The Aging Brain Initiative

White Paper

THE AGING BRAIN INITIATIVE AT MIT

Executive Summary

Recovery from dementia or Alzheimer's disease (AD) is not yet possible and current approaches have not yielded any effective therapies to halt the development or the progression of the disease. This isn't someone else's problem. One in three who read this will die from Alzheimer's or age-related dementia. This means that each and every one of us will be personally affected - if not as a victim, then as a caregiver.

Faculty from the Massachusetts Institute of Technology (MIT) are concerned with the lack of progress, lack of funding, and lack of basic investment into innovative solutions. By pursuing radically different approaches we have discovered compelling data to suggest we can: 1) slow or halt the disease and 2) may be able to re-activate memories and boost cognitive capacity. Some of the procedures do not require antibodies or inhibitors and have about 80-90% effectiveness in animals.

To pursue these very different discoveries into the clinic and build an aggressive, innovative pipeline of solutions, we are mounting an Aging Brain Initiative -- a group endeavor to: (1) pursue a new whole-systems approach, (2) commit a broad and institute-wide skill set, (3) achieve, in parallel, an ambitious portfolio of projects and, (4) apply our leading model of biotech commercialization (Kendall Square) and technology transfer prowess to develop effective treatments and technologies to solve the problem.

WHY NOW

I. STRATEGIC RATIONALE

Why Now?

In 1906 Ramon y Cajal and Santiago Golgi shared the Nobel Prize in Physiology for their work on the structure of the nervous system. The relentless work of Cajal and Golgi led to a detailed map of the brain that stands as the pillar of contemporary neuroscience. The advances in understanding the brain's connectivity, its synchronous patterns of communication, and how the brain and mind converge have been detailed beyond what Cajal and Golgi could have ever imagined.

Neuroscience has entered into a golden age of remarkable progress and as technology allows scientists to map the brain from neurons to cognition, it is expected that brain disorders will be better treated if not cured. Indeed, by the middle of the 20th century a flurry of medications were released that were the first to successfully treat psychopathologies like bi-polar disorder, depression, anxiety, and Schizophrenia[1]. Yet, as humankind celebrated entry into the 21st century and the grand technological leaps that pushed human life in the United States from an average age of 49 years (1906) to 79 years (2016), unexpected consequences of extended life came into focus, namely that of the aging brain.

At the time when the complexity of the nervous system was first being unraveled, a grave discovery was made that has since plagued neuroscientists and individuals with advanced age. One month before Cajal and Golgi were awarded their Nobel Prizes, Dr. Alois Alzheimer gave a lecture in the small university town of Tübingen Germany where he detailed, for the first time, a form of dementia that would earn the eponym, Alzheimer's disease[2]. The uninterested audience listened to Dr. Alzheimer's clinical and pathological findings of his patient that exhibited what seemed to be a unique type of dementia. Although unremarkable at the time the thorough observations presented by Alzheimer would come to define the most common form of dementia worldwide and portend a silent epidemic. In his clinical notes, that would later outline his lecture, Dr. Alzheimer writes about his encountering the first person to be diagnosed with the disease, Mrs. Auguste Deter[3]:

Alzheimer: She sits on the bed with a helpless expression. What is your name?
Deter: Auguste.
Alzheimer: Last name?
Deter: Auguste.
Alzheimer: What is your husband's name?
Deter: Auguste, I think.

Throughout Alzheimer's clinical interview with Mrs. Deter he identifies hallmark characteristics of the disease, namely, memory loss, hallucinations, delusions, paranoia, language deficits, and confusion. Though the clinical symptoms that underlie the disease are grim, perhaps the most frightening consequence of Alzheimer's disease is the slow erasure of one's own identity. From Alzheimer's notes:
"When she has to write Mrs. Auguste D, she writes Mrs. and we must repeat the other words because she forgets them. The patient is not able to progress in writing and repeats, *I have lost myself*."

With dementia, one's identity and humanity is lost, the inside world crumbles, and the outside world disappears as the connection between person and nature falls apart. The brain allows us to navigate the external world, talk to loved ones, and reflect on those special life events whether they be sad, happy or bittersweet. It is precisely these aforementioned cognitive attributes that make humans human and

allow for complex social interactions that are the basis of civilization. The break of connection between internal and external worlds parallels the withering of connections between neurons as the brain slowly degenerates in people with dementia.

It has been nearly 110 years since scientists celebrated the first detailed, albeit incomplete, map of the brain and nervous system. At the very time when connections of trillions of neurons were beginning to be traced into a map, the disease that targets and destroys those very connections (i.e., Alzheimer's disease) was identified. Today, researchers and clinicians are unable to stop the destructive processes in the brains of those with Alzheimer's, there are no cures, no diagnostic tools, and no advances in solving this disease. The staggering increase in the aging populations necessitates immediate development of new therapies before the intractable problem of age related-dementia cripples healthcare systems worldwide.

Public Health and Socio-Economic Impact of Dementia

Aging is the single most important risk factor for Alzheimer's disease and age-related dementia[4]. For the first time in human history the number of people over the age of 65, as a percentage of the global population, will surpass the number of children under the age of 5[5]. The potential burden of advanced age-related dementia on a shrinking younger generation is enormous. Those entering advanced age are showing a sharp decrease in infectious diseases but are exhibiting a startling rise in chronic afflictions such as Alzheimer's disease[6]. While individual longevity is cause for great celebration, governments around the world now need to curtail astronomical expenditures on aging-related social and health care. Instead of age, healthy life expectancy will be the new metric of success for health systems that are now desperate to delay the human and financial cost of disability in their populations.

Because the aging population is growing rapidly the number of people with dementia is estimated to surpass 115 million by 2050[7]. There are now 46 million people with Alzheimer's disease and related dementias and only 1-in-4 people with the disease are diagnosed, suggesting that millions of individuals do not receive proper medical attention[8]. In 2010 the total societal costs associated with dementia was $604 billion[7] and it will reach $2 trillion in the next 15 years[8]. Without an effective treatment for Alzheimer's disease the US Medicare system will be bankrupt within 30 years[9].

No Funding, No Results

Great strides have been made in diagnosing and treating other morbidities of aging like diabetes, cancer, and heart disease. But those strides have not occurred for Alzheimer's disease and the dementias of aging. Alzheimer's expenses are the greatest direct health care cost to the United States economy, **greater than cancer or heart disease**. Yet, funding support for Alzheimer's disease ($566 million) is paltry in comparison to the annual U.S. funding for cancer ($5.4 billion), HIV/AIDs ($3 billion), and heart disease ($1.2 billion).

To successfully create and treat the degenerative processes of dementia it is necessary to understand the genetic, biochemical, cellular, circuit, behavioral, and environmental factors that contribute to cognitive decline. A richer understanding of the healthy, aging, and Alzheimer's diseased brain is necessary, from mapping brain pathways and memory function to linking genetic and cellular interactions throughout the brain. Aging is the single most important risk factor for Alzheimer's disease and age-related dementia[2] yet we know very little about how the brain ages and what aging factors

contribute or protect us from cognitive decline. Although decades of research on Alzheimer's disease and dementia have provided great insight, there has been no translation into human treatments.

Unfortunately, it is largely the lack of funding, the inability to disengage from failed strategies, and the narrowed focus that have stymied treatments and diagnostic tools from being created.

The Amyloid-Beta Hypothesis: A History of Results Without Progress

The hallmark characterization of Alzheimer's disease was detailed during examination of August Deter's brain, which showed severe degeneration[11]. Clusters of proteins between neurons called senile plaques as well as dead or dying neurons that form neurofibrillary tangles were also identified. In the early 1980s it was discovered that senile plaques were made up of an overproduction and accumulation of a protein called amyloid-beta[12], which was due, in part, to a genetic mutation in the amyloid gene[13]. Soon after amyloid-beta was discovered the protein tau was identified and shown to make up the neurofibrillary tangles[14]. By the mid 1990s the amyloid-beta hypothesis was developed[15], which argues that amyloid-beta drives the development of Alzheimer's disease by altering tau to form neurofibrillary tangles. Thus, if it were possible to stop the accumulation of amyloid-beta and tau alterations, then brain degeneration that underlies Alzheimer's disease could be stopped.

After the amyloid-beta hypothesis was developed research institutions and pharmaceutical companies invested heavily into targeting amyloid-beta. Pharmaceutical companies spent billions of dollars and decades of research to find medications that would disrupt Alzheimer's disease progression. However, 30 years of clinical trials have only produced four approved Alzheimer's medications, which show only mild transitory effects and do not slow down brain deterioration. Clinical trials have had a 99.6% failure rate and have been unable to improve Alzheimer's disease using the amyloid-beta hypothesis[16]. In comparison, the failure rate for cancer drug candidates is 81%. Current strategies for medication development have stubbornly stayed the same course since the 1980s, which is to focus on targeting amyloid-beta or the tau protein. Almost all potential Alzheimer's treatments have focused on just a single biological pathway that leads to amyloid-beta accumulation. Other causes remain largely unexplored.

The amyloid-beta hypothesis is being challenged and more researchers think of amyloid-beta as a piece of a large, complex, and multi-dimensional picture that makes up Alzheimer's disease. For example, although amyloid-beta is linked to brain pathology in most of those with Alzheimer's disease, there is a 20- to 30-year interval between enhanced levels of amyloid-beta and dementia[17]. Additionally, having increased levels of amyloid-beta does not necessarily mean someone will develop Alzheimer's disease. Researcher's have made a startling discovery showing that 25% of individuals with a diagnosis of Alzheimer's disease have no or very sparse accumulation of senile plaques (i.e., amyloid-beta) in their brains [18]. Moreover, even medications that reduce amyloid-beta have not been able to curb Alzheimer's disease progression in clinical trials[19]. In fact, clinical trials that have greatly reduced amyloid-beta have accelerated dementia in some cases and increased the risk for skin cancer[19].

Clearly, a new model for drug discovery, treatment, and detection is necessary to interrogate the failing mechanism of the aging brain[18].

WHY MIT

II. MIT'S VISION

An institute-wide call to action - The Aging Brain Initiative at MIT

Faculty at Massachusetts Institute of Technology (MIT) have created the Aging Brain Initiative. The vision is a multi-disciplinary, joint effort, devoted to ambitious research on brain aging and dementia. Our goal is to reduce the impact of cognitive decline, alleviate patient suffering, and prevent the looming and unsustainable global dementia-related medical costs.

The Aging Brain Initiative is a multi-dimensional collaborative effort that integrates research from the fields of neuroscience, genetics, biology, computer science, urban planning, chemistry, engineering, medicine and finance. The expansive collaborative effort of the Aging Brain Initiative allows us to tackle Alzheimer's disease and dementia through a whole-systems approach. Additionally, because MIT is the predominate model for **technology transfer** we can effectively bridge concepts to practical applications in the market place. MIT sits at the epicenter of the **largest concentration of biotechnology companies** and research centers in the world. Given the institutions proven history of innovative solutions to the world's toughest problems the Aging Brain Initiative is confident that it can halt the progression of enhance the cognitive deficits in those with Alzheimer's disease and dementia.

A Whole-Systems Model to Alzheimer's Research

The Aging Brain Initiative purposefully engages in parallel high-risk, high-reward projects, and approaches Alzheimer's disease and dementia research at a whole-systems level. Our whole-systems research program will be actualized by a four-pronged research approach that includes: (1) applying artificial intelligence to identify aging biomarkers; (2) developing brain-circuit specific therapies; (3) personalizing individual care; and (4) identifying healthy markers of brain resilience. Below is a detailed outline of our four-pronged strategy:

Area I. Artificial Intelligence to Identify Aging Biomarkers

Mapping the human genome was accomplished a decade ago and was heralded as laying the foundational map for linking genetic variation to human disease. However, much remains to be understood about how and when genetic information is produced and controlled in and across different body parts and cells types, and how this information can be leveraged to impact the development of medicinal discoveries. Recent breakthroughs in bioinformatics and rapid genome editing and analyzing procedures, make big data approaches to biological sciences possible and data mining essential. In collecting large data sets we will train deep-learning artificial intelligence tools to analyze this tremendous volume of multi-dimensional genetic information to find the targets for aging biomarker and drug development.

Area II. Develop Brain-Circuit Specific Therapeutics

The past five years have witnessed impressive advances in neuro-circuit technologies, many of which were developed by MIT professors -- from optical control of neurons to new clarifying techniques that allow visual access deep inside the brain -- all with incredible potential to accelerate our understanding of disease mechanisms. We can now see, hear, and precisely regulate the neural circuits and brain activity patterns that encode our memories, translate our movements, and predict our decisions. We

can leverage these new technologies and results to retrieve and rebuild lost memories that compromise high-level cognitive function. Our goal is to produce invasive and non-invasive technologies that prove more effective than existing therapies.

Area III. Personalize Approaches to Treatment

Personalized molecular-based medicine or the customization of health care using molecular analysis, is increasingly necessary for effective medical decision making. Improved clinical practice and products tailored to the individual patient will be critical in defining and treating dementia and AD in each patient as every case is unique. Even within Alzheimer's disease, there are expected sub-category pathologies with differences in disease progression that will need individualized study and screening to develop proper treatments. Collaborative projects in this area will build upon our research and clinical partnerships for an application-oriented strategy leading to rapid advances in precision or personalized medicine.

Area IV. Uncover the Demographics of Healthy Aging

By developing strategies to promote healthy aging we will help ensure that age and experience expand life's possibilities rather than lead to decline. Neuroscientists do not yet know why specific categories of older people positively adapt to late-stage life while others do not. Collaborative projects in this area would seek to find mind and body answers through new approaches including brain and cognitive sciences, urban planning, economics, systems engineering, and artificial intelligence.

The whole-systems approach the Aging brain Initiative is only possible through the strength of our diverse array of amazing research teams. The multi-dimensional backbone of our initiative makes us uniquely suited in creating novel treatment options, developing preventative behavioral programs, and engineering diagnostic tools and smart home technologies. We expect to apply the outcomes of our four-pronged approach to clinical and home markets within two to fifteen years. As progress accelerates, collaborative networks will expand to include larger research platforms and new biological aging resources for researchers worldwide. Our ultimate goal is to bring immediate and practical solutions for the treatment and care of people with Alzheimer's disease and dementia.

*BOX 1

EXAMPLE FLAGSHIP PROJECT 1. – Alzheimer's as a Disease of Memory

The Aging Brain Initiative has organized a team of the world's leading memory experts that takes the view that Alzheimer's disease is one of memory and brain systems function. The first brain regions to show degeneration from Alzheimer's disease are critical for memory of everyday events and our internal global positioning systems (i.e., navigation)[21]. Likewise, the first symptoms in those with Alzheimer's disease and dementia are forgetfulness, misplacing things, and wandering or getting lost[22]. In identifying the exact networks and activity patterns affected by Alzheimer's disease breakthrough technologies can be used to improve memory capacity and cognitive ability.

CLARITY and SWITCH - Unbiased 3D brain mapping: Although the general brain regions that are affected by Alzheimer's disease are believed to be known the origins of the disease and the precise pathways within these regions that hold specific memories are beyond reach with traditional and clinical anatomical approaches. MIT Chemical Engineering Professor and Aging Brain Initiative member Kwanghun Chung created the breakthrough technology called CLARITY, which makes brains see-through

– even human brains that were preserved decades ago. With a clear brain and his new SWITCH labeling techniques, an exceptionally detailed map of neuronal circuits and their connections, together with their interactions with other cells in the brain, can be seen. With CLARITY, MIT Neuroscientist and Lead Aging Brain Investigator Li-Huei Tsai is working with Chung to identify the molecular pathology of Alzheimer's disease with anatomical precision that were impossible just a few years ago. In finding the disrupted memory networks and pathology origins in Alzheimer's disease it is feasible to identify specific memories that are attributed to those networks and how those memories are disrupted in Alzheimer's disease. It is also possible to see when, where and how pathological plaques, blood vessels, and immune cells among other things interact with neuron circuits in a single whole brain all at once.

Optogenetic Reactivation of Lost Memories: As Alzheimer's disease progresses, memories fade away as the connections that make up those memories break apart. However, if the connections that hold memories together can be maintained or strengthened it may be possible to prevent memory loss or perhaps bring back lost memories. Founding Aging Brain Initiative member and Bioengineer, Ed Boyden, is the co-developer of a revolutionary technology that allows for specific networks of neurons to be activated by a laser-light. Professor Boyden's technology is called optogenetics, which uses light-sensitive proteins that can be genetically added to neurons. Neurons that contain the light-sensitive protein can be turned off or on by flickering light. This molecular tool enables ultraprecise control of neuronal networks to such a degree that single memories and even complex behaviors can be activated or inactivated. Founding Aging Brain Initiative members, Li-Huei Tsai and Nobel laureate Susumu Tonegawa, are using optogenetics in mouse models of Alzheimer's disease to see if disease pathology can be stopped and lost memories can be restored by strengthening memory networks with optogenetics.

Diagnosis and Treatment Through Brain Waves: Anesthesia alters the brain differently as people age. Because anesthesia primarily affects the brain scalp, electrodes that record brain waves can be used to create a brain age calculator. Founding member, practicing clinician, and computational neuroscientist, Emery Brown, developed the brain wave age calculator and characterized the differences in brain waves in patients between the ages of 18 and 90 years of age. The brain wave calculator has the potential to find differences in patients with and without Alzheimer's disease and serve as a diagnostic tool before individuals become symptomatic. Brain waves can also be altered by non-invasive methods in humans. Aging Brain Initiative Lead Investigator, Li-Huei Tsai, is working with Brown and Boyden to alter brain waves to enhance the synchronizing of neuronal circuits and her results are startling. By making brain waves align in synchrony the pathology of Alzheimer's disease is halted and the symptoms are reduced.

Investing in The Aging Brain Initiative

Investment into brain-aging research offers the most efficient and cost-effective approach to fight age-related diseases. Recent work by MIT Professor of Finance, Andrew Lo, supports a strong and directed investment approach to stave off economic pitfalls of Alzheimer's disease and dementia. For example, a new therapy resulting from basic research that could delay the onset of Alzheimer's disease by just five years would save the US Medicare and Medicaid system $200 billion over the next decade and $1.5 trillion over the next 30 years[23]. The future cost savings of effective Alzheimer's disease therapy to Medicare and Medicaid far exceed investment. Historically, funding basic research results in a wealth of innovation advantages that allows for prevention and treatment of intractable epidemics. Investments into the Aging Brain Initiative is investing into detecting Alzheimer's decades in advance, into creating technologies that offer advanced home-care that supports family and caregivers, and in establishing

health solutions that slow or halt disease progression and improve function and quality of life for people of advanced age.

The Aging Brain Initiative's whole-systems approach disrupts the single nexus therapeutic model (i.e., amyloid-beta) of Alzheimer's disease research. The Aging Brain Initiative is specifically for high-risk and high-reward projects. However, it is our goal to provide risk-adjusted return on investment by implementing multiple collaborative projects simultaneously. In spreading research over several collaborative but independent laboratories overall risk to The Aging Brain Initiative is minimized and probability for success is maximized. Moreover, by incorporating a whole-systems approach we aim to systematize a new model of research into practice versus focusing on single entry points for treating Alzheimer's disease and dementia. The Aging Brain Initiative is designed to achieve specific scientific milestones in Alzheimer's research critical for developmental transition into biotechnology for deliverable products.

MIT is unlike any technology hub on Earth. Over 120 biomedical firms including new research centers built by Pfizer, Novartis, and Takeda pharmaceuticals surround the institute. Microsoft, Google, and Amazon have moved into MIT's Kendall Square. IBM has also relocated to Kendall Square, bringing the power of the Watson computer system to work on health data research. The worlds top companies are desperate for top talent and that talent comes from MIT. MIT is ranked first in undergraduate and graduate sciences and engineering in the U.S., the world's leading model of biotechnology commercialization, and with 85 affiliated Nobel Laureates it stands as a powerhouse in creating and attracting the world's best and brightest. Kendall Square is entering a biotech and information technology renaissance. MIT has provided $2 Billion in investments for new companies and is expanding the Kendall Square corridor by creating nearly 1-million square feet of office and research space to attract biotechnology and information technology companies to foster academic-industry innovation. Massachusetts also ranks as the top innovative state in the US, which is due to MIT and the surrounding technology companies[24]. In the Silicon Valley, information technology development happened in a garage. In Kendall Square, an industrious complex is woven into the academic powerhouse of MIT to create breakthrough technologies. There is no better place to invest into creating the first successful diagnostic tools and therapies to treat Alzheimer's disease and dementia. From leading the Human Genome project, to creating RADAR, optogenetics, GPS, e-mail, encryption, Dropbox, Hewlett-Packard, Bose, canned food safety, the transistor, to the Apollo Moon Landing MIT has a proven record of transforming the impossible into the American fabric of ingenuity and identity.
100 years ago the Massachusetts Institute of technology moved from Boston across the Charles River to settle on a plot of landfill in Cambridge, Massachusetts. Since moving the institute was challenged with nearly insurmountable odds of surviving. Yet, today MIT stands as the pinnacle of US engineering and technology development. MIT's hallmark neo-classical domes sits atop a purposefully networked architecture engineered to enhance interaction, collaboration, and chance interactions. While other institutions were compartmentalizing MIT was integrating. MIT's culture is grounded in translating concepts to practical application and with over 30,000 companies started by MIT alumni that have generated over $2 trillion, the Aging Brain Initiative is uniquely situated to bring Alzheimer's disease therapies to the market place.

OUR TEAM

IV. OUR TEAM

Founding Members

Li-Huei Tsai, PhD
Director, The Picower Institute for Learning and Memory; Lead Investigator, MIT's Aging Brain Initiative; Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, MIT; Associate Director of the Glenn Labs for Aging Research at MIT; Associate Member, Broad Institute

Professor Tsai combines molecular, genetic and circuit approaches to understanding the pathophysiology of neurological disorders affecting cognition as we age. Her discoveries in Alzheimer's-like disease research, including therapeutic reversal strategies for cognitive defects have been highlighted in Nature, Cell, and Neuron. The author of over 190 peer-reviewed articles, she is an Associate Member of the Broad Institute, a member of the Institute of Medicine of the National Academy of Sciences and an Academician of the Academia Sinica in Taiwan, and a recipient of the NIH Cantoni Lecture Award and the Glenn Award For Research in Aging.

Edward Boyden, PhD
Associate Professor of Biological Engineering and Brain and Cognitive Sciences, MIT Media Lab and the McGovern Institute for Brain Research.

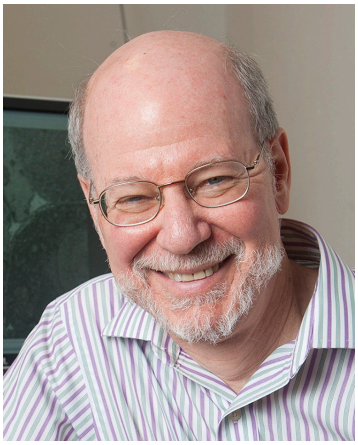
Professor Boyden engineers tools for mapping, controlling, observing and building dynamic circuits of the brain. He has developed *optogenetic* tools to activate and silence neurons with light. In 2010 his approach was recognized as the "Method of the Year" by Nature Methods and is now in worldwide use. He received the 2013 Grete Lundbeck European Brain Research Prize, the world's largest neuroscience prize, and was named among the "Top 35 Innovators Under the Age of 35" by Technology Review and the "Top 20 Brains Under Age 40" by Discover magazine. Professor Boyden is also the 2016 recipient of the Breakthrough Prize in Life Sciences

Emery N. Brown, MD, PhD
Professor, The Picower Institute for Learning and memory, Edward Hood Taplin Professor of Medical Engineering, Institute for Medical Engineering and, MIT and Massachusetts General Hospital.

An anesthesiologist-statistician, Professor Brown has developed signal processing algorithms that characterize how the brain represents and transmits information. He has made important contributions to understanding how anesthetics act in the brain and how their impact changes with age. He is a member of the NIH BRAIN Initiative Working Group, the National Academy of Sciences, the Institute of Medicine, and governing councils of the NIH, NSF and the American Academy of Arts and Sciences. He has been featured on NPR and in Scientific American, Technology Review and the New York Times.

Leonard Guarente, PhD
Novartis Professor of Biology, MIT

Professor Guarente is an expert in the longevity of species from yeast to mammals and has identified potent anti-aging regimens. He found sirtuin proteins central to diet and stress adaptation and to combating diseases of aging like cancer and neurodegenerative disease. He is the author of Ageless Quest and editor of Molecular Biology Of Aging. He serves on the editorial boards of Cell, Genes and Development, and EMBO Reports and is a member of the French Academie des Sciences and the American Academy of Arts and Sciences. He is Director of the Glenn Labs for the Science of Aging and an affiliate of the Koch Institute for Integrative Cancer Research.



H. Robert Horvitz, PhD
David H. Koch Professor; Member, McGovern Institute for Brain Research; Member, David H. Koch Institute for Integrative Cancer Research; Investigator, Howard Hughes Medical Institute

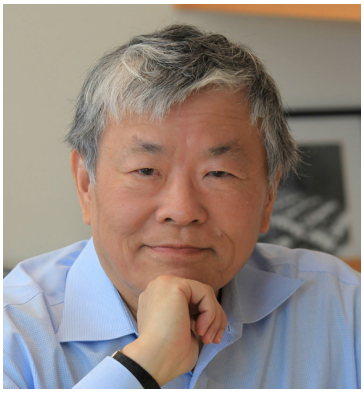
Professor Horvitz uses the genetics of the nematode worm (C. Elegans) to understand neurodevelopment, behavior and neurodegenerative disease. He received the 2002 Nobel Prize in Physiology or Medicine for his discoveries concerning the genetic regulation of organ development and programmed cell death. He is a member of the National Academy of Sciences, the Institute of Medicine and the American Academy of Sciences, an Investigator at the Howard Hughes Medical Institute and a member of the McGovern Institute for Brain Research.

Manolis Kellis, PhD
Professor of Computer Science, MIT, Computational Biology Group, Computer Science and AI Lab, Broad Institute of MIT and Harvard

Manolis Kellis is a Professor of Computer Science at MIT, a member of the Computer Science and Artificial Intelligence Lab at MIT where he directs the MIT Computational Biology Group (compbio.mit.edu), and an Institute Member of the Broad Institute of MIT and Harvard. He has helped direct several large-scale genomics projects, including the NIH Roadmap Epigenomics project, the comparative analysis of 29 mammals, the Encyclopedia of DNA Elements (ENCODE) project, and the Genotype Tissue-Expression (GTEx) project. He received the US Presidential Early Career Award in Science and Engineering (PECASE), the NSF CAREER award, the Alfred P. Sloan Fellowship. He obtained his Ph.D. from MIT, where he received the Sprowls award for the best doctorate thesis in computer science. He lived in Greece and France before moving to the US.

Susan Lindquist, PhD
Professor, Department of Biology, MIT and The Whitehead Institute, Associate Member Broad Institute, and David H. Koch Institute for Integrative Cancer Research at MIT.

Professor Lindquist has pioneered studies of protein homeostasis and protein folding, particularly as it pertains to heat-shock proteins and prions. She has discovered processes in the rapid evolution of new traits, cancer, neurodegenerative disease and microbial drug resistance. She is a co-founder of biotech companies FoldRx (producer of Tafamidis) and Yumanity (therapeutic discovery platforms for human pathologies in yeast). She was awarded the President's National Medal of Science in 2010 and has been highlighted in Forbes, the Financial Times, and National Geographic. She is an Investigator at the Howard Hughes Medical Institute.



Susumu Tonegawa, Ph. D.
Nobel Laureate
Picower Professor of Biology and Neuroscience, Director, RIKEN-MIT Center for Neural Circuit Genetics, Director, RIKEN Brain Science Institute

Professor Tonegawa is the sole recipient of the 1987 Nobel Prize in Physiology or Medicine, for his seminal discovery on the genetic origin of antibody diversity. Since the late 1980s, Professor Tonegawa has made a series of equally seminal discoveries in the field of neuroscience of learning and memory, in health and in disease. His recent studies conducted by combining molecular genetic and optogenetic technology have revolutionized memory research, and were recognized in 2014 as one of The Top 10 Discoveries by the journal Science. Professor Tonegawa's genetic and optogenetic approaches are currently being used to treat enhance cognitive abilities in mouse models of Alzheimer's disease.

Current Collaborators

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