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3D Pathology-Guided Tissue Micromachining for Targeted Molecular and Spatial Multi-Omics Analysis

Researchers at Stanford have developed TRIM3D (Tissue-Referenced Integrated Micromachining in 3D), a precision tissue extraction platform that couples 3D pathology imaging with guided physical retrieval of specific tissue regions.

Modern 3D pathology methods can generate detailed, high-resolution volumetric images of intact biological tissues. However, no reliable method currently exists to extract specific volumes of interest or 2D tissue sections from defined depths and angles within a 3D specimen. A common workaround is to serially section thick specimens prior to identifying the best regions for molecular analysis, but this approach makes it impossible to obtain continuous-depth 3D pathology data and requires exhaustive sectioning before any region of interest can be identified.

TRIM3D solves this problem by leveraging the physical properties of a standard tissue-clearing agent to stabilize and immobilize specimens during precision micromachining. This enables accurate retrieval of user-defined 3D tissue volumes for downstream molecular profiling. Critically, the platform also supports extraction of thin, slide-ready 2D sections at any prescribed depth or angle within a specimen, making them directly compatible with spatial multi-omics platforms such as spatial transcriptomics and proteomics.

Stage of development: Proof of Concept

Applications

- Targeted extraction of tissue volumes for whole-genome sequencing and molecular profiling
- Preparation of slide-ready 2D sections for spatial transcriptomics and proteomics platforms
- 3D imaging-guided spatial phylogeny studies of tumor invasion and cancer biology

Advantages

- First method enabling 3D pathology-guided extraction of both tissue volumes and 2D sections
- Non-destructive workflow preserves intact specimens for 3D imaging before any physical extraction
- Fully compatible with all commercial spatial multi-omics platforms requiring thin 2D sections

Publications

- Hsieh, H.-C., Gao, G., Han, Q., et al. (2026). 3D pathology-guided microdissection. Nature Methods, 23, 1313–1317.

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