Capture of circulating tumor cells using nanomagnetic technology

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INTRODUCTION

Detection of biomarkers like circulating tumor cells (CTCs), nucleic acids and exosomes in peripheral blood is an increasingly popular method for early diagnosis of cancer and has been gaining prominence as an alternative to invasive biopsies. “Liquid biopsy” has potential to be a next generation diagnostic and prognostic tool for point of care testing by clinicians

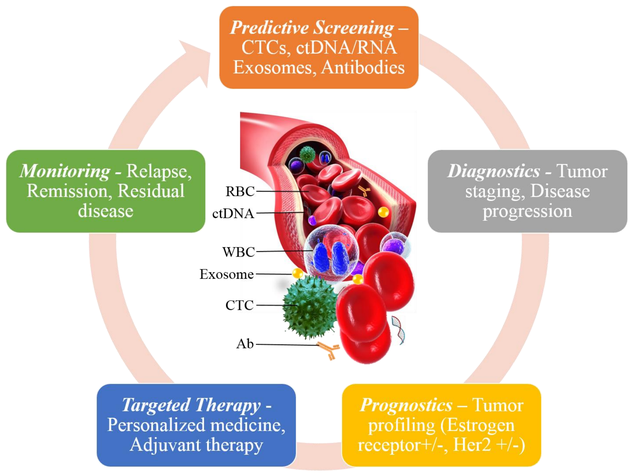

Fig 1. *Liquid biopsy as a diagnostic and prognostic tool.* The information derived from liquid biopsy can be used for continuous monitoring of the patients, from initial screening to personalized treatment.

SCHEMATIC OF THE MICROCHIP

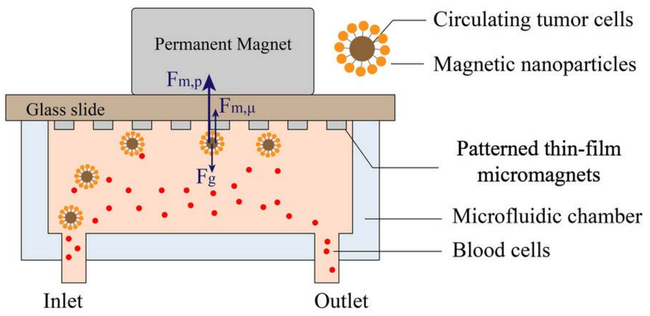

Fig 2. Concept of nanomagnet array integrated with the microfluidic channel for capturing CTCs. Chen at al., 2015.

METHOD

- **Controls** – We pipette 200 SKBR3 cells’ worth of solution onto control glass slides and allow them to dry
- **Experimental** – We mix a separate 200 cells’ worth of solution with 100 micrograms of nanoparticles and incubate them
- **Capture** – After 2 hours of incubation, we run the experimental samples through the magnetic capture machine
- **Analysis** – Both experimental and control slides are frozen, fixed, stained, then counted under fluorescent microscope display

RESULTS

The images below display a portion of a microscope slide used for CTC capture. The CTCs have been stained with a green fluorescent dye FITC (which stains cytokeratin) and a blue fluorescent dye DAPI (which stains nucleus).

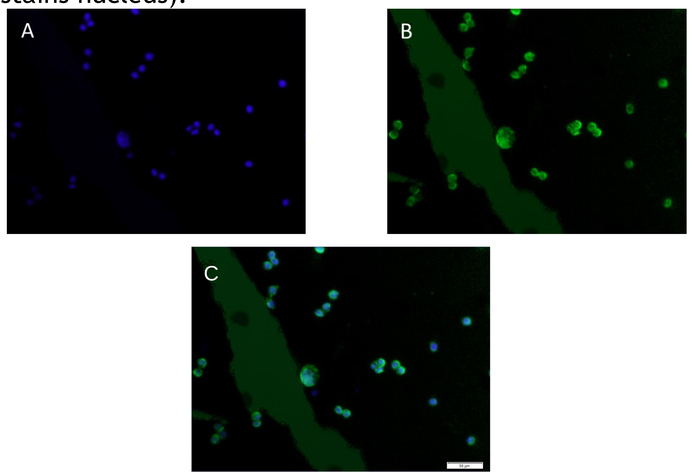

Fig 3. *SkBr3 cells labelled with anti-EpCAM conjugated magnetic NPs. (A) DAPI + (B) FITC-labeled anti-cytokeratin + (C) Overlay of DAPI and CK.*

DATA

100 nm NP conjugated with EpCAM (Source)	NP Conc. (μg/ml)	Incubation Time (Hours)	Incubation Conditions	Capture Rate (%)
Dartmouth	100	2	Closed/37 ˚C	82
Dartmouth	75	2	Closed/37 ˚C	80
CellSearch	100	2	Closed/37 ˚C	83

Table 1:*Capture rate of the CTC using the magnetic nanoparticles conjugated with EpCAM. The capture rate is defined as the ratio of average number of cells captured during the screening process to the average number of cells counted on control slide. We compared the performance of the nanomagnetic particles conjugated at Dartmouth against those which are commercially available.*

CONCLUSIONS AND FUTURE DIRECTIONS

Immunomagnetic separation is a reliable means of CTC capture. Our techniques yield promising results in buffer-based tests. Our particles and machine perform at commercial level.

Future directions include the use of negative enrichment, which would capture white and red blood cells while eluting the CTCs as a means of separation. We are also exploring the integration of microfluidic techniques into CTC separation.

REFERENCES

Chen, Peng, et al. "Microscale magnetic field modulation for enhanced capture and distribution of rare circulating tumor cells." *Scientific reports* 5 (2015).

ACKNOWLEDGEMENTS

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