

Collaborative 3D Atlas and Brain Development

The National Institutes of Health (NIH) announced on April 2 the results of a first major study based on an NIH-supported collaborative 3-dimensional atlas of the developing human brain that incorporates gene activity along with anatomic reference atlases and neuroimaging data. Miller, from the Allen Institute for Brain Science (Seattle, WA), and researchers from a consortium of U.S. centers, published “Transcriptional landscape of the prenatal human brain” in the April 10 issue of *Nature* (2014;508:199–206). The study uses data from the BrainSpan Atlas of the Developing Human Brain, which aims to profile gene activity throughout the course of brain development. The NIH-funded atlas and associated resources, freely available to the public, will enable researchers to explore questions related to the early origins of brain-based disorders such as autism and schizophrenia.

“Many neuropsychiatric diseases are likely the result of abnormal brain development during prenatal life,” said Ed Lein, PhD, from the Allen Institute and senior author of the study. “An anatomically precise molecular atlas of the brain during this time period is a first step to understanding how the human brain develops normally and what can go wrong.” The researchers studied 4 donated, intact, high-quality human prenatal brains from preterm stillbirths (from 15 to 21 wk postconception) as a framework for the atlas. Contributing labs provided data from a variety of genomic and imaging techniques. Among other findings, the authors identified significant differences between mouse and human brains in the subplate zone, a developmentally transient structure critical in cortical development. The researchers also identified unexpected similarities between mouse and human brains.

The BrainSpan atlas currently includes 4 central resources for studying transcriptional mechanisms involved in human brain development: (1) developmental transcriptome data: RNA sequencing and exon microarray data profiling up to 16 cortical and subcortical structures across the full course of human brain development; (2) prenatal laser microdissection microarray data: high-resolution

neuroanatomical transcriptional profiles of ~300 distinct structures spanning the entire brain for 4 midgestational prenatal specimens; (3) in situ hybridization image data: high-resolution data covering selected genes and brain regions in developing and adult human brain; and (4) a reference atlas: full-color, high-resolution anatomic reference atlases of the prenatal and adult human brain, accompanied by a systematic, hierarchically organized taxonomy of developing human brain structures. The consortium developing the BrainSpan atlas includes the Allen Institute for Brain Science, Yale University (New Haven, CT), the Zilkha Neurogenetic Institute of the Keck School of Medicine of the University of Southern California (Los Angeles), the Athinoula A. Martinos Center at Massachusetts General Hospital/Harvard Medical School–MIT History of Science and Technology/Computer Science and Artificial Intelligence Laboratory (Boston, MA), the University of California Los Angeles, and the University of Texas Southwestern Medical Center (Dallas), with collaborative support from the Genes, Cognition, and Psychosis Program, part of the Intramural Research Program of the National Institute of Mental Health (NIMH).

“Although the many genes associated with autism and schizophrenia don’t show a clear relationship to each other in the adult brain, the BrainSpan Atlas reveals how these diverse genes are connected in the developing brain,” said NIMH Director Thomas R. Insel, MD. “Findings of what goes on early in the prenatal brain can lead to the development of biomarkers for diagnosing brain disorders and for matching patients to treatment options most likely to be successful. This atlas is a clear example of the progress that can be made when the public and private sectors work together.”

These resources are freely available for viewing, searching, and data mining as part of the BrainSpan Atlas of the Developing Human Brain (<http://brainspan.org>) and can also be found through the Allen Brain Atlas data portal (www.brain-map.org).

National Institutes of Health