THE MULTIDIMENSIONAL MIND

PART 1: Creative Brains: Music, Art and Emotion

Bruce L. Miller, MD

BIOGRAPHY:

Dr. Miller is Professor of Neurology at the University of California, San Francisco (UCSF) where he holds the A.W. & Mary Margaret Clausen Distinguished Chair. Dr. Miller directs the busy UCSF dementia center where patients in the San Francisco Bay Area receive comprehensive clinical evaluations. His goal is the delivery of model care to all of the patients who enter the clinical and research programs at the UCSF Memory and Aging Center. Dr. Miller teaches extensively and runs the Behavioral Neurology Fellowship at UCSF.

Dr. Miller is a behavioral neurologist focused in dementia with special interests in brain and behavior relationships as well as the genetic and molecular underpinnings of disease. His work in frontotemporal dementia (FTD) emphasizes both the behavioral and emotional deficits that characterize these patients, while simultaneously noting the visual creativity that can emerge in the setting of FTD. He is the principal investigator of the NIH-sponsored Alzheimer’s Disease Research Center (ADRC) and an NIH-funded program project on FTD called Frontotemporal Dementia: Genes, Imaging and Emotions. He oversees a healthy aging program supported through the Larry H. Hillblom Foundation and the Hellman Center, which includes an artist in residence program. In addition, he helps lead two philanthropy-funded research consortia, the Tau Consortium and Consortium for Frontotemporal Research, focused around developing treatments for tau and progranulin disorders respectively.

Dr. Miller has received many awards including the Potamkin Award from the American Academy of Neurology, the Raymond Adams Lecture at the American Neurological Association, the Elliot Royer Award from the San Francisco Neurological community, the UCSF Annual Faculty Research Lectureship in Clinical Science, the UCSF Academic Senate Distinction in Mentoring Award, and the Gene D. Cohen Research Award in Creativity and Aging from the National Center for Creative Aging. He has authored The Human Frontal Lobes, The Behavioral Neurology of Dementia and extensive publications regarding dementia. He has been featured in Fortune Magazine, Charlie Rose Show, The PBS NewsHour, The New York Times, and other media. For nearly three decades, Dr. Miller has been the scientific director for the philanthropic organization The John Douglas French Alzheimer’s Foundation, a private philanthropic organization that funds basic science research in Alzheimer’s disease.

BIBLIOGRAPHY:


PART 2: Mouse Models, Jellyfish and Stem Cells: Mechanisms for Disease

Keith Vossel, MD, MSc

BIOGRAPHY:
Keith Vossel, MD, MSc is a Staff Scientist in the Gladstone Institute of Neurological Disease and Assistant Professor of Neurology in the UCSF Memory and Aging Center. Dr. Vossel received a BS in engineering science and mechanics and MSc in biomedical engineering at the University of Tennessee. He received an MD at the University of Tennessee and subsequently completed residency training in neurology at Massachusetts General Hospital and Brigham and Women’s Hospital, where he served his final year as a chief resident. In addition to caring for patients, Dr. Vossel investigates mechanisms and novel treatment approaches for neural network dysfunction in Alzheimer’s disease. His laboratory investigation focuses on the microtubule-associated protein tau and regulation of axonal transport and his clinical study investigates seizures and epileptiform activity in Alzheimer’s disease and related dementias.

BIBLIOGRAPHY:


FINANCIAL STRENGTH

Grants from the National Institutes of Health (NIH) and other federal agencies are Gladstone’s major source of support. Foundations and private donors contribute other significant funding—which is critical towards advancing our mission to overcome some of the world’s most devastating diseases.

2011 SOURCES OF FUNDING

<table>
<thead>
<tr>
<th>Source</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>External Grants (including NIH)</td>
<td>$60 Million</td>
</tr>
<tr>
<td>Philanthropy</td>
<td>6 Million</td>
</tr>
<tr>
<td>Other revenues</td>
<td>6 Million</td>
</tr>
<tr>
<td><strong>Total Revenue</strong></td>
<td><strong>$72 Million</strong></td>
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EMPLOYEES

At the beginning of 2012, we had approximately 400 employees.

UCSF AFFILIATION

Gladstone has a vibrant partnership with the University of California, San Francisco (UCSF), one of the nation’s premier medical schools. All of Gladstone’s principal investigators are seamlessly integrated faculty members at UCSF, where they regularly teach and mentor UCSF graduate students.

GLADSTONE HISTORY

Established in 1971 from the estate of J. David Gladstone, the Gladstone Trust is a 501(c)(3) tax-exempt charity. Valued at about $8 million at the time of Mr. Gladstone’s death, this original bequest has since multiplied more than 20-times its original value—while also supporting more than three decades of biomedical research and training.

Mr. Gladstone was a real estate developer who made his fortune as the first developer to create enclosed shopping malls (such as the Northridge Fashion Center mall) in Southern California. His accidental death in 1971 left an estate dedicated to supporting medical students interested in research.

The Gladstone Trust was used to launch The J. David Gladstone Institutes in 1979, under the leadership of Robert W. Mahley, MD, PhD. Through an affiliation agreement with UCSF, Gladstone was founded as a research and training facility at San Francisco General Hospital. Initially focused on cardiovascular research, Gladstone added expertise in virology and immunology in 1991 and in neurological disease in 1998.

In 2004, the Gladstone Institutes moved to a new and dedicated facility in San Francisco’s Mission Bay, ushering in a renewed sense of collaboration among Gladstone’s growing scientific staff. In 2010, after three decades of leading Gladstone, Dr. Mahley stepped down in order to return to more active research.

That same year, R. Sanders “Sandy” Williams, MD, left Duke University, where he had been Dean of the School of Medicine—as well as Senior Vice Chancellor and Senior Advisor for International Strategy—to become Gladstone’s new president. The following year, the independent and philanthropic Gladstone Foundation formed with the mission of expanding the financial resources available to drive Gladstone’s mission.

ABOUT US

Gladstone is a nimble and independent nonprofit biomedical-research organization dedicated to rigorous, cutting-edge science—our mission is to unravel the basics of biology in order to better understand, prevent, treat and cure cardiovascular, viral and neurological conditions such as heart failure, HIV/AIDS and Alzheimer’s disease.

OUR SCIENCE

Gladstone combines the best of basic science with expertise in cardiovascular, viral and neurological diseases. Our scientists are at the forefront of stem cell biology research, using induced pluripotent stem cell (see graphic) and other cellular reprogramming technologies in their research. We have a robust translational research effort to transform our basic discoveries into solutions for patients. Another key component of our work at Gladstone is training tomorrow’s physicians and researchers. We are passionate about science and determined in our goal of preventing, treating and curing some of the world’s most relentless illnesses.

LEADERSHIP

Gladstone’s president, three research directors and three trustees strategically guide the organization to foster and enrich innovation, talent, entrepreneurship and financial strength.

R. Sanders Williams, MD  
President, Gladstone Institutes

Deepak Srivastava, MD  
Director, Cardiovascular Research

Warner C. Greene, MD, PhD  
Director, Immunology and Virology Research

Lennart Mucke, MD  
Director, Neurological Research

TRUSTEES

Richard D. Jones, JD
Albert A. Dorman
Andrew S. Garb, JD

GLADSTONE INSTITUTES | BACKGROUNDER

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Part II: Mouse Models, Jellyfish and Stem Cells: Mechanisms for Disease

Overview

Part II: Mouse Models, Jellyfish and Stem Cells: Mechanisms for Disease

- Mouse models of Alzheimer’s disease
- Jellyfish proteins illuminate inner workings of cells
- Transforming skin cells into stem cells

Alzheimer's Disease

- 5.4 million Americans have Alzheimer’s
- 6th leading cause of death in US
- Impending public health crisis

www.alz.org
Alzheimer's Disease

Normal Brain  Alzheimer's Patient Brain

Alzheimer's Disease: Multiple Factors

Why study mice?

- Short life span (30 months)
- Entire genome mapped
- Transgenic models isolate effects of single genes
- Relevant functional measures
- Biomarkers validated in humans

Transgenic Mouse Models of AD

Morris Water Maze: hAPP Mice Show Learning and Memory Deficits

Nontransgenic (Normal)  hAPP (Alzheimer's)

What hAPP Mice Have Taught Us

Cognitive/Behavioral Deficits

Seizures

Cell and Molecular Changes

Biomarkers

Therapies

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2008 Nobel laureates from Miyawaki: Cell 2008; Mouse cortex image courtesy of Robert Cudmore
Mitochondrial Transport in Living Brain

Overview

Part II: Mouse Models, Jellyfish and Stem Cells: Mechanisms for Disease
- Animal models of Alzheimer’s disease
- Jellyfish proteins illuminate inner workings of cells
- Human-derived stem cells

What are stem cells?
- Definition: any cell with the capacity to differentiate into a more mature cell type
- Therapeutic applications
  - Neurodegenerative disease
  - Epilepsy
  - Stroke
  - Spinal cord injury
  - etc
Induced Pluripotent Stem Cells (iPS Cells)

Shinya Yamanaka
2012 Nobel Prize

iPS-derived Neurons
with FTD Mutation

Corrected Mutation
Increased FTD Mutations

Yadong Huang, MD, PhD, Gladstone/UCSF

Physician Scientists

Research Scientists

Clinical Trials
Personalized Medicine
Regenerative Applications of Stem Cells
Gladstone
Leonard Mucke
Pascal Sanchez
Jorge Palop
Laure Verret
Jean Brodieck
Steve Finkbeiner
Aaron Daub
Punita Sharma
Eva LaDow
Aisha Holloway
Yading Huang
Dimitrios Davalos
Katerina Alexasoglou
Jordan Xu
Tim Sweeney
UCSF
Bruce Miller
Heidi Kirsch
Paul Garcia
Srikant Nagarajan
Susanne Honma
Anne F. Dowling
John Housle
Manu Hegde
Mary Mandie
Gil Rabini
William Jagust
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http://memory.ucsf.edu