SmartBioSurface® slides: from cell monolayer to multimodal analysis and easy single-cell laser-based microdissection

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1. INTRODUCTION

Single-cell analysis is essential for understanding cellular heterogeneity.
However, multimodal single-cell analysis of non-adherent cells remains challenging due to poor adhesion and workflow incompatibility.
Non-adherent cells, White Blood Cell (WBC) suspensions, and rare cells are difficult to immobilize on standard Laser Capture Microdissection (LCM) slides, while cytospin often results in low recovery and potential cell damage.

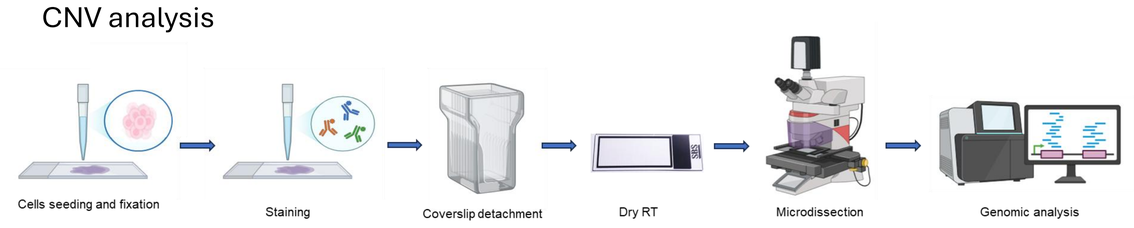
SmartBioSurface® slides, featuring a **nanostructured TiO_2 coating**, promote stable cell **adhesion**, preserve **morphology**, and enable **efficient laser microdissection** coupled with downstream **molecular analysis** [1].

Left Image: SmartBioSurface® slides in different formats. Right Image: Atomic Force Microscopy (AFM) of the nanostructured titanium surface showing homogeneous nanoscale features.; thickness: 47.6 ± 5.68 nm; specific surface area: 1.38 ± 0.03; RMS roughness: 9.5 ± 0.1 nm. *Specific surface area is defined as the ratio between 3D surface area and projected scan area.*

2. METHODS

LCM Analytical Workflow

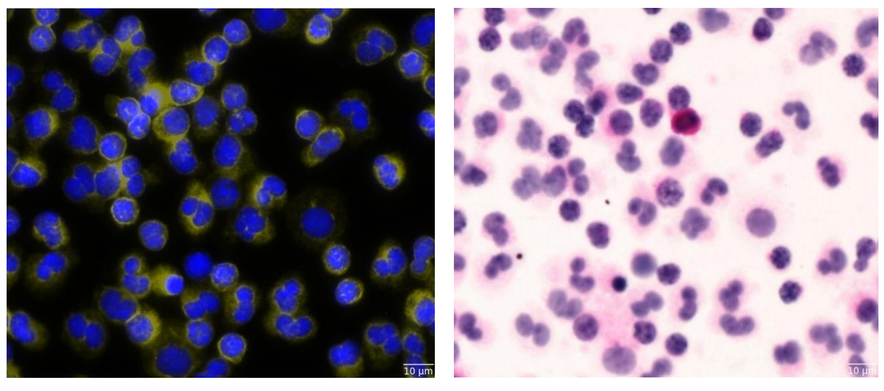
- **Cell seeding** – Non-adherent cells are pipetted onto the slide and spontaneously adhere to the nanostructured surface
- **Staining** – Brightfield or immunofluorescence enables clear cell identification
- **LCM isolation** – Target cells are precisely isolated by laser microdissection
- **Molecular analysis** – Single cells are compatible with WGA, NGS library prep, and CNV analysis



Schematic description of the analytical workflow starting from cell seeding on SmartBioSurface® slides to single-cell genomic analysis.

Sequential Staining

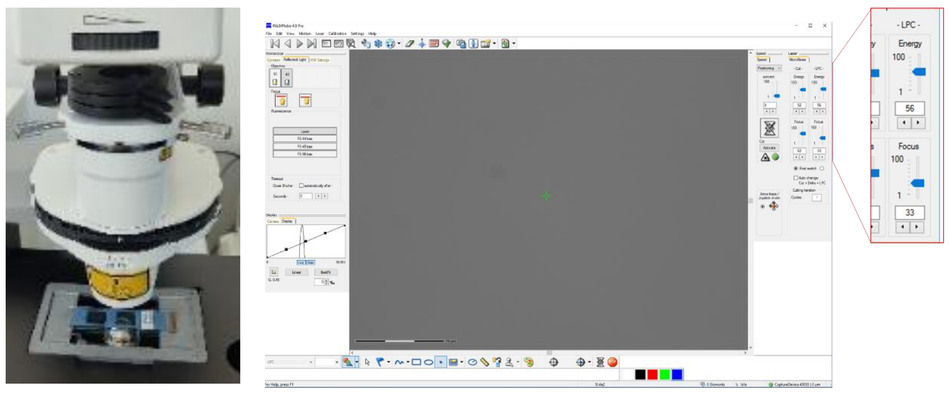
SmartBioSurface® enables a **sequential staining** workflow tailored for LCM, where **immunofluorescence** (IF) is performed first to identify target cells, followed by **brightfield** (BF) staining for morphological confirmation [2].



WBCs from a healthy donor, seeded on SmartBioSurface® (SBS) and fixed with 4% paraformaldehyde (PFA), after sequential staining for LCM. Left: IF image (Alexa Fluor® 647 anti-CD45 and anti-CD66b in yellow, DAPI in blue) used for target identification. Right: the same FOV after hematoxylin and eosin (H&E) staining in BF for morphological assessment (40× objective).

LCM System and Software Interface

SmartBioSurface® slides are fully compatible with LCM systems based on **laser pressure catapulting** (LPC), enabling clean-cut, precise, and efficient single-cell isolation [3,4].

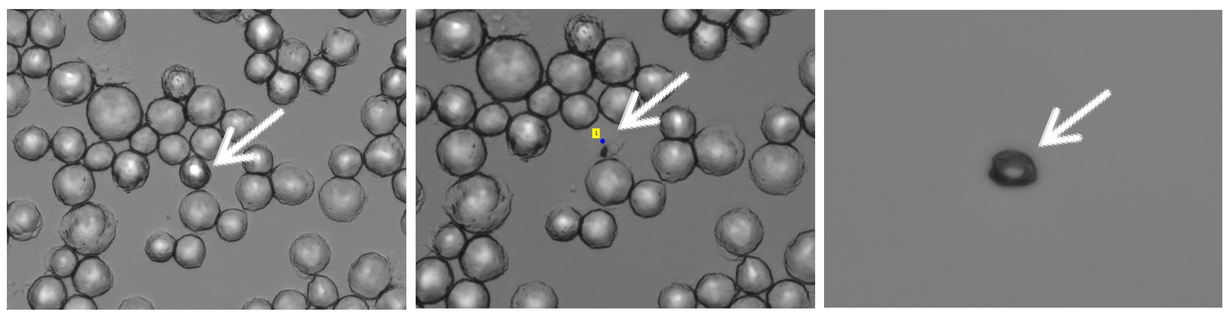


Left: SmartBioSurface® (SBS) slide mounted on the microscope stage for LPC-based microdissection. Right: PalmRobo software interface showing LPC parameters (energy and focus) used for precise single-cell isolation.

3. RESULTS

Single-cell LCM and capture confirmation of BT-474 cells

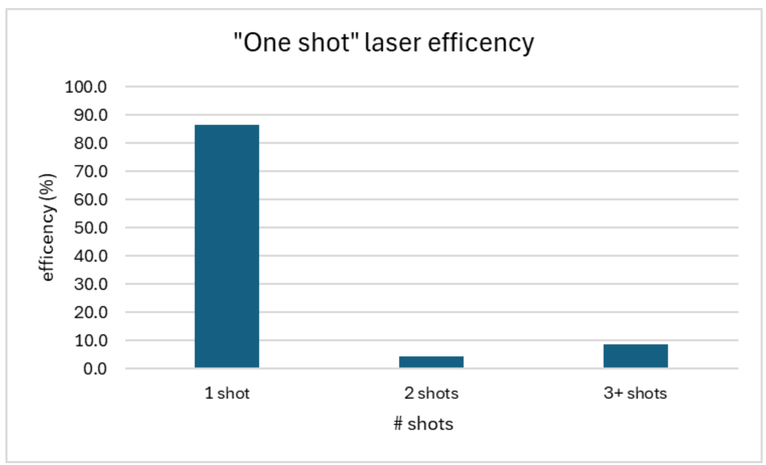
SmartBioSurface® slides enable **clear target identification** and **clean laser-based** release with LCM systems, allowing **efficient single-cell recovery**.



On the left: target cell before microdissection; in the middle: target cell after microdissection; on the right: target cell into the cap.

Efficiency of cell microdissection

Across more than 200 **individual targets**, the SmartBioSurface® slide provided a **100% success rate**, with most cells requiring only a single laser shot.

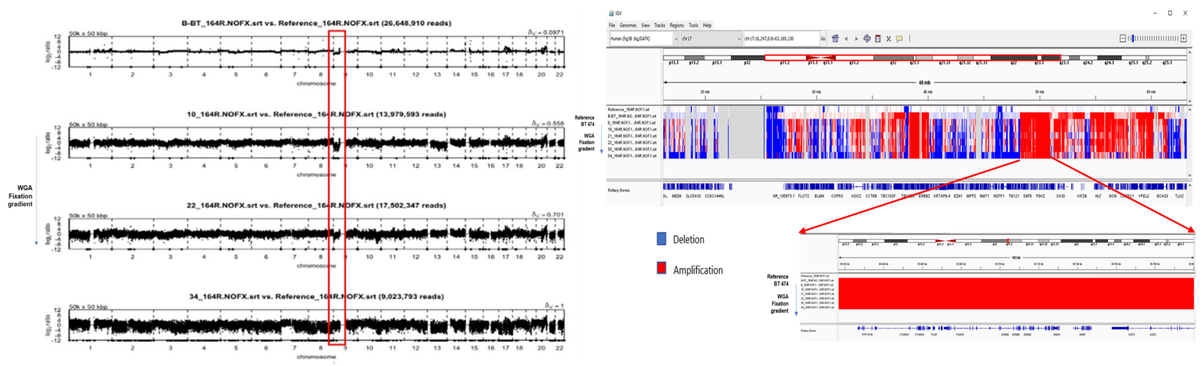


Distribution of Laser Shots per Cell (n=216)
1 Shot: 86.6%
2 Shots: 4.6%
3+ Shots: 8.8%

Molecular analysis of BT474 for Her2 amplification

WGS of single BT-474 cells after LCM demonstrates robust detection of key **CNVs**.

- Although PFA fixation (0–4%) increases background noise, CNV detection remains reliable
- **Chr17 ERBB2** (*HER2*) amplification is consistently detected across all cells



On the left: Effect of PFA fixation on single-cell CNV profiles. On the right: Detection of high-amplitude CNVs is preserved across fixation conditions

4. CONCLUSIONS

SmartBioSurface® slides enable **efficient single-cell isolation** by LCM and support reliable downstream genomic analysis, even in fixed samples

Workflow advantages

- Ready-to-use slides (no pre-treatment required)
- Efficient capture of non-adherent and rare cells
- Compatible with brightfield & immunofluorescence imaging

Performance

- High-efficiency single-cell isolation by LCM (up to 100%)
- Compatible with downstream molecular analysis (WGS)
- Robust CNV detection despite PFA-induced noise

References

1. Carbone R, et al; Biomaterials, 27(17), 3221-9 (2006).
2. Krol I, et al; Br J Cancer, 125, 23–27 (2021).
3. Visci G, et al; PLoS One, 19, e0297739 (2024).
4. Mastromarino MG, et al; Biomedicines, 11, 153 (2023).

SmartBioSurface®
Where efficient adhesion meets precise laser microdissection

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