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Expanded Vacuum-Stable Gels for Multiplexed, High-Resolution Spatial Biology

Stanford scientists developed a new chemistry technique involving embedding tissue in hydrogel for mass spectrometry (MS), without the need for water to prepare samples for MS, that provides better resolution, better maintenance of X-Y distances and subsequent improvement in visualization of single cells.

Visualizing molecular tissue organization is essential for understanding normal and abnormal biological functions. Various highly multiplexed imaging technologies available today can be used to visualize intra- and inter-cellular molecular features at the nano- and microscale. Although these technologies can determine cellular positioning in tissues, their ability to resolve subcellular elements is limited. Those that can overcome these spatial resolution problems are burdened by high water content limits, challenges in multiplexed imaging, difficulties in retaining protein epitopes for antibody-based imaging, and applications to archival formalin-fixed paraffin-embedded tissues. The Nolan lab developed the current invention to overcome the above limitations.

The current invention enables the interrogation of biomolecular organization in physically expanded hydrogel-embedded tissues and the subsequent complete removal of water molecules in the hydrogel while retaining the expanded lateral dimensions. High-content visualization of tissue organization across multiple scales can then be achieved using analytical methods, including mass spectrometry imaging (MSI).

Stage of Development
Proof of Concept

Applications

- Imaging assays for the detection of biomolecular neighborhood signatures in tissue samples at high-plex dimensions and sub 100nm resolutions.

Advantages

- Fourfold or greater axial resolution improvements with the same instrumentation
- Improved signal-to-noise ratio
- Fast acquisition times
- Effective single-cell resolutions for methods (including MALDI-MSI) that was previously unattainable

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