

Table S2. Tissue Transparency Methods for Intact Analyses

Selected techniques currently available for achieving intact tissue transparency and covering a broad range of capabilities are summarized. In light of the focus of this primer, methods with demonstrated capacity to clear intact adult mouse brains are listed. We divided these published whole-brain transparency techniques into three main categories: hydrogel-based methods (e.g., CLARITY), organic methods (e.g., iDISCO/3DISCO), and aqueous non-gel methods (e.g., Scale, CUBIC). Under each general heading, we then list extensions, variations, and new directions, as well as published demonstrations of use and papers reporting biological discoveries made using these methods. N.D., not determined in the original literature as of this writing.

Tissue Transparency Method	Initial method references	Clearing mechanism	Optical quality (intact adult mouse brain)	Reversibility	Labeling				Extensions/ variations and new directions	Biological demonstrations and discoveries in the brain (beyond the initial papers)	Biological demonstrations and discoveries in non-brain tissues (beyond the initial papers)
					Protein (native fluorescence)	Protein (immunostaining)	Nucleic acid	Lipid dye			
CLARITY and hydrogel variations	Chung, 2013	Formation of a hydrophilic tissue-polymer composite, followed by aqueous solvent-based disruption and removal of unbound components such as lipids by diffusive, mechanical, thermal, electrical, or other means	Fully transparent	Irreversible gel transformation, reversible labeling and imaging	Yes	Yes	Yes	No	Passive CLARITY (Tomer 2014, Zheng 2015), PACT/PARS (Yang, 2014), COLM (Tomer, 2014), ExM (Chen, 2015a), Stochastic electrotransport (Kim, 2015), SWITCH (Murray, 2015), ACT-PRESTO (Lee, 2016), SPED (Tomer, 2015), EDC-CLARITY (Sylwestrak, 2016)	Rodent brain: Hsiang, 2014; Spence, 2014; Lerner, 2015; Menegas, 2015; Adhikari, 2015; Plummer, 2015; Zhang, 2014; Tomer, 2015; Unal, 2015; Sylwestrak, 2016 Human brain: Ando, 2014; Liu, 2015a	Rodent: Lung (Joshi, 2015; Saboor, 2015), Liver (Font-Burgada, 2015), Whole animals/embryo/multiple organs (Epp, 2015; Yang, 2014), Spinal cord (Zhang, 2014) Plant: Palmer 2015
3DISCO and hydrophobic (organic solvent) variations	Erturk, 2012	Organic solvent-based lipid removal by dehydration/rehydration and bleaching on native tissue	Fully transparent	Irreversible	Rapid quenching	Yes (especially with iDISCO)	N.D.	No	iDISCO (Reiner, 2014)	Rodent brain: Weber, 2014; Zapiec, 2015; Garofalo, 2015 Human brain: Theofilas, 2014	Rodent: Thymus (Ziętara et al, 2015), Skin (Maksimovic, 2014; Oshimori, 2015), Islets (Juang, 2015), Bone marrow (Acar, 2015), Lymph node (Liu, 2015c), Spinal cord (Papa, 2016; Soderblom 2015; Zhu, 2015) Human: Lung (Hoffmann, 2015)
Aqueous non-gel variations	Hama, 2011 (Scale) Susaki, 2014 (CUBIC)	Chemical cocktail-based lipid removal and decolorization on native tissue (also compatible with CLARITY/hydrogel variants)	Mostly transparent	Irreversible	Yes	Yes	N.D.	No	Whole body CUBIC (Tainaka, 2014); Scales (Hama, 2015)	Rodent brain: Singh 2015; Asai, 2015; Ozkan, 2015	Rodent: Lung (Noguchi, 2015; Peng, 2015; Jain, 2015), Heart (Machon, 2015; Chabab, 2016), Spinal cord (Hinckley, 2015), GI system (Higashiyama, 2016; Liu, 2015b), lymph node (Jafarnejad, 2015; Moalli, 2015), Whole animals/embryo (Huang, 2015; Roccaro, 2015; Hirashima, 2015; Dorr, 2015; Hartman, 2015) Bird: Botelho, 2015 Xenopus: Tsujioka, 2015 Human: Intestine (Clairembault, 2015)

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