

# Neurogenomics and the Allen Brain Atlas

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A Decade of Neuroscience Informatics: Looking Ahead  
William H. Natcher Conference Center, NIH  
April 26, 2004

# Principles and Practices

## 1900-1953

- Body as a machine
- Matter and energy
- Biochemistry, physiology
- Small molecules, organs
- Rates, concentrations
- Pathways and cycles
- Simulations
- Integrative

## 1953-2003

- Body as a computer
- Information
- Molecular Cell Biology
- Macromolecules, cells
- Enumerations, interactions
- Pathways and signals
- Models
- Reductionistic



# A Century of the Gene

- 1960s Genetic Code
- 1970s Recombinant DNA technology
- 1987 “Genomics” coined by T. Roderick
  - **Gene + Chromosome + “ics” = Genomics**
- 1990 Human Genome Project launched
- 1998 Human Genome Project accelerated
- 2000 “Draft” sequence available in June
- 2001 Historic & controversial publications in February
- 2003 “Finished” sequence in February – 50th Anniversary of Watson & Crick

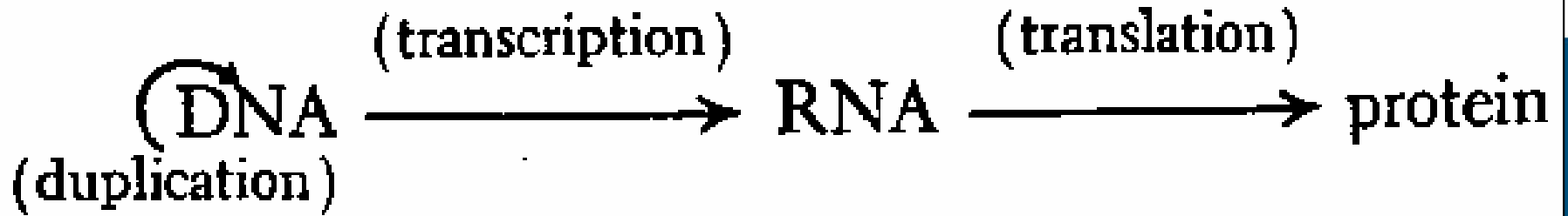


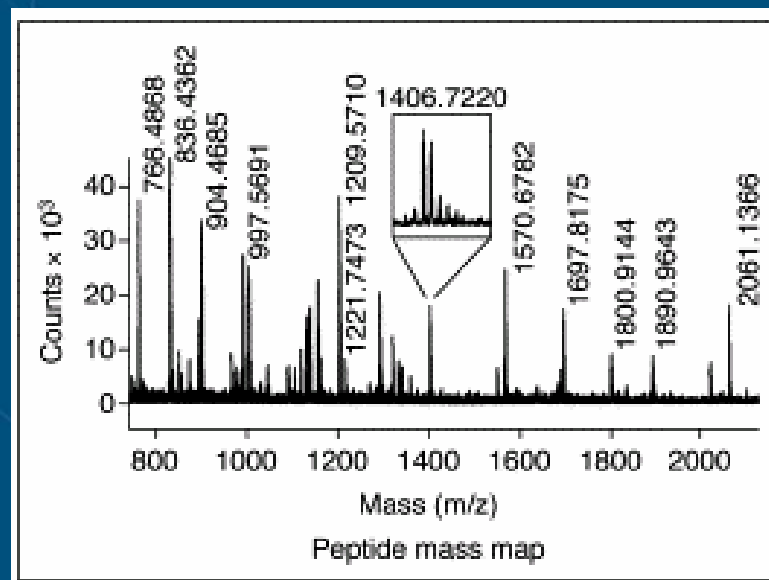
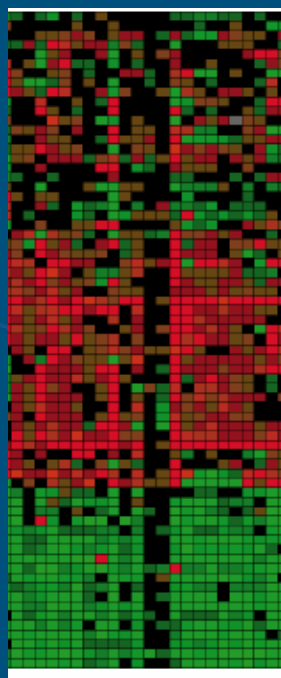
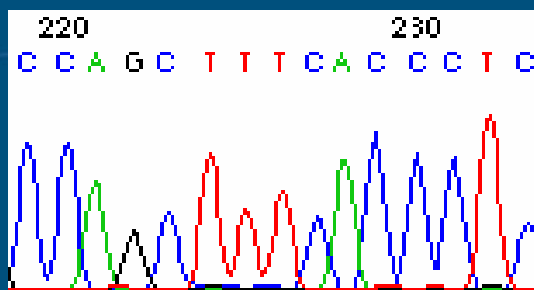
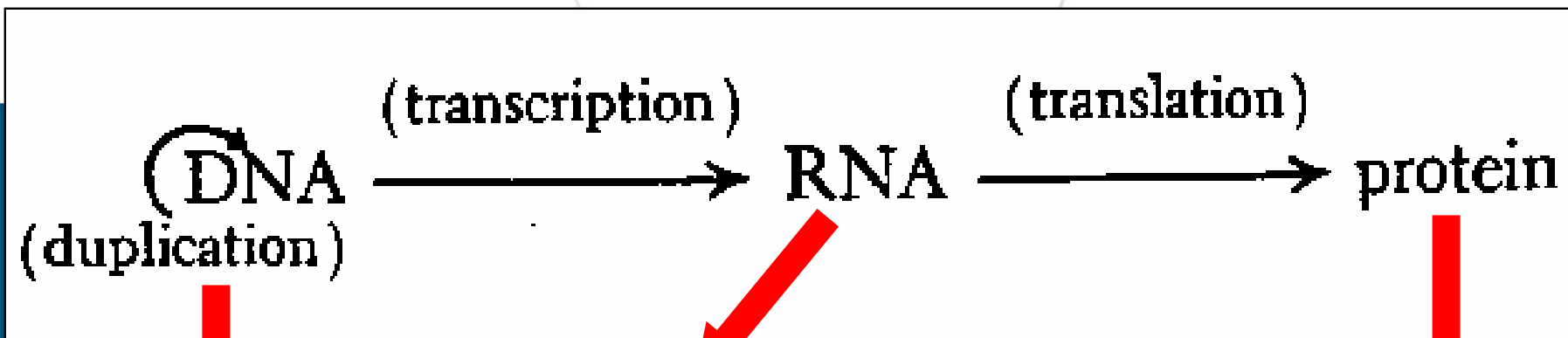
# The “omics” Transformation of Biology

- Cell & Mol. biology = “Functional Genomics”
- Protein structure = “Structural genomics”
- Protein biochemistry = “Proteomics”
- Descriptive biology = “Phenomics”
- Reading the literature = “Mining the bibliome”

“There’s no place like ome”

J.D. Watson (1965). *Molecular Biology of the Gene*, W.A. Benjamin, NY





# Consilience

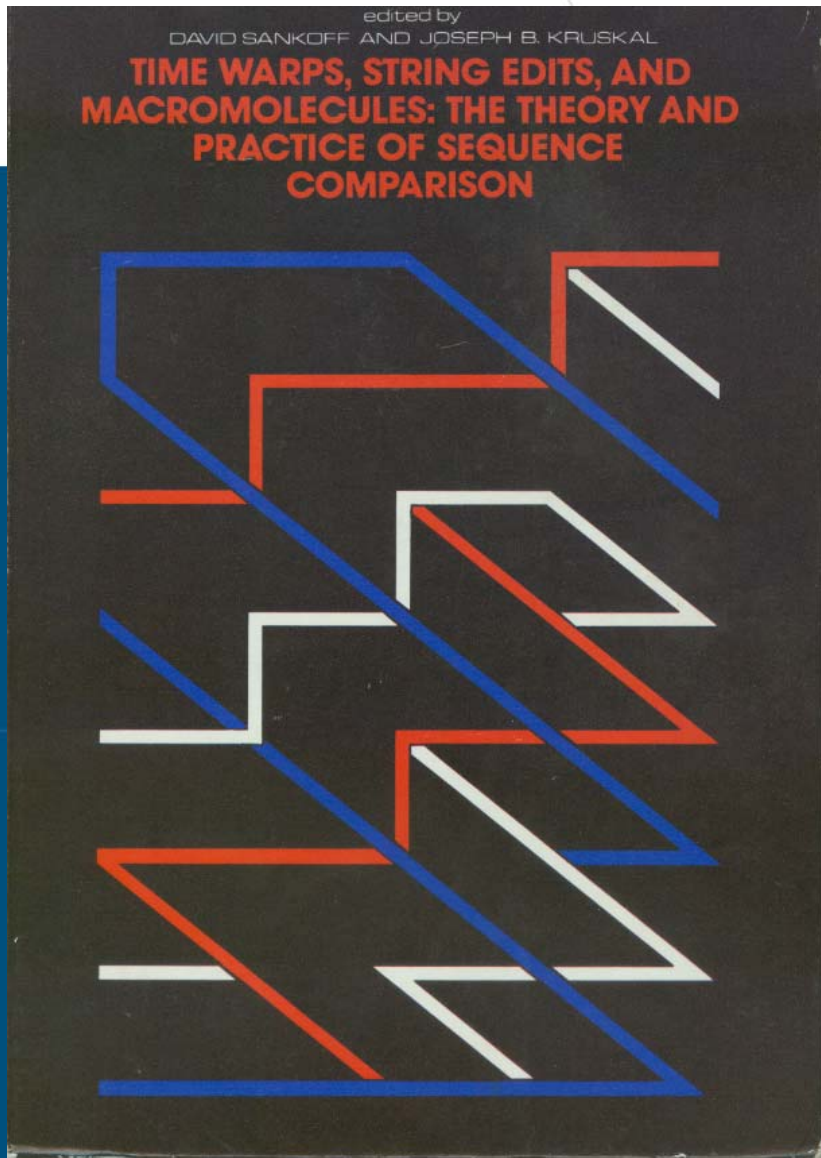
## 1900-1953

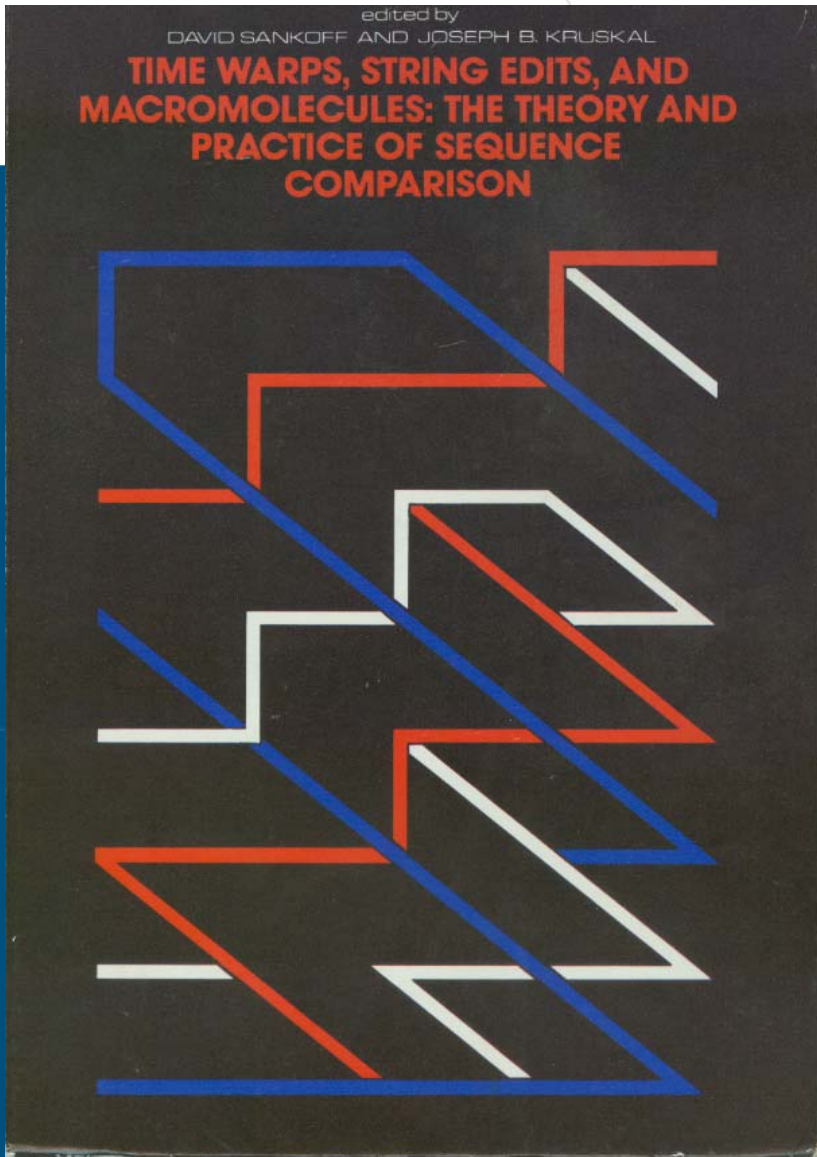
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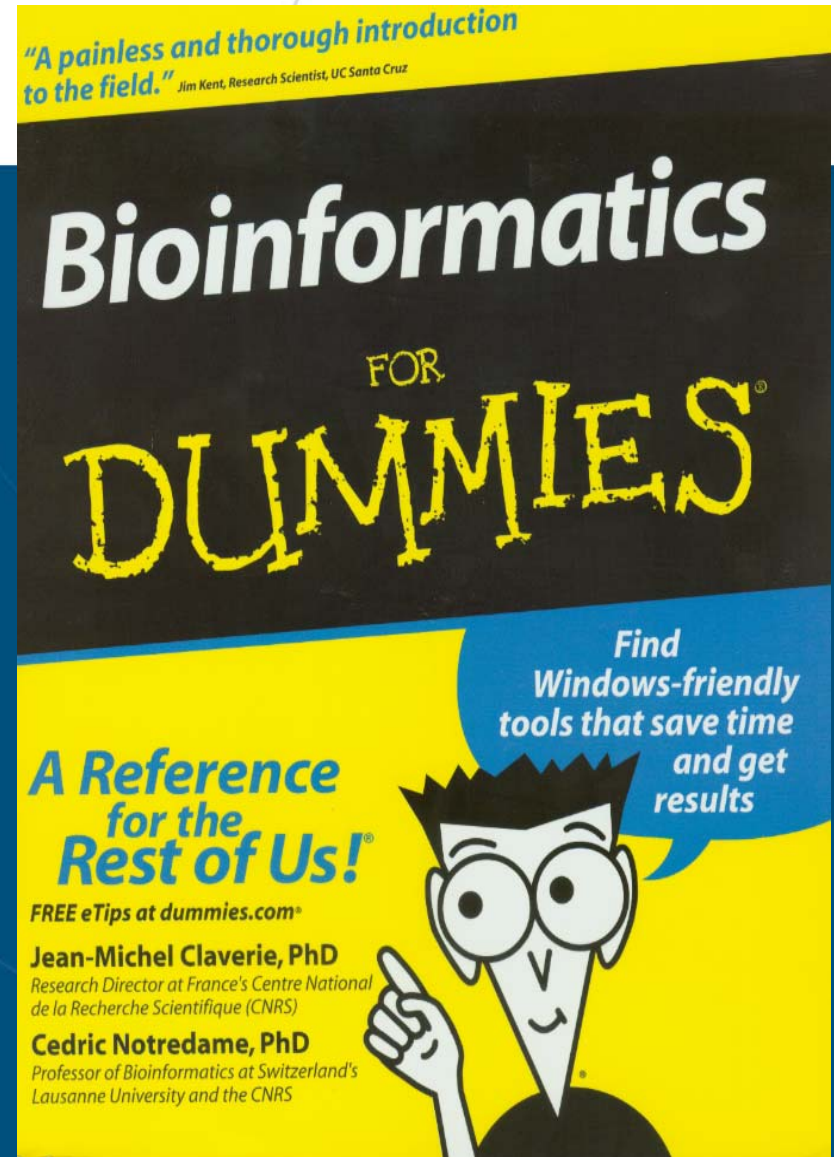
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- Reductionistic

Advanced technologies, multidisciplinary teams





Sankoff and Kruskal, 1983



Claverie and Notredame, 2003

# Brains & Genomes

1990-2000 “Decade of the Brain”

1990-2000 Beginning of the “Genome Era”

“Brains were brains and genes were genes and rarely the twain did meet.”

1998 *Neuron*

2002 Laguna Beach

# Lessons learned, promises kept: a biologist's eye view of the genome project

Lessons

Promises

S. Tilghman, *Genome Res.* 6:773, 1996

# Lessons learned, promises kept: a biologist's eye view of the genome project

## Lessons

- Information is power
- The power of collective action
- The power of high-volume data collection

S. Tilghman, *Genome Res.* 6:773, 1996

# Lessons learned, promises kept: a biologist's eye view of the genome project

## Lessons

- Information is power
- The power of collective action
- The power of high-volume data collection

## Promises

- Connections
- The power of model organisms
- The freedom to do biology

S. Tilghman, *Genome Res.* 6:773, 1996

# Allen Institute for Brain Science

- Founded in 2001 by Paul G. Allen and Jo Allen Patton as a 501(c)(3) nonprofit corporation
- Scientific Advisory Board chartered Fall 2002
- Hiring of full-time staff commenced Q1/2003
- Inaugural project begun Q1/2003
- Public announcement of \$100MM, 5-year “seed” funding on September 16, 2003

# Allen Institute for Brain Science

- Senior Advisors: James D. Watson, Steven Pinker
- Scientific Advisory Board:
  - Marc Tessier-Lavigne, Genentech Inc.
  - David Anderson, Caltech
  - Joseph Takahashi, Northwestern University
  - Gregor Eichele, Max Planck Institute and Baylor
  - Richard Gibbs, Baylor Genome Center
  - Arthur Toga, UCLA
  - Steven Paul, Lilly & Co.
  - Catherine Dulac, Harvard University



# Allen Institute for Brain Science

- The inaugural project is a genome era atlas of the mouse brain
- The goal is to construct an objective and consistent map with the goals of anatomic fidelity and cellular resolution
- This map will be based upon the expression patterns and levels of up to 20,000 genes

# Allen Brain Atlas

- A secondary goal is to develop a high-throughput technology platform to
  - Examine other strains
  - Perform perturbation experiments
  - Construct subsequent generation maps, e.g. proteome
- The timeline for the project is three years

# Allen Brain Atlas

- Work is being carried out in a 30,000 SF facility in Seattle
- Current staff is ~26 FTE and represents a multidisciplinary team with experience in
  - Neuroanatomy
  - Genomics
  - Engineering
  - Process development
  - Image analysis
  - Data mining
- Staff will expand to ~50 FTE by Q4/2004

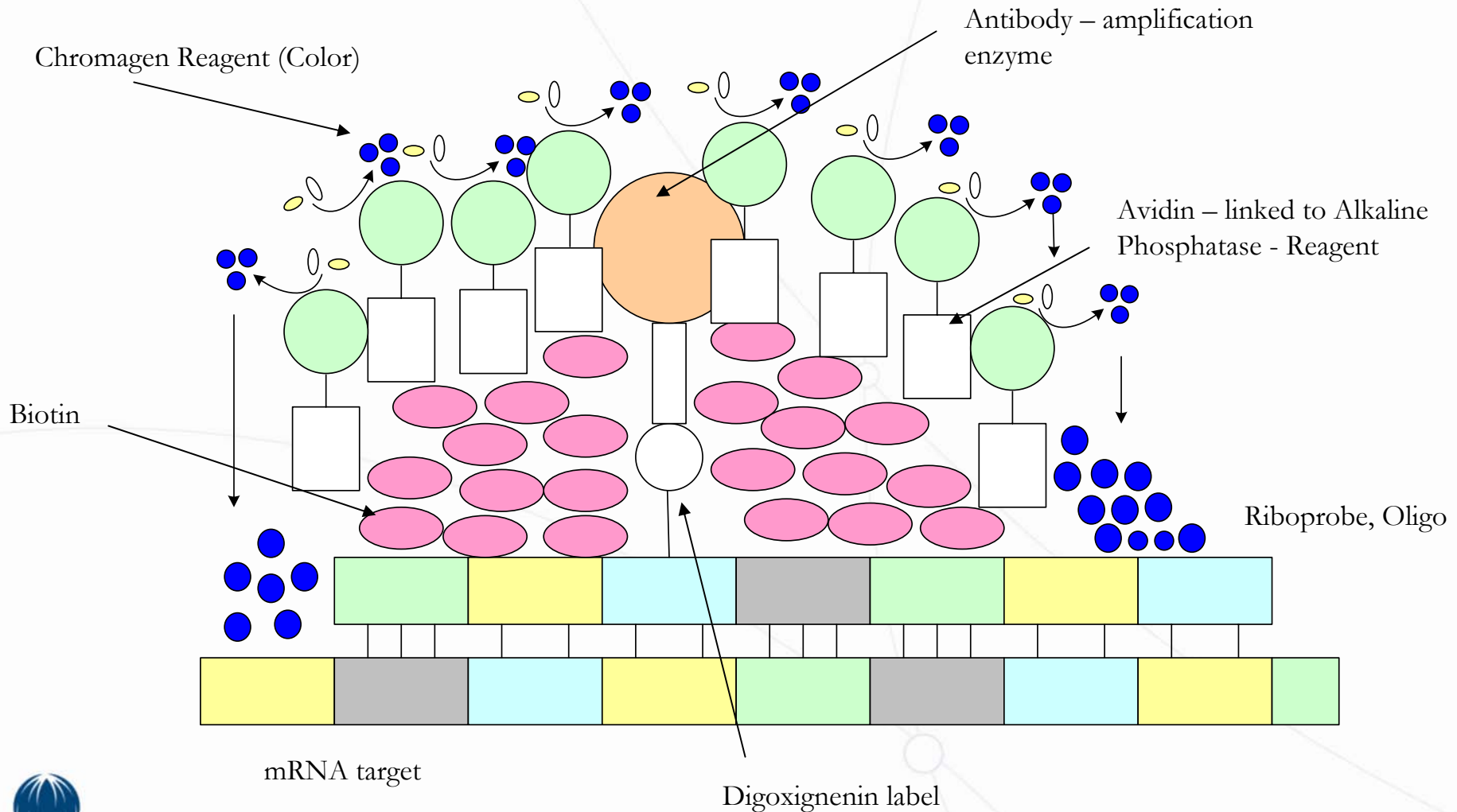


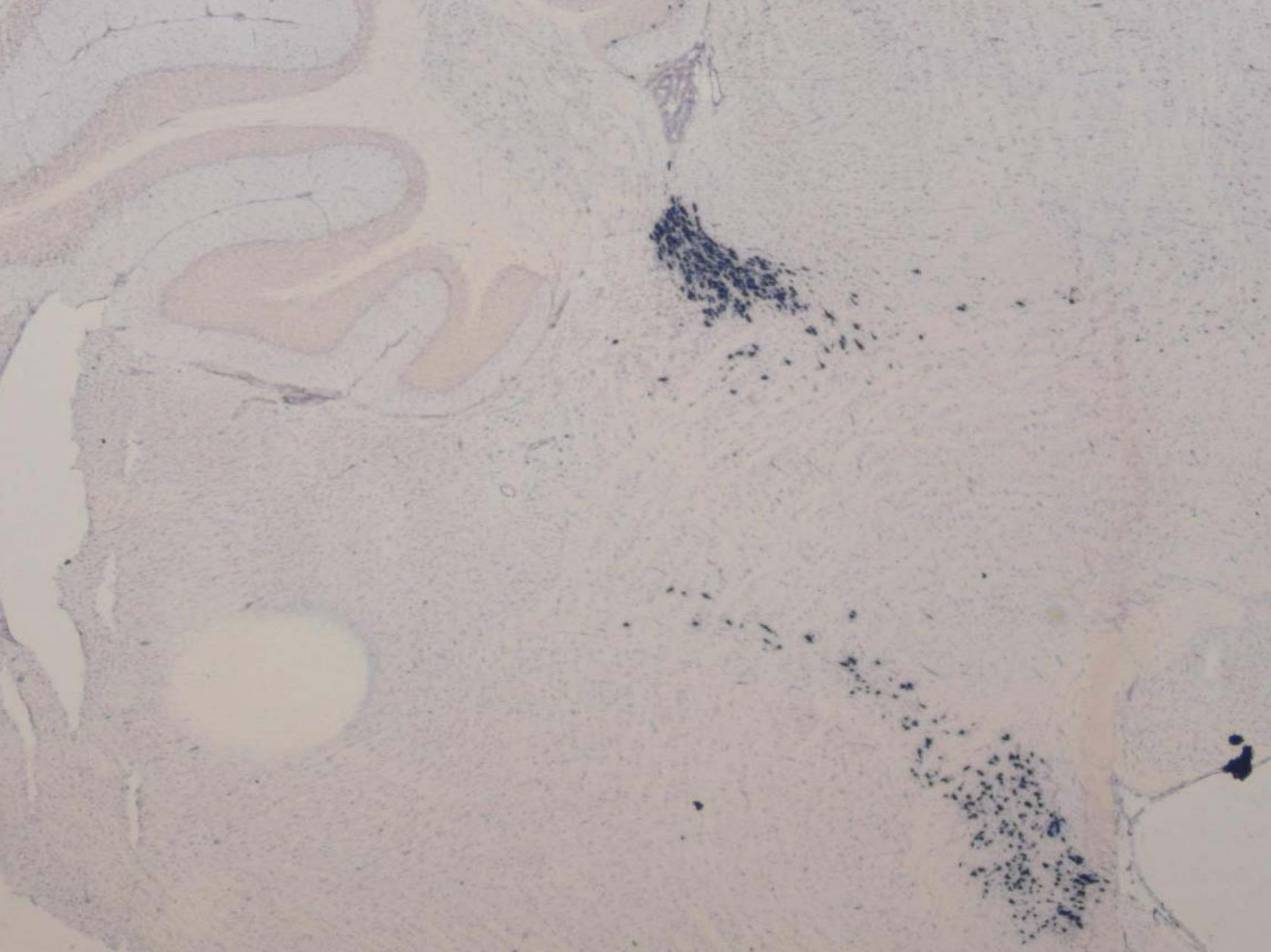
# Allen Brain Atlas

- During the first year we have a dual focus on
  - Medium-throughput data production
  - Process and technology R&D in preparation for scale up
- Milestones achieved to date
  - LIMS development
  - Pilot data production
  - Database, application and user-interface
  - Gene selection and probe design pipeline for *in situ* hybridization

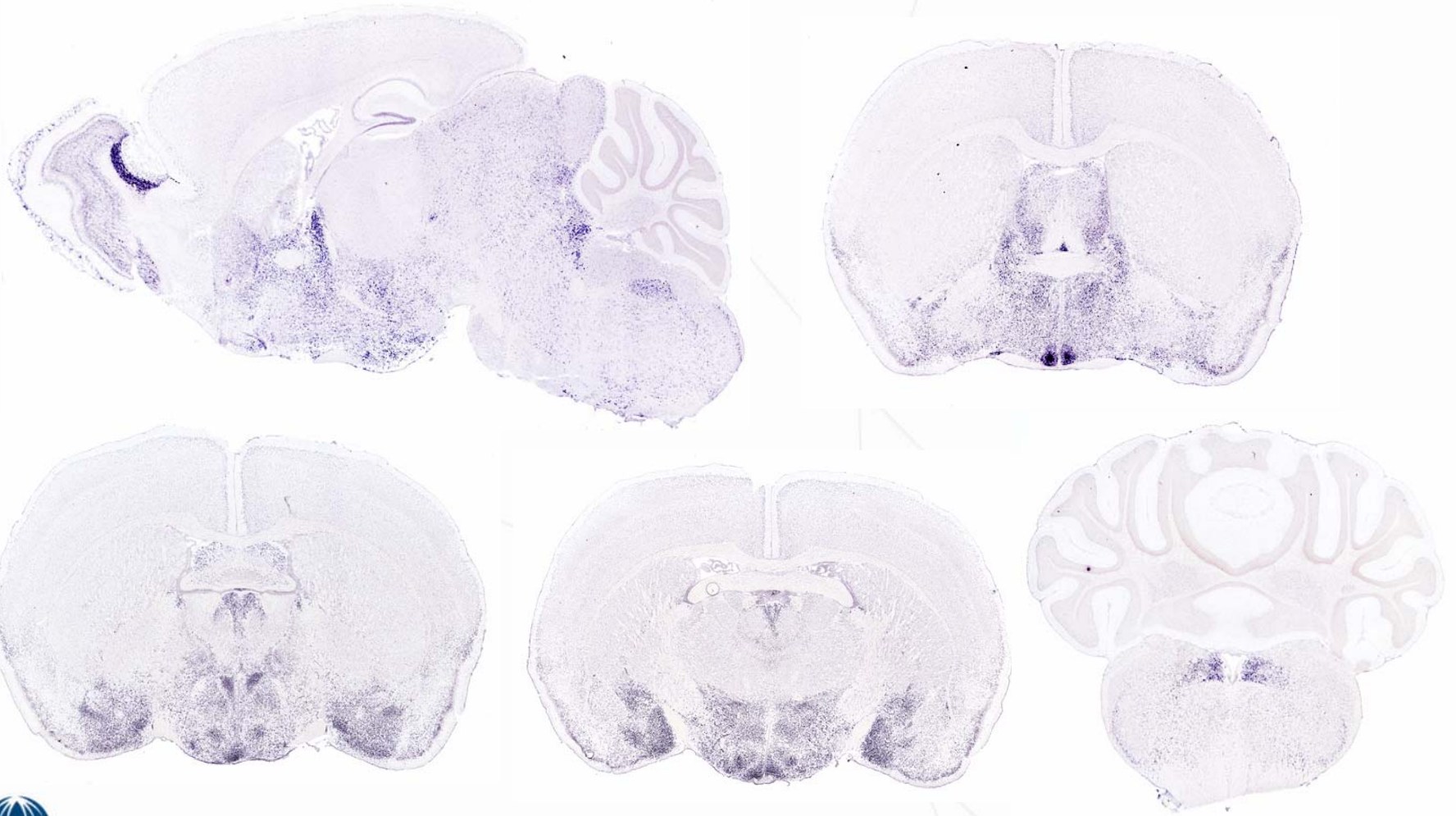


# *In situ* Hybridization



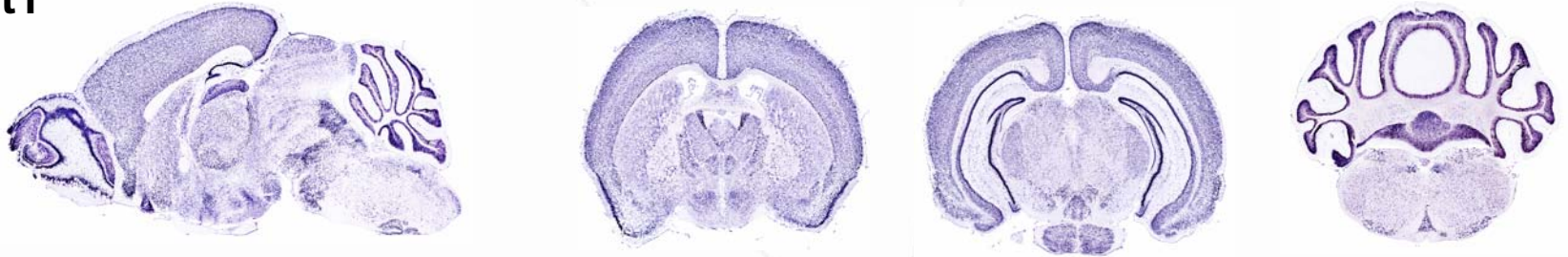


# Huntingtin-associated protein HAP1

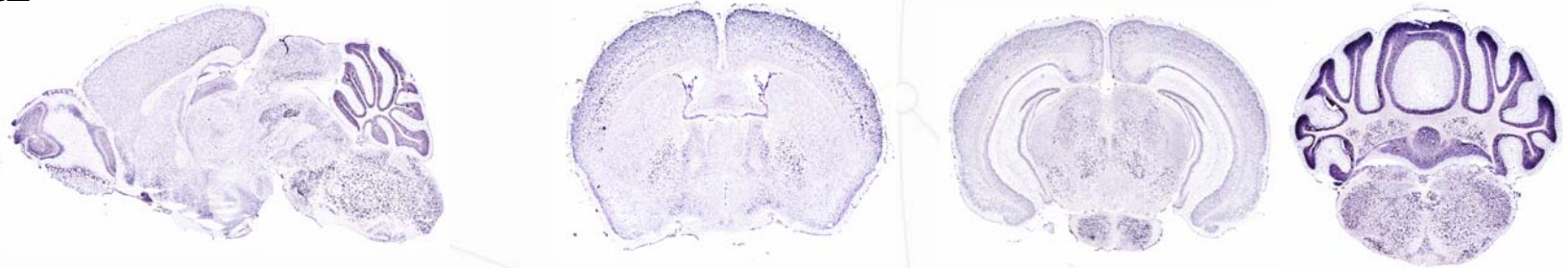


# Differential expression of Synaptotagmins

**Syt1**



**Syt2**



**Syt10**



# ABA User Application



ALLEN  
BRAIN ATLAS | a project of the Allen Institute for Brain Science

HOME APPLICATION SETTINGS HELP LOG OUT

## GENE LIST

<< Hide Pane

- ▶ fibroblast growth factor receptor 1 (posted 01/14/2004)
- ▶ glutamate receptor, ionotropic, NMDA1 (zeta 1) (posted 01/13/2004)
- ▶ L1 cell adhesion molecule (posted 01/13/2004)
- ▶ calmodulin 1 (posted 01/13/2004)
- ▶ ectodermal-neural cortex 1 (posted 01/13/2004)
- ▶ proprotein convertase subtilisin/kexin type 1 inhibitor (posted 01/13/2004)
- ▶ erythroid differentiation regulator 1 (posted 01/13/2004)
- ▶ chloride intracellular channel 6 (posted 01/12/2004)
- ▶ cannabinoid receptor 1 (brain) (posted 01/12/2004)

## NEWS

- ▶ Mouse model could ID mental illness gene  
Melissa Trudinger :: BIO-IT World  
July 2003
- ▶ Genome Architecture: Where Genomics  
and Nanotechnology Meet  
Nancy Touchette :: Genome News  
Network  
July 2003

## GENE SEARCH

To view sample queries, [click here](#).

Search Database: Images for c

GO

RESET

## GENE SEARCH RESULTS: 6 Results

Select one or two image sets for viewing

Select Set	Gene Name	Symbol	Plane	Orientation	Accession #	Organism	Strain	Age	Gender	Date
<input type="checkbox"/>	histone 1, H2bc	Hist1h2bc	coronal	Antisense	NM_023422	Mus musculus	C57BL/6J	56	male	2003-08-26 00:00:00.0
<input checked="" type="checkbox"/>	histone 1, H2bc	Hist1h2bc	sagittal	Antisense	NM_023422	Mus musculus	C57BL/6J	56	male	2003-08-26 00:00:00.0
<input type="checkbox"/>	histone 1, H2bc	Hist1h2bc	sagittal	Sense	NM_023422	Mus musculus	C57BL/6J	56	male	2003-08-26 00:00:00.0
<input type="checkbox"/>	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C	Sema3c	coronal	Antisense	NM_013657	Mus musculus	C57BL/6J	56	male	2003-11-10 00:00:00.0
<input type="checkbox"/>	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C	Sema3c	sagittal	Antisense	NM_013657	Mus musculus	C57BL/6J	56	male	2003-11-10 00:00:00.0
<input type="checkbox"/>	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C	Sema3c	sagittal	Sense	NM_013657	Mus musculus	C57BL/6J	56	male	2003-11-10 00:00:00.0

CLEAR SELECTION

VIEW SELECTED

# ABA User Application



ALLEN  
BRAIN ATLAS

a project of the Allen Institute for Brain Science

HOME

APPLICATION SETTINGS

HELP

LOG OUT

## VIEW IMAGE SETS

Hist1h2bc-BrainSagittal-H1889 Accession #: NM\_023422

HIDE METADATA

Gene Symbol: Hist1h2bc  
NCBI Nucleotide: [NM\\_023422](#)  
NCBI Locus ID:  
UCSC: [Mouse Genome](#)  
Ensembl: [Mouse ContigView](#)  
Gene Name: histone 1, H2bc

Organism: Mus musculus  
Strain: C57BL/6J  
Age: 56  
Gender: male  
Date of Dissection: 2003-08-26 00:00:00.0  
RNA Probe: 0  
Sectioning Plane: sagittal

Add all Thumbnails to Image Viewer - 40 images

GO TO IMAGE VIEWER



Hist1h2bc-H1889-001a  
Position: 75.0000

Add to Image Viewer



Hist1h2bc-H1889-001a  
Position: 75.0000

Add to Image Viewer



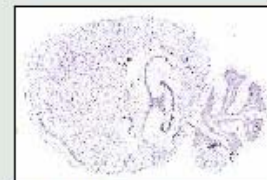
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Add to Image Viewer



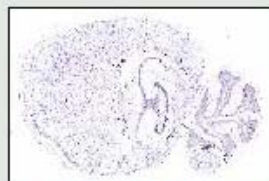
Hist1h2bc-H1889-001b  
Position: 275.0000

Add to Image Viewer



Hist1h2bc-H1889-001c  
Position: 475.0000

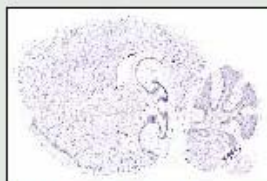
Add to Image Viewer



Hist1h2bc-H1889-001c  
Position: 475.0000



Hist1h2bc-H1889-001d  
Position: 675.0000



Hist1h2bc-H1889-001d  
Position: 675.0000



Hist1h2bc-H1889-002a  
Position: 875.0000



Hist1h2bc-H1889-002a  
Position: 875.0000

# www.brainatlas.org



**ALLEN  
BRAIN ATLAS**

a project of the Allen Institute for Brain Science

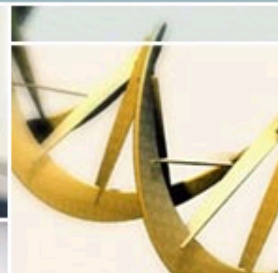
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## ALLEN BRAIN ATLAS PROJECT

Paul G. Allen had a vision that recent advances in computer science, bioinformatics, image analysis and the sequencing of the human genome could be brought together to answer one of the most complex questions in human biology—what is the brain and how does it work? He brought this vision to a renowned group of neuroscientists and advisors, and the Allen Institute for Brain Science was born.

Paul G. Allen has committed an initial \$100 million in seed money for the Institute. Its inaugural project is a massive and ambitious undertaking: creating a 21st century map of the brain. The Allen Brain Atlas will be publicly accessible and will have immediate utility and far-reaching implications for brain science.

Employment opportunities at the Allen Institute for Brain Science and Allen Brain Atlas are listed on the Vulcan Inc. Web site at [jobs.vulcan.com](http://jobs.vulcan.com).

## OUR MISSION

The Allen Brain Atlas project, named for its founder Paul G. Allen, will combine the disciplines of neuroanatomy and genomics to create the most comprehensive map of the brain at the cellular level, illustrating the functional anatomy of the brain through a collection of gene expression maps, brain circuits and cell locations. The Allen Brain Atlas will be the cornerstone of 21st century brain science. Researchers around the world will leverage information from the Brain Atlas to gain insights into some of the most profound and challenging questions facing science in this century.

## NEWS

09-17-03: *Seattle Times*  
**Curiosity feeds Allen's goal to speed up brain...**

09-17-03: *Seattle P-I*  
**Allen's brain project praised**

09-16-03: **Paul G. Allen Commits \$100 Million To Brain Research**

09-16-03: *Bio IT World*  
**Paul Allen Invests US\$100M in Brain...**

09-16-03: *New York Times*  
**Public Atlas of the Brain in the Works**



# Allen Institute for Brain Science

- Atlas-related research
  - Neuroinformatics/computational biology
  - Comparative genomics and data-mining
  - Collaborations around use of platform
  - Murine transgenesis/KOs and behavioral phenotyping
- Future research areas
  - “Proteoarchitecture” and connectivity mapping
  - Live animal imaging
  - Closing the “gene gap”

# Closing the Gene Gap

- *C. elegans*
  - 19,000 genes
  - 302 neurons
  - ~7000 synapses
- *Homo sapiens*
  - 24,000 genes
  - 100 billion neurons
  - $\sim 10^{15}$  synapses

