Sequential blood samples & circulating tumour DNA

To get the most out of clinical trials and studies we include optional sub-studies to enable the collection of additional samples from patients that are taking part. Personalised Breast Cancer Program has a sequential blood sub-study. Blood samples are collected at specific time points throughout treatment and up to 5 years post surgery. The main reason for collecting these samples is for circulating tumour DNA analysis (ctDNA).

What is circulating tumour DNA?

The nucleus is often described as the command centre of a cell controlling its growth, function and reproduction. Each cell nucleus contains a copy of the individuals DNA sequence which serves as a template for the production of proteins to regulate cell activities, and a template for cell division and growth. All cells shed DNA into the bloodstream, including cancer cells. Sensitive techniques can be used to isolate and sequence the ctDNA in the plasma fraction of a blood sample. The sequence of the ctDNA and the amount of it in the blood can give us useful information about cancer.

These kind of tests are sometimes referred to as “liquid biopsies” as we can find out information about an individuals cancer with a blood sample rather a tissue biopsy which requires a more invasive procedure.

What can we learn from ctDNA?

Early Detection

The sooner a cancer is detected, the better the treatment outcomes. At present, mammography is the method used for surveillance of the population most at risk of breast cancer, or they are detected by physical changes in the breast. Cancers could be detected at an earlier stage through analysing ctDNA in blood samples. The ctDNA could also provide information about the cancer is it is too small or inaccessible to biopsy. The EMBED study is looking for ctDNA early markers of Breast Cancer from blood samples collected when women attend routine screening Mammograms.

Monitoring treatment response

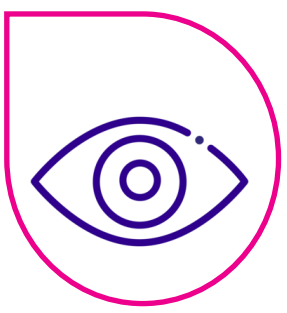
It is helpful for patients and oncologists to know early into a course of treatment whether it is working. This gives reassurance to the patient, but also allows for treatment to be stopped or changed if it is not working. Currently, this can be estimated by physical exam or imaging examination.
There is potential for ctDNA to be used to monitor the response of a cancer to treatment to give us a much earlier indication if treatment is working than can be achieved through standard imaging techniques. It could also help monitor for early cancer recurrence along side routine mammograms.

Mutation-directed Therapy

ctDNA can give us information about the gene alterations that might be driving the cancer, without the need for a biopsy. The PlasmaMatch clinical trial used ctDNA to detect the mutation of four different genes that align to targeted treatments. Early results demonstrate a good response to drugs that target two of the gene alterations detected in ctDNA. The ctDNA analysis was also shown to have 93% accuracy when compared to sequencing of tumour tissue samples.

Prognostic markers

Low levels of ctDNA on completion of treatment are related to a long progression-free survival and overall survival in certain breast cancer types. This means ctDNA could be used as a prognostic marker on completion standard treatment, and to inform whether additional treatment is recommended.



Tumour heterogeneity

A cancer is constantly changing as it grows in response to its environment, surrounding cells and treatments. A tumour is made up of different groups of cells which have developed alterations that drive their growth and division. Circulating tumour DNA can give us a snapshot of these mutations and how they change in response to treatment over time.

Analysis of ctDNA is not currently part of standard care in the NHS. Research is ongoing to develop the evidence and techniques to introduce this as a diagnostic and monitoring tool along side tissue biopsies, imaging and clinical examination.

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