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Isolation & analysis for single circulating tumor cells (CTC) in an integrated microsystem

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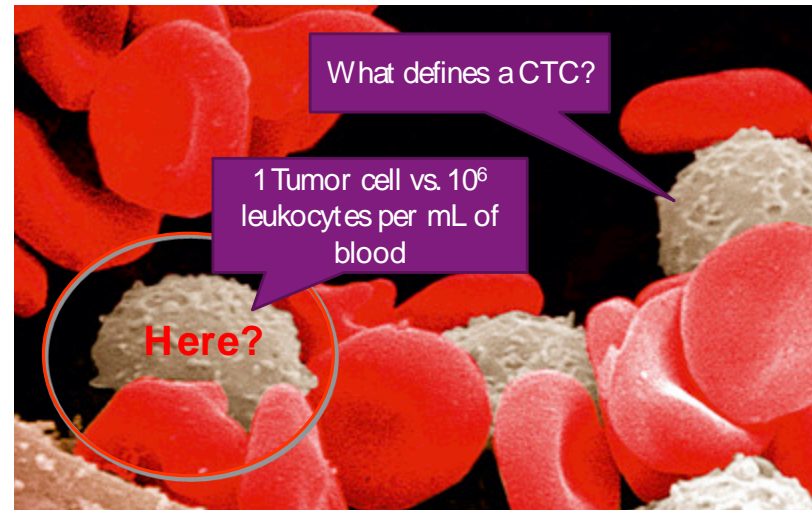
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Motivation and challenges for CTC

isolation

- Motivation
 - Mediated by CTC, metastasis caused 90% cancer deaths.
 - Oncologists need a screening tool which captures rare CTCs very early to maximize therapy success
 - A relevant screening tool is a complete instrument starting from relevant patient samples
- Challenges
 - Down to 1 CTC/mL among billions of normal cells
 - Similar size & morphology to WBCs
 - No generic CTC-specific marker



Rare single cells

Blood sample

Multi-gene analysis

The consortium

Molecular
biology



Nanoelectronics



MIRACLE



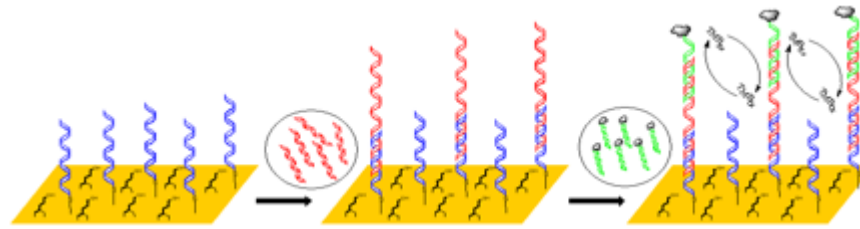
ConsulTech GmbH

Clinical
validation

Instrumentation

- **Project type:** FP7 integrated project
- **Project number:** 257743
- **Project duration:** 01.09.2010 – 31.08.2014
- **Total cost:** 10 million euro
- **Project coordinator:** Prof. Liesbet Lagae (imec)

MIRACLE technology overview

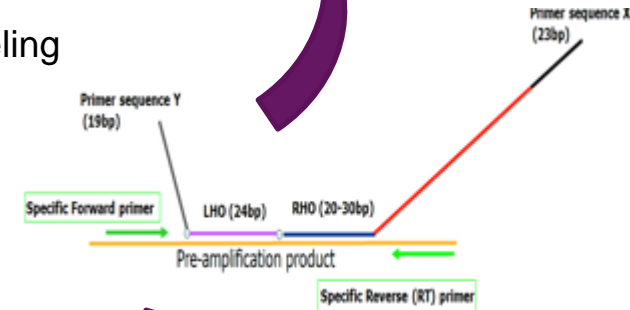


Probe immobilization

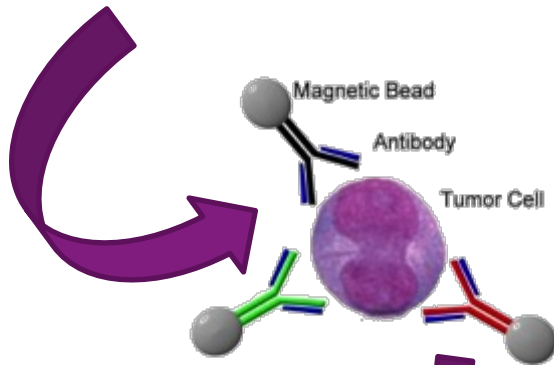
DNA hybridization

HRP labeling and detection

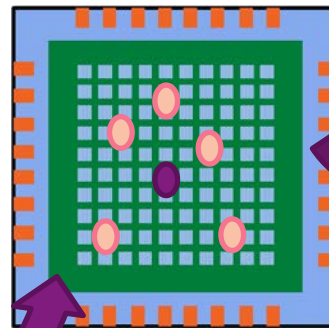
ⁿ Multiplexed gene detection



Multiplexed gene amplification (MLPA)





Immunomagnetic cell isolation



Active sieve for CTC identification by electrical cell impedance measurement

Unique objectives of MIRACLE

- Viable single CTC isolation from blood sample
- Multi-gene analysis for CTCs
- Fully automated system

	Veridex CellSearch 	MIRACLE 
CTC isolation	<ul style="list-style-type: none"> ▪ Single-marker based ▪ CTC not viable after isolation ▪ Multi-cancer type 	<ul style="list-style-type: none"> ▪ Multi-marker based ▪ Viable CTC after isolation ▪ Multi-cancer type
Gene analysis	<ul style="list-style-type: none"> ▪ No (separate product) ▪ Not compatible with RNA analysis 	<ul style="list-style-type: none"> ▪ Yes (integrated module) ▪ 7 (Breast cancer) and 16 genes (Prostate cancer)
Automation	<ul style="list-style-type: none"> ▪ User experience based visual CTC identification 	<ul style="list-style-type: none"> ▪ Automatic electrical CTC detection



MIRACLE: distance to the market

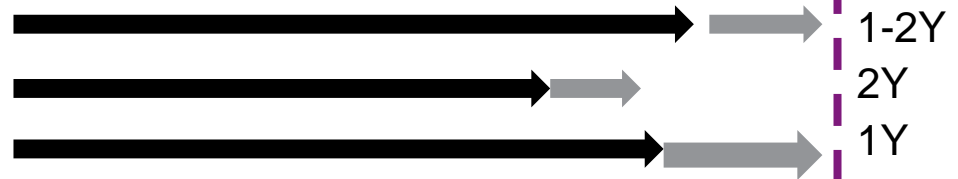
➡ Current

➡ By the end of project

Component fabrication & QA Lab proof-of-principle Pre-clinical test Commercialization

Single cell isolation technology

- Novel magnetic nanobeads
- New tumor markers
- IC for single cell impedance meas.



Multi-gene analysis technology

- Multi-gene amp. probe mix
- Multi-gene detection chip
- Ultra fast electrochemical reading

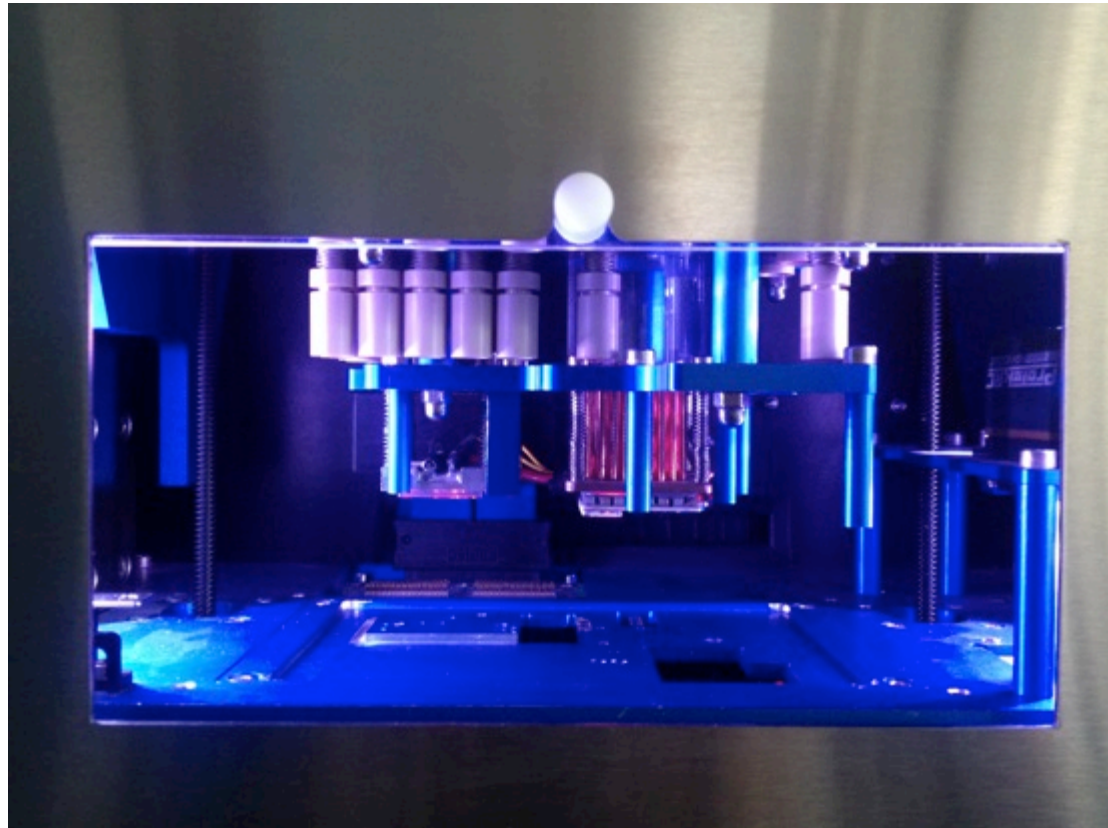


Integrated module / system

- Immunomagnetic rare cell isolation
- Single cell multi-gene analysis
- Full CTC isolation & analysis platform



MIRACLE: instrument perspective today



MIRACLE: recent progress relevant for the end user

- On-chip single cell amplification and detection demonstrated in the MIRACLE amp-det chip
- Integrated MIRACLE system close to completion, including the injection-molded cartridge
 - Complete instrument
 - Proper sample handling
 - Designed for clinical evaluation
- Scientific confirmation relevant for assay development
 - Novel EMT marker identified
 - promising for CTC isolation assays using biomarkers
 - Measurements of imec's active sieve confirm the trend of single cell impedance on cell invasiveness
 - promising for markerless CTC isolation assays



MIRACLE: bringing the innovation to the user

■ Technical steps

- Clinical validation of discrete technologies
- (Continued) integration of functional modules and the entire system including product *design* aspects
- System evaluation & benchmarking (lab & clinical)

■ Non-technical steps

- Continuous market analysis update
 - conventional system and impedance chip-based analysis & sorting
- Know-how and IP valorization
 - follow-up projects, synergies with other projects (e.g. CanDo)
- Workshop organization (e.g. ECCO conference, focus on users)
- Accessing the market
 - Showcasing in business-to-business conference & fairs (e.g. Analytica)
 - VC identification & contact
 - Contacting biomedical instrument firms for licensing or partnership

MIRACLE: road to exploitation

	IP ownership	Licensing	Direct exploitation	Partnership
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Single cell isolation technology

- Novel magnetic nanobeads
- New tumor markers
- IC for single cell impedance meas.

Partial	Yes	Yes	Yes
Full	Yes	Yes	
Full	Yes	Yes	Yes

Multi-gene analysis technology

- Multi-gene amp. probe mix
- Multi-gene detection chip
- Ultra fast electrochemical reading

Full		Yes	
Full	Yes		Yes
Full	Yes		Yes

Integrated module / system

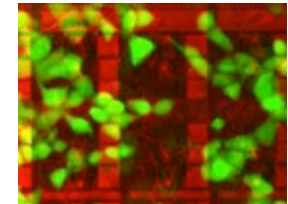
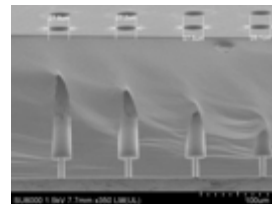
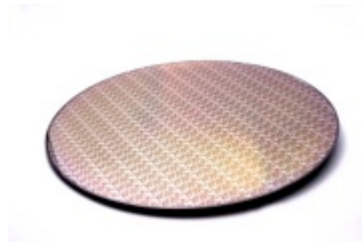
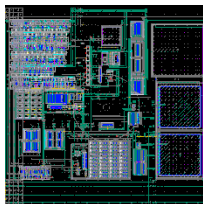
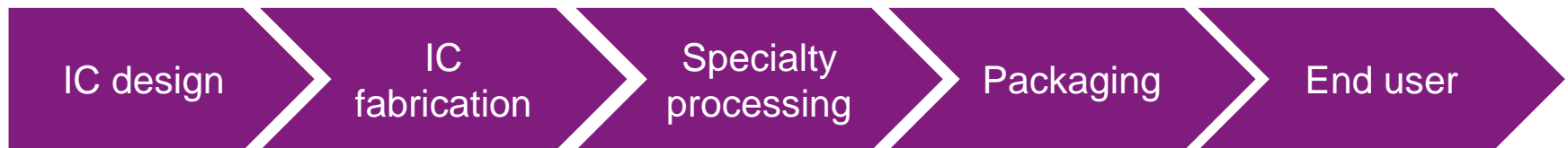
- Immunomagnetic rare cell isolation
- Single cell multi-gene analysis
- Full CTC isolation & analysis platform

Partial	Yes	Yes	Yes
Partial	Yes	Yes	Yes
Full	Yes	Yes	Yes



Complete value chain enables exploitation

- Reliable & realistic innovation
 - Industrial **standard** methodology → quality & efficiency (i.e. IC design)
 - Compatibility with **mass production** → low cost (i.e. injection molding)
 - **Flexibility** (technology, module or system) → technology evolution & market coverage



(MCF7 cancer cell on IC chip)

After MIRACLE



Molecular
biology



Nanoelectronics



ConsulTech GmbH

Clinical
validation

Instrumentation

<http://www.miracle-fp7.eu>

