# Personalised Breast Cancer Program

## What happens to samples?

The journey of blood and breast cancer samples collected as part of the Personalised Breast Cancer Program (PBCP) is long and complex. We have summarised what happens to samples below so that patients can understand how we determine both **somatic** (tumour) and **germline** (inherited) genetic codes.

## The journey of blood and tissue samples in PBCP

### Blood and tumour tissue collection

Precision Breast Cancer Institute, Cambridge Breast Unit, Oncology Outpatients & theatres

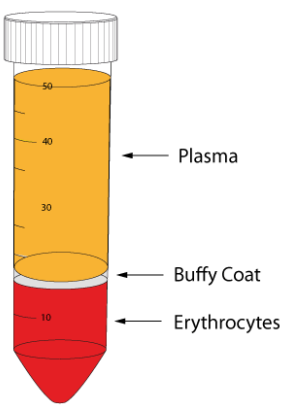
As part of routine care, blood and a tissue biopsy will be taken. If a patient gives consent to take part in the personalised Breast Cancer Program, we collect additional blood and tissue samples, either from a biopsy or surgery. Blood is sent straight to the Cancer Molecular Diagnostic Lab (CMDL). Tissue is collected by a member of the PBCP team and is frozen very quickly in liquid nitrogen and stored in an ultra-cold freezer at -80$^{o}$C. The samples will be anonymised using a numerical ID. Only a select number of people can link the samples back to the patient.

Senior Research Nurse, Justine Kane, freezing a tissue sample

### Blood processing for germline (familial) DNA

Cambridge Molecular Diagnostic Labs

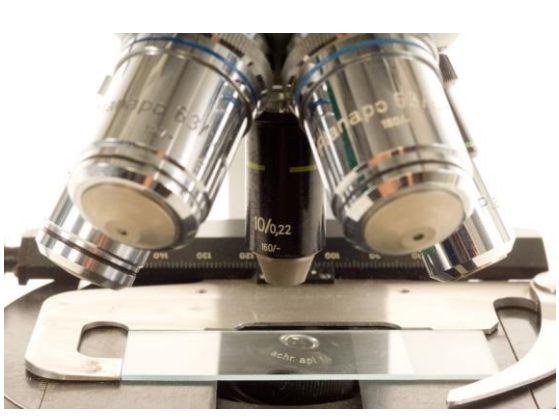
Blood samples will be received by scientists at CMDL where they are spun at a very high speed in a centrifuge. This separates the blood into three distinct layers: plasma, buffy coat and erythrocyte (red blood cells) layer. To isolate DNA, we are in are interested in the buffy coat layer which contains leukocytes (white blood cells). The plasma layer is removed and stored, the buffy coat is carefully removed for DNA isolation and the red blood cells are discarded.




### Processing tumour sample for somatic (tumour) DNA

Human Research Tissue Bank

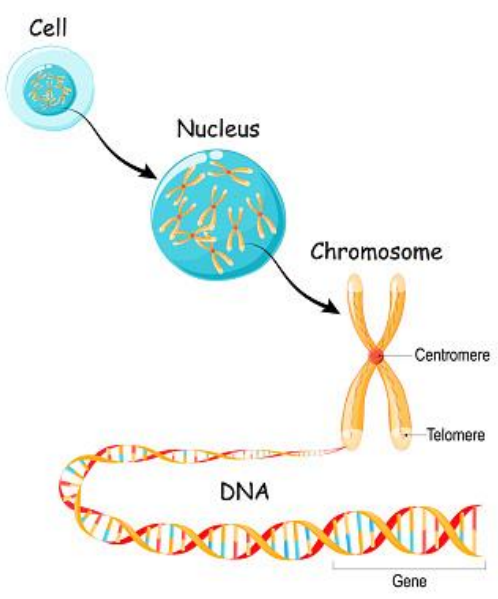
The tumour sample is taken to the Human Research Tissue Bank and Cambridge University Hospital. They will cut a very thin slice of the tumour, lay it on a glass slide and view the tissue under a microscope.. First they assess how much of the sample is made up of cells as opposed to structural and non cellular content – this is called the sample cellularity. Then the count the number of normal breast cells and breast cancer cells to determine the tumour content. A sample with a high cellularity and high tumour content will give us the best sequencing data. This information helps us choose which sample should go to CMDL for DNA isolation



### DNA Isolation

Cambridge Molecular Diagnostic Labs

At CMDL, the samples are handles carefully to make sure there is no cross contamination of the samples. In order do access the DNA in the nucleus, the white blood cells from the buffy coat are lysed (burst open) and the tissue samples is broken up. The DNA from each sample is extracted from all the other components inside the cells. The team then measure the amount of DNA in each sample and the assess the quality. The DNA samples are frozen before sending on for the next step.




### DNA Sequencing

Illumina, Chesterford Research Park.

Both germline (from the blood) and somatic (from the tumour) DNA samples are sent to Illumina by courier. The samples are still anonymised and can be identified with the numerical ID assigned when the samples were collected.

DNA is made up of four building blocks called bases: Adenine (A), Guanine (G), Thymine (T) and Cytosine (C). The germline sequence of these provide the instructions to make all the proteins that are needed to make our bodies function and make us all unique. The somatic DNA may contain alterations in the sequence that can provide clues to why the cancer is growing.

Illumina use state-of-the-art technology to work out the entire sequence of both sample. Follow this link to see a cartoon that explains the Illumina method of sequencing. The data is sent to scientists at the University of Cambridge for analysis.

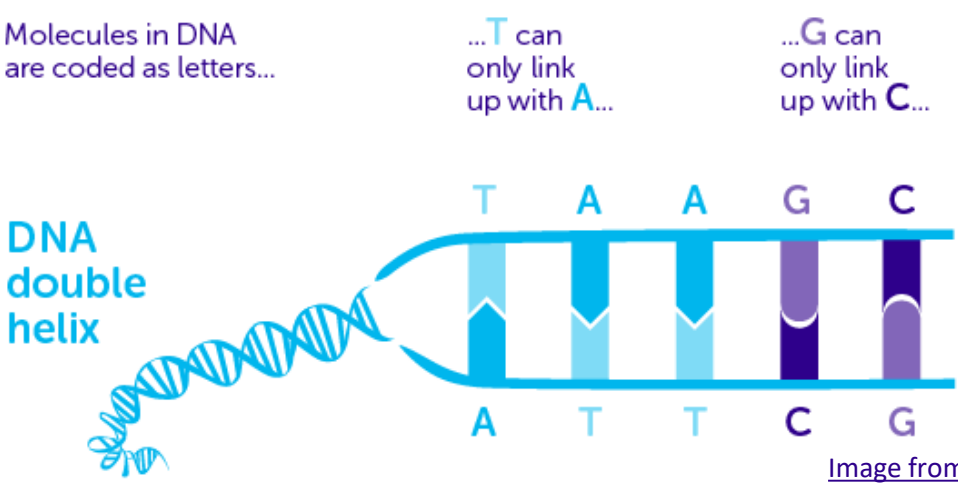
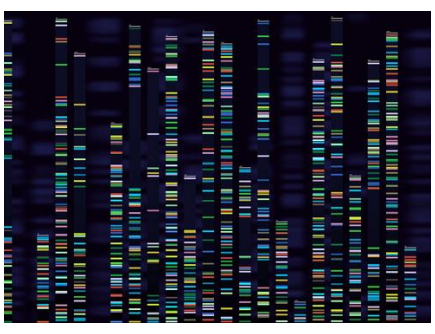



Image from CRUK.org

### Sequencing Data Analysis

Precision Breast Cancer Institute

A whole human DNA sequence contains a lot of data, with approximately 3 million bases per genome. The data needs to be stored and analysed on the secure High Power Computer system at the University of Cambridge by specialist data scientists called Bioinformaticians. The germline and somatic genomes are carefully analysed and compared to identify any changes that might be linked to the patients breast cancer. This information is summarised in a report for the PBCI coordination team.



### Omics Review Board

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The PBCI team will prepare reports that bring together clinical data collected through PBCP with the information that has been summarised by the Bioinformaticians. The report, which is anonymised, is discussed at the Omic Review Board (ORB) where a multidisciplinary team (MDT) of specialists in oncology, genetics, pathology and bioinformatics discuss the genomic information for each participant of PBCP. The MDT will decide whether any of the genetic changes are likely to have a potential impact on the patients future care.

### Results are returned the PBCP participants

Precision Breast Cancer Institute

The PBCI team will make sure the outcome of the ORB is recorded in the patients medical record, and compose an individualised report for the patient. The patients will be able to have further discussion with their consultant about the results. If an alteration is found in the germline sequence that increases the patients risk of breast or other cancers, they will be referred to the Clinical Genetics team and another blood test will be collected to validate the results. The Clinical Genetics team will support the patient and their family members in managing the risk of carrying a gene alteration that makes them at higher risk of developing cancer.

## 12 weeks from samples collection

We aim for this process to take a maximum of 12 weeks, but it is often completed within 6-9 weeks. The data will continue to be securely stored and used for research to try any learn more about breast cancer that might lead to future trials and treatment changes to personalise how we treat breast cancer.