

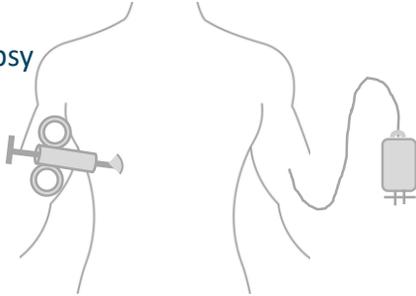
# exosomics

## The challenge:

Traditional biopsies are invasive and do not represent tumour heterogeneity. Liquid biopsies instead are minimally invasive, they capture the whole tumour picture but tumour-derived material is scarce and its detection in the bloodstream is challenging

### 1. Traditional Biopsy

- Invasive.
- Time consuming.
- Does not represent the whole tumour.
- Cannot be used for monitoring.
- Risk associated.



### 2. Liquid Biopsy

- Minimally invasive.
- Cheaper.
- Tumour heterogeneity detectable -> better treatment indications
- Can be easily obtained and repeated -> ideal for screening, staging, profiling and monitoring.
- Preferred approach for unresectable tumours.

#### Circulating free nucleic acids (cfDNA & cfRNA)

- Come mostly from dead cells.
- Tumour causing mutation is barely detectable because of the confounding background noise: Needle in a haystack problem.
- Free circulating RNA is usually degraded, not good if looking for fusions.

#### Circulating Tumour Cells (CTCs)

- Cancers may shed cells into the bloodstream.
- Very rare.
- Requirement of very expensive instrumentation for detection.

#### Exosomes

- Exosomes (40-100nm) are released into the bloodstream especially from tumour cells.
- They contain and protect from degradation DNA, RNA and proteins, multi-analyte analysis possible.

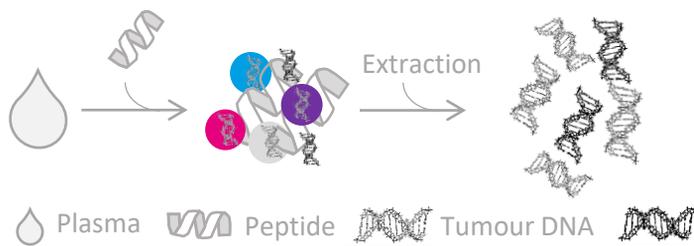
## The solution:

Exosomics has a range of pre-analytical solutions to selectively isolate tumour-derived exosomes from biofluids and extract their tumour-derived content. This allows easier detection of tumour-causing mutations from liquid biopsies and enables the next generation of tumour screening, staging, profiling and monitoring tests.

#### Tumour-derived Exosomes

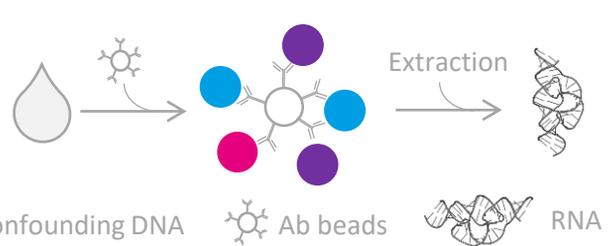
- Exosomics solutions allow selective isolation of tumour-derived exosomes and extraction of DNA or RNA through peptide-affinity or antibody-affinity methods, respectively.
- This allows better performance of any downstream analytical assay such as qPCR, ddPCR, hybridisation and NGS.

### SeleCTEV™ Enrichment Kit (RUO)



- Peptide affinity purification
- Exosome isolation and DNA extraction workflows combined.
- Peptide pulls down tumour-derived exosomes and circulating DNA
- Best pre-analytical method to harvest as much as possible DNA from biofluids.
- It's easy, does not require complex ultracentrifugation or chromatography steps
- Enables better downstream analytical performance

### SoRTEV™ Enrichment Kit (RUO)



- Antibody coated beads pull down tumour-derived exosomes selectively.
- Best pre-analytical method to harvest the purest tumour-derived RNA from biofluids.
- It's easy, does not require complex ultracentrifugation or chromatography steps.
- Enables the next generation of RNA-based tumour diagnostics assays.



Plasma



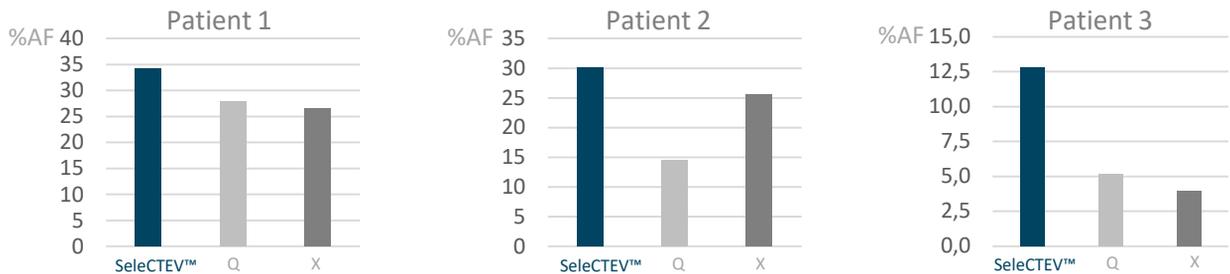
Tumour-derived material enrichment

qPCR  
ddPCR  
Hybridization  
NGS  
Your Analytical Assay

Lower % AF detectable  
Improved stratification  
More accurate staging  
Earlier detection  
Better Patient Outcomes

## Case study #1: SeleCTEV™ – Metastatic Melanoma Patients, *BRAF*<sup>V600E</sup> detection

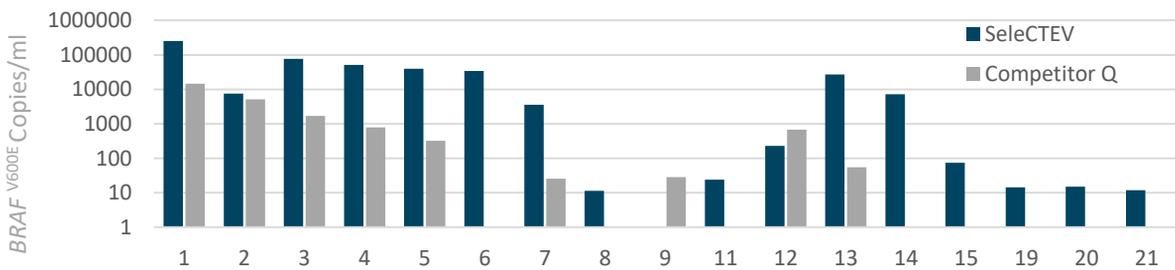
Plasma from three metastatic melanoma patients with *BRAF*<sup>V600E</sup> mutation was processed with either SeleCTEV™, Company X or Competitor Q to obtain DNA. Such DNA was then tested for *BRAF*<sup>V600E</sup> by ddPCR (BioRad®).



The bar represents the % of allelic frequency (%AF) of *BRAF*<sup>V600E</sup> detected. For all three patients the use of SeleCTEV™ as the pre-analytical step yielded tumour-enriched DNA as shown by a higher allelic frequency. Note that the lower is the allelic frequency in the patient the bigger is the difference between SeleCTEV™ and the competitors. This suggests the SeleCTEV™ performs better by increasing the signal to noise ratio especially in cases when the copy number of mutated DNA molecules is low and confounding background is high. **Data generated by Company X, Belgium**

## Case study #2: SeleCTEV™ Metastatic Melanoma Patients, *BRAF*<sup>V600E</sup> detection

Plasma from twenty-one metastatic melanoma patients was processed with either SeleCTEV™ or Competitor Q to obtain DNA. Such DNA was then tested for *BRAF*<sup>V600E</sup> by ddPCR (Thermo®).

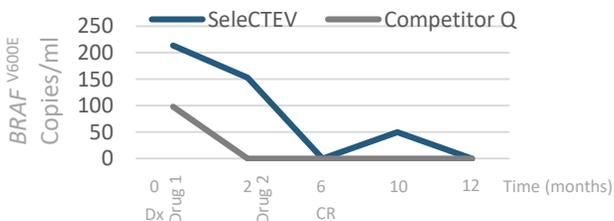


The bar represents the number of copies of *BRAF*<sup>V600E</sup> DNA detected. For almost all but 2 patients, the use of SeleCTEV™ as the pre-analytical step yielded a higher number of *BRAF*<sup>V600E</sup> - mutated gene copies. In seven cases SeleCTEV™ could detect the mutation whilst the competitor did not. **Data generated by University of Brescia, Italy, manuscript in preparation.**

## Case study #3: SeleCTEV™

### *BRAF*<sup>V600E</sup> Monitoring

Plasma from a single patient was withdrawn every two months from diagnosis and then processed with either SeleCTEV™ or Competitor Q to obtain DNA. Such DNA was then tested for *BRAF*<sup>V600E</sup> by ddPCR (Thermo®).

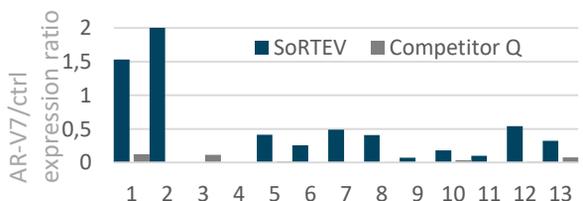


The lines represent the number of mutated DNA copies detected every two months from diagnosis. The use of SeleCTEV™ as the pre-analytical step yielded a higher number of copies of DNA mutated for *BRAF*<sup>V600E</sup> than the competitor Q. **Data generated by University of Brescia, Italy, manuscript in preparation.**

## Case study #4: SoRTEV™

### Androgen Receptor V7 (AR-V7) Detection

Plasma was withdrawn from thirteen prostate cancer patients and then processed with either SoRTEV™ or Competitor Q to obtain RNA. The ratio between AR-V7 and a control (ctrl) mRNA was tested by RT-ddPCR (Thermo®).



AR-V7 mRNA can be detected when SoRTEV™ is used as the pre-analytical step whilst it is not or barely detectable when Competitor Q is used. High levels of AR-V7 correlate with poor response to first and second line novel hormonal therapy in castration-resistant prostate cancer. **Data generated by University of Brescia, Italy.**