CHIEF SCIENTIST OFFICE

CODE: ETM/433

RESEARCH PROJECT BRIEFING

Testing new methods to analyse cancer using tumour DNA in blood samples

AIM

Currently, many cancer patients undergo surgery to take samples of tissue from their tumours which are used to diagnose their cancer and manage its treatment. We aimed to develop new methods to process blood so that blood samples from cancer patients can be used to understand and analyse a patient's tumour without needing surgery.

KEY FINDINGS

- Microfluidics is a branch of engineering in which fluids are processed and analysed by passing them through very narrow tubes.
- One of the research team (Maiwenn Kersaudy-Kerhoas) has shown that microfluidics can be used to remove all of the cells from blood samples without having to spin them in a centrifuge. The liquid produced is called plasma.
- Human plasma contains a small amount of free DNA. In a cancer patient, some of this cell-free DNA is mutant DNA which has come from their tumour. We have shown that this can be purified using microfluidics.
- The polymerase chain reaction (PCR) is a method to make many copies from a small number of DNA molecules in a sample. We have developed a new PCR based method to detect mutant tumour DNA within a background of healthy DNA which does not need expensive specialist equipment so can be performed in most laboratories

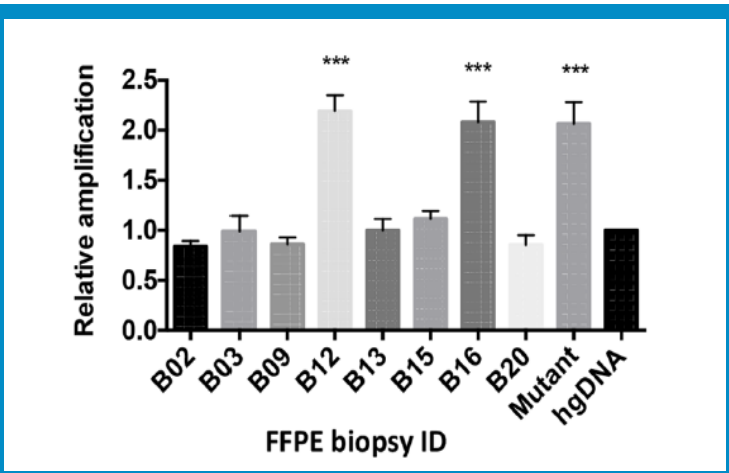
WHAT DID THE STUDY INVOLVE?

We collected just over 50 blood samples, 28 from breast cancer and 23 from brain tumour patients. Each blood sample was split in two and then plasma was prepared from both halves by removing the cells either by microfluidics or by the standard method of using a centrifuge. We then purified DNA from each plasma sample and tested whether we could detect mutant tumour DNA in the plasma DNA samples by sequencing the DNA or by using a method called digital droplet polymerase chain reaction (ddPCR). As part of the study, we also developed new simpler methods of detecting tumour DNA by simple quantitative PCR, a technique which can be achieved in most laboratories.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

We were able to get a normal yield of DNA from the plasma purified by both microfluidics and by centrifugation. Importantly, using both ddPCR and sequencing we were able to detect tumour DNA in the plasma samples of some cancer patients and at similar levels. We also showed that our new simple PCR based detection method was able to identify mutant DNA in DNA samples taken from tumour tissue and from mixtures in which the % of tumour DNA was as low as 5%. However, this new method was not sensitive enough to detect the very low levels of mutant tumour DNA in most plasma samples, which are often <1%.

Detecting tumour DNA in DNA samples purified from blood samples by microfluidics has not been done before and is important because efforts are underway to develop bedside devices to analyse tumour DNA in blood samples in one process.



The graph show the successful accurate detection of a specific cancer mutation (PIK3CA H1047R) in cancer patients samples. 8 samples were analysed (each with a B number), two of which were known to carry the mutation being tested for. The amplification method successfully identifies patients B12 and B16. Taken from Alvarez-Garcia et al, Sci Rep, 2018.

WHAT IMPACT COULD THE FINDINGS HAVE?

- The easier cheaper characterisation of tumours and assessment of disease burden using blood samples should improve disease management for many solid cancers and reduce the number of cancer patients who need to have surgery to diagnose their cancer.

- The project has also provided a significant boost for the development of a Spin Out company funded by Scottish Enterprise, Natantis, which now has 4 staff and is developing a bedside device to purify cell free DNA from blood

HOW WILL THE OUTCOMES BE DISSEMINATED?

The new PCR method has already been published in Scientific Reports (Alvarez-Garcia et al, Sci Rep, 2018, 8, 4290). The data addressing microfluidic recovery of ctDNA will be published in a further paper

The co-applicants and I have presented the research at international conferences (myself as a speaker at “Molecular Diagnostics Europe” in April 2017 and the funded researcher Dr Alvarez-Garcia in a poster at the Circulating Biomarkers World Congress in Boston 2017) and we will do so again in the future.

CONCLUSION

This work helps confirm the potential of microfluidics as a method to analyse tumour DNA in blood samples from cancer patients. This has the potential to greatly reduce the need for invasive biopsies making the care of cancer patients both more reliable and cheaper.

RESEARCH TEAM & CONTACT

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Additional Information

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