CLINICAL TRIALS UPDATE:

Immune therapies show promise as early-stage Alzheimer’s treatment

As the hunt for an Alzheimer’s cure continues, immune therapy remains one of the most promising treatment approaches — and an increasing number of studies will test whether it can slow or stop the disease before the worst of its symptoms emerge.

Immune therapy approaches for addressing Alzheimer’s disease use the body’s immune system to remove amyloid plaque, a harmful protein that builds up in Alzheimer’s-affected brains. The body’s immune system naturally creates antibodies to remove viruses and bacteria from the body; however, antibodies can also be made in a laboratory. The resulting antibody drugs specifically attach to amyloid in the brain and remove it — and, in theory, removing amyloid from the brain should slow or even stop the progression of Alzheimer’s.

In reality, initial research studies have found mixed, but useful results. Studies of these drugs in animals found that they did remove amyloid and improve performance on memory tests. Similar drugs were then tested in human clinical trials, including bapineuzumab, also known as bapi. The Boston University Alzheimer’s Disease Center was part of the effort to test whether bapi could effectively slow or stop mild to moderate dementia. Unfortunately, researchers had to stop the trial because they found no significant differences between the participants receiving doses of bapi and those receiving an inactive placebo; both groups had similar results on tests of memory and cognitive functioning and their ability to do daily activities. However, the researchers also found that some measures of biological function — called biomarkers — indicated that bapi did successfully reduce the amount of amyloid in participants’ brains. While the drug didn’t ultimately improve the health of patients in the study, it still seemed to accomplish its goal of removing amyloid from the brain.

To understand this contradiction, you need know how Alzheimer’s develops. The changes that occur in the brain that lead to Alzheimer’s actually start decades before the first symptoms appear. In fact, a study reported in the New England Journal of Medicine by Bateman and colleagues showed that changes in amyloid can be detected up to 25 years before memory problems are reported. By the time a patient gets diagnosed with Alzheimer’s, the disease has done a lot of damage, including the irreversible brain cell loss and brain atrophy that create memory loss and other cognitive problems. That damage isn’t solely caused by amyloid; researchers believe it’s driven by tau tangles, which also accumulate in Alzheimer’s-affected brains. Once tau starts accumulating in the brain, it leads to even more tau. It’s like a traffic jam that builds and builds during rush hour. But unlike a traffic
jam, which clears up eventually, the tau sticks around and keeps damaging brain cells. Many researchers believe Alzheimer’s comes from a sequence of changes in the brain: Amyloid comes first, and then the tau — which causes more tau, which leads to brain damage, which creates dementia symptoms.

Researchers now understand that if amyloid-removing antibody drugs are going to help slow patients’ decline, they need to be used by Alzheimer’s patients who haven’t had much tau buildup — patients who are in the milder, earlier stages of the disease. Results from a clinical trial of a medication similar to bapi — solanezumab — found a small clinical effect on participants with milder stages of dementia. This result was encouraging enough for drug makers to plan for a phase three clinical trial in patients with mild Alzheimer’s.

Drug makers and researchers are also testing other immune therapies for Alzheimer’s, including a vaccine. Vaccines work by introducing a small portion or safe version of something that might otherwise cause a disease into the body — like a flu virus or, in the case of Alzheimer’s, part of the amyloid protein. Adding this intruder causes the immune system to respond to and attack it, developing antibodies that will flag the intruder (and future intruders with the same characteristics) for removal. An amyloid vaccine for Alzheimer’s was first tested many years ago, but studies were stopped because the immune response was too intense in some patients, resulting in inflammation and mild swelling of the brain. Scientific understanding of the immune response has greatly increased since then, and the vaccines being tested now have been modified to reduce this risk.

As we move forward with the lessons learned from bapi and other clinical trial research, studies of anti-amyloid immune therapies will be tested on patients very early in the disease course, among people with Mild Cognitive Impairment (MCI) and possibly among those who have no symptoms, but do possess risk factors and biomarkers for Alzheimer’s. Clinical trials of these drugs are now available for patients who have very mild symptoms of memory loss or cognitive impairment, including trials offered through the Boston University Alzheimer’s Disease Center.

Want to learn more about clinical trials offered through the BU ADC?
Visit our website: bu.edu/alzresearch/research/
Contact our Recruitment Coordinator: joinadc@bu.edu or 617-414-1078

BU ADC joins Walk to End Alzheimer’s
Friends, faculty and staff of the Boston University Alzheimer’s Disease Center teamed up to raise awareness and funds for Alzheimer’s disease.

More than 20 people joined in, completing the Sept. 23 Alzheimer’s Association Walk to End Alzheimer’s and raising more than $5,700 for research.

The BU ADC team supported the Alzheimer’s Association at the Greater Boston Walk to End Alzheimer’s.

About Us
The Boston University Alzheimer’s Disease Center (BU ADC) aims to reduce the human and economic costs of Alzheimer’s disease through the advancement of knowledge. We conduct cutting-edge Alzheimer’s research and provide education about aging and dementia to professionals and communities in Boston and beyond. The BU ADC Education & Outreach team publishes the BU ADC Bulletin twice per year. It includes stories about research findings, new studies and more. Our center is also associated with the BU Center for the Study of Traumatic Encephalopathy.
Researchers from the Boston University Alzheimer’s Disease Center and the Center for the Study of Traumatic Encephalopathy shared their cutting-edge expertise at a variety of recent professional and community events. The BU ADC provided speakers and volunteer support for the 2012 Community Forum on Memory Loss, a free, daylong health education event coordinated by the Alzheimer’s Association and attended by more than 400 people. BU researchers also hosted two continuing medical education events this fall: “Aging or Alzheimer’s? How to Detect and Treat Memory Loss in the Primary Care Setting” and “Brain Trauma and the Athlete.” Both events aimed to provide detailed knowledge that professionals can use to help patients and families, from best practices for managing a concussion to non-pharmacologic treatments for memory loss and dementia.

Questions about our education events? Want the BU ADC to speak at your community event?
Contact the Education Programs Manager: 617-414-1077 or edaube1@bu.edu

Neil Kowall, director of the BU ADC, answers questions about the testing from course attendees.

Robert Stern, director of the BU ADC clinical core, adds some humor to his course presentation.

ADC staff members helped serve lunch during the Community Forum on Memory Loss.

Stern also presented at the Alzheimer’s Association’s 2012 Community Forum on Memory Loss.

Catch the latest Alzheimer’s news: BU ADC on Facebook, Twitter
Alzheimer’s disease makes news every day in cities around the globe. Sorting through all the headlines takes time, and some of the research can be tough to understand.

The Boston University Alzheimer’s Disease Center is helping people stay up to date on the latest Alzheimer’s news and what it means for them. With a revamped website and an expanded presence on Facebook and Twitter, the BU ADC now shares and comments on noteworthy Alzheimer’s articles, videos and more.

Want to know more?
Find us online, and stay in touch.

bu.edu/alzresearch
facebook.com/BUmemoryloss
twitter.com/BUmemoryloss

HOPE study to host thank-you event for volunteers
The Boston University Alzheimer’s Disease Center’s main research registry – HOPE, or Health Outreach Program for the Elderly – is planning a special event for the study’s 400 volunteers. The HOPE APPRECIATION BRUNCH, scheduled for Friday, June 21, will give BU ADC leadership an opportunity to thank HOPE participants for the contributions they make to a variety of studies and to a future without Alzheimer’s.

HOPE participants will receive more details in the mail soon. Please contact Angela Dwyer at 617-414-1189 with any questions.
### Actively Recruiting Studies

**STUDY TITLE** | **CURRENTLY RECRUITING** | **STUDY DESCRIPTION**  
--- | --- | ---  
BU ADC Registry–Health Outreach Program for the Elderly (HOPE) | Healthy Adults, MCI, AD | HOPE is the main registry of participants at the BU ADC. People who join HOPE attend a yearly visit in which their memory and thinking abilities are evaluated. They also participate in other BU ADC-affiliated studies. Interested volunteers may join this important registry if they can attend a yearly visit with a study partner and are 65 or older with or without memory concerns or 55 or older with memory concerns.  
AD Neuroimaging Initiative (ADNI-2) | MCI, AD | ADNI-2 is an important nationwide study that uses brain scans and biomarkers, along with tests of participants’ memory and thinking abilities, to help researchers better diagnose and track AD and related disorders. The study is currently recruiting volunteers who have memory concerns and who are between the ages of 55 and 90. Participants are compensated for their time.  
Gantenerumab (Roche clinical trial) | MCI | This is a double blind, randomized, placebo-controlled clinical trial to evaluate the effects of a monoclonal antibody, gantenerumab, on cognition in patients with MCI and early Alzheimer’s disease. Study participation is open to adults between the ages of 50 and 85 who have an MCI diagnosis.  
False Memory in AD | Healthy Adults, MCI, AD | The False Memory study seeks to understand why patients with AD and other dementias frequently remember things that never happened. The goal of this study is to find ways to reduce false memories in patients with dementia. Study participation is open to adults age 65-85 with or without memory concerns.  
Amylin, Amyloid-beta Peptide, and Alzheimer’s disease | Healthy Adults, MCI, AD | The goal of this study is to develop a blood test that can be used to diagnose MCI or dementia due to Alzheimer’s disease. The study uses an FDA-approved medication called pramlintide and involves one visit, which will include one injection of the medication, followed by several blood draws. Volunteers may be eligible if they do not have diabetes.  
Health Pathways | Healthy Adults, Caregivers | The Health Pathways study looks at how caring for a person with dementia affects physical and emotional health. Participants attend four annual face-to-face interviews in which they are asked questions about their health and about the person they care for. They also complete lab work. Participants may be eligible if they have no memory concerns and are age 60 or older.  
Memory Benefits of Sleep in Healthy Young, Elderly and Mild AD Patients | Normal Controls | The goal of this study is to examine the effects of sleep on memory processing for healthy young adults and healthy elderly individuals. Volunteers participate in a daytime nap study or an overnight study. Participants may be eligible if they are between the ages of 65 and 80, in good physical and mental health and do not have any sleep complaints.  
Cardiovascular Integrity Risk for Cognitive Decline in Aging (CIRCA) | Healthy Adults, MCI | Both AD and cerebrovascular disease can cause changes in the brain that are associated with changes in memory, thinking and organizational skills. This study is looking closely at how brain structures relate to cognitive changes and how risk factors for cerebrovascular disease may affect individuals with and without MCI. Volunteers may be eligible if they are between the ages of 45 and 85 and have MCI or no memory concerns.  
Effects of Parkinson’s Disease on Perception and Gait | Healthy Adults | Parkinson’s disease is a neurological disease that affects both motor and non-motor abilities. This study is looking at neurological changes associated with Parkinson’s and the relationships between basic vision, visuospatial abilities and daily function. Volunteers may be eligible to participate if they have no memory concerns, good vision and no conditions that affect walking ability.  
PAIRS Program | AD | This program pairs first-year Boston University medical students with patients who have early-stage AD. The program educates medical students about the care and support issues faced by patients with AD and provides patients with an opportunity to mentor students. Student-patient pairs meet monthly to participate in social activities throughout the academic year.  
Association Between Cerebral Blood Flow and Glucose Metabolism | Healthy Adults, MCI, AD | Using various brain imaging techniques, this study examines the association between cerebral blood flow and glucose metabolism as it relates to memory decline in older adults. Comparing the information from the different brain imaging techniques, the researchers hope to develop better methods for monitoring the progression of Alzheimer’s disease. Volunteers between the ages of 60 and 99 may be eligible.  
Emotional Perception, Neuropsychiatric Symptoms and Caregiver Experience in AD | Healthy Adults, AD | Researchers are examining how changes in emotional perception in people with dementia due to Alzheimer’s disease impact the experience of their caregivers. The goal is for the results of this study to be used to improve services for people with Alzheimer’s disease and their caregivers. The researchers are looking both for couples affected by Alzheimer’s disease and couples in which both spouses are not experiencing memory loss.  

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**AD = Alzheimer’s Disease; MCI = Mild Cognitive Impairment**

**Interested? Contact the BU ADC recruitment coordinator at 617-414-1078 or joinADC@bu.edu.**
Research Updates

Some hypertension medications may delay the development of Alzheimer’s Disease
Dr. Wendy Wei Qiao Qiu, along with colleague Dr. Haihao Zhu and student volunteer Max Wallack, discovered that angiotensin-converting enzyme (ACE) inhibitors, a class of hypertension medications, are associated with lower risk of developing Alzheimer’s disease (AD) compared to those who had not been taking this class of medications. They believe the ACE inhibitors, which can enter the brain, might help prevent the onset of AD.

New findings on the effects of aerobic fitness on memory
Dr. Karin Schon’s presentation of her research findings, “High-confidence recognition memory is associated with greater aerobic capacity in healthy young adults,” was selected as a “hot topic” at the Annual Meeting of the Society for Neuroscience. Schon’s study of young adults found subtle effects of aerobic capacity — measured with a treadmill test — on recognition memory for complex visual outdoor scenes. Schon’s ongoing research will focus on the effects of an exercise intervention for older adults on hippocampus-dependent memory function and structural integrity of the medial temporal lobes.

Regulated protein aggregation: a new paradigm for Alzheimer’s disease
The Journal of Neuroscience and Molecular Neurodegeneration recently published findings from Dr. Ben Wolozin and colleagues. Protein aggregation that occurs in Alzheimer’s disease is classically thought to occur as an undesirable, nonfunctional byproduct of protein misfolding. However, RNA-binding proteins use protein aggregation as part of a normal, regulated, physiological mechanism controlling protein synthesis and form stress granules in response to stress. Wolozin and his team recently demonstrated that the microtubule-associated protein tau regulates stress granule formation and that stress granules massively accumulate in the Alzheimer brain. This finding provides a novel approach to understanding degeneration in Alzheimer’s disease and potentially intervening in the disease process.

False memory in Alzheimer’s disease: testing the ‘imagination inflation effect’
Dr. Maureen O’Connor, along with colleague Dr. Andrew Budson, recently completed a study that analyzed the imagination inflation effect in healthy older adults and patients with Alzheimer’s. Imagination inflation is a memory distortion in which people are more likely to falsely remember an imaginary item as having been performed. O’Connor’s team found that imagining performing actions increased the tendency of both healthy older adults and patients with AD to falsely recall the action as having been performed. The effect was more pronounced for patients with AD. Understanding the imagination inflation effect in patients with Alzheimer’s disease is important because increased vulnerability to the imagination inflation effect could have significant consequences in daily life. (For example, a patient with AD may mistakenly believe they took their medications or shut off the stove when they had only imagined doing these actions, which raises safety concerns.)

Neurogenic therapy on Alzheimer’s disease mouse models
Dr. Tsuneya Ikezu presented his research, “Enhancement of Neurogenesis and Cognitive Function by Adeno-Associated Virus-Mediated Gene Therapy,” at the Federation of European Neuroscience Societies 8th Forum of Neuroscience in Barcelona, Spain. In this study, his team found that viral gene delivery of fibroblast growth factor-2 gene into the hippocampus of a mouse model enhances the growth of new brain cells, amyloid clearance and learning even after the onset of learning impairment. This work was also recently published in Proceedings of the National Academy of Sciences.

Music and memory
Neuropsychologia recently published findings from Dr. Andrew Budson’s laboratory. Led by colleagues Nicholas Simmons-Stern and Dr. Rebecca Deason, the study examined whether music could enhance memory for activities related to daily functioning (such as taking your pills) and also whether memory for both general and specific details of the lyrics was improved by music. They found that both healthy older adults and patients with Alzheimer’s disease showed better memory for the general content of the lyrics when they had been accompanied by a sung recording. The study also demonstrated some limitations of this effect, as memory for specific content did not seem to be improved by music. The results will help guide the development of music-based therapies designed to improve the quality of life of those living with Alzheimer’s disease.

Epigenetic mechanism of neurodegenerative disorders
Dr. Hoon Ryu’s research on the epigenetic regulation of heterochromatin condensation in Huntington’s disease was recently published by the journal Cell Death & Differentiation. Aberrant chromatin remodeling is involved in the pathogenesis of Huntington’s disease, but its mechanism is not known. In this study, Ryu and colleagues validated the contribution of the ATRX gene to Huntington’s pathogenesis through epigenetic modulation of heterochromatin condensation. ATRX participates in organizing the structure of pericentromeric heterochromatin by elevating trimethylated histone H3K9 levels in striatal cells. These findings suggest that ATRX-mediated epigenetic modifications contribute significantly to the development of neurodegeneration in Huntington’s and that neuronal ATRX levels may be an indicator of aberrant chromatin remodeling in other neurological disorders.
Welcome

The Boston University Alzheimer’s Disease Center (BU ADC) and its affiliate, the Center for the Study of Traumatic Encephalopathy (CSTE), would like to extend a warm welcome to new staff and interns:

Lauren Murphy, Executive Assistant. She was previously the Senior Program Manager at the American Islamic Congress in Boston, MA. She will work with Dr. Bob Stern, providing support for ADC and CSTE activities, and with CSTE directors.

Alyssa Blood, CSTE Research Intern. Alyssa received her Bachelor of Arts from Brown University in 2011 and completed a pre-medical program at Georgetown University in 2012.

Daniel Wigmore, CSTE Intern. Daniel is an undergraduate at Northeastern University.

Goodbyes

Many thanks and best wishes to departing BU ADC and CSTE staff:

Patrick Curtis, who worked at the BU ADC and then as CSTE Assistant for more than three years, has taken a new opportunity as Executive Assistant to the Dean at Massachusetts Institute of Technology’s School of Humanities, Arts and Social Sciences.

Theresa McGowan, ADC Study Coordinator, recently moved to New York City. She has been accepted to New York University’s accelerated nursing program.

Sumati Raghavan, ADC Clinical Research Coordinator, has taken a new position coordinating clinical research studies at the Boston Center for Memory, a private clinic run by Andrew Budson, MD, BU ADC Education & Outreach Director, and his colleagues.

The HOPE Study Team: Danielle Borin & Liza Elkin

What do they do?

Liza and Danielle both work for the Boston University Alzheimer’s Disease Center’s Health Outreach Program for the Elderly (HOPE) study, a research registry that evaluates memory and thinking abilities of older adults and provides ongoing opportunities to participate in related studies. Liza and Danielle spend much of their time with HOPE participants, conducting interviews and administering neuropsychological tests. In addition, Liza requests medical records and scans that allow the team to make a diagnosis for each participant, and Danielle coordinates the brain donation program. Danielle explained that the donations are “critical to HOPE” because the information gained from examining brain tissue — collected after death — allows researchers to double-check an Alzheimer’s diagnosis and “can ultimately help us learn more about the disease and improve treatment for future patients.”

Why do they do it?

Danielle has enjoyed working with older adults for years. As an undergraduate, she led a volunteer group that partnered students with elderly residents of a local assisted living facility for weekly activities. She hopes to contribute to improving the health and quality of life for older adults. Liza is driven by her desire to understand Alzheimer’s disease and discover its mysteries. “There is so much research to be done on the disease: how it affects individuals and their families, best methods for treatment and prevention,” she said. “It’s an honor to be contributing to this body of knowledge that’s going to have a great and lasting impact on the lives of millions of people.”

Which part of the job do they enjoy most?

Danielle loves interacting with HOPE participants. “Seeing the love and strength our participants and their loved ones have makes each day worth it — and so much fun,” she said. Liza highlighted the educational opportunities that arise at the ADC, from lectures hosted at the School of Medicine to ordinary staff meetings. “I feel like I learn something new nearly every day,” Liza said. “Our interactions with HOPE participants give me the opportunity to see and apply what I’m learning in real time.”

What do they do outside of the ADC?

Liza is an avid yoga enthusiast and currently training for a half-marathon. She also recently joined a dance team and stays busy practicing for competitions. Danielle doesn’t have much free time because she’s studying for the Medical College Admission Test, in the hope of eventually becoming a geriatrician or neurologist. Still, she plans to spend a week in the spring volunteering with Global Medical Brigades in Honduras, building housing and water systems in a remote village.

BU ADC Happenings

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Making History

Solomon Fineblum made his mark in the Space Race. Now he’s helping the BU ADC fight to end Alzheimer’s.

Solomon Fineblum’s belief in the benefits of research has kept him in the Boston University Alzheimer’s Disease Center’s HOPE study for 11 years and counting. After witnessing a variety of breakthroughs during his lifetime, he felt compelled to give back in some way. “I’ve lucked out,” said Fineblum. “I’m the beneficiary of generations of people who have participated in research.”

It’s not the first time that Fineblum has helped advance knowledge and make history. The former aircraft engineer spent eight years working on the National Aeronautics and Space Administration’s Apollo program, where he focused on heat transfer and fluid dynamics.

The end result? His team put a man on the moon for the first time. “It was comparable, in terms of labor, to building a couple of pyramids,” he said. But Fineblum believes in the power of intense effort toward a common goal, whether it’s space travel or a cure for Alzheimer’s. He inherited a special appreciation for new technology from his father, who believed that developments like television — not yet popular when Fineblum was a child — would fix most of society’s problems by increasing public access to knowledge. In retrospect, Fineblum said, this was a naïve prediction; but it instilled an enthusiasm for improving the human condition that Fineblum has carried with him.

As a HOPE study participant, he’s picked up tips that could help prevent or slow the effects of memory disorders. Fineblum and his wife, Carol, particularly enjoy trying to stay active and social. “We consciously look for new experiences,” he said, from trying out a new theater to taking a cruise to Bermuda.

Although the couple married in 1946, Fineblum notes that they were friends for a long time first, which might be the secret to their 66 years of marriage (and counting.) “We were across-the-street neighbors,” he said. “She was my sister’s best girlfriend.”

The possibility of losing his memories to Alzheimer’s upsets Fineblum, even though he hasn’t been diagnosed with the disease. “All I have of any value is right here,” he said, gesturing toward his brain. While his work on the Apollo program might be a far cry from volunteering for an Alzheimer’s study, researchers undoubtedly share his belief — that if we keep trying and learning, we’ll eventually find a cure.

“In wasn’t a miracle,” he said, recalling the Apollo missions. “A lot of people worked hard, and we accomplished something.”

Honorary and Memorial Contributions

The Boston University Alzheimer’s Disease Center is involved in a variety of clinical, research and educational activities. Research study participants, families and community leaders often wish to contribute to the fight against Alzheimer’s disease. We welcome honorary and memorial donations. These gifts are an excellent way to honor a family member or friend while contributing to the advancement of Alzheimer’s research. To make a donation, please call Lawrence Crimmins in the BU Development Office at 617-638-5676 or visit us online: www.bu.edu/alzresearch/donate

The BU ADC would like to recognize the following private donors for their greatly appreciated contributions, which were made between June 12 and Dec. 12, 2012. Please note that anonymous donors are not listed.

In Memory of Eleanor Burns
Evelyn Allen
Mary Anderson and Robert J. Anderson
Mary F. Boudreau
Frank F. Burns and Mary E. Burns
Rose Burns and Thomas Burns
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Shirley A. Young and Thomas E. Young

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Lionel E. Racicot

In Memory of Steve Thorne
Philip Gilley, Jr.

In Memory of Bride S. Van Anglen
Susan Farrell
THE NEWSREEL:

Head Games highlights BU researcher’s work on sports concussion crisis

The critically acclaimed documentary Head Games, based on a 2006 book by Christopher Nowinski, is now available on demand via Amazon Instant Video, iTunes and other digital video providers. Produced by Steve James, the award-winning director of Hoop Dreams, the film examines the concussion crisis in sports. It features the groundbreaking findings of researchers at the Boston University Center for the Study of Traumatic Encephalopathy (BU CSTE) and highlights the experience and advocacy of Nowinski, who is the current BU CSTE director and a former World Wrestling Entertainment wrestler.

Find more about the film: www.headgamesthefilm.com
Learn more about chronic traumatic encephalopathy: www.bu.edu/cste

Now Recruiting: Repetitive Brain Trauma Study

A new study at the Boston University Alzheimer’s Disease Center and Center for the Study of Traumatic Encephalopathy needs volunteers who have participated in contact sports that put them at higher risk for experiencing repetitive brain trauma.

Eligible participants will be between ages 50 and 79 with at least five years’ experience in boxing, football, rugby, ice hockey or wrestling. Two of those years must have been on the collegiate, semi-professional or professional level or as part of an organized recreational league.

Want more information? Contact Eric Steinberg: egstein@bu.edu or 617-638-5368