



**ANGLE**

**Shares Cenkos  
Innovators & Investors Forum**

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Cancer Research UK: “One in two people born after 1960 in the UK will be diagnosed with some form of cancer during their lifetime.”

- ❖ Each patient's cancer is different
  - ❖ Patient's cancer changes over time
  - ❖ Effective treatment requires personalised care
  - ❖ Reducing healthcare costs
- ❖ Major pharma developing more selective drugs
    - Colorectal cancer KRAS- Erbitux (Merck Serono)
    - Lung cancer EGFR+ Iressa (AstraZeneca)
    - Breast cancer HER2+ Herceptin (Genentech)



## Obtaining cancer cells for analysis

### Existing approach: solid tumour biopsy

- ❖ Clinicians cut out part of the tumour and analyse the cancer cells
  - Breast cancer mastectomy or lumpectomy
  - Colorectal cancer colonoscopy tumour biopsy
  - Prostate cancer fine needle biopsy and prostatectomy
- ❖ Difficulty in accessing some tumours
  - Pancreatic cancer, Lung cancer, Brain cancer
- ❖ Repeat tumour biopsy problematic

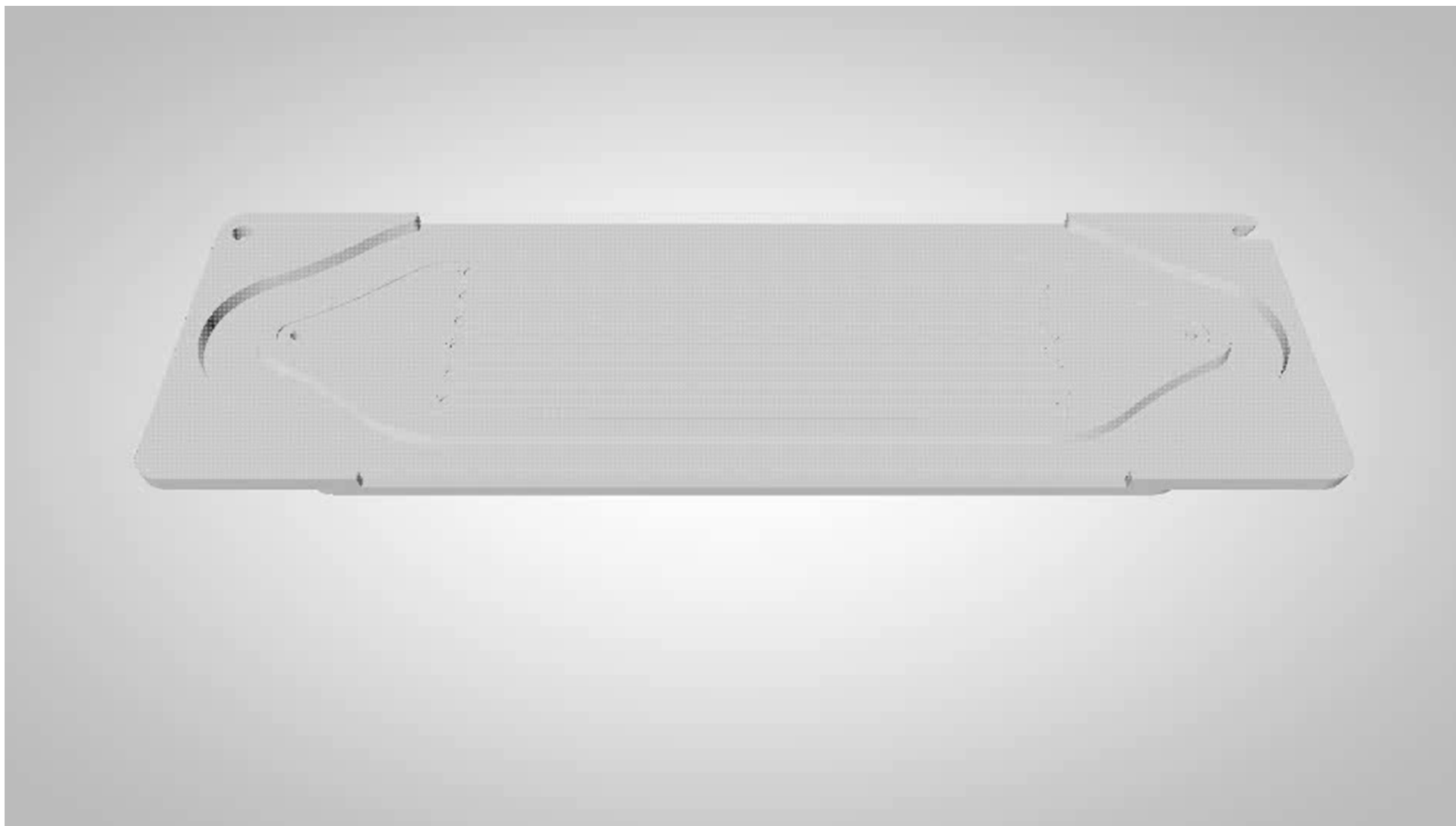
### New approach: liquid biopsy

- ❖ Harvest intact cancer cells from blood
- ❖ Non-invasive, repeatable, real time, cost effective
- ❖ But only one CTC in one billion blood cells



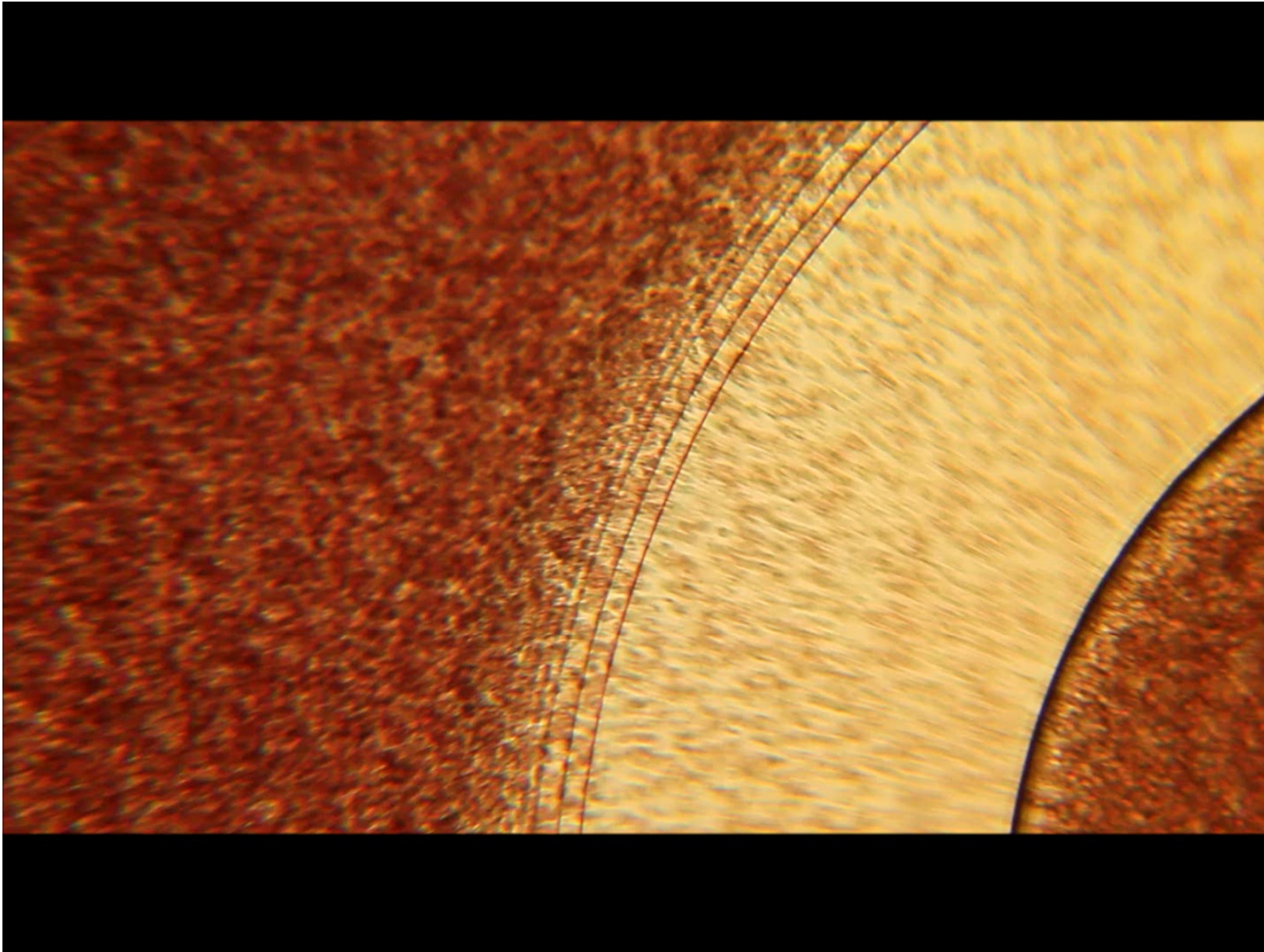
Whole blood from a simple peripheral blood draw contains approximately one cancer cell per ml of blood. The cancer cells are circulating tumor cells shed by the primary tumour in the process of metastasis. The CTCs travel in the blood and if they take root in another organ are the cause of a secondary cancer at a new location.

## Animation showing Parsortix patented steps





## Video showing blood flowing in Parsortix cassette





## ANGLE's patented Parsortix system



- ◆ Stepped, microscale cell separators for fluid flow and cell separation
- ◆ Two granted US Patents
- ◆ Patents pending worldwide
- ◆ Granted patents in China, Canada and Australia
- ◆ European patent expected

## Market size and drivers

- ❖ Total addressable market for liquid biopsy US\$14 billion in the United States market alone by 2025
- ❖ Four key market segments
  - Diagnostic screening
  - Therapeutic decision-making
  - Minimal residual disease
  - Post treatment monitoring
- ❖ Liquid biopsy comprises ctDNA and CTCs
  - “Whole cells (CTCs) offer the advantage of providing a clinician access to cellular morphology along with other genetic content such as RNA”
  - “CTCs are exceedingly rare ... and more difficult to isolate than ctDNA”

Source: The Goldman Sachs Group, Inc. Global Investment Research “Liquid Biopsy: Could a simple blood test revolutionize cancer care?” Equity Research 6 October 2015

**ANGLE is changing the paradigm by making it easy to isolate CTCs from patient blood for a wide range of cancers**





## Parsortix™ and the advantages of CTCs for liquid biopsy

Solid Biopsy				Liquid Biopsy	
		Primary Tumor	Metastatic	cfDNA <sup>1</sup>	CTCs <sup>2</sup>
Sample Type		Intact cells	Intact cells	Fragmented DNA	Intact cells
Accessibility		Invasive Not always accessible	Invasive Not always accessible	Non-invasive <sup>3</sup> Accessible	Non-invasive <sup>3</sup> <b>Accessible using Parsortix<sup>4</sup></b>
Repeatability		Difficult	Difficult	Easy	Easy
Molecular analysis	DNA RNA Protein	Yes Yes Yes	Yes Yes Yes	Yes Difficult No	Yes Yes Yes
Live cells	Cell culture Xenograft	Yes Yes	Yes Yes	No No	Yes Yes

- ❖ ANGLE's Parsortix™ system is a patented product, competitively differentiated in a \$ multi-billion market
- ❖ Parsortix™ provides a unique product based solution where others are offering only a laboratory-service based approach

ANGLE is offering customers a Parsortix system for purchase comprising a desktop instrument and a one-time use consumable. Many competitor systems are so complicated that they have to offer a CLIA (certified laboratory) solution where the customer sends them the sample and they operate the system and provide a result. This approach is commercially less attractive as it requires large in-house investment, is less scalable and deprives the clinical customer of much needed revenue in processing the samples.

## Competitive differentiation in a \$ multi-billion market

Technology	Name	Simple process	Low cost	Captures all types of cancer	Captures mesenchymal CTCs involved in metastasis	Able to easily harvest cells for analysis	High purity of harvested cells	Cell viability (alive)
<b>Microfluidic step</b>	<b>Parsortix</b>	✓	✓	✓	✓	✓	✓	✓
Antibody-based system	CellSearch (only FDA authorised system)	✗	✗	✗	✗	✗	✗	✗
	CTC iChip Magsweeper Cynvenio Biocept Isoflux Gilupi AdnaTest	✗	✗	✗	✗ ✓	✗ ✓	✗	✗
Membrane-based	ISSET Screencell CellSieve	✓	✓	✓	✓	✗	✗	✗ ✓
Centrifugation	Dean Flow Fractionation	✓	✓	✓	✓	✗	✗	✗ ✓
Cell-free DNA <sup>(1)</sup>	Alternative process using plasma from blood	✓	✗	✓	✗	N/A	✗	✗

(1) Cell-free DNA (known as cfDNA or ctDNA) are DNA fragments of dead cells and can only be analysed for DNA using expensive NGS sequencing techniques. RNA analysis is very difficult and limited and protein analysis is not possible with ctDNA. ctDNA fragments thus contain less information than fully intact viable cancer cells and, as they originate from dead cells, may provide less relevant information and miss information on treatment resistant cancer. Viable (live) CTCs can also be used for cell culture and xenografts.

## Research use sales to support drug trials and other research

- ❖ Following successful evaluations of the system by KOLs, ANGLE commenced research use sales in Q4 CY15 addressing a research use market of £250m p.a.
- ❖ Secondary market providing establishment revenues, building market awareness and third party evidence to support clinical applications in multiple cancer types
- ❖ 750 addressable Phase II cancer drug trials p.a.
  - typically 100 patients two years 3 blood tests per patient
  - each trial potential to generate >\$150,000 revenue for ANGLE
- ❖ 120 addressable Phase III cancer drug trials p.a. initiated each year
  - typically 1,000 patients three years 5 blood tests per patient
  - each trial potential to generate >\$1m revenue for ANGLE
- ❖ Securing 5% of the Phase II and Phase III trials as customers offers potential Parsortix revenues of £8m p.a.
- ❖ Cancer drug trials leading to a new drug may lead to the adoption of Parsortix as a companion diagnostic (CDx) for that drug

	Machine	Cassette
Price <sup>1</sup>	£40,000	£150
Cost	£12,000 <sup>2</sup>	£17
Margin	70%	89%
1. High margins allow flexibility in pricing for competitive advantage		
2. Includes maintenance, technical support, sales and distribution		

- ❖ Sales of the Parsortix system for clinical use is the primary objective for commercialisation of the business
- ❖ Estimated clinical market available to ANGLE in excess of £8 billion p.a.
- ❖ Requires both regulatory authorisation and patient data
- ❖ ANGLE has a comprehensive strategy to deliver clinical sales
  - regulatory authorisation
  - key opinion leaders
  - patient studies
  - corporate partnerships



- ❖ Multiple KOL studies in progress to investigate new clinical applications for the treatment of patients



## FDA authorisation progress

- ❖ Seeking to be first FDA authorised system for harvesting cancer cells from blood
  - full-time FDA experienced clinical studies director
  - detailed study plans have been developed and reviewed with the FDA
- ❖ FDA authorisation of the system first for metastatic breast cancer with ovarian cancer and other cancer types to follow
  - breadth of authorisation to provide flexibility in clinical deployment, allowing a range of downstream analytical procedures
  - base authorisation to which (i) additional cancer types and (ii) specific clinical uses can be added facilitating roll out across a wide range of applications
- ❖ Three world-leading US cancer centres selected
  - patient accrual and clinical evidence to secure the FDA authorisation
  - major customers in the future
  - Key Opinion Leaders in securing uptake of the Parsortix system once FDA secured
- ❖ Approach adopted provides a strong competitive advantage

## Medical University of Vienna

- ❖ Highly successful patient study
  - 100% specificity in primary epithelial ovarian cancer (no false positives)
  - 78/80% sensitivity with 7 RNA markers
  - 100% sensitivity with 30 RNA markers
- ❖ Parsortix results “sensational”
  - best CTC alternative only 24.5% sensitivity
- ❖ Clinical application in triaging patients with abnormal pelvic mass
  - to identify those at high risk of ovarian cancer
  - in US, 200,000 women p.a. have surgery on abnormal pelvic masses c. 10% have cancer
  - Medicare reimbursement of \$516/test
- ❖ Ovarian sales potential >£300m p.a.

### Parsortix effectiveness compared to other tests

#### Sensitivity

The test correctly identifies those with the disease (true positive). A low sensitivity means the test may miss many people who have cancer (false negative).

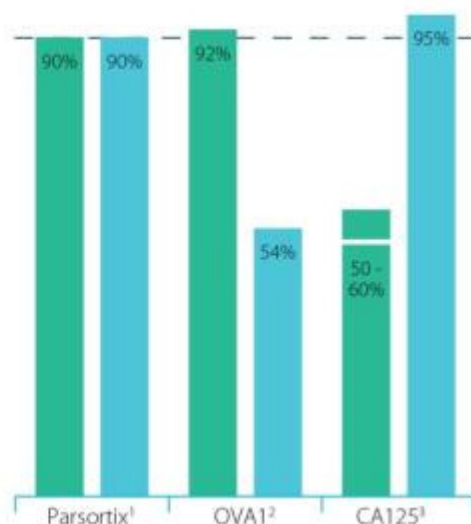
#### Specificity

The test correctly identifies those without the disease (true negative). A low specificity means patients are told they may have the disease when they do not (false positive).

<sup>1</sup> Target for clinical studies

<sup>2</sup> Vermillion Inc

<sup>3</sup> Patient.co.uk / Fritsche HA, et al. (1998). CA-125 in ovarian cancer: advances and controversy. Clinical Chemistry. 44(7):1379-1380



#### Key

■ Sensitivity

■ Specificity

-- Target level

	Cancer	No cancer
Test Result	Sensitivity	Specificity
Positive	True Positive	False Positive
Negative	False Negative	True Negative

## Barts Cancer Institute

- ❖ CTCs harvested in 100% of patients (n=52)
- ❖ Barts study demonstrates Parsortix harvested cells are clinically relevant in prostate cancer
- ❖ Mesenchymal cells (involved in metastasis) as well as epithelial cells
- ❖ Clinically relevant cells harvested
- ❖ Barts researchers now investigating molecular biomarkers on the harvested cells to guide effective treatment

2. Different populations of CK+/Vimentin-/CD45-, CK+/Vimentin+/CD45-, and CK-/Vimentin+/CD45- cells were identified in clinical samples using 4-colour immunofluorescence (Figure 3).

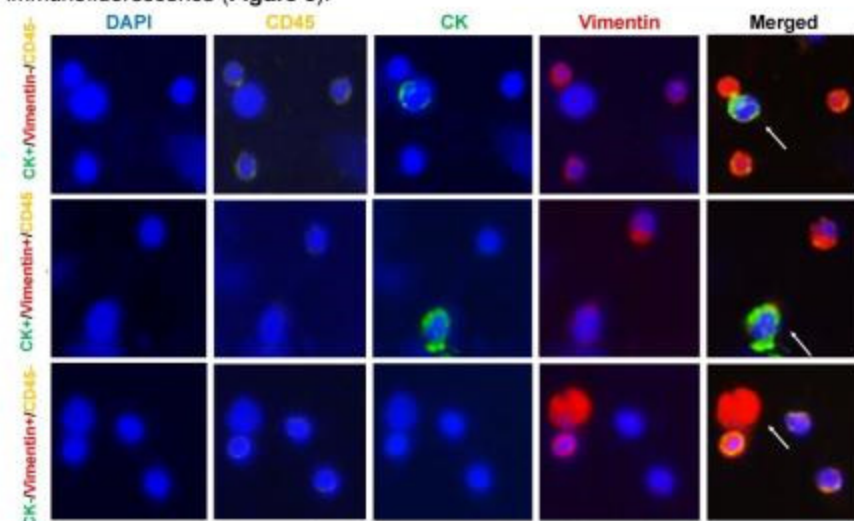
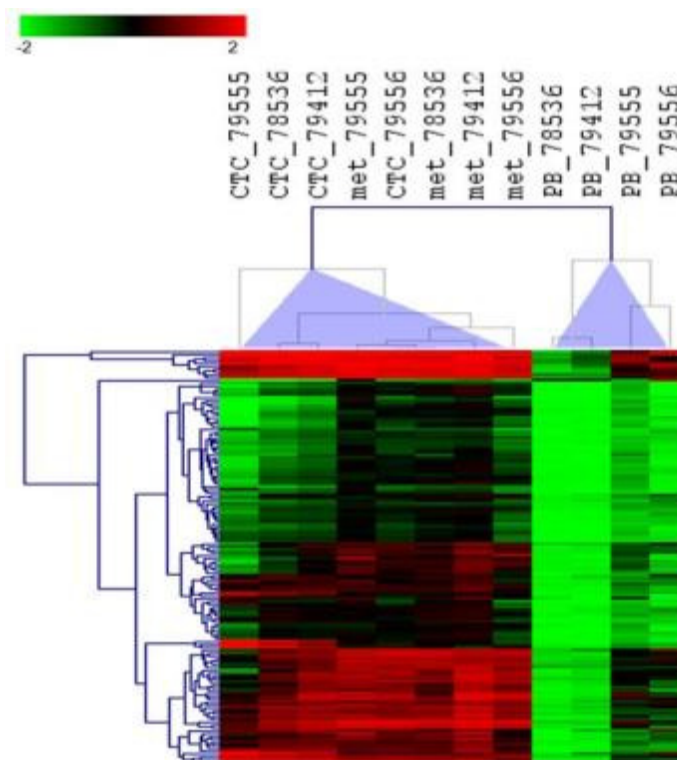


Figure 3. Representative images for different populations of detected cells in prostate cancer patients. The upper row: a CK+/Vimentin-/CD45- cell surrounded by CD45+ lymphocytes. The middle row: a CK+/Vimentin+/CD45- cell next to a CD45+ lymphocyte. The lower row: a CK-/Vimentin+/CD45- cell surrounded by CD45+ lymphocytes.

### University of Southern California Norris Comprehensive Cancer Center

- ❖ CTCs harvested for RNA Seq analysis in 100% of patients
- ❖ CTCs from Parsortix liquid biopsy had similar patterns of gene expression to the traditional biopsy of cancer cells from metastatic sites in all cases (n=4)
- ❖ Parsortix liquid biopsy also provides additional clinical information beyond the biopsy of a single metastatic site
- ❖ Metastatic biopsies invasive, often requiring surgery, expensive and may delay treatment

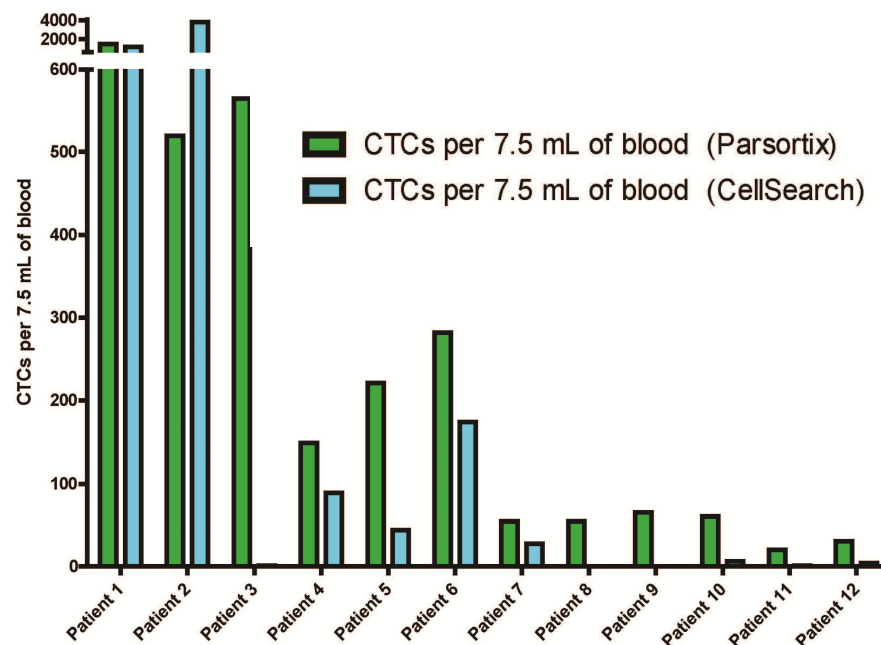


Hierarchical two dimensional heat map of 214 genes differentially expressed in CTC and met vs peripheral blood.



## Cancer Research UK Manchester Institute and Christie Hospital

- ❖ CTCs harvested 100% patients (n=12)
  - Parsortix harvested >5 cells from 100% of patients compared to 58% by leading competitive system
- ❖ Suitable for at least four days at room temperature
- ❖ Simple plug and play device
- ❖ Enables analysis of CTCs not detected by epitope dependent technologies
- ❖ Parsortix enables processing a single blood sample for both CTCs and cfDNA



Ged Brady, Cancer Research UK Manchester Institute

"The Parsortix system has a unique combination of features making it suitable for routine clinical analysis of patient blood samples. We have now incorporated the Parsortix workflow into multiple clinical trials and have been accumulating many hundreds of stored enriched samples that will be of immense value in our future CTC studies."

Parsortix™ patented system provides cells for precision medicine changing the paradigm in a \$ billion emerging market

- ❖ High performance in ovarian, prostate, breast and lung cancers
- ❖ Growing research use sales with a clear competitive advantage
- ❖ CE Mark authorised. FDA authorisation in process
- ❖ Ovarian cancer first clinical application in development

~~MD Anderson~~  
~~Cancer Center~~





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