

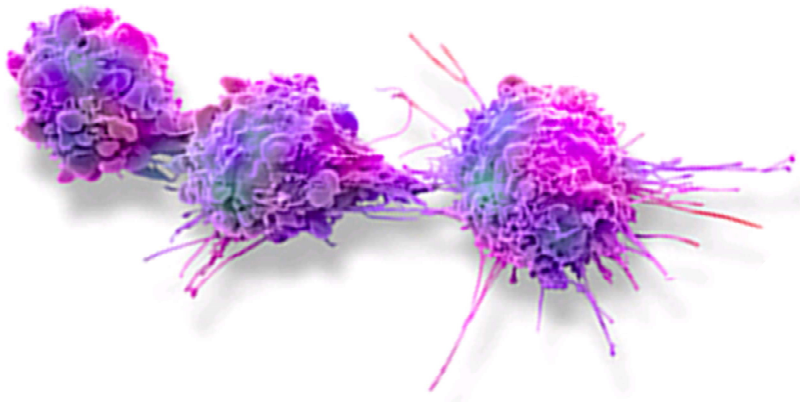
CellCelector™ – an automated system for detection and isolation of CTCs

2016-09-16 Prague

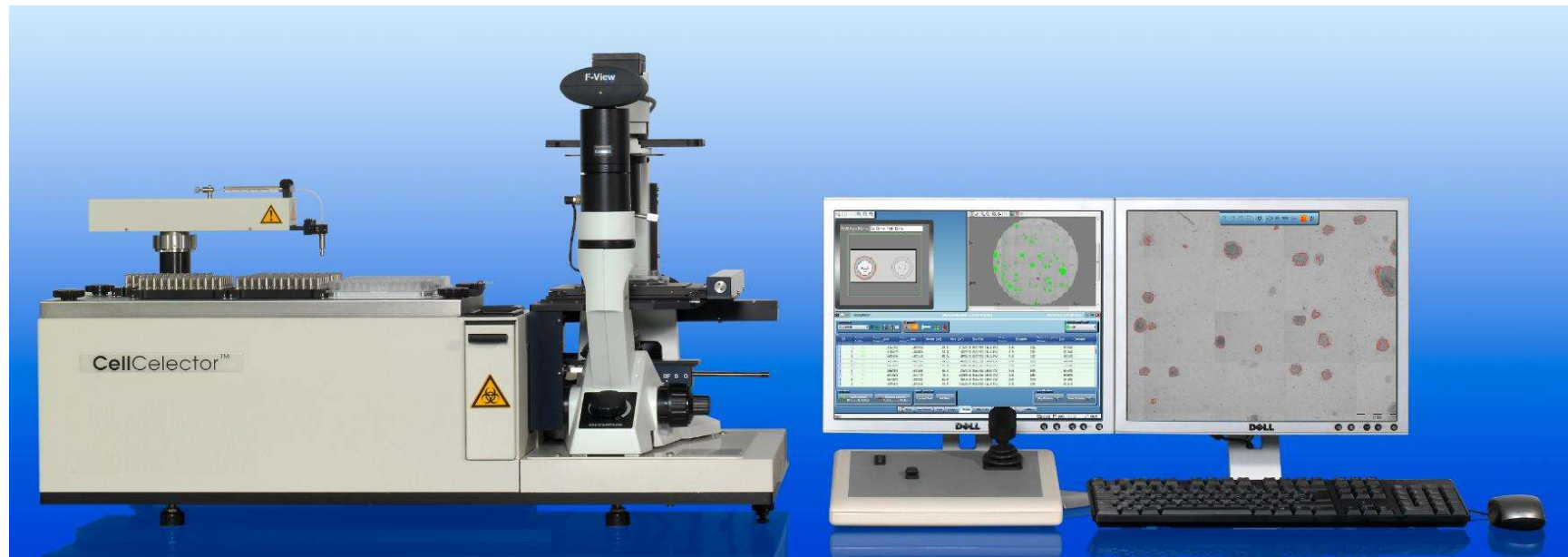
Dr. Katharina Uhlig



ALS Automated Lab Solutions GmbH



CellCelector™



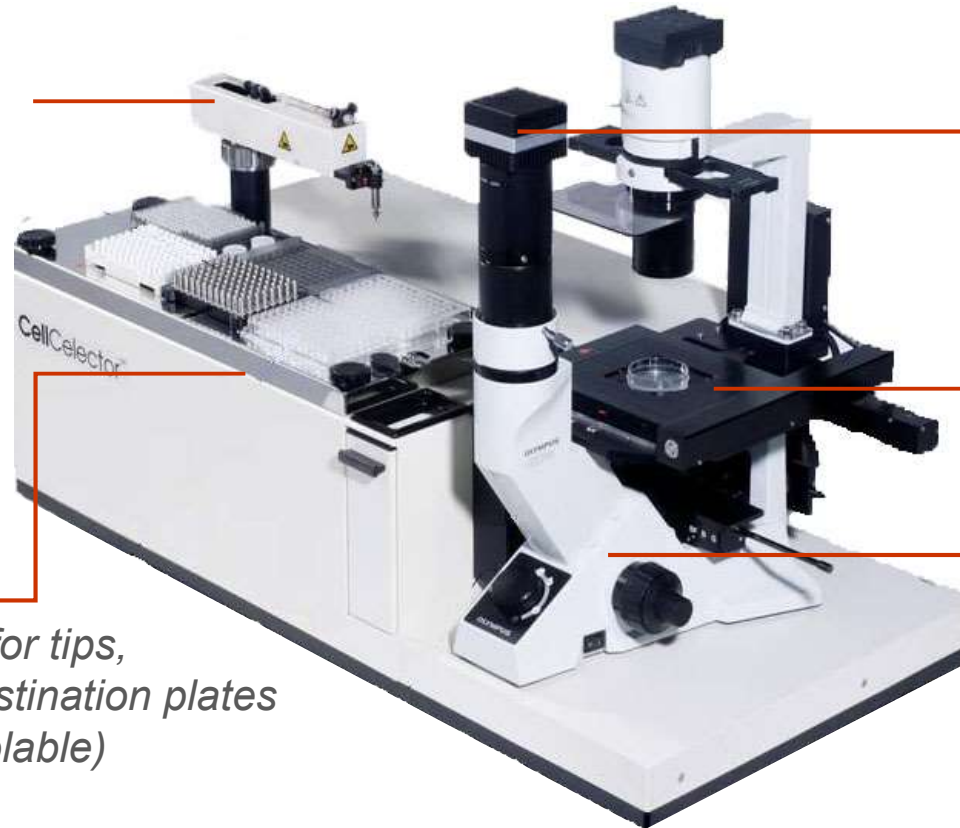
Robotics unit

Optical unit

Workstation

CellCelector™

Picking tool



CCD camera

- cooled
- 14 bit

Motorized XY stage
with source plate(s)

Inverted microscope

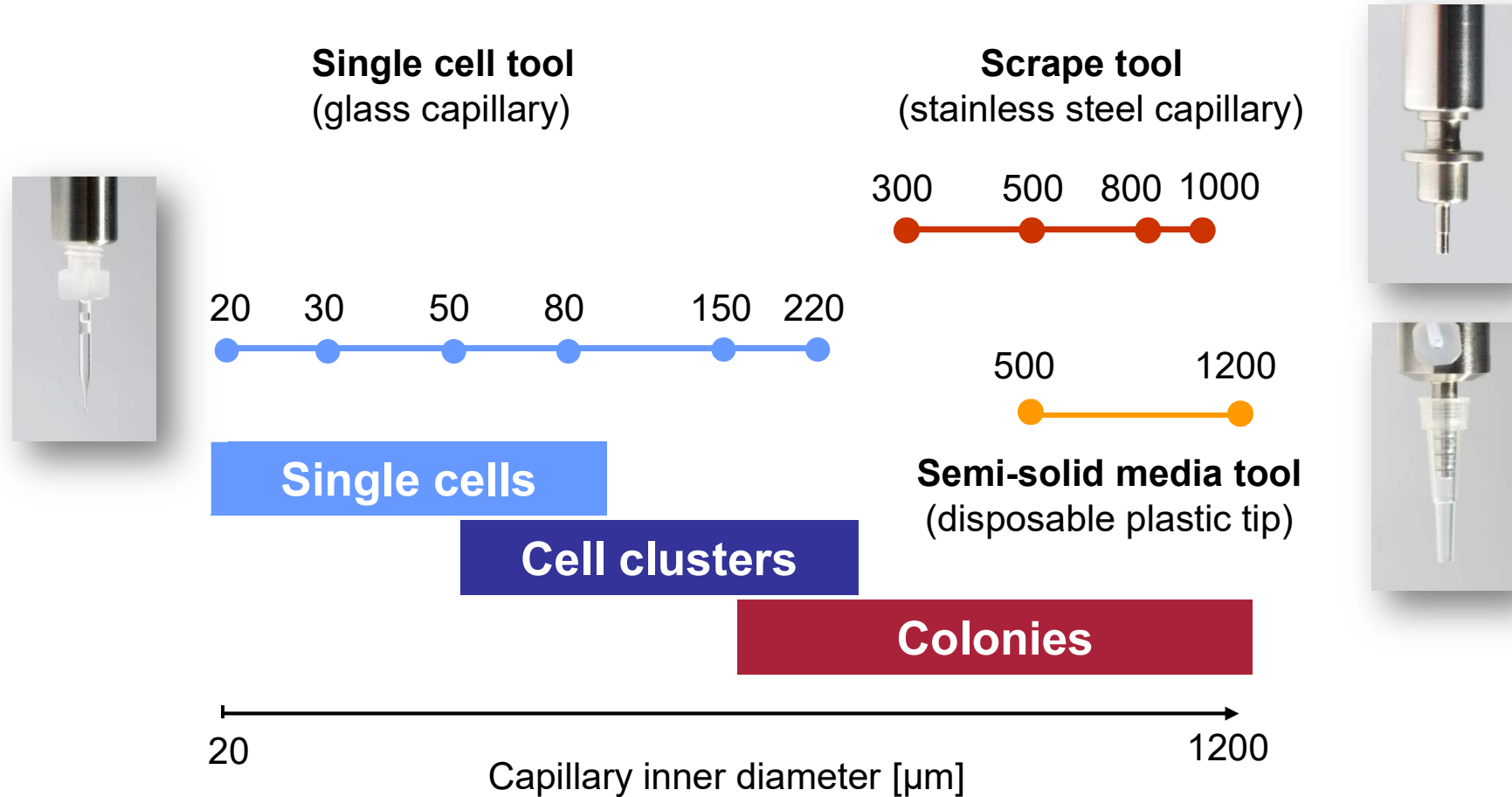
- Bright field
- Phase contrast
- Fluorescence

- Different magnifications
- Autofocus

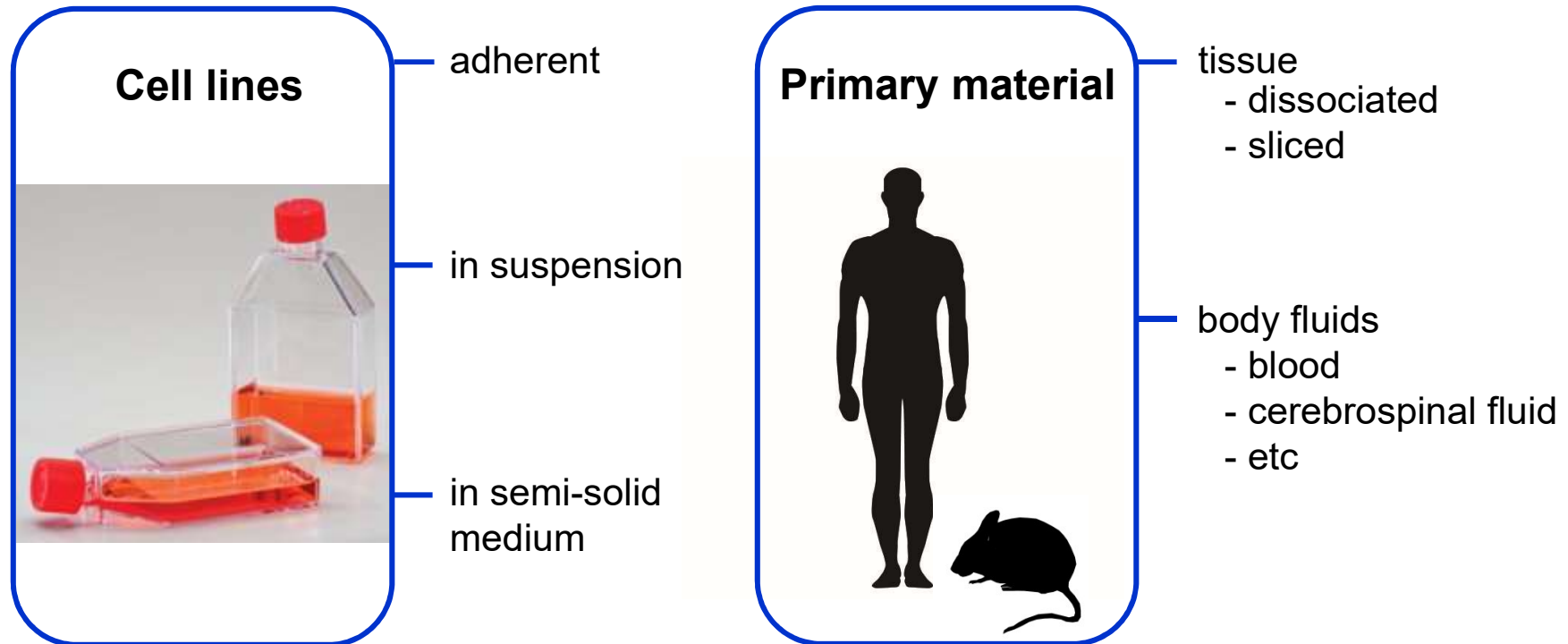
Decktray

with positions for tips,
buffers and destination plates
(heatable / coolable)

Picking tools and applications

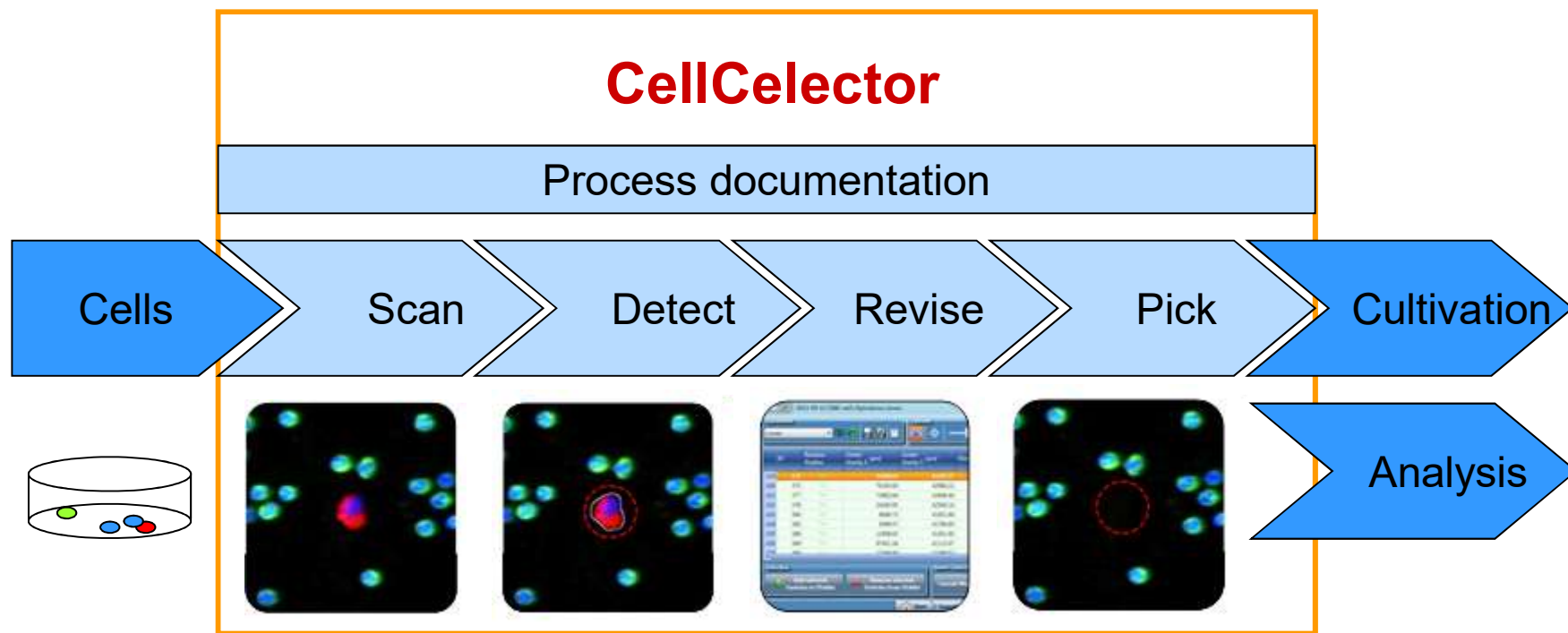


Source material

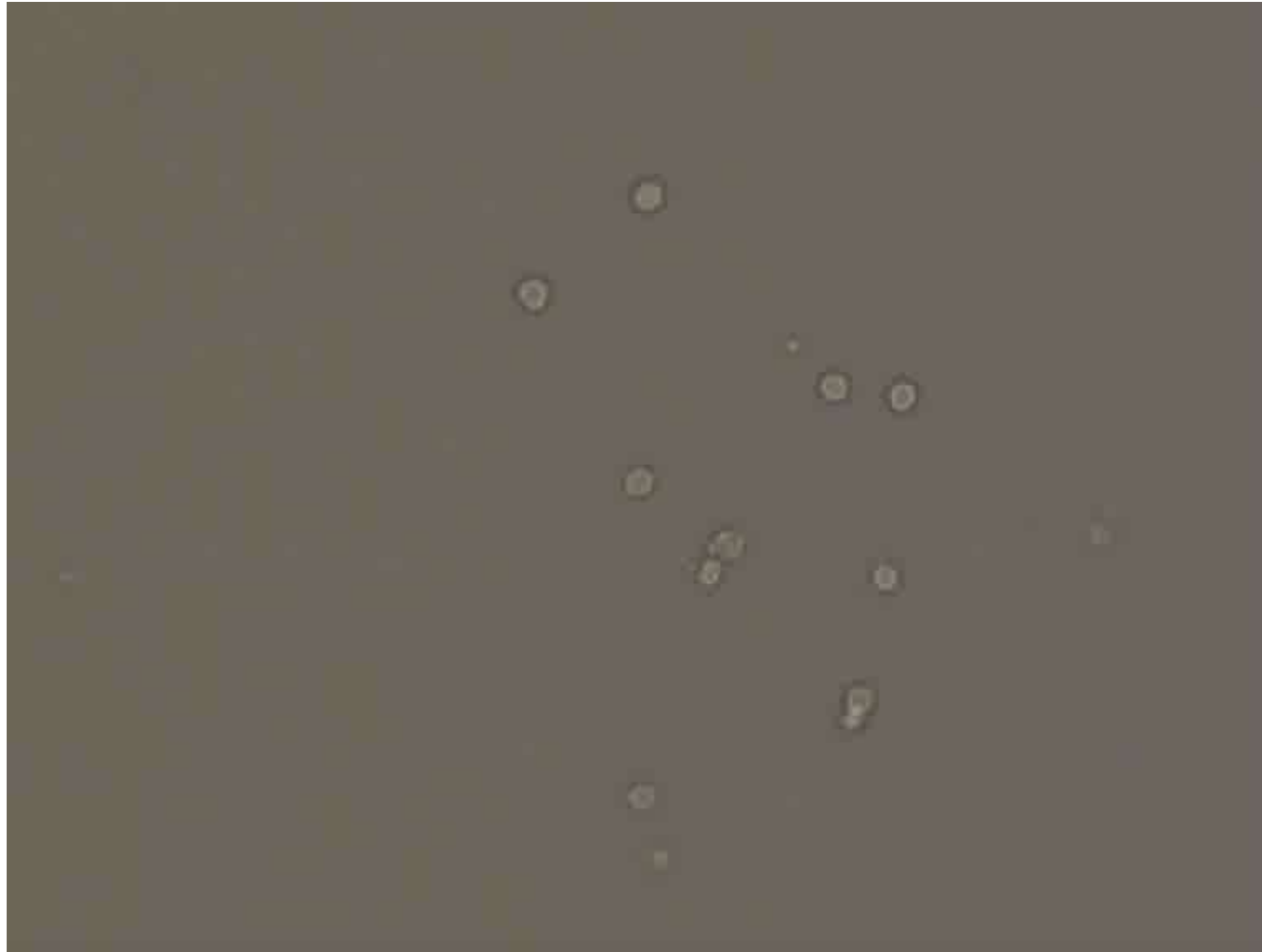


- ▶ Source material can be living or fixed
- ▶ Huge variety of commercially available source vessels can be used

Overview of the general workflow

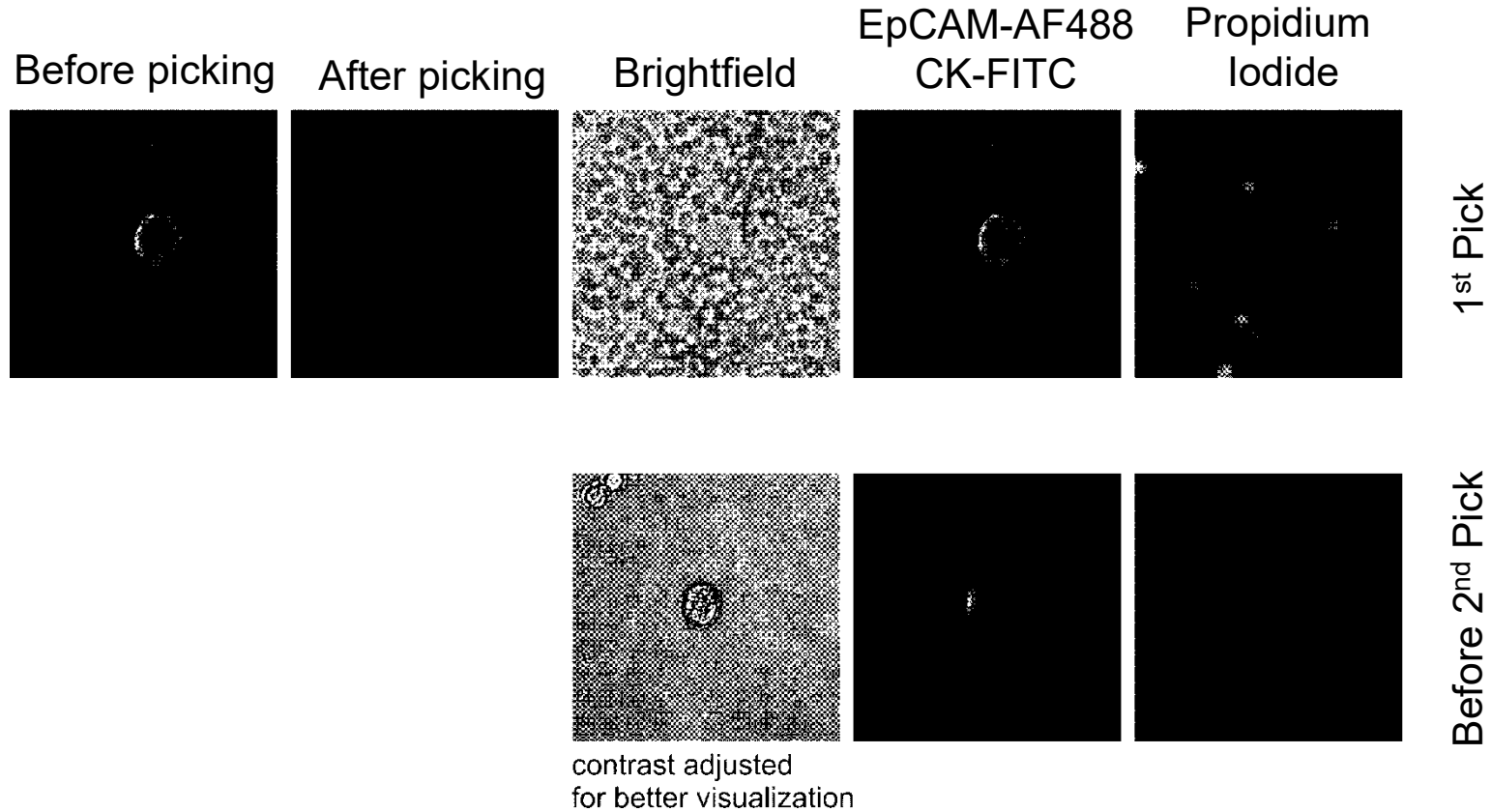


Picking of circulating tumor cells from suspension



Isolation of rare cells

Example: Isolation of viable CTCs from PBMC fraction of whole blood

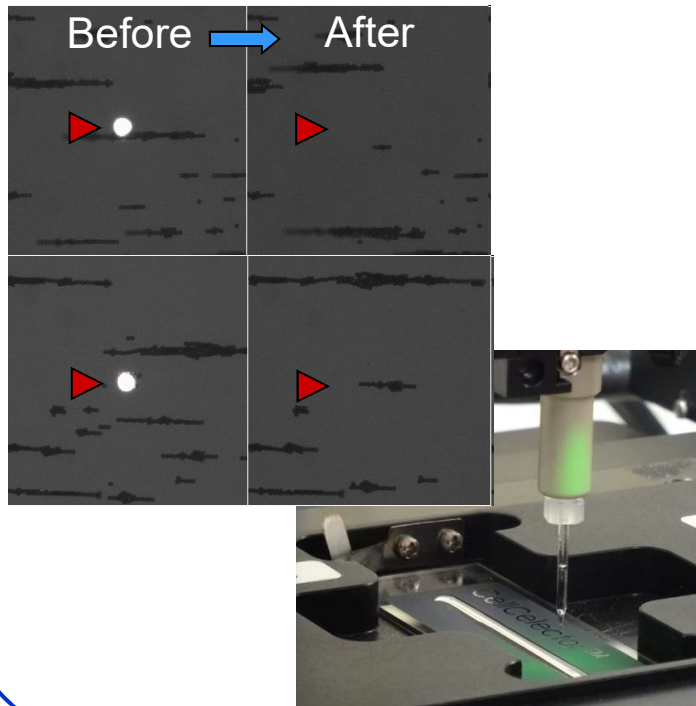


Courtesy of N. Neumann, University Hospital Duesseldorf, Germany

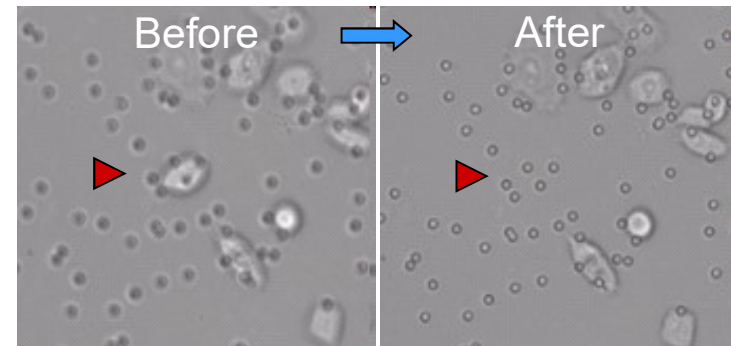
Enrichment of CTCs from blood

Immunomagnetic enrichment

SK-BR-3 (DAPI⁺)
bound to magnetic beads



Size-based enrichment



MCF7 cells on ScreenCell filters

CellCelector housing options

Safety housing

- ✓ User protection



*Installation at Aceto Lab,
Basel University, Switzerland*

Laminar flow cabinet

- ✓ User protection
- ✓ Sterility



*Installation at Inserm U935/ESTeam,
Paris region, France*

Incubator Flowbox

- ✓ User protection
- ✓ Sterility
- ✓ Temperature, CO₂ and humidity control



*Installation at Rudbeck Lab,
Uppsala University, Sweden*

Examples of downstream analyses

Nucleic acids

DNA

- PCR
- WGA
- Sequencing
- aCGH

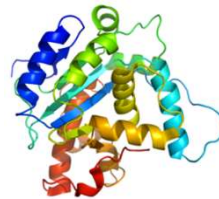


RNA

- qPCR
- WTA
- RNA sequencing

Proteins

- Protein microarrays





Functional assays


- Injection into mice




Published data


Neumann M.H. *et al.* Isolation and characterization of circulating tumor cells using a novel workflow combining CellSearch® and CellCelector™. *Biotechnol Prog. Epub* (2016) [PubMed](#) 


Blassl C. *et al.* Gene expression profiling of single circulating tumor cells in ovarian cancer - Establishment of a multi-marker gene panel. *Molecular Oncology. Epub* (2016) [PubMed](#) 

Schneck H. *et al.* EpCAM-Independent Enrichment of Circulating Tumor Cells in Metastatic Breast Cancer. *PLOS One*. 10(12):e0144535 (2015) [PubMed](#) 

Lohr, G.J. *et al.* Whole-exome sequencing of circulating tumor cells provides a window into metastatic prostate cancer. *Nature Biotechnology* 32, 479–484 (2014). [PubMed](#) 

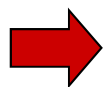
Yao, X. *et al.* Tumor cells are dislodged into the pulmonary vein during lobectomy. *J Thorac Cardiovasc Surg*. 148 (6), 3224-31 (2014). [PubMed](#) 

Heidary, M. *et al.* The dynamic range of circulating tumor DNA in metastatic breast cancer. *Breast Cancer Res*. 16(4), 421 (2014). [PubMed](#) 

Adalsteinsson, V.A. *et al.* Single cells from human primary colorectal tumors exhibit polyfunctional heterogeneity in secretions of ELR+ CXC chemokines. *Integr. Biol. (Camb)*. 5(10):1272-81 (2013). [PubMed](#) 

Summary

Allows isolation of different cells of diverse origin	<ul style="list-style-type: none">- Single cells, cell clusters or cell colonies- Cell culture (suspension, adherent) & primary material (body fluids, dissociated tissue, tissue slices, etc)
Flexibility	<ul style="list-style-type: none">- Use of any commercially available source and destination vessels- Bright field, phase contrast or fluorescence imaging
Reliability	<ul style="list-style-type: none">- No dead volume → no intrinsic cell loss- Picking success > 95%
Compatibility with upstream enrichment	<ul style="list-style-type: none">- Flow cytometry- Filters- Immunomagnetic separation
Compatibility with downstream analyses	<ul style="list-style-type: none">- Fast (~ 10 – 30 sec / single cell) and gentle isolation of intact cells- Low aspiration (≥ 5 nl) and dispensing volumes (≥ 50 nl)- WGA, WES, RNA sequencing, etc.



CellSelector is a highly flexible and reliable device for automated isolation of cancer cells