

Report 11: 3D Atlas of Cell Types in the Nervous System Defined By Molecular Phenotypes and Connectivity

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Brief History: Over the past ten years a large number of tools have been developed to analyze gene expression in the nervous system. However, the functional unit of an organism is the cell and not a gene. Analysis of gene expression with these tools is not dynamic. There is a clear need to define cell types by their position, connectivity, and the genes expressed. Technology such as TRAP technology is now making possible the identification of cell types based on molecular phenotypes. Identification of cell types on the basis of molecular phenotypes provides the basis for creating tissues to screen toxicants and to examine dynamic changes that occur in cell types based on changes in expression.

Discussion Highlights:

- What resolution is needed to define a cell type in the nervous system?
- What is the best organism to use to visualize dynamic changes produced by environmental toxicants and stressors?
- Identification of conserved dynamic changes in gene expression in cell types exposed to toxicants will be useful for identifying mechanisms of action.
- Definitions of cell types provide the basis for tissue engineering that enable screening of toxicants and overcome limitations of screening tissue culture cells.
- Zebrafish is an ideal organism to combine morphological changes with changes in gene expression in defined cell types. The zebrafish is transparent where morphological changes can be imaged with synchrotron computer tomography and at the same time visualized epigenetics and gene expression in defined cell types in real time.
- Developed advanced imaging methods that can probe changes in gene expression in single cells in at any level within the human brain.

Recommendations:

Create 3D atlas of cell types in the nervous system of mouse and zebrafish as baseline for measuring dynamic changes in cell types.

Develop statistical algorithms for defining cell types that are needed.

Use Molecular phenotypes as standard for creating tissues from embryonic stem cells. These tissues can be used for high-through screening of toxicants.

Combining synchrotron computer tomography to identify morphological changes with dynamic changes in gene expression in cell types, defined by molecular phenotype, in response to environmental insults in zebrafish.

Identify conserved dynamic changes in cell types in response to environmental stressors in vivo across species.

Develop new technologies that can image changes in gene expression in defined cell types in the human brain.

NIEHS should encourage grantees to take advantage of existing molecular neuroanatomy resources.

Discussion Participants:

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