APPLICATION NOTE

PRECISION BIOANALYSIS FOR THE DEVELOPMENT OF DERMAL THERAPIES

Aliri BIOANALYSIS

Unique spatial multi modalities platform

A deep understanding of pharmacokinetics (PK) and pharmacodynamics (PD) is critical for successful drug development. Aliri's integrated PK-PD platform combines Quantitative Mass Spectrometry Imaging (QMSI) with spatial omics while preserving tissue architecture. This spatial multi-modal approach offers unmatched insights into drug penetration, distribution, metabolism, and mechanism of action. By mapping the spatial localization of drugs and metabolites alongside molecular changes in the tissue, we enable precise characterization of disease pathology, patient stratification for treatment response, and the optimization of drug development strategies particularly in dermatology and tissue-targeted therapies.

Label-free quantitative small molecule distribution using QMSI

Choice of the compound and selection of the formulation composition are critical to obtain expected penetration. Critical elements to unreveal during development are about ensuring compound reaches its target (layer or cell type) at appropriated concentration and though a defined penetration route and pattern. The QMSI results allow visualization of small molecule drug distribution (<2.5 kDa) in a specific, label-free and quantitative way from frozen ex vivo samples or biopsies to be collected. This technique can be applied to exogenous (ie drug, API, metabolites) as well as endogenous molecules (ie lipids, histamine, Hyaluronic acid).

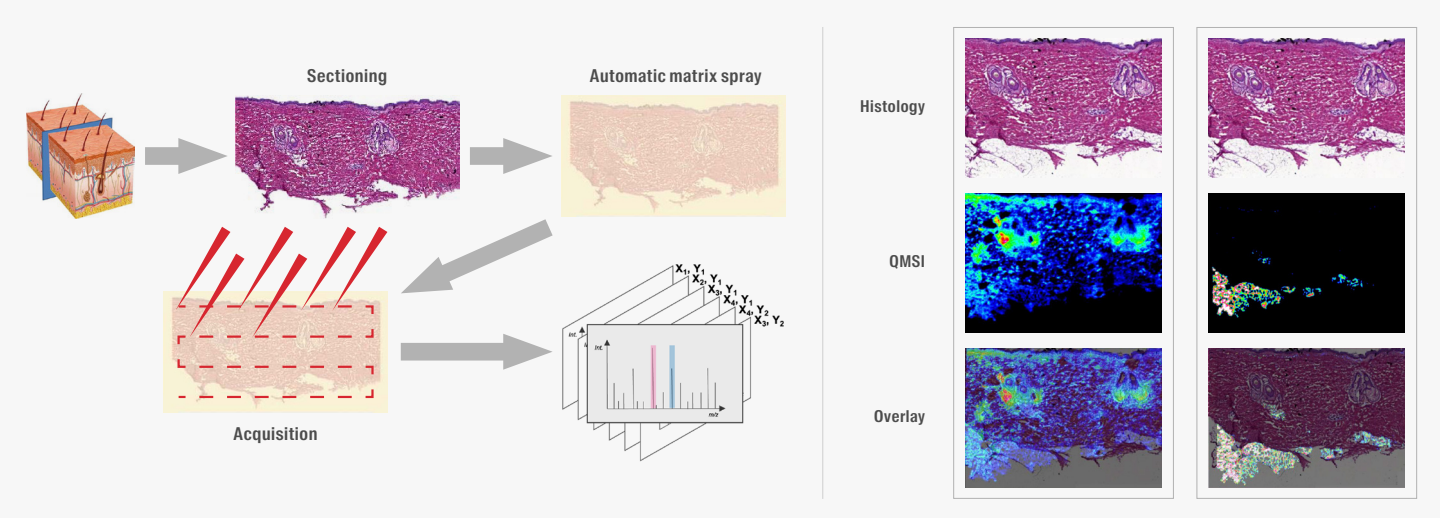
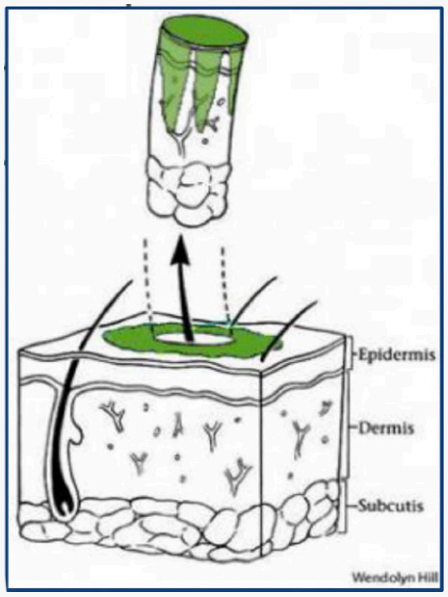
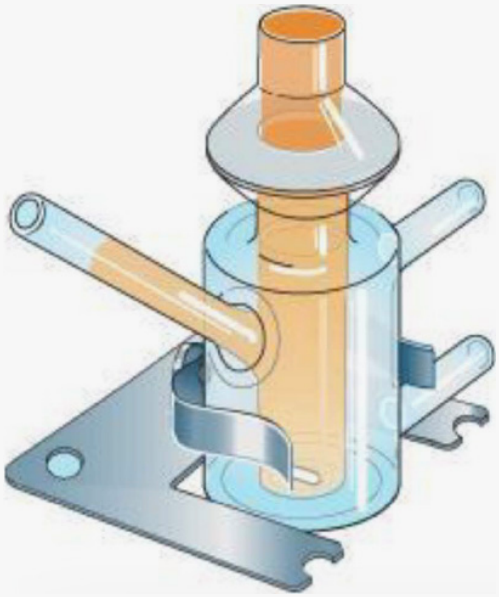


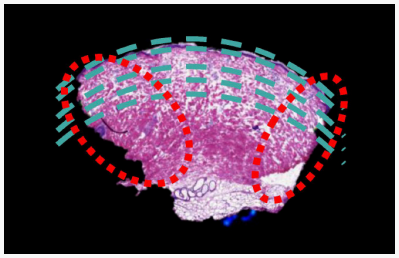
FIGURE 1. QMSI workflow and illustration of label free small molecule quantitative distribution with histological concordance.

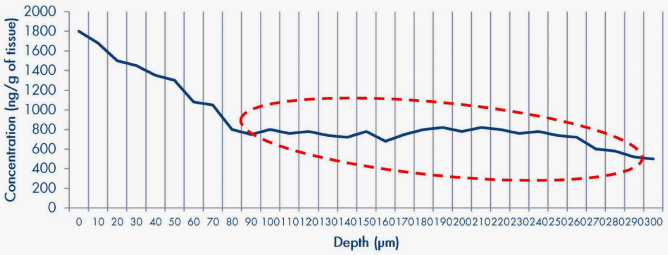
De-risk your decision-making

Diffusion analysis of compound into skin is traditionally associated with in vitro Franz cell experiments and/or in vivo skin punch biopsies testing. Nevertheless, major risk of tissue contamination and false positive results are associated with the sampling process. The combination of standard histology and QMSI allows discarding experimentally-induced diffusion effect to correlate only actual compound diffusion and concentration while preserving histological integrity.

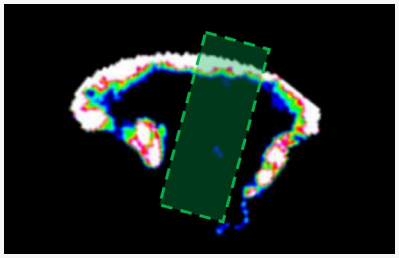








False positive risk without the imaging dimension!



ROI	HISTOLOGICAL REGION	CONCENTRATION (ng/g OF TISSUE)
1	Stratum corneum	1500
2	Epidermis	1200
3*	Dermis	nd

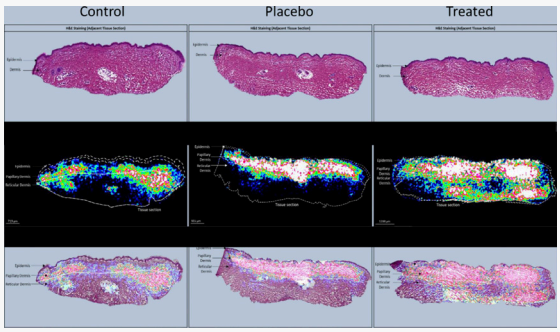
- Avoid false positive due to punch contamination and Franz cell systems (85%) with imaging
- Possibility to focus on histological features

FIGURE 2. Avoid false positive results

Select Your Formulation

QMSI approach is particularly useful comparing multiple formulations. As illustrated, it is possible to select a formulation based on the penetration profiles and in situ concentration of target exposure. A quick comparison of formulations provide confident decision-making for further topical drug application success.

https://pubmed.ncbi.nlm.nih.gov/35650447/



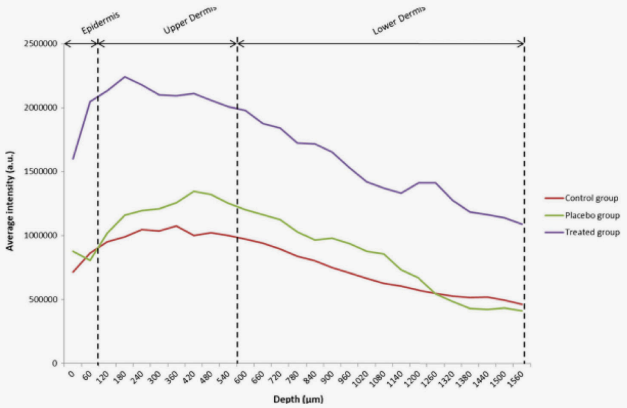


FIGURE 3. Representative images of label-free Hyaluronic Acid distribution and related penetration profiles

Legouffe R, Jeanneton O, Gaudin M, Tomezyk A, Gerstenberg A, Dumas M, Heusèle C, Bonnel D, Stauber J, Schnebert S. Hyaluronic acid detection and relative quantification by mass spectrometry imaging in human skin tissues. Anal Bioanal Chem. 2022 Aug;414(19):5781-5791. doi: 10.1007/s00216-022-04139-8. Epub 2022 Jun 2. PMID: 35650447.

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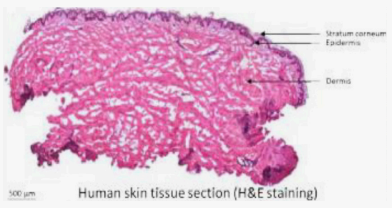
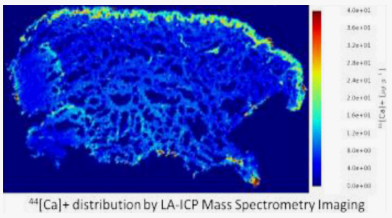
Cellular mechanism of action, from elemental imaging to spatial proteo-transcriptomics

Beyond in situ drug distribution, Aliri also provides elemental imaging capabilities to deepen biological insights. Using LA-ICP-MSI (Laser Ablation Inductively Coupled Plasma Mass Spectrometry Imaging), we offer precise, quantitative detection of elemental ions (e.g., Fe, Mn, Ca, Zn, K) at resolutions down to 1 µm. This is complemented by spatial proteomic and transcriptomic profiling, which enables cell-type identification and reveals localized changes in tissue architecture and signaling pathways. Together, these approaches allow us to address critical questions in drug development and translational research including mechanism of action, target engagement, biomarker discovery, immune infiltration, and patient response stratification.





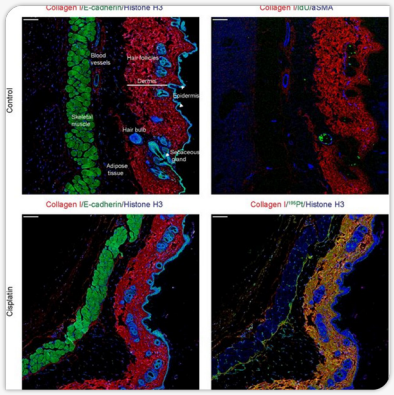


FIGURE 4. (*Left*) Distribution and quantification of calcium in Human skin at 20µm resolution with LA-ICP-MSI

FIGURE 5. (*Right*) Phenotyping and cellular interaction Aliri provides ready to use and customized immunofluorescence (IF) and Imaging Mass Cytometry (IMC) multiplex panels allowing to detect simultaneously up to 40 proteins in a single tissue section. Workflows integrates image segmentation and statistical analysis to identify cell subpopulations and deep tissue architecture. For deeper spatial proteomic insights, the Digital Spatial Profiler (DSP) platform provides access to over 1000 protein targets, integrated seamlessly into Aliri's data science pipelines.

In addition to high-plex proteomic capabilities, Aliri provides transcriptomic spatial profiling expertise thought multiple platforms (RNAscope, GeoMx, Visium, Visium HD). From single targeted transcript to Whole Transcriptome Altas (WTA) analysis, revealing transcriptomics modulations is widely used to identify new drug targets, characterize disease, identify relevant biomarkers and drug mechanisms of action. Aliri's data analysis proprietary workflow can spatially map gene expression clusters preserving histological and biological concordance.

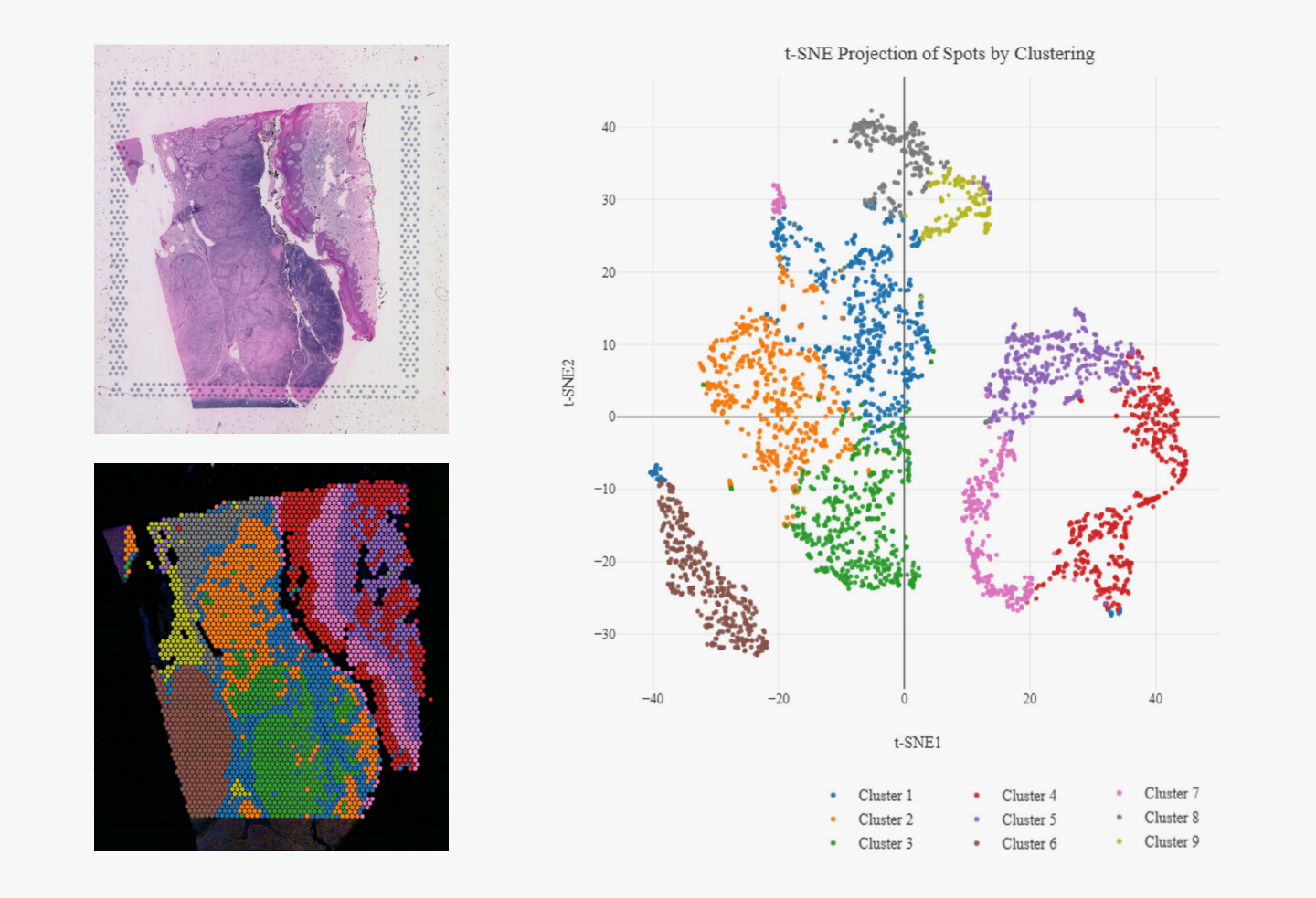


FIGURE 6. WTA spatial profiling in melanoma tissue

H&E-stained tissue captured post-CytAssist alignment preserves morphology, enabling accurate downstream spatial registration.

Using graph-based clustering, spatial transcriptomics data is analyzed to define biologically distinct regions. Clusters are projected back onto tissue coordinates, revealing transcriptionally distinct zones within the histological context. A t-SNE dimensionality reduction plot, where each dot represents a transcriptomic spot, colored by its assigned cluster, highlights transcriptional diversity across the sample.

Global Conclusion

With deep skin biology expertise and advanced multi-omics platforms, Aliri enables actionable insights across the R&D continuum. From identifying new drug targets to optimizing treatment response evaluation, our spatial-omics workflows accelerate translational decisions in dermatology and beyond.

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