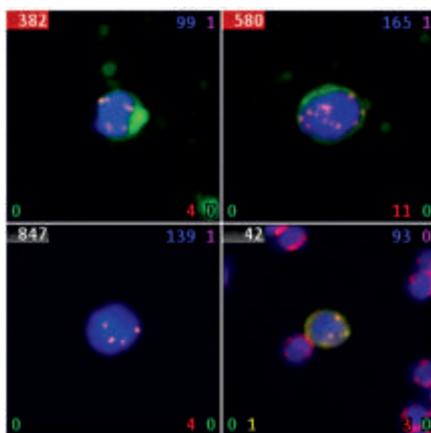
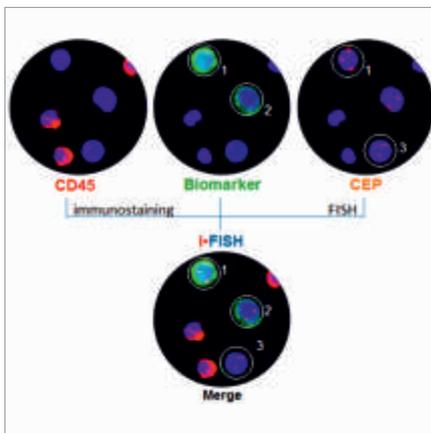


Circulating Tumor Cells

Automated identification and analysis of CTCs enriched and isolated by SE-i•FISH®



Metafer CTC Application

Circulating Tumor Cells (CTCs) are cancer cells shed from primary or metastatic solid tumors into peripheral blood. Enumeration and characterization of these rare cells holds promise as a non-invasive means of detecting, diagnosing, and monitoring cancers.

The Cytelligen SE-i•FISH® kit uses an unbiased approach called subtraction enrichment (SE), which combines non-haemolytic removal of red blood cells and immuno-magnetic removal of white blood cells to enrich for CTCs. In contrast to most other methodologies, this is independent of cell size and independent of molecular markers, such as the commonly used EpCAM and Cytokeratins (CKs), and can therefore find cells that are overlooked by these other approaches. The SE-enriched samples are stained by immunofluorescence for CD45 and other markers of interest, as well as centromeric FISH for chromosome 8 as an indicator of aneuploidy.

The Metafer CTC Application was developed to detect CTCs processed by SE-i•FISH®**, and analyze these within a clinically relevant time frame. Metafer's on-screen review of candidate cells and their morphological and molecular properties, ensures reliable confirmation of all CTC types. A combination of automatic and interactive measurements classifies these cells by size, marker status and ploidy. Clinical labs can output these complex results directly in a customizable report.

Top Left: *The novel SE-i•FISH® method combines multiple marker immunostaining with centromeric FISH for chromosome 8 (Lin PP, The Principle of iFISH, Diagnostics 2018).*

Left: *Example gallery of CECs* (upper row) and both marker negative and positive CTCs (lower row) identified by the Metafer CTC Application*

CTC APPLICATION

References

Metafer users publish their results in many peer-reviewed journals, and the Metafer CTC user base is growing. Please find below a list of recent publications using Metafer for the study of Circulating Tumor Cells (the authors have referred to the Metafer CTC Application as 'Metafer-iFISH').

- Comprehensive in situ co-detection of aneuploid circulating endothelial and tumor cells. Lin PP *et al.*, *Sci Rep.* 7(2017).
- Quantified postsurgical small cell size CTCs and EpCAM+ circulating tumor stem cells with cytogenetic abnormalities in hepatocellular carcinoma patients determine cancer relapse. Wang L *et al.*, *Cancer Lett.* 412(2018).
- Aneuploid CTC and CEC. Lin PP. *Diagnostics (Basel)*. 8(2018).

The SE-i•FISH® technique has also been used independently to identify and study CTCs. A selection of related publications is listed below.

- Clinical significance of phenotyping and karyotyping of circulating tumor cells in patients with advanced gastric cancer. Li *et al.*, *Oncotarget* 5 (2014)
- Aneuploidy of chromosome 8 in circulating tumor cells correlates with prognosis in patients with advanced gastric cancer. Li *et al.*, *Chin J Cancer Res* 28(2016)
- Enhanced detection and comprehensive in situ phenotypic characterization of circulating and disseminated heteroploid epithelial and glioma tumor cells. Ge *et al.*, *Oncotarget* 6(2015)

* Circulating Endothelial Cells (CECs) (described in Lin PP *et al.*, 2017), can also be identified by the Metafer CTC Application, using the additional endothelial marker CD31.

** Metafer is a powerful platform and is not restricted to the detection of CTCs processed by SE-i•FISH®. If you would like to learn how MetaSystems can help with your own proprietary needs, please contact us.

MetaSystems

EUROPE & RUSSIA

Germany, Altlusheim

info@metasystems-international.com

Italy, Milan

info@metasystems-italy.com

Russia, Moscow

info@metasystems.su

AMERICAS

USA, Medford

info@metasystems.org

Argentina, Buenos Aires

info@metasystems-latam.com

ASIA

China, Hong Kong

info@metasystems-asia.com

China, Taizhou

info@metasystems-china.com

India, Bangalore

info@metasystems-india.com



CTC APPLICATION

 MetaSystems

info@metasystems-international.com

www.metasystems-international.com

