breast cells that are characteristic of cancer.

The work began January 2016 and was completed in 2017.

Description of results by Dr Silva

The alarming increase in the incidence of breast cancer worldwide cannot be explained solely by hereditary factors and evidence suggests that exposures to environmental contaminants, including those that disrupt normal hormone functions (so-called endocrine disrupting chemicals, EDCs), are involved. Scientific research linking endocrine disruptors to cancer is currently inconclusive. Experimental work has shown that chemicals such as plasticisers, pesticides and cosmetic additives cause effects in animal and cell-based models that promote breast cancer. However, many of these effects are only seen at levels of the chemicals that are much higher than those found in human tissues. Also, most studies examining links between exposure to individual EDCs and breast cancer in humans have produced unconvincing results. Taken together, these observations often lead to

the assumption that the concerns associated with the role of endocrine disruptors in breast cancer are unfounded, as their levels in tissues are not high enough to increase breast cancer risk. The problem with this assumption is that humans are exposed to low levels of large numbers of chemicals that could act together to increase breast cancer risk. However, to date, this possibility has not been investigated.

Our project aimed at addressing this question by studying the way EDCs act together at low levels to potentially cause breast cancer. For this, we analysed the impacts of four EDCs and investigated how they impacted on the structure and behaviour of breast cells grown in a three dimensional (3D) system that resembles the human breast. The four compounds tested were: Bisphenol A, a chemical found in plastics, DDT, a pesticide that accumulates in our tissues, propylparaben, a preservative found in cosmetics and benzophenone-3 a UV filter found in sunscreens. All four are also ubiquitously found in human tissues.

We observed that all four compounds led to a disruption of breast structure that resembled what occurs in the early stages of breast cancer. We were also able to use the information on the chemicals to predict the effects they would cause if combined at levels found normally in human tissues. We showed that, together, these chemicals affect the function and structure of the breast more significantly than when tested alone, indicating that mixtures of EDCs, even at low levels, can potentially lead to breast cancer.