NEUROSCIENCE

‘Google of the Brain’: Atlas Maps Brain’s Genetic Activity

With his Microsoft money, Paul Allen has funded a gene-expression database of the mouse brain

In 2002, Microsoft co-founder and philanthropist Paul Allen asked a handful of neuroscientists how best he could use some of his fortune to advance their field. The researchers recommended the creation of a map of gene expression in the mouse brain, which they said would combine with knowledge gained from the Human Genome Project to illuminate how our brains work. The idea became the inaugural project of the Allen Institute for Brain Science in Seattle, Washington; $40 million and 4 years later, the map is now finished.

The completion of the Allen Brain Atlas, announced this week, caps a painstaking effort that involved analyzing more than 250,000 slices of mouse brain to determine which of the 21,000 or so known genes in the animal’s genome are turned on in the brain, as well as where and to what extent. The result is a freely accessible, searchable digital database (www.brain-map.org). Researchers are ecstatic: They say the gene-expression map will accelerate the search for drugs to treat psychiatric illnesses and help address fundamental questions about the development and function of different brain structures. “Some are calling it the Google of the brain,” says Joanne Wang, a pharmaceutics researcher at the University of Washington, Seattle. “I could not think of a better term than that.”

The interdisciplinary project involved neuroscientists and geneticists, as well as bioinformaticists and software engineers who worked on automating the analysis. “It took more than a year just to integrate the microscope to the software,” says Allan Jones, the chief scientific officer of the project. Having mice as the object of study allowed for a high degree of experimental control, Jones notes; not only were the animals genetically identical, but they were also given the same diet and handled the same way to the same age—56 days—before brain tissue was drawn from them.

The map shows that 80% of genes in the mouse genome are expressed in the brain—higher than the 70% figure that researchers previously thought. “Also, roughly 25% of the genes expressed in the brain show some kind of regional restriction,” Jones says. Among the things that the data set will allow researchers to do, he adds, is “group cells in the brain that have similar patterns of gene expression, which could reveal functionally relevant brain structures that are still unknown.”

The atlas, whose data have been made available in installments since December 2004, is already saving researchers a lot of time and trouble, says Jane Roskams of the University of British Columbia in Vancouver, Canada. Roskams, who studies the development of neurons in the vertebrate embryo, has been using the map to test how combinations of glutamate receptors on neurons in the olfactory bulb may be responsible for differences in how likely they are to undergo programmed cell death. The map helps narrow down alternative hypotheses quickly instead of testing them all through hours of lab work, says Roskams.

Wang has found that the atlas aids her work on using molecules known as membrane transporters, which ferry cargo into and out of the brain, to deliver drugs to targeted brain areas. Doing this requires understanding where and how abundantly drug-transporter genes are expressed in the brain, which is “not a trivial task for individual labs,” she says. “I had a graduate student work for almost a whole year to map the brain expression pattern of a single transporter gene discovered in our lab.” Now, she can simply type a gene’s name into the site and click a button to view its expression profile.

Jones says the institute is now embarking on a project to create a similar gene-expression map for the human cortex; he and his colleagues have already begun talks with brain banks and neurosurgeons. “It’s going to be more of an experimental venture,” says Jones, “because we will have no control over the genetic background and the environmental factors behind the samples we end up analyzing.”

Still, he believes the new project will provide important insights into genetic drivers of the overall structure of the cortex as well as how developmental abnormalities unfold. For example, Karen Berman, a psychiatrist at the National Institute Mental Health in Bethesda, Maryland, plans to use the current mouse atlas as well as the planned human cortex map to home in on the specific gene defects that cause Williams syndrome, a developmental disorder she’s studied for several years.

“This will also help us to look at interactions between genes of interest and how their effects develop in the brain over time,” she says. “That could help us intervene before the disorder sets in.” Researchers say the atlas will definitely quicken the development of such interventions and prove that Allen spent his money wisely.

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