

Automated Digital Cytology for Rare Cell Detection:

Enhancing Personalized Cancer Medicine with Standardized Liquid Biopsy Workflow



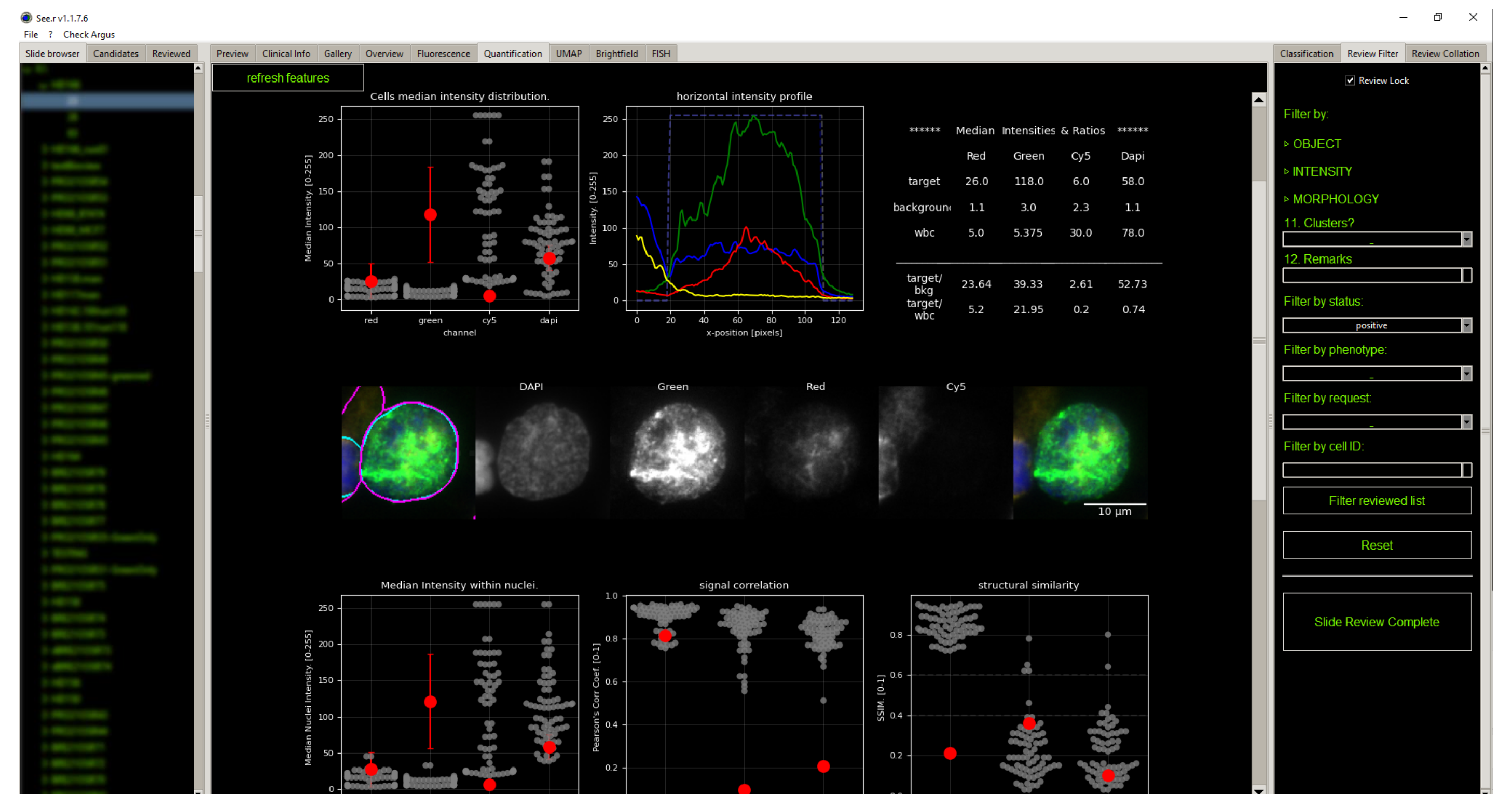
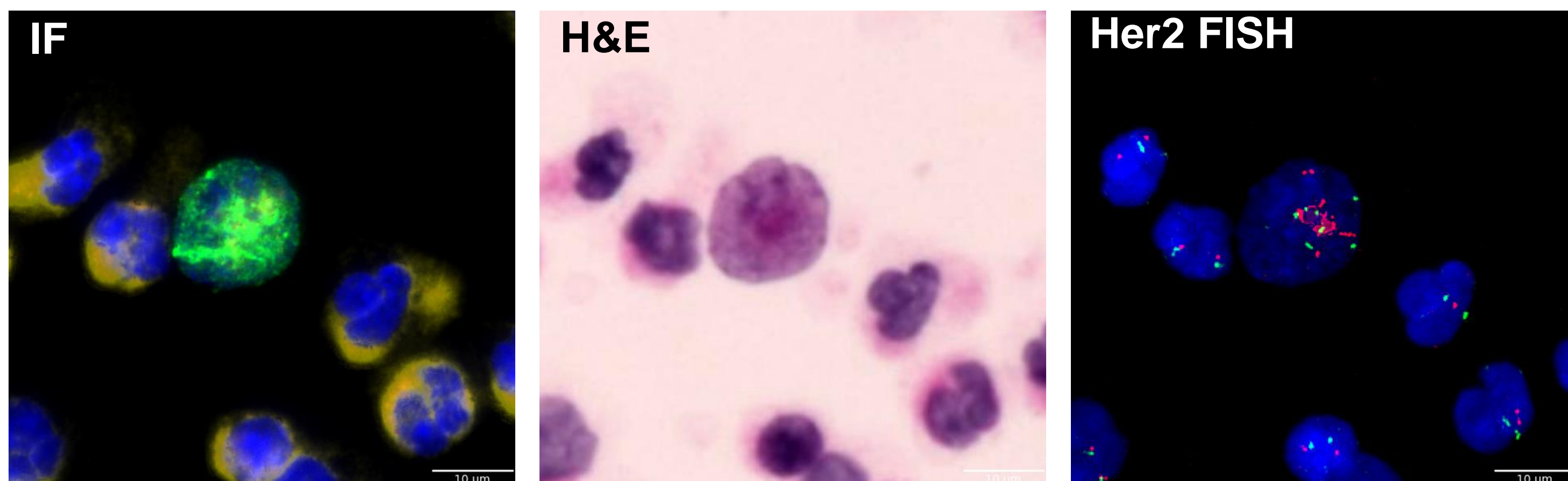
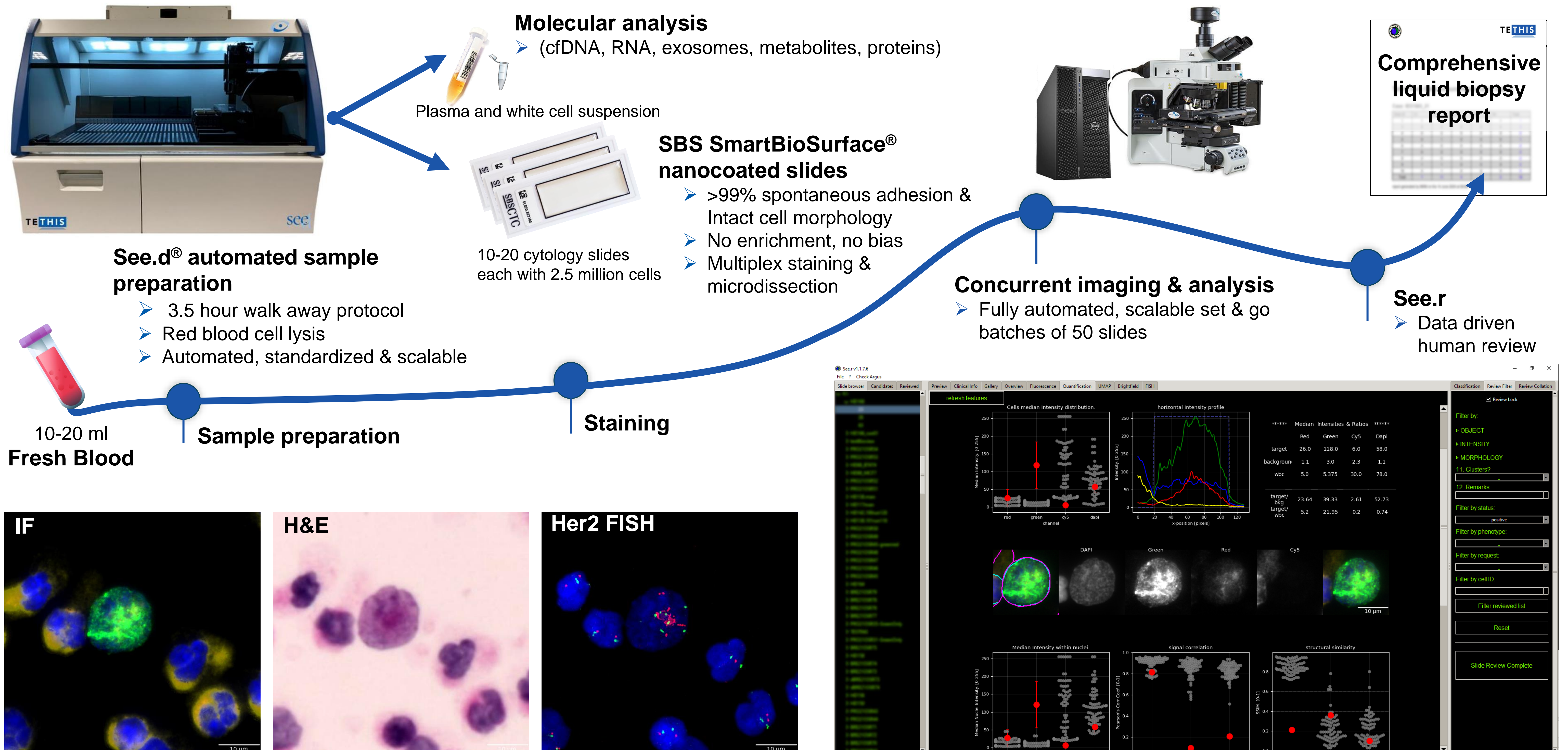
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Introduction

Liquid biopsy is emerging as a critical tool in personalized cancer medicine, allowing for the non-invasive detection and monitoring of circulating tumor cells (CTCs). However, the reliable and standardized processing of these samples is essential for accurate analysis and clinical application [1]. Tethis S.p.A introduces an innovative workflow that automates and standardizes the preparation of liquid biopsy samples, enhancing the detection of CTCs. Our technology leverages SmartBioSurface® (SBS) slides [2-4] and the See.d® system, transforming blood samples into a homogeneous monolayer of cells, ready for comprehensive analysis using advanced imaging techniques and AI-powered algorithms. This approach promises to significantly improve the accuracy and efficiency of CTC detection, making it a valuable tool in cancer management.

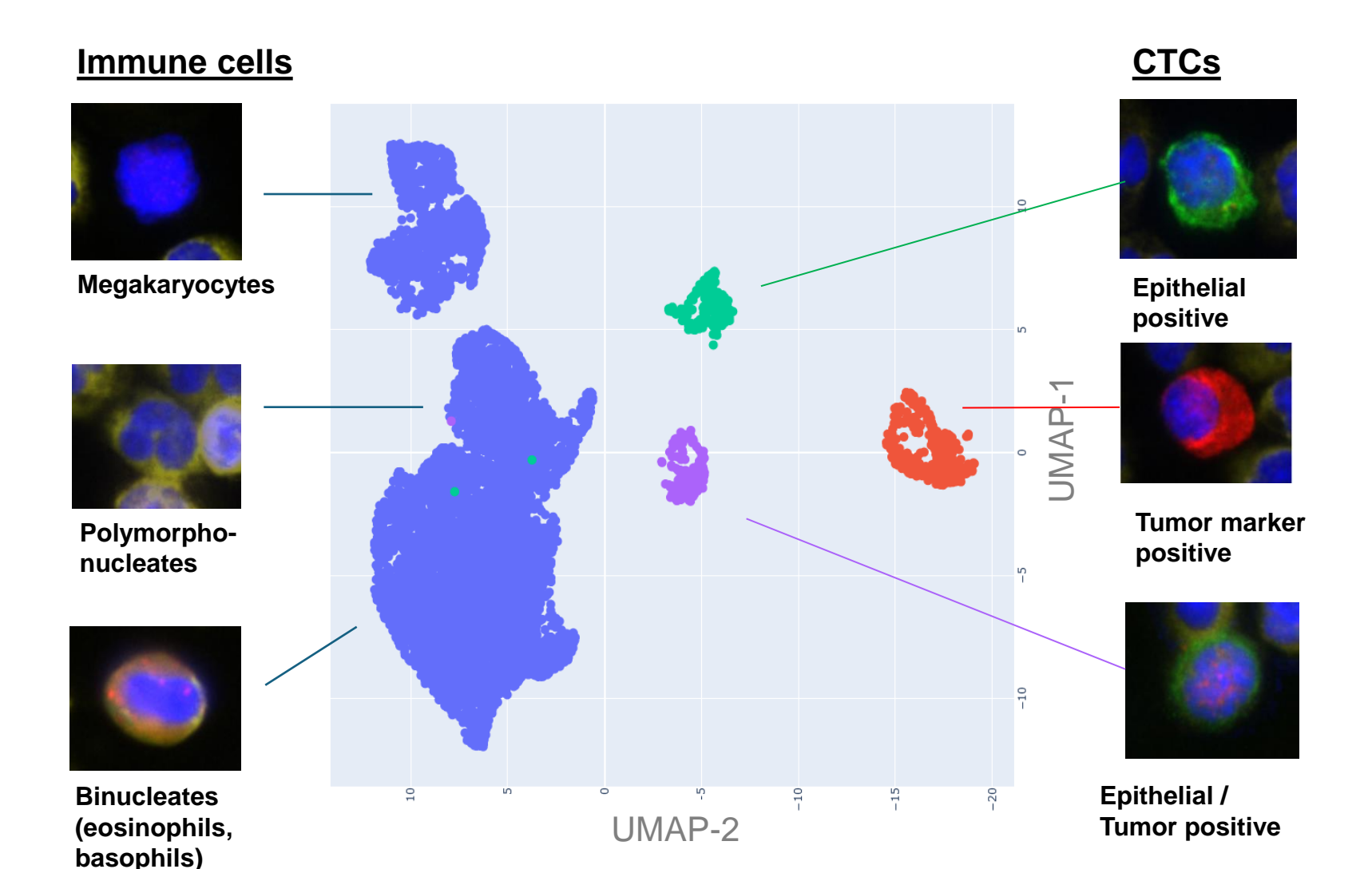
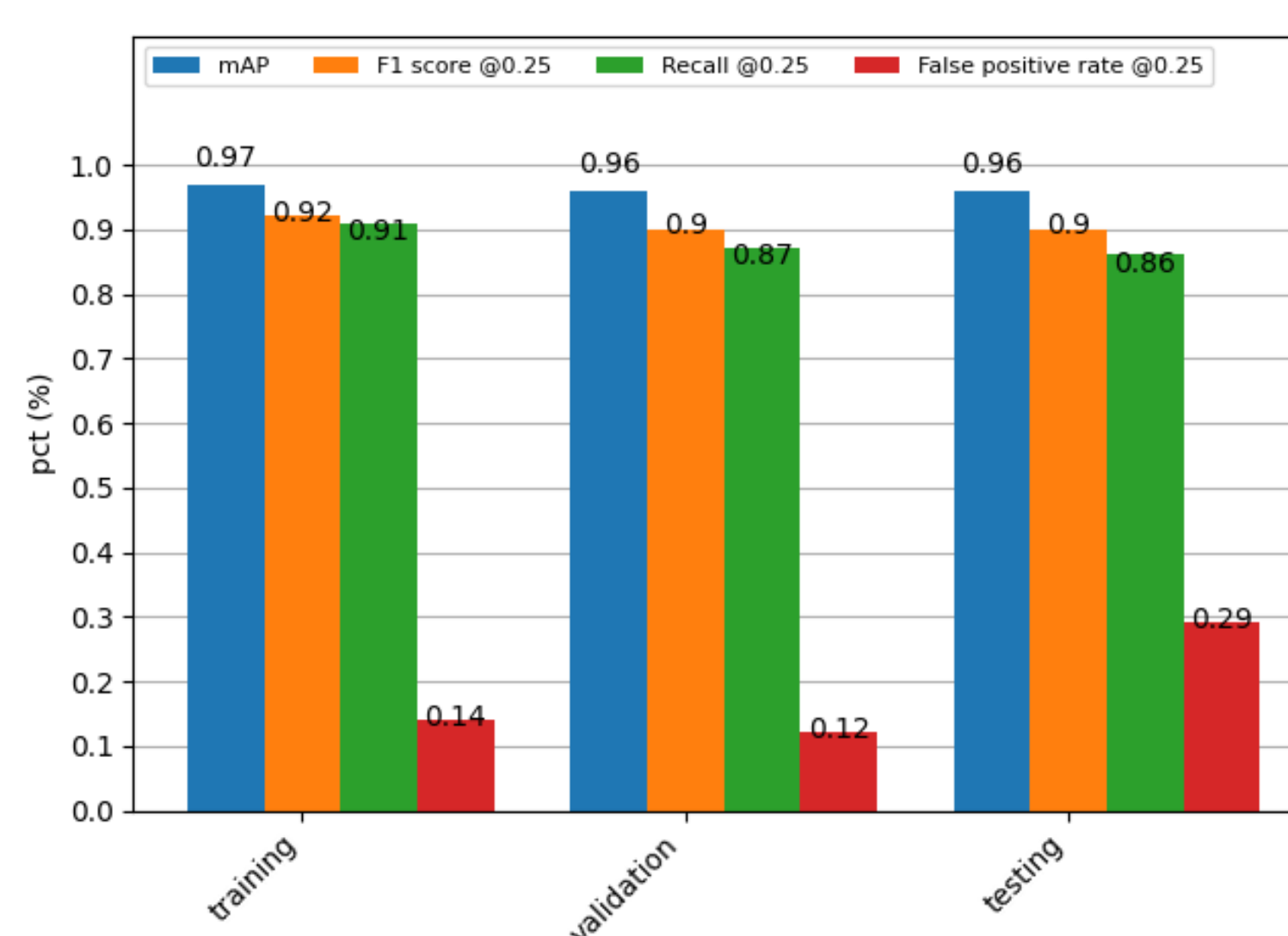
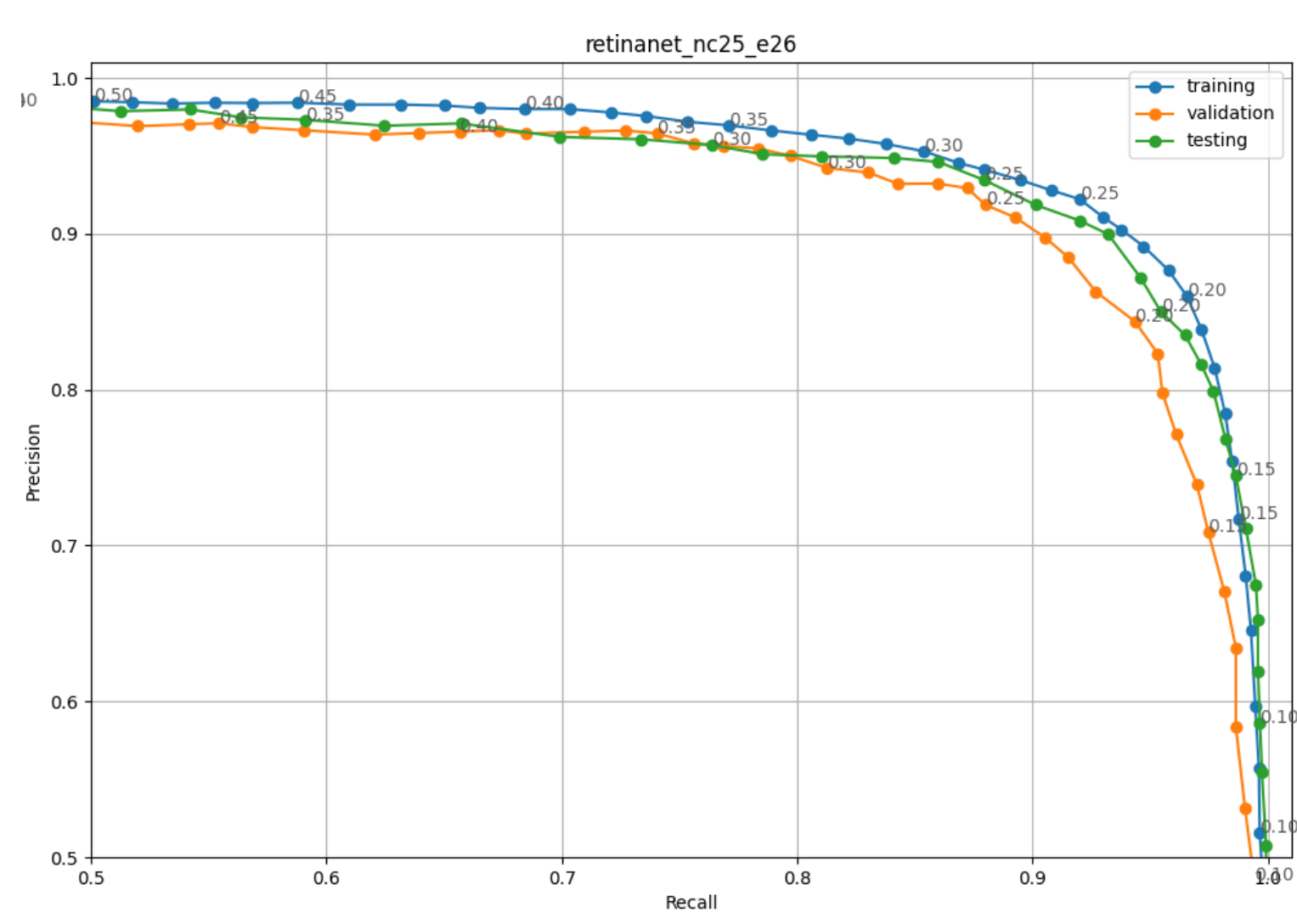
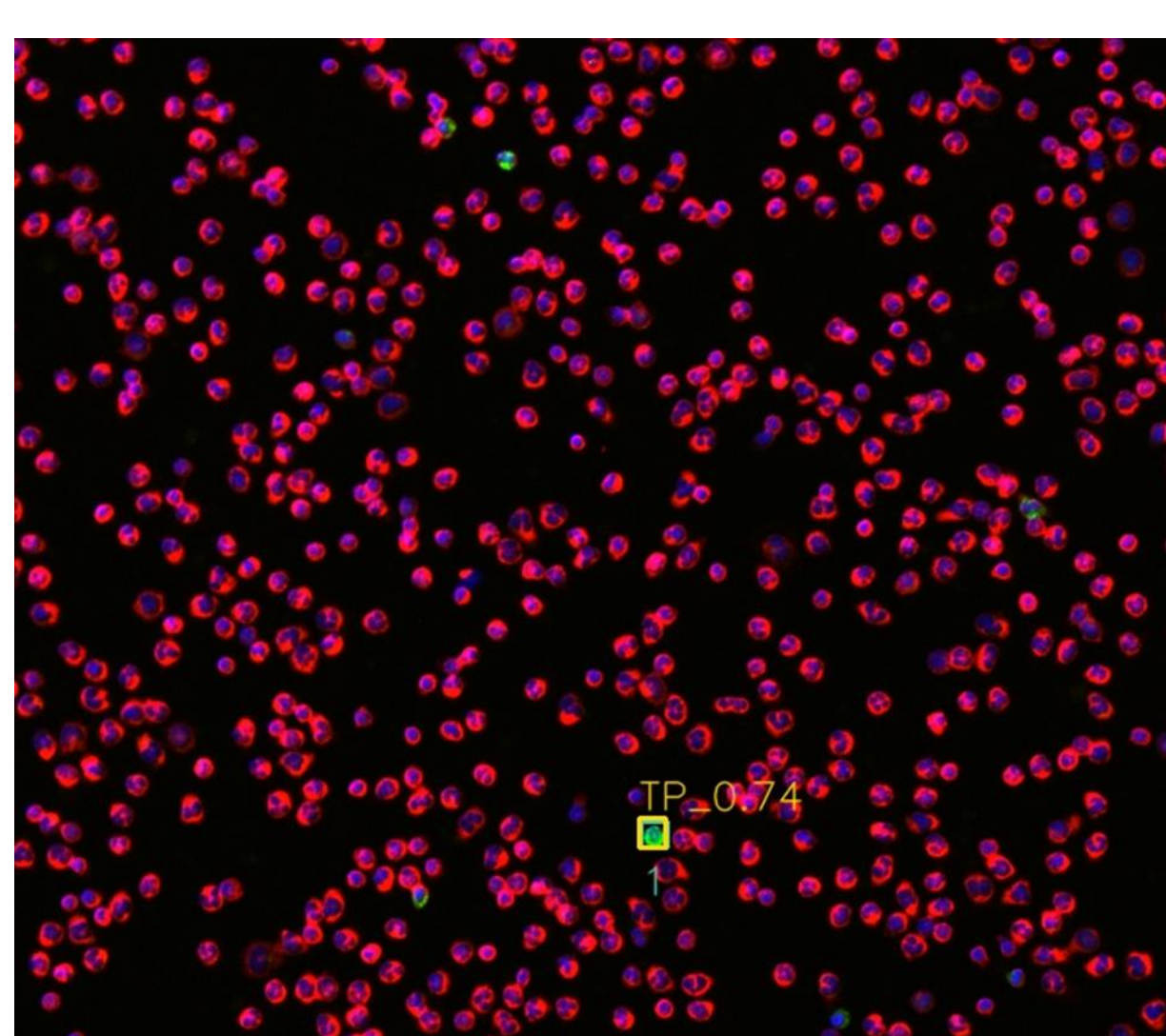
Tethis S.p.A liquid biopsy processing workflow



Multimodal imaging: Immunofluorescence (IF), Brightfield (BF) & Fluorescence In Situ Hybridization (FISH) on the same slide. Connect specific biomarker expression to cytologist cell review and FISH gene amplification

See.r software allow operators to review cells and confirm classifications based on: Quantitative information on intensities and cell morphology features, Brightfield picture, Single-cell molecular analytics information & Patient information

Rare cells detection and classification on clinical samples based on Immunofluorescence



Cell biology expert annotation

Breast & Prostate cancer patient CTCs Detection datasets:

Datasets	N cells	Precision	Recall
Training	5400	88%	96%
Validation	1030	86%	93%
Testing	1170	87%	95%

IF low resolution cell detection:

- Retinanet architecture-based object detection model tailored for detecting rare events with high accuracy by focusing on difficult-to-detect instances using Focal Loss [5].
- Highly effective at identifying as rare cells. The high mean Average Precision (mAP) score indicates that the model also maintains strong precision, balancing the ability to detect true positives while reducing the number of false positives.
- Sorting 2.5 million cells into about a hundred region of interests per slides

Immunofluorescence characterization:

- Balanced Random Forest model for automated classification of targets
- Digitalized rare cell fluorescence intensity and cell morphology features
- Trained UMAP features 2D projection

Conclusion

- Standardization** - See.d® system automates and standardizes liquid biopsy sample preparation, ensuring consistency and reliability.
- High-Quality Specimens** - SBS slides provide high adhesion rates and preserved cell morphology, enabling accurate analysis.
- Advanced AI-Powered Detection** - The model improves CTCs detection with high recall and precision, guaranteeing reliable cancer diagnostics.
- Multimodal Imaging Integration** - Integration of IF, FISH and BF microscopy allows comprehensive molecular characterization of rare cells.
- Clinical Relevance** - Streamlined workflow supports for routine clinical use, improving cancer management and patient outcomes.
- Personalized Medicine** - Accurate CTCs characterization makes this approach a valuable tool for personalized cancer treatment.

CONTACT INFORMATION

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