A MESSAGE FROM OUR CHIEF

It feels like eons since we’d last produced another issue of our Center’s KEEP IN MIND newsletter, and we’ll like to thank everyone for their patience as we pull together the pieces of a lengthier newsletter this time around.

This issue is of great pride to us, as it showcases some of the talented students and scientists from all over the world who travel to the MGH in order to train in our labs and learn more about outstanding patient care. The accompanying image beside this message is taken from the front page of the October 3, 1996 issue of the Harvard Gazette and it is certainly an ‘ancient’ image of our Center’s Associate Director (Dr. Teresa Gomez-Isla) and I discerning brain-cell images in our lab during that era. Teresa was one of our first international trainees/fellows who had travelled to our shores from Spain to engage in Alzheimer’s disease research for a few years before returning to Spain. It is indeed gratifying to see her come full-circle since that time, returning to MGH after becoming a leading clinician scientist in Europe, to take on the challenge of serving as the Associate Director of our Center! We have had the honor to recruit and train a wonderful set of Harvard students and junior colleagues each year, and often also get to host students from throughout our country and indeed, from Asia, Europe, Australasia, South America and the Middle East each year. As you peruse this issue, you will be thrilled to learn more about the awards & achievements of some of these teammates who join us in our fight against devastating brain diseases.

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To mirror and reinforce our efforts in training the next generation of first-rate clinician-scientists, we held our inaugural “John H. Growdon, MD symposium” at the MGH on November 25, 2019. The symposium is named in honor of Dr. John Growdon – the founder of our Center and of the MGH’s Memory Disorders Unit (MDU) clinic and the MGH’s Movement Disorders Unit clinic. Dr. Growdon had welcomed and trained so many of our mentees since the beginning of memory and dementia care at the MGH, and we all owe our heartfelt appreciation to all the speakers, panelists and Keynote Speakers --- all trained by Dr. Growdon – who'd contribute to our growing collection of specimens in our Center’s “biobank” in order to partner with us in this innovative research!

I know that many of us are concerned about developing dementia in early midlife, right when we are still providing for our families and actively engaged in our workplaces and our beloved communities. I would urge everyone to check out page 28 for a study (the ‘HATCH’ study – yes, an acronym again!) led by Dr. Jill Goldstein to identify the risks of developing Alzheimer’s disease in early midlife. A close MGH colleague of ours, Dr. Goldstein has led the federally-funded Clinical Neuroscience Laboratory of Sex Differences in the Brain (www.cnl-sd.mgh.harvard.edu) for decades and she is an expert on sex differences in health and diseases associated with the central nervous system such as depression and its connection to heart disease.

In past issues, we had sometimes showcased the talents of research participants and patients (when they permit us!) and in that tradition, we are honored to feature the works and life of novelist Shiao-Shen Yu in the centerfold of the newsletter. I am sure that you will enjoy learning more about her books!

On the home front, I am certain that many of you have already met our wonderful Ambassador of Clinical Research – Judy Johanson. We had last featured a piece written by her in the Spring/Summer 2016 of our newsletter and four years later, we again welcome her perspectives on her life-paths on page 36!

In closing, I want to thank each of you for being part of the family – it is your dedication and effort that makes it possible to do everything humanly possible to help each other fight these diseases, and we take great strength and comfort in coming together. All my colleagues join me in saying “thank you”!

~ Brad
Alois Alzheimer (1864 –1915): “It was here in the years 1886/87 that he presented the disease named after him to the public for the first time in 1906 at the local psychiatric university clinic.”
CONGRATULATIONS to Nancy Coppelman of our Outreach, Recruitment & Education (ORE) Core --- on her receiving the 2020 Partners in Excellence Award (category: Fostering Community).

“I see this award as a recognition of all my colleagues at MADRC, MGH, CNY & BWH - all of us who work in outreach and recruitment. I think the award acknowledges the importance of connecting with local communities, particularly those that have traditionally been underserved. We have worked very hard to build a welcoming path for research participants from all walks of life, along with their care partners. Much of our outreach involves education: increasing awareness about memory loss and aging in a conversational way, establishing rapport and being available to people wherever they may be. We do a lot of listening – the education process definitely goes both ways! I see outreach as connecting the dots, seeing how one person can help another and finding creative solutions to very real, often tragic problems. It is an organic process similar to being a crafts person — weaving random threads into patterns and relationships, creating a human design to support the groundbreaking scientific work being done at the Massachusetts Alzheimer’s Disease Research Center. My role is to be a welcoming presence at the door to this essential research.”

MORE CELEBRATORY NEWS!

by Liang Yap, PhD

Much congratulations to Yakeel Quiroz, PhD of our ORE Core for receiving the MGH’s 2019 Ernesto González Award last Fall. Together with Martha Muniz – a clinical research coordinator of the Harvard Aging Brain study who had also receive the award – both are commended for their outstanding efforts to the Latino community!

For more information, visit:: https://www.massgeneral.org/news/hotline/HTL100419/community-contributions
I am originally from Brazil, specifically from the state of Minas Gerais, the country’s storehouse of mineral riches (as indicated by the name). The state is the largest producer of coffee in the country (you’re welcome!) and an important contributor to farming and agriculture, which has provided the ingredients to great food and drinks. My entire family is in Brazil and yet, I have lived in the US over the years on three separate occasions. When I was a child, we lived in San Diego for one year while my mother was studying Psychology. Then back in Brazil, I took up volleyball and ended up returning to the US to go to college in Idaho on an athletic scholarship. After college I returned to Brazil and took up my graduate studies in Nutrition. During this time, I joined a multidisciplinary research group treating cancer patients who suffered from debilitating pain. This was my introduction to neuroscience. I was fascinated by the possibility of using nutrients to modulate neurotransmitters and help improve our patients’ quality of life and I decided I wanted to study the brain. I joined Dr. Angela Ribeiro’s neuroscience and cognition laboratory at Universidade Federal de Minas Gerais (UFMG) as a research fellow and learned about molecular and behavioral deficits in thiamine deficient rats. At this time, I contacted a researcher in Boston who used a prenatal malnutrition model that we were establishing at UFMG. Through this contact I ended up coming to Dr. Douglas Rosene’s laboratory at Boston University. In my PhD project I was able to combine my background in nutrition and my interest in the brain to investigate the long-term effects of prenatal...
protein malnutrition in the brain of adult rats. After having used animal models to study the brain, I decided to pursue research that utilized human brains and that was more clinically relevant. I transitioned to a postdoctoral research position in Dr. Teresa Gomez-Isla lab at MGH. Teresa's expertise as a neurologist has helped me design and conduct experiments that translate to human disease. In her lab, I have worked on two main projects: 1) I used a transgenic mouse model to study the spreading of pathological tau in the brain, and 2) my current research focuses on deciphering the traits of resilience to Alzheimer's pathology using post-mortem human brain tissue. Earlier this year I received a Poster of Distinction Award for a poster I presented at ECOR (“Executive Committee on Research”)/MGH titled: “Selective partial decrease of glycogen synthase kinase 3 beta (GSK-3β) diminishes tau phosphorylation, propagation, and formation of tau aggregates in the mouse brain”. Presenting the results of my work to the MGH research community was a truly rewarding experience and receiving the award a gratifying recognition for the hard work over the past couple of years.

I consider it a privilege to be part of this research community at MGH and to personally handle such invaluable brains daily. I am looking forward to joining MGH faculty as an Instructor in Neurology soon, to continue my work on Alzheimer’s disease amidst other talented colleagues at the MassGeneral Institute for Neurodegenerative Disease (MIND). It seems like the third time was the charm and, after having been in the US for over thirteen years now, I consider Boston my home away from home.
I am a neuropathologist and post-doctoral fellow at the Massachusetts Alzheimer’s Disease Research Center (ADRC). Recently, I was awarded the Alzheimer’s Association Clinician Scientist Fellowship (AACSF) for my project entitled “Tau aggregation and toxicity in patient derived iPS neurons”. This research project uses stem cells made from ADRC brain bank donors to study the mechanisms of Alzheimer’s disease.

I am originally from Glen Carbon, Illinois, and attended Washington University in St. Louis for my undergraduate studies. To complete my MD and PhD degrees, I moved to Columbia University in New York City, largely due to its strengths in neuroscience and the emerging field of human stem cell biology. Subsequently, I completed anatomic pathology residency and neuropathology fellowship at the Massachusetts General Hospital/ Harvard Medical School, where I solidified my interests in dementia.

At this time, I also began building a patient-derived cohort of induced pluripotent stem cells (iPS cells) for research in Alzheimer’s disease and related dementias. I am using this group of iPS cells to perform the research in my AACSF fellowship under the mentorship of Dr. Brad Hyman, director of the MADRC, and Dr. Matthew Frosch, director of the MADRC neuropathology core. Broadly, the project will seek to understand how aggregated forms of the protein “Tau” effect neurons in Alzheimer’s disease.

In Alzheimer’s disease, brain cells (neurons) become sick and develop aggregations of proteins within the cell bodies. Tau, a protein normally present in neurons, is the major component of these aggregates.

“I am using stem cells derived from autopsy-confirmed Alzheimer’s disease patients to create personalized human models of the disease in a dish.”

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The spread of tau aggregates is thought to drive cognitive decline in Alzheimer’s disease. However, the scientific community does not have a complete understanding of how tau aggregates in neurons lead to the neuronal dysfunction and death seen in Alzheimer’s disease.

I am using stem cells derived from autopsy-confirmed Alzheimer’s disease patients to create personalized human models of the disease in a dish. Our approach uses time-lapse microscopy to watch individual stem cell-derived neurons in a dish over a period of up to one month, to induce the formation of tau aggregates in these cells, and to then determine what happens to the neurons afterwards. Preliminary data suggest that human stem cell-derived neurons may become sick and die once tau aggregation has occurred - an observation that has not been directly seen in animal models of Alzheimer’s disease. During my fellowship, I will perform experiments to confirm this observation and use patient-specific stem cells to see if neurons derived from Alzheimer’s disease patients are more sensitive to tau aggregates than those derived from people without this disease. We will also attempt to determine exactly which of the multiple forms of tau seen in aggregates is most responsible for the negative impacts in neurons. Hopefully, this project will help improve our understanding of one of the major brain-changes that occurs in Alzheimer’s disease. It will also produce an experimental system that can be used for many future studies, including drug discovery.

Being a member of the group at the MADRC and beginning this research project is a fantastic opportunity. I am thankful for the support of the Alzheimer’s Association and very grateful to the patients and families that participate in and support this work.
Growing up in the idyllic central Texas hill country, I developed a love of Texas sports and BBQ and all things sun and summer. I also experienced firsthand, in my close-knit Italian family, the devastating impact of neurodegenerative disease: I witnessed my grandmother, an Italian immigrant and one of my primary caregivers, struggle with the movement and behavioral changes of Parkinson’s Disease.

Seeking to better understand this disease process, and, ultimately, to be able to do more to help her and others who were similarly affected, I went on to pursue MD/PhD training in the Baylor College of Medicine Medical Scientist Training Program. There, I worked with Dr. Huda Y. Zoghbi, an extraordinary scientific and professional role model, and modeled mechanisms of neuronal death and dysfunction in mice and in cells in a dish. This work, which led to the discovery of an insulin signaling pathway shared across affected brain regions in neurodegenerative disease, further fueled my drive to develop approaches to prevent or slow neuronal degeneration. Together, these early personal and scientific experiences were formative in motivating me to pursue a career as a physician scientist in geriatric psychiatry, working at the interface of mental health and neurodegenerative disease.

Following my medical school and graduate school training, I went on to complete Psychiatry residency at Massachusetts General Hospital/ McLean Hospital, and then the Harvard Medical School Geriatric Psychiatry Fellowship Program. As I cared for older adults with debilitating late life depression, anxiety and memory disorders, I became increasingly interested in determining mechanisms underlying these behavioral and cognitive symptoms. Drawing...
from my graduate school work, and further motivated to investigate these pathways in patients using neuroimaging and fluid biomarkers, I sought the guidance of a diverse “dream team” of research mentors at Harvard: Dr. Deborah Blacker, and Geriatric Psychiatrist and epidemiologist; Dr. Gad Marshall a Behavioral Neurologist with expertise in neuropsychiatric symptoms in Alzheimer’s Disease (AD); and Drs. Reisa Sperling and Keith Johnson, leaders of the landmark Harvard Aging Brain Study, designed to identify the earliest signs of memory decline in otherwise healthy older adults. I additionally benefited from the mentorship of Drs. Brent. Forester and Olivia Okereke (Geriatric Psychiatrists) and Dr. Steven Arnold (Psychiatrist and Neurologist), all accomplished scientific mentors with diverse expertise in neuropsychiatric disorders in older adults.

These mentors have provided critical guidance as I learned clinical research principles. Working with them, I was additionally awarded a BrightFocus Foundation fellowship in 2016 to support my work investigating mood and behavioral changes in AD. In AD, changes occur not only in a person’s memory and thinking, but also in their mood and behavior. Symptoms such as depression, apathy and withdrawal are common and distressing to patients and their families, and can be just as debilitating, if not more so, than changes in memory and thinking. These psychiatric and behavioral symptoms may occur very early in the disease process, in the “pre-Alzheimer’s” disease stage, when a person may have the AD proteins, amyloid beta (Aβ) and tau, in their brains, but before they have developed overt signs of the disease. There is currently not a clear understanding of why and how these debilitating psychiatric and behavioral symptoms occur, and there are few effective treatments. The goals of my BrightFocus project were to determine the association between mild psychiatric and behavioral symptoms, memory decline, and build-up of Aβ, tau, and brain pathway changes in normal older adults and those in the pre-Alzheimer’s and early AD stages. Results from this project, published in the Journal of Alzheimer’s Disease and JAMA Network Open, showed that in healthy older adults, mild depressive symptoms are associated with tau in two brain regions of initial deposition in older adults. We also found that brain amyloid influences the association between depression and memory, such that worsening depression over time is closely associated with declining memory and thinking in those with evidence of elevated amyloid. These findings from my BrightFocus project have implications for clinical trials in AD. Indeed, they suggest that targeting behavioral symptoms could be a potential strategy to prevent the clinical symptoms of AD, a hypothesis that merits testing in future work. To follow up on these findings, I am now carrying out an NIH/NIA K23 project

“Although my grandmother ultimately lost her battle with neurodegenerative disease, her memory, and the motivation to help other older adults like her, continues to drive me today.”
examining associations among mood, memory and pathology in older adults with more severe depression. In recognition of these efforts, in 2017 I was selected to receive the Outstanding Emerging Research Scientist award by the BrightFocus Foundation, and in 2019, the Hartford-Jeste Award for Future Leaders in Geriatric Psychiatry by the American Psychiatric Association.

Although my grandmother ultimately lost her battle with neurodegenerative disease, her memory, and the motivation to help other older adults like her, continues to drive me today. Indeed, my clinical research interests are sub-served by a more fundamental desire to have an even larger impact in the lives of patients and their families, whether by promoting healthy brain aging and mental health, training the next generation of geriatric psychiatrists, or advocating for legislative action to support patients and families. I enjoy giving talks on these topics in the community and to fellow clinicians and scientists across all disciplines, and raising awareness, which can translate into an overall larger support network for patients and families.

While I have come a far distance from the idyllic Texas hill country, Boston has become a second home to me. When not carrying out research, I enjoy entertaining (and being entertained) by my two Russian blue cats, Cosmo and Mr. Whiskers. My love of Texas football and BBQ have persisted, but have broadened to include Boston sports teams, and to sampling and cooking a wide range of diverse cuisines with family and friends, including Italian recipes handed down through generations of my family. To balance this out, I am an enthusiast of personal training and fitness (running, interval training, pilates, and yoga), fashion and style, volunteering at my faith community, the Paulist Center, and maintaining steadfast pursuit of the most beautiful beaches near and far.
I was born and raised in Málaga, a mid-sized city in the Southern Mediterranean coast of Spain. Professionally, it’s been 11 fantastic years in the US, but I cannot help missing Málaga sunny weather throughout the year, the amazing food and, above all, my family. I try to go back home a couple of times every year to spend quality time with my parents and siblings.

I am a neurologist specialized in memory disorders and a wet lab researcher on Alzheimer’s disease and related dementias. My career path has been rather atypical. I received my MD in 2001 at the University of Málaga School of Medicine and then completed my first neurology residency in 2006 at the University Hospital Virgen del Rocío in Seville (Spain). During those years, I became very motivated to specialize on dementias and decided to do a 2-year research and behavioral neurology fellowship at the same institution. I came to the US in 2008 attracted by the ground-breaking research being conducted by Dr. Brad Hyman at our Massachusetts Alzheimer’s Disease Research Center. Under Dr. Hyman’s mentorship, I investigated the associations between cognitive decline and brain autopsy findings in patients with Alzheimer’s disease and age-matched healthy individuals. I am extremely grateful to our research participants for their generosity with our brain donation program; without this invaluable ultimate gift, we would not have the possibility of advancing the research on these terrible diseases. My scientific publications during this period (2008-2013) resulted in my PhD at the University of Seville in 2013. Next, to become a board-certified neurologist in the US and caring for dementia patients while continuing my research program, I pursued a second neurology residency, which I completed at the University of Iowa in 2017. Lastly, I returned to MGH to complete a second research and clinical dementia fellowship, directed by Dr. Teresa Gómez-Isla, and was recently recruited to the MGH Memory Division Faculty. To be part

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There are few forces as powerful as the will to live – a stubborn conviction to keep breathing and to fight for the right to stand by your grandchild at his 17th birthday, high school graduation, and first day of college. This summer, I was witness to this formidable fortitude as my grandmother battled respiratory failure, a complication of end-stage Progressive Supranuclear Palsy (PSP).

PSP is a rare and rapidly progressive neurodegenerative tauopathy which has afflicted my grandmother for the past decade. Though the disease has rendered her unable to speak, see, nor swallow, when I played top hits of the 70s in her ICU room, my grandmother gripped my hand and swayed her limbs to the beat of the music. She was determined to dance.

It is this unrelenting spirit which, since 7th grade, has inspired me to pursue research in neurodegeneration. I am a rising high school senior at Phillips Exeter Academy, and am deeply fortunate to have the opportunity to participate in research efforts at the Massachusetts Alzheimer’s Disease Research Center. Mentored by Dr. Sudeshna Das and Dr. Alberto Serrano-Pozo, I am committed to helping further enterprising research initiatives and seek to contribute to the effort to develop better treatment options for patients with neurodegenerative disorders.

Over the past year and a half, I have conducted a meta-analysis of published human gene expression data across Alzheimer’s disease, Lewy body dementia, and amyotrophic lateral sclerosis (ALS) to identify the shared cellular pathways which underlie neurodegeneration. This project involved comprehensive computational analyses of diverse datasets, with a plan to validate these results in worm (C. elegans) models of disease. To image the worms and track their health and lifespan I built the WormBot, an open-source robot from the University of Washington. For this research, I was happy to receive 1st place in Biology at the New Hampshire state science fair this spring, and was a Finalist at the 2019 International Science and

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of this team of smart and dedicated clinicians and scientists is highly motivating.

I have just been honored with the 2019 NACC New Investigator Award (NACC stands for National Alzheimer’s Coordinating Center and represents the consortium of about thirty Alzheimer’s Disease Centers across the US). In my initial neuropathological studies, I had made several intriguing observations supporting a role of glial (non-nerve) cells in the progression of Alzheimer’s disease, therefore they became my research focus. These brain cells—called astrocytes and microglia—are known to respond to the plaques and tangles that accumulate in the brain of Alzheimer’s disease patients, but whether this response is protective or deleterious remains unclear and is currently a hot topic in Alzheimer’s research. In this specific award-winning project, I have proposed to investigate further the nature of the astrocytic and microglial responses in Alzheimer’s disease by applying a novel multi-staining technique on single human autopsy brain slices from our brain bank. This method will allow a deeper profiling of these cells with many more markers than traditional staining methods (i.e. more than 10 instead of 2 or 3) and a better understanding of the effects of plaques and tangles on these non-nerve cell types.

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My number one aspiration in the lab is to help find the mechanism that fuels the progression of cognitive decline in Alzheimer’s disease, so that we could eventually develop neuroprotective therapies to slow down or even arrest this decline. Next, I am planning to test the hypothesis that these glial cells are crucial to disease progression using Alzheimer’s mouse models. I feel privileged to have the opportunity of developing my lab research program while caring for patients with dementing conditions at MGH memory clinic.
Engineering Fair (ISEF) in Phoenix, AZ. ISEF is the largest pre-collegiate science competition in the world, and I was galvanized by sharing my research with like-minded peers engaged in pioneering investigations across the frontiers of all disciplines of science. This unforgettable experience has energized my resolution to continue to unmask the secrets of neurodegeneration, and instilled in me optimism that we, the next generation of scientists, will leave an enduring impact on patient care globally.

I am indebted to Dr. Hyman and the Massachusetts ADRC for investing in the research endeavors of students like myself and am lucky to have selfless mentors like Dr. Serrano-Pozo and Dr. Das who have altered the trajectory of my research path. In turn, I hope to one day serve in the same role for young scientists who may not have access to the incredible resources I have been offered. I plan to further my work by studying computational neuroscience in college. Ultimately, though my grandmother may not live to see my first day of college, the stories and courage of patients like her will forever fuel my passion for research and help ensure that our team of scientists will keep hunting for a cure. This promise of perseverance gives both her and I hope, and for that, I am grateful.

Ayush approached me about a year and a half ago when he needed help with analyzing data. His objective was to find a common gene-expression-signature for neurodegenerative diseases, an aim that most of us with much more experience would find daunting! He was fourteen. Though only in high school, Ayush quickly learned the skills required to conduct research at a post-graduate level. His meticulous work succeeded in identifying molecular pathways deregulated in Alzheimer’s, Lewy body dementia, and Amyotrophic Lateral Sclerosis. Ayush has consistently impressed me with his exceptional energy, creativity, and motivation. He brings a humanitarian perspective to the work he conducts inside the laboratory: he is driven by his passion for and personal investment in the issues that he is addressing through his research. I have little doubt that one day this young man will bring us closer to treating a disease that affects millions and for which there is currently no cure! – Sudeshna Das, PhD (mentor)

...the stories and courage of patients like her will forever fuel my passion for research and help ensure that our team of scientists will keep hunting for a cure.

Photo caption: Phillips Exeter Academy Library designed by architect Louis Kahn
My name is Iman Aganj, and I am a researcher at the Martinos Center, Mass General Hospital, Harvard Medical School. I was born and raised in Iran, received my Bachelor’s degree in Computer Science in France, and my Master’s and PhD in Electrical Engineering from the University of Minnesota. Besides my research, I like watching movies, playing the piano, and hiking.

My graduate research focused on electron microscopy and brain MRI, under Prof. Guillermo Sapiro’s supervision. I have always been fascinated by how different branches of science, engineering, and medicine came together to build a device that makes an image of my brain without opening my skull, and I was determined to be a part of the research community that keeps improving it. I joined Prof. Bruce Fischl’s Lab for Computational Neuroimaging as a postdoc fellow in 2011, where I am currently a faculty member. Under his guidance, I managed to receive a pilot grant from Mass. ADRC, which then led to a 3-year Alzheimer’s Disease Research grant from the BrightFocus Foundation.

The main purpose of the BrightFocus grant project is the study of brain connectivity in Alzheimer’s disease. The human brain has complex structural and functional networks. Network-based analysis of brain white-matter connections is helpful
in revealing the structural changes in aging and Alzheimer’s disease, and in discovering biomarkers that are important for diagnosis and treatment. The goal of the project is to build on my background in brain imaging to develop new computational methods, especially those that take indirect neural pathways into account, and derive more accurate imaging connectomic biomarkers for Alzheimer’s disease, which will help us to better understand how the brain is affected in this disease. At the core of the project are new mathematical models to account for the brain’s indirect structural connections that may not have been considered by standard techniques. We recently published our methods and results (led by my postdoc fellow Dr. Aina Frau-Pascual) in NeuroImage.

I am working towards securing future funding for this project, so I can continue working on imaging Alzheimer’s disease. Generally, my research is focused on innovating technology and developing new medical image analysis techniques (and improving the ones that already exist), so researchers and clinicians can extract as much useful information as possible from their medical images. My research is focused on innovating technology and developing new medical image analysis techniques, so researchers and clinicians can extract as much useful information as possible from their medical images, with the ultimate goal of improving human health. I have sought to apply theoretical ideas, such as deriving mathematical formulas or designing algorithms, to health-related practical problems, with the long-term goal of helping ease patients’ suffering from diseases.

http://iman.mgh.harvard.edu
I am currently a postdoctoral research fellow in Dr. Brian Bacskai’s laboratory at the Massachusetts General Hospital and Harvard Medical School, in Boston. I have been fascinated by science since I was a little kid. My interest in neuroscience and neurodegenerative disorders was sparked when I started my pre-doctoral training. How connections are made, how neurons establish contact with other neurons, and how everything is interconnected in the brain (neurons, glia, vessels…) intrigues me. I completed my PhD in 2015 at the University of Valladolid (Spain), my hometown university. The aim of my PhD project was to identify intracellular calcium alterations in healthy aging and disease, specifically in neurodegenerative disorders such as Alzheimer’s disease, using primary cells collected from rat brains. After receiving my PhD, I decided to focus my post-doctoral research on translating the phenomena that I studied in cells to a more complex and integrated system, the living brain. In 2016, I was very fortunate to join the group of Dr. Bacskai, an internationally renowned expert in the field of intravital imaging. Currently, I use state-of-the-art microscopy techniques that allow me to observe even the smallest subcellular structures like a mitochondrion in the living mouse brain. My current research in the Bacskai group focuses on mitochondrial dysfunction in Alzheimer’s disease, particularly in mitochondrial calcium dysregulation and associated oxidative stress and the neuronal cell death that occurs.
in Alzheimer’s disease. Specifically, I use in vivo multi-photon microscopy to study mitochondrial alterations in neurons in mouse models of Alzheimer’s disease. I was recently awarded the Junior Faculty Award at the International Conference on Alzheimer’s and Parkinson’s disease that took place this last March in Lisbon, Portugal, for the project entitled “In vivo mitochondrial calcium dysregulation in neurons in a mouse model of Alzheimer’s disease”.

Now, I want to continue with my research and extend these novel findings to astrocytes, which are a relatively understudied cell type, that potentially play a key role in the pathophysiology of Alzheimer’s disease. Malfunction in the regulation of mitochondrial dynamics in astrocytes may reduce the production of ATP, which may disturb glial-neuronal interactions and cause neuronal death. I recently received a BrightFocus Foundation Fellowship that will fund this project. This study aims to find alterations in the correct function and dynamics of mitochondria in astrocytes during the development of the pathology of Alzheimer’s disease, with the final goal of identifying new therapeutic targets. With this project I hope I can contribute my grain of sand and advance the research towards finding a cure for this disease.

Out of the lab, I like practicing sports because it helps me relaxing and meeting lots of people. Back in Spain, I used to be a spinning and aerobics instructor! Now my favorite activity in Boston is kayaking in the Charles river when the weather is good. I also enjoy making crêpes for breakfast on Sundays, going to Chinatown for dumplings, and travelling to new places.

“With this project I hope I can contribute my grain of sand and advance the research towards finding a cure for this disease.”
Induced pluripotent stem (iPS) cells technology was developed in 2006 at Kyoto University/Japan. In the same year at the same place, I was an undergraduate student and thus was lucky enough to find how impressively this technology impacts scientific community all over the world. This experience naturally inspired me to become a scientist.

During my time as a graduate student, I was trained by Dr. Ayae Kinoshita (who worked for Dr. Brad Hyman’s laboratory at MGH as a post-doc/instructor and now a professor at Kyoto University) and I could obtain broad range of technical skills in molecular biology. My work investigating the roles of diet and exercise in Alzheimer’s disease (AD) mouse models resulted in a series of publications that support the beneficial roles of exercise. It was an honor to be selected one of my first author papers as The Journal of Biological Chemistry Paper of the Year 2012.

In 2014, I moved to Dr. Berezovska lab at MGH as a post-doc fellow to learn cutting-edge techniques in microscopy that include Förster resonance energy transfer (FRET) imaging and multiphoton microscopy. I have mainly focused on presenilin (PS)/γ-secretase biology in the Dr. Berezovska lab since PS/γ-secretase is not only involved in many essential biological events (e.g., development, neurogenesis, neuronal survival, etc.) but also plays significant roles in the broad range of diseases that are related to brain, skin, immune system, etc. Most clear link is with Alzheimer’s disease (AD) since dominantly inherited missense mutations in the genes encoding PS have been identified in the families of Alzheimer’s disease (FAD), highlighting its importance in AD pathogenesis.
Dr. Berezovska’s strong expertise has allowed me to recently develop and validate a novel FRET-based biosensor that enables monitoring PS/γ-secretase activity in real time. PS/γ-secretase activity can be color-coded and mapped over the entire image of a cell. Therefore, our novel biosensor would permit to “visualize” the activity of PS/γ-secretase within the cell. Fortunately, I was able to receive the BrightFocus Foundation Fellowship, which would support to 1) improve the sensitivity of biosensor that we have recently developed to monitor PS/γ-secretase activity in cells and 2) express and validate the optimized biosensor in the brain of live mice. Our novel biosensor(s) would allow for the first time to study dynamic behavior of endogenous PS/γ-secretase longitudinally in different anatomical and subcellular regions in living mice. Upon completion of this work, the proposed studies will provide a necessary tool for better understanding of the dynamics of PS/γ-secretase and its association with diseases (e.g., AD, skin cancer, etc.). It could also enable a breakthrough needed for more efficient preclinical drug testing and for a successful clinical trial design.

My future endeavor is to develop new assays that are useful in translational studies (i.e., drug discovery and testing its efficacy in vivo) by utilizing my extensive experience in molecular biology and microscopy since I believe this would be crucial for the transition of findings from basic research to clinic. At last, I am deeply grateful to the donors of BrightFocus Foundation who made this research possible.

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I grew up in Phoenix, Arizona and have been interested in the brain since I took a high school field trip to a brain bank, which stores tissues donated to research, similar to the Massachusetts Alzheimer’s Disease Research Center at MGH. I remember one of the scientists pulling out a small microscope and a slide with a tiny piece of cortex on it that had been stained for Alzheimer’s disease plaques. On the slide we saw neurons and cells packed together with splotchy, plaque-like protein deposits spread throughout the section. When I looked at it, it felt like an “ah-ha!” moment: using a few simple science techniques researchers could make Alzheimer’s disease changes visible. Being able to actually see the disease drove me to ask questions about the brain works and specifically, what causes it to stop working in Alzheimer’s.

I joined Brad Hyman’s Alzheimer’s disease research lab as a postdoctoral fellow in 2014 to try to answer some of these questions. I was drawn to the lab because Brad is at the forefront of developing microscopy tools to help visualize changes taking place in the brain. As a recent neuroscience graduate, I initially focused on neurons and watching what happens to them as Alzheimer’s proteins accumulate, but sitting at the microscope one day we happened to notice that blood vessels in diseased brain looked different than in healthy brain. This observation set us on a path to exploring new ideas about how the brain (and not just neurons!) is altered by disease and I am increasingly fascinated by the incredibly interesting biology of brain vasculature.

Blood vessels play an important role in supplying the brain with the oxygen and nutrients necessary to keep neurons alive, and the blood vessels in your brain are unlike those found in other parts of the body. Like neurons, blood vessels can also
be affected by the same proteins that accumulate in Alzheimer’s, which causes them to become inflamed, changing their shape and recruiting white blood cells to their surface. Similar to clogging a pipe, these changes restrict blood flow vessels and could have devastating consequence to brain health.

Identifying these important vascular changes has led to an innovative way of thinking about how we might treat Alzheimer’s — if we can find treatments that reduce inflammation and white blood cell “clogs” in brain vasculature we might be able to slow or prevent neuronal loss.

This research was funded by the BrightFocus Foundation and I was recognized as their 2018 Outstanding Emerging Scientist and in 2019 as one of three Donors Cure New Vision Investigators. In the future, I am excited to continue this research by testing drugs that are already FDA-approved to treat vascular inflammation to see if they might be effective in Alzheimer’s models. I am fortunate to be at MGH and have access to world-class collaborators in the Radiology Department who are developing new MRI and brain imaging methods that will help us identify individuals who might benefit from these treatments. It’s thrilling to see a small observation turn into a full-blown research project that has real implications for helping in the clinic and I’m looking forward to guiding this project forward over the next few years.

“Identifying these important vascular changes has led to an innovative way of thinking about how we might treat Alzheimer’s”
I was born more than 30 years ago in Belgium. After spending 5 years there, we moved to France where I grew up near the city of Lille! Lille is a quite nice and active city at the intersection of Paris, London and Brussels, all linked by a high-speed train!! My father is a nurse and my mother a professor of neuropsychology at the university of Lille so I guess that I had a “background” for science but surprisingly, I really found a passion for science only in high school when I realized how perfect and beautiful Life is! I decided then to join an undergrad program of engineering in biotechnologies in Paris and obtained a master there. While I studied mostly genetics of hematology during my undergrad, i wanted to join a program studying cell biology and physiology and therefore I did a second master in cell biology at the university of Lille where I started to study neuroscience. Again, what struck me right away is the beauty and perfection of this network of cells all interconnected with specific functions. Reacting in microseconds and all based on biochemical reactions. I think I really found my way at that moment! I pursued with a PhD program in Lille and started to study the dysfunction of a protein called tau in Alzheimer’s disease. After my PhD, I wanted to improve again and nothing better for that purpose than joining Massachusetts General hospital / Harvard Medical School! So I joined the lab of Pr. Bradley Hyman, one of the most prominent scientist worldwide working in Alzheimer’s, here at MGH and continued to study tau. I developed a project to understand how tau dysfunctions
progress through the brain and ultimately invade the whole brain killing neurons on its passage... more importantly we are trying to translate this knowledge in novel potential diagnosis and therapeutic tools. We actually had great results confirming our hypothesis that the progression of tau dysfunction in the brain is closely associated with cell death and disease progression in patients. We identified a specific species of tau that was particularly prone to induce pathological formation. We also understood partially how this pathology spreads in the brain of patients. Finally, we try to tackle the formation of tau dysfunction by the use of antibodies and got promising results even if the way is still long before the translation to clinic. I got awarded a grant from the Alzheimer’s Association to continue and extend this work and I also obtained the junior faculty award from the Alzheimer’s disease and Parkinson’s disease international conference! I have now the ambition to extend these results and pursue other studies that we are currently developing in the lab. Long term, I wish I could settle a lab and continue to work in these passionating subject! But the way is still long!
I am a neuroscientist studying pathogenic mechanisms of Alzheimer’s disease. I was born in Incheon, South Korea, a mid-sized city in the northern area, which is quite close to North Korea. Actually, my father was a refugee from North Korea. He escaped to the South before the Korean war. As many Korean parents do, my father and mother scarified a lot for the better education of their children, my brother and me. My father wished me to study law, but my strong interest in science and engineering made me to choose a track toward science and engineering. I had entered the college as the mechanical engineering major but later switched to the biology, fascinated by complicated biological machineries that make the life exist.

After getting Ph.D. degree in cell biology at Korea Advance Science and Technology (KAIST), South Korea, I had been looking for the best place to study neuroscience and neurological disease mechanisms, which seems to be much more challenging and interesting (to me) than general cell biology. I wrote a letter to Dr. Rudolph E. Tanzi and Dora M. Kovacs (mADRC faculty member) in early 2001. Rudy and Dora are top Alzheimer’s disease experts and extremely popular among Korean scientists. I was surprised (and happy) to get their response in a couple of days. They became by mentors and my journey towards a cure for Alzheimer’s disease started.

In 2014, we developed a three-dimensional (3D) human brain cell culture model of Alzheimer’s disease (a.k.a. AD-in-a-dish) (Choi et al. 2014). In a conventional cell culture system, brain cells are growing in two-dimensional surfaces as a flattened single layer, which limits the recapitulation of 3D brain cell networks in human brains. Therefore, we created a 3D cell culture system where human brain cells are growing in 3D gels that are composed of...
brain matrix proteins. Interestingly, we found that 3D culture system was not only increasing brain cell interactions but also robustly accelerated toxic amyloid beta accumulation and amyloid beta-driven damages when we grew human Alzheimer’s disease brain cells, which is the central pathogenic mechanism of Alzheimer’s disease. We soon realized that this unique 3D human Alzheimer’s disease brain cell culture system can provide an exciting cellular model to study Alzheimer’s disease in a dish.

Since then, we started multiple collaborative projects around our human 3D Alzheimer’s disease models. We have been awarded grants from Cure Alzheimer’s Fund and NIH/NIA (1R01AG057635-01A1), together with Dr. Stephen Wong (Huston Methodist Hospital) to screen ~2400 compounds including FDA-approved drugs for their efficacy in reducing pathological markers of Alzheimer’s disease in our 3D culture model. In this project, we are using bioinformatics tools to accelerate identifying additional candidate drugs for Alzheimer’s disease. Recently, we have been awarded another NIH/NIA grant (1R01AG062547-01), together with Dr. Winston Hide (Beth Israel Deaconess Medical Center) to identify resilient pathways for Alzheimer’s disease patients using human brain transcriptomic database and our 3D culture models. Our 3D Alzheimer’s disease brain models play a central role in these two projects. If the similar projects were performed using mouse models, it would cost much higher price and pose potential ethical problem due to the sacrifice of too many mice.

My goal of our studies, of course, is to find a cure for Alzheimer’s disease. I also hope that our studies contribute to develop more precise and comprehensive human brain models that can be used to study various neurological diseases as well as Alzheimer’s disease. In line with this direction, we recently developed modified 3D Alzheimer’s brain models that mimics the brain inflammation (Park et al., 2018) and the deficits in blood vessels in Alzheimer’s disease patients (Shin et al., 2019). Of course, many challenges lie ahead. But I am optimistic and will continue my research path aimed at ending this horrendous disease.
I joined ACTRU, the Alzheimer’s Clinical & Translational Research Unit, as a staff scientist last winter to work with the MADRC biobank and biomarker core.

I am originally from Sweden and completed my medical and graduate degrees at the Karolinska Institute in Stockholm before moving to the Cleveland, Ohio, to do a post-doctoral fellowship. My intention was to stay in the U.S. for four years, but I met my husband in Boston and am still here 20 years later!

An important part of my current position is to collect biospecimens such as blood and cerebrospinal fluid (CSF) that can be used to investigate biomarkers, which are molecules that provide information about a disease or condition, in these samples. I am especially excited about working with CSF. We all have about a pint of this crystal-clear fluid that circulates in and around the brain and spinal cord. CSF functions as a cushion or “shock absorber” for the brain, but because it is in direct contact with the brain tissue itself, CSF reflects many of the molecular changes taking place locally within the brain in diseases like Alzheimer’s disease. These proteins and other molecules are not detectable in more easily accessible fluids, like blood samples.

A small sample of CSF can be obtained through a lumbar puncture, also called an LP or a spinal tap. An LP is a relatively easy procedure that can be done without any special preparations. The clinician performing the test numbs the skin with a local anesthetic before inserting a thin needle between two of the lumbar vertebrae into the lumbar cistern, a long sac containing CSF and some of the nerve roots extending below where the spinal cord itself has ended. CSF collection is a routine procedure in the clinical work-up of many brain disorders and LPs are commonly done in patients with dementia to determine CSF levels of Alzheimer biomarkers such as amyloid and tau. In research, we also measure many other brain proteins to detect if there is any inflammation, metabolic abnormalities, or other markers of brain cell injury. We learn

Continued on next page
We learn a tremendous amount about the molecular ecosystem of the brain through analyzing CSF.

A tremendous amount about the molecular ecosystem of the brain through analyzing CSF. Many people have heard rumors of how difficult an LP is and are scared of having the procedure done, but it is a safe and well-tolerated procedure which is usually easier than people expect it to be. As one study subject expressed "I expected a movie version of an epidural and got less than a tetanus shot". The main complication of an LP is that 10-20% of all subjects develop "low-pressure" headaches, which are harmless and typically resolve on their own without treatment. Very rarely, the headache can be severe and persistent. If this happens, it can be treated with an epidural blood patch, where a small amount of the person's own blood is injected in the site of the LP to form a clot sealing the hole. The risk of headaches can be reduced by proper technique and by using thin needles with a blunt rather than a cutting tip.

Studies have shown that changes occur in the brain at least ten, and perhaps even 20-30 years before symptoms of Alzheimer start to appear. During this time, it is possible to see changes in the protein composition of the CSF providing a unique opportunity to study the disease at an early stage before extensive brain damage has occurred and when it may still be possible to find effective treatment strategies. We hope that information from our CSF studies will not only help in the early diagnosis of dementia, but also in predicting the outcome of the disease in individual patients, in providing insights into the mechanisms driving the disease that can be used to identify new treatment targets, and in identifying markers that can be used as read-outs for the effects in clinical trials. We currently have CSF from around 800 subjects stored in our biorepository and are working on increasing this number and in obtaining samples from a more diverse population. We hope that this will be a valuable resource to the scientific community helping future patients with dementia overcome their disease and are very grateful to each and every person that is willing to donate CSF to our studies!
Eighteen percent of the U.S. population is older than 60 years of age, with projections for this group growing to 25-30% by 2050, two thirds of whom are women. Thus, maintaining healthy brain aging and prevention of Alzheimer’s disease (AD) are critical public health priorities. Most research on memory aging and AD begins with people over age 65 and does not investigate sex or gender differences. However, we now know that processes that lead to cognitive decline begin at much earlier ages in midlife, a period during which women undergo menopause. This provides a naturalistic opportunity to understand the impact of ovarian decline on risk factors implicated in AD to contribute to our understanding of sex differences in AD. Thus, it is critical to develop tools to identify in early midlife prior to disease manifestation, those who are at highest risk for AD later in life and incorporate our understanding of differences between women and men. With initial support from the BrightFocus Foundation, the Goldstein lab (http://cnl-sd.mgh.harvard.edu) and Innovation Center on Sex Differences in Medicine (ICON) (http://icon.mgh.harvard.edu) engaged multiple departments to
It is critical to develop tools to identify in early midlife prior to disease manifestation, those who are at highest risk for AD later in life and incorporate our understanding of differences between women and men.

initiate the development of such a tool, a clinical risk algorithm, that will be sensitive to potential differences between men and women.

We are recruiting from the Partners Biobank to create a Healthy Aging Translational CoHort (HATCH). The HATCH study begins with acquiring information from Electronic Health Records to create two groups people that are “high risk or low risk” for AD. High risk individuals have high genetic risk along with a diagnosis of either major depression, hypertension, and/or diabetes, which are known risk factors for AD. Low risk individuals are defined as those who do not have these conditions.

The Goldstein lab and team of MGH collaborators are extensively characterizing these individuals (ages 50-70) with respect to immune function, genetics, and hormonal, neurovascular, metabolic, and clinical functions to create an integrated profile to predict who may have accumulated amyloid in early midlife but without clinical manifestation of the disease. The profile will be validated using advanced brain imaging techniques such as MRI and amyloid PET imaging.

We envision a time when we can predict AD prior to its manifestation for early intervention and therapeutics sensitive to sex differences. Ultimately, we hope to create a healthy aging cohort of 5000 people as a learning laboratory for disorders of aging, a platform for integrating aging research across fields and organ systems (brain, heart, gut, lungs), and a potential pool of people who may be ideal candidates for clinical trials.

We have engaged multiple departments across Massachusetts General Hospital (MGH), including the departments of psychiatry, neurology, and cardiology, and the McCance Center for Brain Health to join efforts with our team and ICON. Our highly qualified group of experts are excited and committed to the development of the clinical risk algorithm. Further, and importantly, we believe that our unique focus on sex differences will provide novel insights into understanding AD and the development of sex-dependent therapeutics.

For more information about the program, contact the administrative assistant, Ms. Kayla Jashinsky at kjashinsky@mgh.harvard.edu, who will direct your contact appropriately.
A CONVERSATION WITH NOVELIST - MS. SHIAO-SHEN YU

Q: What brought you to America?

Ms. Yu: More job opportunities for myself and my two daughters when they grow up. I left Canada for the USA in 1979. My daughters were 10 and 9 years old at that time.

Q: Have you had a variety of meaningful experiences throughout the years in this country?

Ms. Yu: Yes. Both in Canada and in the United States. Here’s an overview of my years in North America thus far…

1974 to 1979 – I worked as a bookkeeper in Canada;

1979 to 1985 (Pueblo, Colorado, USA) – I worked as a bookkeeper and an office manager while I attended university for more courses, and I passed the teachers’ certificate test;

1986 to 1998 (Pueblo, CO) – I was a media specialist, a teacher-librarian and as a newspaper columnist;

1998 (3 months in San Jose, CA) – I made a living by being a bookkeeper;

1998 to 2006 (Cambridge and Boston, MA) – I worked as an accounting clerk, an ESL teacher and as a Chinese instructor;

I eventually retired in 2007. Since then, I have been doing a bit of writing and a lot of reading!

Q: Tell us about the books you’ve written. Why did you decide to write these books?

Ms. Yu: I have written 2 books so far:

-- Chinese Mosaics, which consists of my memoirs, short stories, essays and columns,

-- Two Swordmasters. Note that the two martial arts masters in this book are the teachers featured in the movie Crouching Tiger, Hidden Dragon.

My reasons for writing are…

1 - My two daughters and 3 half Chinese grandchildren do not know Chinese. I hope these books will tell them something about their Chinese heritage, and

2 - I’d like to tell the ‘lives’ of the Chinese women in the 19th century.

Continued on page 17
besides writing, what hobbies are you indulging in? What drives you?

Ms. Yu: I read a lot, both Chinese and English books. I play the game “Sudoku’ on the iPad a lot. I teach myself to ‘play (the) piano’. I have a keyboard and so far, I can only play poorly a few songs.

I try to keep busy and active, but most of the time I am very lazy. Like the lyrics in the song ‘old man river,’ I am now “tired of living and scared of dying.”

In terms of what drives me, I think I’d like to leave some kind of ‘marks’ of the years I am on this earth.

TWO SWORDMASTERS: CHIANG SHIAO-HO & LEE MO-BAI

BOOK REVIEW (Kirkus)

The fates of a pair of Chinese master martial artists and the women who love them play out in this two-part historical novel. Inspired by the 2000 film Crouching Tiger, Hidden Dragon (based on the work of Chinese author Wang Dulu), this book offers two interconnected stories about star-crossed lovers in a 19th-century world of Chinese martial arts, intrigue, and cultural constraints. In “Chiang Shiao-ho and a Willow Tree,” young Chiang rises from humble beginnings to fame as a master martial artist. He is determined to kill his father’s murderers and his childhood foes, including the dangerous patriarch of a feared martial arts school.

Chiang’s desire for revenge is complicated by his love for the patriarch’s granddaughter, who has sworn to protect her grandfather with her life. Yu’s (Chinese Mosaic, 2018, etc.) second tale, “Lee Mo-bai and a Living Widow,” takes place many years later. The orphaned son of a wealthy man (Chiang’s sworn brother), Lee is an expert in the literary and martial arts. He diverges from his reluctant path to civil service when he becomes the protector of Yu Ceo-lian, a young woman traveling to meet her betrothed for the first time. The bridegroom-to-be disappears, leaving her, as tradition dictates, to be a “living widow” for life. Although loving Lee, she takes her fate into her own hands, becoming adept at martial arts and seeking to avenge the death of her father.

Lee, meanwhile, earns influential friends and powerful enemies. Despite inadvertent repetition, abrupt scene shifts, and distracting grammatical and English usage...
hitches ("I did not teach you all my skills"; "He knew he will win"), these stories are rich in character and shaped by both thoughtful moral dilemmas and hyper-dynamic action. While the dual epilogues are anticlimactic, the two moving tales are skillfully propelled by acts of treachery, honor, and duty; the suspenseful appearance of legendary martial arts masters; and the author’s pointed examination of the tragic consequences of endless cycles of revenge and the cultural subordination of women.

Engaging storytelling in a vivid setting.

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CHINESE MOSAIC

BOOK REVIEW (Kirkus)

A writer offers autobiographical vignettes, short stories, and reflections on Chinese culture and history. In this book, Yu (Two Swordmasters, 2018, etc.) reveals that her “official and reported” birth date in north China is April 1, 1939. A self-described “unwanted girl child,” she was born after the Nanjing Massacre, when Japanese troops murdered an estimated 3 million Chinese people in a matter of weeks. Her father had been captured by the Japanese to work as an interpreter while her busy mother kept eight children safe from the Japanese army. In 1949, Yu’s family escaped from Communist China to Taiwan. Many years later, the author wrote columns for an American newspaper, the Pueblo Chieftain, and dreamed of publishing a book about China. After battling cancer in 2006, she was determined to realize her dream and pass down stories to her grandchildren. The end result is this heartfelt compilation of childhood memories and tales about Chinese culture and history. Divided into two parts, the book’s first section presents 16 easy-reading selections: autobiographical pieces, short stories, and essays. Sometimes, the volume feels like an informative classroom lecture; for example, in the essay “Three Chinese Poems,” Yu briefly discusses classical Chinese poetry. Other works are much more personal. Once, on a terrible train ride, Yu’s mother hid from Japanese soldiers by disguising herself as a man and her daughters as boys. The author also paints a memorable portrait of the outmoded custom of foot binding. In “My Mother’s Big Feet,” Yu’s mother—whose forward-thinking father wouldn’t allow her feet to be bound—was ridiculed her entire life for having “big” (smaller than size 5) feet. And the tender reflections in “A snowy night in Canada” chronicle the author’s struggles to raise her daughters alone. The second section presents 41 newspaper articles with details that should leave a lasting impression on readers of all ages. For example, “The Archer and the Moon Goddess” explains why ceramic rabbits popular gifts for children during the moon festival are. While they are not chronological, these succinct works are easy to browse, and Yu’s lively prose brings her subjects to life.

Quick, colorful glances at a rich culture.

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Sometimes life can take us down unexpected paths.

If I were asked eight years ago where I thought my husband Steve and I would be in the summer of 2019, our family history would likely have prompted my response, and I would have answered that there was a strong likelihood that we would be vacationing with our kids and grandchildren on the southern coast of Maine. Salty from riding waves during the day, and slightly sticky from ice cream melting down our grandchildren’s arms in the evening, and completely content by celebrating these time-honored family traditions, while creating new memories.

Not in my wildest of imaginings would I have conjured up the response that Steve will have endured a 6 ½ year journey through Alzheimer’s, and will have been gone for over a year, and I will be working as a Clinical Research Ambassador for the Massachusetts Alzheimer’s Disease Research Center at MGH.” But alas, this IS my reality, as I said, sometimes life takes us down paths we never expected to travel.

To say it was a surprise to us when Steve received his diagnosis of Younger Onset Alzheimer’s at age 59, would be a prodigious understatement. Steered by our deep love for each other and hope for our children and grandchildren, we made the decision to face this
diagnosis head on, and to embrace the time we had together with meaning and purpose. With the solicitous guidance we received from Steve’s Neurologist Dr. Teresa Gomez-Isla, in the MDU (Memory Disorders Unit, outpatient clinic) at MGH, we reached out to the Alzheimer’s Association for information and resources to navigate this new path we were travelling. We used our voices and became advocates, we remained socially engaged for as long as it was possible and found an alternative path to creating family legacies by becoming involved with research and ultimately, the donation of Steve’s brain to the MADRC (Massachusetts Alzheimer’s Disease Research Center).

All of these experiences that encompassed a full range of joy and sorrow have led me to my position here at MADRC.

While each person’s approach and understanding is different, I feel there is an innate kinship between those of us who travel this Alzheimer’s and other related dementia journeys.

I vividly recall our visits to the MDU and how travelling to MGH could be stress inducing, and trying to keep calm for Steve’s sake, making sure I delivered accurate accounts of what was going on with his symptoms, and while always pleasant, each visit was a stark reminder of the reality of this disease.

It is my privilege to meet people as they enter the MDU clinic and to be welcomed into their “story”. It is always my hope that along with the excellent clinical care they are receiving, that they feel nurture from everyone they encounter. It is my goal to be able to soften their day and experience even with an extended hand or an exchanged smile.

I am very cognizant of the feelings of hope and hesitation that people may be experiencing as they are approaching the subject of entering the research world. I am always inspired by those who are willing to just ask the question, “is research right for me?”

Our intent as we sit at the research recruitment table in the MDU clinic is to meet people wherever they are on their journey, to listen to their questions, and to offer them enough information to pursue the path that feels most comfortable for them.

There was no question in Steve’s mind about becoming involved in research. His fatherly instinct inspired him to want to contribute to any efforts that would pave a path to a future when no one would ever receive the diagnosis of Alzheimer’s (or other related dementias). He knew he wouldn’t be here to pass on his love of sailing, or climbing mountains to his grandchildren, but by being involved in research, he left a legacy of the importance in giving of yourself for the betterment of all. We spent many hours here in the Charlestown research center. Through my employment here, I am so grateful for the opportunity to continue traveling the path we began together at MGH. Steve left his brain to MGH, and his heart to me. It is my good fortune to be able to work here and keep them together and to be able to extend a hand of hope to others who have been redirected to a new path of AD/ADRD.
A LOOK AT SOME OF THE RESEARCH STUDIES OFFERED AT THE ALZHEIMER’S CLINICAL & TRANSLATIONAL RESEARCH UNIT (WWW.ACTRU.ORG)

Look out for other types of studies in future issues of our newsletters!

<table>
<thead>
<tr>
<th>STUDY NAME</th>
<th>STUDY CRITERIA</th>
<th>STUDY GOALS</th>
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<tbody>
<tr>
<td><strong>AIA AUTONOMICS</strong></td>
<td>AGE RANGE: 55-95</td>
<td><strong>THE GOAL</strong> of the study is to test and re-test the reliability of heart rate changes and skin response changes in individuals who would each be wearing a device called a BioStamp. Individuals’ anxiety, irritability and agitation symptoms will also be measured.</td>
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<tr>
<td></td>
<td>CLINICAL DIAGNOSES ELIGIBILITY*: Cognitively normal, PRAD, FTD, DLB</td>
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<tr>
<td><strong>ACEND-LB</strong></td>
<td>AGE RANGE: 55+</td>
<td><strong>THE GOAL</strong> of the study is to evaluate whether a drug known as Neflamapimod (VX 745) will affect cognitive functions in adults with DLB.</td>
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<td></td>
<td>CLINICAL DIAGNOSES ELIGIBILITY*: DLB</td>
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<tr>
<td><strong>LIFESPAN BIOBANK</strong></td>
<td>AGE RANGE: 18+</td>
<td><strong>THE GOAL</strong> of this study is to determine the effects of methylphenidate (also known as Ritalin) on cognition, behavioral symptoms and daily activities of living in people with either MCI or eAD, by using traditional office-based assessments, daily brain training games and FitBit (see <a href="http://www.fitbit.com">www.fitbit.com</a>) activity tracking.</td>
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<tr>
<td></td>
<td>CLINICAL DIAGNOSES ELIGIBILITY*: Individuals with or without dementia</td>
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<tr>
<td><strong>PACT-METHYLPHENIDATE STUDY</strong></td>
<td>AGE RANGE: 55-95</td>
<td><strong>THE GOAL</strong> of this study is to determine the effects of methylphenidate (also known as Ritalin) on cognition, behavioral symptoms and daily activities of living in people with either MCI or eAD, by using traditional office-based assessments, daily brain training games and FitBit (see <a href="http://www.fitbit.com">www.fitbit.com</a>) activity tracking.</td>
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<td>CLINICAL DIAGNOSES ELIGIBILITY*: MCI or eAD</td>
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<tr>
<td><strong>PEGASUS</strong></td>
<td>AGE RANGE: 55-89 (inclusive)</td>
<td><strong>THE GOAL</strong> of the study is to evaluate the safety, tolerability and effectiveness of a drug called AMX0035 in individuals with either MCI or PRAD clinical diagnoses.</td>
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<td></td>
<td>CLINICAL DIAGNOSES ELIGIBILITY*: MCI, PRAD</td>
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For information on these and additional studies, call 617-643-5200 or check out listings on www.madrc.org

*KEY*

CSF: Cerebrospinal fluid  
eAD: early-onset Alzheimer’s disease  
FTD: frontotemporal degeneration  
MCI: Mild Cognitive Impairment  
FDA: Federal Drug Administration  
PRAD: Probable Alzheimer’s disease  
DLB: Dementia with Lewy bodies

KEEP IN MIND
TO ALL OUR RESEARCH PARTICIPANTS~

As always, we want to give you a hearty and well-deserved “Thank you!” for all you do. Your loyalty to our research and your perseverance in participating over the years are truly amazing. You are the real stars of the Gerontology Research Unit!

JEANETTE GUNTHER, MS
CLINICAL COORDINATOR
GERONTOLOGY RESEARCH UNIT

A CENTRALIZED TELEPHONE NUMBER FOR INQUIRIES ABOUT OUR RESEARCH STUDIES!

INTERESTED IN LEARNING more about research studies and how you can get involved?

Patients, caregivers, family members and healthy volunteers can call 617-643-5200 to learn about all of the exciting research opportunities we have going on!

“For age is opportunity no less Than youth itself, though in another dress, And as the evening twilight fades away The sky is filled with stars, invisible by day.”

by Henry Wadsworth Longfellow

Image courtesy of favpng.com
The inaugural John H. Growdon, M.D. Symposium was held in the Simches Auditorium at MGH on November 25, 2019.

“The Symposium was an extension of a tradition in the Massachusetts Alzheimer Disease Research Center to hold an annual scientific meeting to present the important discoveries being made by Center investigators. The Center was one of the first five funded by the National Institutes of Health in 1984; I was the founding Director and led the Center’s activities for more than 20 years. During this time, I was fortunate to mentor and work with scores of talented young investigators who continue to make important scientific contributions.
to understanding the nature and causes of dementia. I was extremely honored therefore when two of these close colleagues, Drs. Teresa Gomez-Isla and Bradley Hyman, proposed a day-long symposium that would highlight advances in understanding and treating the dementia associated with Alzheimer disease and Parkinson disease. These are the two diseases that have been the focus of my career at MGH. They further proposed that the symposium be personalized so that only my former and current mentees and colleagues would be invited to present papers. The morning session, devoted to advances in Alzheimer disease, opened with a keynote address by Prof. Roger Nitsch from the University of Zurich that detailed the path of discovery of a novel treatment for Alzheimer disease. During the lunch break, attendees visited junior investigators standing by their posters and discussed the novel findings. The afternoon session, devoted to Parkinson disease, opened with a keynote address by Prof. Michael Schlossmacher from the University of Ottawa, centered on the molecular biology of Parkinson disease. By all measures, the Symposium was a great success: strong scientific presentations and an enthusiastic audience. For me, the best part is that only a fraction of the talented physicians and scientists who have worked with me were involved in this inaugural Symposium, and many more are eager to participate in the next one.”

--- John H. Growdon, MD
Welcome to the Spring / Summer issue of

KEEP IN MIND!

A newsletter for friends and supporters of the Massachusetts Alzheimer’s Disease Research Center and the Memory Study

Artist Unknown, Japanese (Circa 1919)

Summer Greeting Card: Thermometer
Taishō era Color lithograph, ink on card stock
Leonard A. Lauder Collection of Japanese Postcards
Museum of Fine Arts, Boston

Dear Summer: Please stay longer!