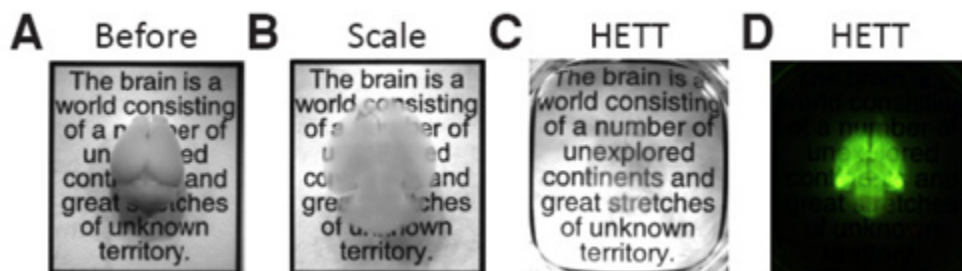


**Docket #:** S12-036

# **CLARITY: Transparent Tissue for 3D Imaging of Neuronal Networks and Subcellular Structures**

Researchers in Prof. Karl Deisseroth's laboratory have patented a revolutionary technique that can be utilized to map neural circuits in the whole brain. This technology, called CLARITY (Clear, Lipid-exchanged, Anatomically Rigid, Imaging/immunostaining compatible, Tissue hYdrogel), employs a hydrogel that preserves proteins, small peptides, small molecules, and nucleic acids in their three-dimensional distribution as found in original tissue. Following a clearing procedure, CLARITY renders tissue ultrastructures highly transparent and permeable to macromolecules, enabling visualization of both three-dimensional structure and fine molecular details of intact whole tissues without mechanical sectioning. Compared to the current *Scale* technology, this process is much faster (2 days vs. 5 weeks) and more effective removing opaque molecules.

Immunostaining the now transparent tissue can reveal subcellular structures in their native three-dimensional context. The same tissue can then be washed and stained again for subsequent analyses. CLARITY has a wide range of applications such as high-throughput mapping and analysis of neuronal networks, mapping cellular components in whole organisms, or clinical histology of biopsies and post mortem tissue.



Images courtesy the Deisseroth Lab

**CLARITY imaging of the whole intact mouse brain.** Photographs of whole mouse brains (4 months old). (A) Before clearing (B) Cleared by the *Scale* method for 5 weeks (C) Cleared by the CLARITY method for two days (D) Fluorescent image of the same brain shown in C.

### **Stage of Development**

Deisseroth Lab researchers regularly use CLARITY in their neural physiology research and actively maintain the CLARITY resource center.

## **Applications**

- **Research:**
  - 3-dimensional mapping of complex neural circuits with cellular resolution
  - research tool for [BRAIN initiative](#) to map the human brain
  - probing and mapping neural networks and other cellular components in the context of intact tissue or organisms
- **Clinical histology:**
  - storing, rendering, and using, and eventually actuating, the full connectivity of a human brain post mortem
  - obtaining 3D structural information from clinical biopsies such as heart, kidneys, tumors and other tissues

## **Advantages**

- **Whole tissue analysis** — no sectioning
  - faster and less laborious than mechanical sectioning
  - compatible with immunostaining or molecular phenotyping that is not possible with optical sectioning
- **Integrated 3D images** reveals structure combined with fine molecular details throughout the whole tissue
- **Maintains tissue** — the same brain or other tissue sample can be used for multiple rounds of staining
- **Improvement over current *Scale* technology** — faster (2 days vs. 5 weeks) and more effective at removing opaque molecules

## Publications

- Deisseroth, K. A., & Chung, K. (2021). *U.S. Patent Application No. [16/950,640](#)*.
- Deisseroth, K. A., & Chung, K. (2020). *U.S. Patent No. [10,545,075](#)*. Washington, DC: U.S. Patent and Trademark Office.
- Hsueh, B., Burns, V. M., Pauerstein, P., Holzem, K., Ye, L., Engberg, K., ... & Deisseroth, K. (2017). [Pathways to clinical CLARITY: volumetric analysis of irregular, soft, and heterogeneous tissues in development and disease](#). *Scientific reports*, 7(1), 1-16.
- Chung, K., Wallace, J., Kim, S. Y., Kalyanasundaram, S., Andalman, A. S., Davidson, T. J., ... & Deisseroth, K. (2013). [Structural and molecular interrogation of intact biological systems](#). *Nature*, 497(7449), 332-337. <https://doi.org/10.1038/nature12107>
- [White House Fact Sheet: BRAIN Initiative](#)
- [New York Times — Brains as Clear as Jell-O for Scientists to Explore](#)
- [Scientific American — Interview with Prof. Deisseroth](#)
- [Nature — See-through brains clarify connections](#)
- [The Verge — Technique to create transparent brains could transform neuroscience](#)
- [Inside Stanford Medicine — Getting CLARITY](#)
- [Stanford News — President Obama's new \\$100 million brain research initiative taps several Stanford scientists](#)

## Patents

- Published Application: [20150144490](#)
- Published Application: [20170219465](#)
- Published Application: [20210215581](#)
- Issued: [10,545,075 \(USA\)](#)

## Innovators

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