

# Prevent Breast Cancer's Molecular Basis of Breast Density Project

## About Prevent Breast Cancer

**Predict. Prevent. Protect.** You could call it our mantra. As the only UK charity entirely dedicated to the prediction and prevention of breast cancer, we're committed to freeing the world from the disease altogether. Unlike many cancer charities, we're focused on preventing, rather than curing. Promoting early diagnosis, screening and lifestyle changes, we believe we can stop the problem before it starts. And being situated at the only breast cancer prevention centre in the UK, we're right at the front line in the fight against the disease.

We **predict**, we **prevent**, we **protect**.

**We predict** – by identifying who is at risk of breast cancer

**We prevent** – by offering preventative interventions, to **stop** breast cancer before it starts

**We protect** – our goal is to **shield future generations** from breast cancer

Prevent Breast Cancer seeks to create a breast cancer free future for the next generation. We conduct ground-breaking research into the prediction and prevention of breast cancer and with **only 3% of all cancer research being spent on prevention, the work we do is vital.**

We are a registered with the Charity Commission in England with the Registered Charity Number 1109839.

## The Breast Density Project

Little is known about the exact cause of many breast cancers. We do know that women described as having high mammographic density (whiteness on the mammogram), have a 4-6-fold increase in breast cancer risk compared to women of the same age, described as having low mammographic density. **Scientists agree that this is one of the strongest predictors of whether a woman will develop breast cancer in the future**, but it is not yet known why. Prevent Breast Cancer is seeking funding for a pioneering new research project which will examine this in depth.

### A project impacting thousands of people across the UK

The impact of this research project could be significant. It could help Prevent Breast Cancer provide more targeted breast screening and early, accurate diagnosis of breast cancer and possibly lead to improved approaches for prevention. This could benefit many thousands of women and men across the UK every year.

Every year 55,000 people are diagnosed with breast cancer– that's 150 a day. And every year we lose a staggering 11,400 people to the disease.



A patient about to receive a mammogram

### The project in more detail

Mammographic density describes how the breasts absorb X-rays and therefore look on a mammogram. On the whole, fatty breasts have low overall mammographic density (fat appears black or grey on the mammogram) while breasts containing a lot of connective tissue (which act as a scaffold for breast ducts and lobules) have high mammographic density. Emerging evidence shows that there are changes within this collagen-rich connective tissue in women with high mammographic density, which in turn promote cancerous changes within the breast cells.

The nature of the changes within the connective tissue, and how these changes subsequently promote breast cancer, is not well understood but our early experiments suggest that it is not the amount but rather the organisation of collagen proteins

within breast tissue may be very important. This altered organisation of collagen may in turn promote a stiffer environment around breast cells that leads to the genetic changes of cancer. We wish to study this further as it will contribute to a very important body of research as well as potentially helping us to provide targeted and more accurate early screening.

To fill this important gap in our knowledge, we will determine differences in tissue composition, structure, stiffness, and expression of genes in high and low mammographic density tissue, and of early breast tumours arising in the same individuals. To do this we will recruit patients undergoing mastectomies for breast cancer.

We will study breast tissue removed as part of the cancer operation, comparing normal breast tissue to cancer tissue in women with high mammographic density and also in women with low mammographic density. Our work will provide completely new insights into the cause of high mammographic density and may identify genetic factors that predispose some individuals to developing high-density breasts.

This project is led by Principal Investigator Charles Streuli, Professor of Cell Biology, Faculty of Life Sciences, University of Manchester from 2002 and Director of the Wellcome Trust Centre for Cell-Matrix Research.

### **Our Team**

We will fund a small team to lead this pioneering research project.

**Laboratory technician** – Angela Leek - Senior Biobank Technician, UHSM Hospital Manchester Cancer Research Centre Biobank CRUK Manchester Institute

Job Description Summary - Organise tissue collection from patients; Collect mammograms (VAS and Volpara); Collect relevant patient information; Get blood samples; Take surgery samples to pathology for dissection; Fix some samples in paraformaldehyde, freeze others, and send to biobank for storage and future analysis.

**Postdoc** – Dr James McConnell - Post-Doctoral Research Associate

Job Description Summary - Arrange to get for H+E & PSR (=picrosirius red) samples from histology; Arrange for cutting of other samples - for various immuno-studies; Complete the micro-mechanics work & determine tissue ultrastructure; Responsible for Atomic Force Microscopy, microCT (microscopic X-ray imaging); Arrange for frozen tissue specimens to be cut for a) micromechanics, b) proteomics, c) RNA-omics, d) DNA analysis; Send samples > proteomics core facility; > RNA core facility; > Illumina for DNA; Collect and analyse data - and write papers for publication & present data at conferences.

### **Length of the Project**

The project began on 1<sup>st</sup> April 2017 and will run for 2.5 years.

### **Methodology**

We will recruit post-menopausal women (aged 53-67) undergoing mastectomies for invasive breast cancer at the University Hospital of South Manchester. Patients with high and low overall mammographic density will be identified at The Nightingale Centre Breast Clinic and their breast tissue will be studied using the following methods:

- a) Following resectional surgery, isolate fresh tissue from women with high and low mammographic density.
- b) Obtain comparative deep sequencing and detailed genomic information of normal breast and invasive breast cancer arising within the same breast, and as controls, distant non-breast tissue.
- c) Determine if any differences between high vs low mammographic density breast, and invasive breast cancers within the same breast, correlate with altered RNA and proteomic composition (by microarray and mass spectrometry), remodelling of breast structure and micromechanics (conventional histology and atomic force microscopy), and local X-ray density variation (by microCT).

### **Your Contact at Prevent Breast Cancer**

For further information or any queries, please contact Vicki Wilkinson, Charity Manager at Prevent Breast Cancer. Phone: 0161 291 4402 Email: [vicki@preventbreastcancer.org.uk](mailto:vicki@preventbreastcancer.org.uk)