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ALLEN INSTITUTE *for* BRAIN SCIENCE

FREQUENTLY ASKED QUESTIONS

GENERAL QUESTIONS ABOUT THE INSTITUTE AND THE ALLEN BRAIN ATLAS

What is the Allen Institute for Brain Science?
Founded in 2003 by philanthropists Paul G. Allen and Jody Allen Patton, the Seattle, Wash.-based Institute is a non-profit medical research organization with about 80 employees. Started with $100 million in seed money from Paul Allen, the Institute was created to identify and address key issues in neuroscience.

Why did Paul Allen decide to launch the Allen Institute for Brain Science?
Paul has always been interested in high-impact initiatives that change the world, and is well known as one of the leading philanthropists in the country. The majority of Paul's philanthropy has been dedicated to health and human services and toward the advancement of science and technology. In 2002, Allen gathered together leading scientists from around the world and posed a critical question: "What is the one thing that will make the biggest difference in the field of brain science?" The Allen Brain Atlas is the result.

What is the Allen Brain Atlas?
Publicly accessible at no cost, the Atlas is a Web-based, three-dimensional map of the normal mouse brain that pinpoints the anatomical location of over 21,000 genes. The Institute's inaugural project, it shows in which brain regions and cells the genes are expressed, and thus can help elucidate which genes are turned on during particular brain functions. Since 2004, the Institute has been releasing data via the Atlas as it becomes available.

How does a mouse brain correlate to the human brain?
Humans share more than 90 percent of their genes with mice, making the mouse a good model system for learning more about disorders and diseases rooted in the human brain.

How significant is the completion of the Atlas?
The Atlas represents a groundbreaking intersection of genomics and neuroscience, providing the most comprehensive look to date at gene activity in the brain at a cellular level. The data provided by the Atlas can help lead scientists to major advances in detection, prevention and treatment of brain disorders and diseases.

What does the Atlas mean to scientists and researchers?
Referred to as "Google for gene activity in the brain," the Atlas allows scientists to see which genes are active in the brain, which cells they are expressed in, and which genes are turned on during particular functions. Providing data on over 21,000 genes in one resource dramatically propels neuroscience forward, saving scientists several steps in their research programs and thus giving them an invaluable gift of time.

How is the Atlas being used so far?
The Atlas can help unlock brain functionality in a wide range of applications – from helping a pharmaceutical company understand the potential side effects of new drug therapies to enabling a researcher to understand the causative gene(s) for autism. It is being used by scientists at large

pharmaceutical companies, as well as by government labs, academic labs, the military and biotech companies. Anecdotal evidence shows that the Atlas is already moving research programs forward. A Harvard researcher is using it in his work on treating obesity. A genomics research institute in Arizona used the Atlas to confirm its findings on short-term memory, and the U.S. Department of Defense commissioned the Institute to study the effects of sleep deprivation on the brain.
We know that the Atlas is being used often – it receives >4 million hits a month, and approximately 250 scientists worldwide access it each day.

How might the Atlas benefit the average person?
The Atlas holds great promise for profound discoveries that could affect millions of lives worldwide. An estimated 26 percent of Americans – 57.7 million people – suffer from a diagnosable mental disorder in a given year, according to the National Institute of Mental Health.

- Nine out of every 1,000 people treated for epilepsy in the last five years
- 4.5 million Americans with Alzheimer's disease
- 3.4 out of every 1,000 children ages 3 to 10 diagnosed with autism

By establishing a baseline of a normal brain against which scientists can compare brains affected by diseases and disorders such as addiction, autism and schizophrenia, among many others, the Atlas offers vast potential for further understanding of those conditions.

How is the Atlas different from other brain atlases that have previously been developed?
The Allen Brain Atlas provides a comprehensive map of gene expression in the brain at a level of detail previous unavailable. Some atlases have provided anatomic maps that show the location of various structures in the brain but provide little or no information about the genetic activity within them. Others have identified the location and activity – or "expression" – of genes in the brain, but none have been as comprehensive as the Atlas, which includes every major structure in the brain and most of the smaller structures, and covers essentially the entire genome.

How does the Atlas correlate to the Human Genome Project?
The scale of the two projects is similar - the Human Genome Project, completed in 2003, identifies all of the 20,000-25,000 genes contained in human DNA but does not identify where they are turned on in the body. The Allen Brain Atlas adds the *where*, showing both the genetic makeup of the brain and where in the brain those genes are turned on.

Why did it take until 2006 for a comprehensive brain atlas to be developed?
In a word, resources. A project on the scale of the Atlas, which cost about $41 million, would have been virtually impossible to achieve through traditional government funding sources. In addition, the 32,000-square foot facility housing the Allen Institute for Brain Science is also much larger than traditional research laboratories. Paul Allen's vision and contribution have provided the world with critical knowledge that is expected to help further brain research on a global scale.

How was such an enormous project completed within three years?
Structured more like a biotech or pharmaceutical company than a traditional research facility, the Institute represents a new paradigm for science. The Atlas project was conducted by a multi-disciplinary team comprised of neuroscientists, mathematicians, technical experts and others focused on a specific goal. The funding provided by Paul Allen enabled the project to avoid financial delays and be completed on time and under budget.

Why was the mouse brain used in the Atlas project rather than a human brain?
Neuroscientists can obtain donated human tissue from brain banks to conduct research, but supplies are limited and the quality of the tissue is highly variable. Donated brains typically come from people who suffered from various diseases and disorders, compounding the challenge of securing "normal" brains for baseline research.

How much data is contained in the Allen Brain Atlas?
The completed project contains more than 600 terabytes of data, enough to fill up about 20,000 iPods of the 30 gigabyte variety. The Atlas project has generated more than 85 million total images of gene data and brain scans. While the project was underway, it created more than 1 terabytes (1,000 GB) of data daily.

Can scientists download the data?
Yes. The Atlas is intended as a freely and publicly available resource. Downloading the data is subject to the project's terms of use and privacy policy, which are available online or by request.

Are there restrictions on use of the data?
The Institute is Paul Allen's gift to science. The use of data for scientific research and discovery is encouraged. Users are asked to credit the Institute if its data is included in published work. There is no "reach-through" on intellectual property associated with the Atlas data.

What will the Institute work on next?
The Institute will be focusing on the cortex, the region of the brain associated with behavior and most "higher order" functions. The goal is to build an atlas of cell types within the cortex, utilizing the data obtained from the mouse brain and building on that through study of human tissue. The Institute is also seeking opportunities to collaborate with scientists at other institutions on research programs addressing a variety of questions in neuroscience.

How will the Institute be funded in the future?
The Institute envisions a public-private funding partnership with both federal and state funding, as well as private contributions. Its founders feel that the Institute's success thus far and its potential for future collaborations will allow it to become self-sustaining.

TECHNICAL QUESTIONS ABOUT THE ALLEN BRAIN ATLAS

How many genes were done and in what timeframe?
Begun in 2003, the Atlas project completed a survey of over 21,000 genes in 2006.

What are you doing about alternate splicing?
The Atlas project's objective is to use one probe per gene. Probes are designed to be pan-specific for multiple transcripts of the same gene.

What mouse strain are you using? Age? Sex?
C57BL/6J from The Jackson Laboratory. The animals are 8 week (56 days) old males. This strain of mice is the same as used in the creation of *The Mouse Brain in Stereotaxic Coordinates* by George Paxinos and Keith Franklin. This age/sex/strain is the same as used to generate the data for the Atlas project.

Why do some genes have both coronal and sagittal data sets, while others only have sagittal?
Expression data for genes demonstrating particularly compelling specificity of expression are replicated at higher sampling density in the coronal plane of section that most neurobiologists and anatomists are familiar with.

Why didn't you use radioactivity?
The Allen Brain Atlas project chose the non-isotopic methodology because it allows the visualization of cellular morphology to a greater extent than radioactive measures. These methods produce a label that fills the cell body, in contrast to autoradiography that produces scattered silver grains surrounding each labeled cell. In addition the non-isotopic procedures are more environmentally friendly, a significant consideration for a project the size and high-throughput nature of the Allen Brain Atlas project.

Why did you create other reference atlases?
The decision to construct in-house mouse brain atlases was made to correspond to the methodology of brain tissue preparation used for Allen Brain Atlas *in situ* preparation. Additionally the reference atlas data hierarchy provides the common anatomical framework utilized during informatics processing in the Atlas data pipeline.

What platforms and browsers are supported by the Allen Brain Atlas?
The Allen Brain Atlas supports both PC and Mac users, ensuring access to data. For optimal performance, the minimum suggested requirements for each platform are: Microsoft® Windows® XP with either Internet Explorer 6.0 or Firefox 1.5; and Macintosh® OSX 10.3.6 with Safari 1.2.4.

What are the requirements for running 3D Brain Explorer?
For requirements for installing and running 3D Brain Explorer, follow the "Download and Install" link in the 3D Brain Explorer section at www.brain-map.org.

What are the Allen Reference Atlases and how do I use them when viewing a gene image?
The Allen Reference Atlases (ARAs) are brain atlases that provide an anatomic framework for brain regions, in both the sagittal and coronal planes, for the images you have selected. The ARAs are annotated using abbreviations to label the regions within the mouse brain. To view the ontology legend, click the "Show Legend" button in the Allen Brain Atlas Image Pane. When you select an ISH Image Pane, the relevant reference atlas automatically updates to the nearest corresponding reference atlas section.

How do I get search results for more than one gene at a time?
The Application bulk query search should be used to search for large gene sets. The query should be comma delimited. Then, select up to three genes for viewing simultaneously within our Image Viewer by clicking the "Add" box next to the genes of interest in the results set. Then select the "View Detailed Images" button to launch the Image Viewer. For more information, go to the help files via the "Help" tab on the Application.

Can I use Boolean search? Yes. You can use Boolean Search to build more complex queries to generate more refined results.

Can I link to information from other data and publication sources while viewing a gene image? Yes. Follow the "Links" link located in the gene search results table and then click the

active links to other sources.

If there are additional features that would enhance my experience with the Allen Brain Atlas, how do I submit my request? If you have suggestions for how we can improve the Atlas application, please submit your comments via the "Feedback" link under the "Contact Us" tab at the top of each application page.

Will there be any restrictions on use of the data? Will I be able to file for intellectual property on discoveries that I make using the data?
The use of data for scientific research and discovery is encouraged. Users are asked to credit the Institute if its data is included in published work. There is no "reach-through" on intellectual property associated with the Atlas data. For more detailed information, follow the "Terms of Use" link at the bottom of the Atlas home page: www.brain-map.org.

For more information:
www.brain-map.org