New biopsy technology for analyzing multiple tumor tissue biomarkers

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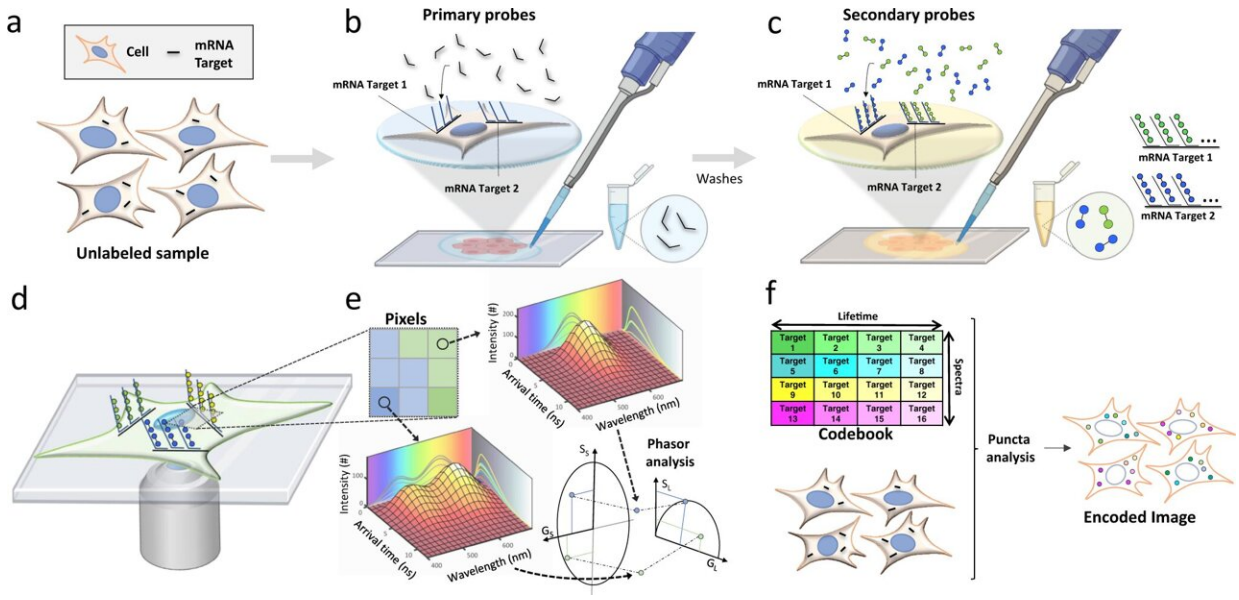

Fig. 1: Schematic of the MOSAICA approach for labeling and analysis of spectral and time-resolved components. a Sample(s) can be fixed cells or tissues. RNA transcripts from genes of interest are targeted for detection. Protein targets can be stained too in mRNA and protein codetection. b Primary labeling probes are designed to include two functional regions: a target region which is complementary and can bind to the mRNA target and an adjacent readout region which can subsequently bind to fluorescently labeled oligonucleotides. c Secondary fluorescent probes are added to bind to the primary probes to form different combinations (combinatorial labeling) through a “readout” domain. d Labeled targets are measured under a fluorescent microscope to interrogate the spectral and lifetime characteristics of the labeled moieties. e Phasor analysis is used to identify which fluorophore labels are present in each pixel and puncta. f Labeled targets eliciting the encoded intensity-based and time-based signature

are decoded to reveal the locations, identities, counts, and distributions of the present mRNA targets in a multiplexed fashion. Credit: DOI: 10.1038/s41467-021-27798-0

A team led by University of California, Irvine researchers has developed a new biopsy technology that can profile multiple tumor microenvironment biomarkers simultaneously, revealing cellular spatial organization and interactions that will help advance personalized disease diagnosis and treatment. Current single-biomarker biopsies lack the ability to analyze many different markers and often fail to predict patient outcomes.

Called the multi-omic, single-scan assay with integrated combinatorial analysis, the fluorescence imaging-based technology can spatially profile a large number of mRNA and protein markers in cells and tissues, including clinical tumor tissues. A study published today in *Nature Communications* shows that MOSAICA enables direct, highly multiplexed biomarker profiling in a 3D spatial context using a single round of staining and imaging instead of the repeated processing steps typically needed in conventional methods.

Clinicians and scientists will now have a holistic view of the different immune and cancer cell types in tumor tissues, providing greater insight for determining patient prognosis and treatment.

"Spatial biology is a new science frontier and mapping out each cell and its function in the body at both the molecular and tissue level is fundamental to understanding disease and developing precision diagnostics and therapeutics," said Weian Zhao, Ph.D., UCI professor of pharmaceutical sciences and study co-corresponding author. "Many cancer immunotherapeutics, including immune checkpoint inhibitors,

don't work and scientists realized that was because of the spatial organization of all the tumor tissue cell types, which dictates drug efficacy. The MOSAICA can characterize the spatial cellular compositions and interactions in the tumor immune microenvironment in biopsies to inform personalized diagnosis and treatment."

More information: Tam Vu et al, Spatial transcriptomics using combinatorial fluorescence spectral and lifetime encoding, imaging and analysis, *Nature Communications* (2022). DOI: 10.1038/s41467-021-27798-0

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