On a drizzly spring day in April 2009, I walked into the elaborate lobby of the historic Omni William Penn Hotel in downtown Pittsburgh, notebook in hand, for a group interview with a family from North Dakota. I had no notion of the impact that the interview would have on my life nor how important these people would become to me.

I was there because the Alzheimer Disease Research Center (ADRC) at the University of Pittsburgh had hired me to write an article for Pathways about the DeMoes of Tioga, N.D., who were long-time contributors to a study headed by ADRC Co-Director William Klunk. I knew relatively little about Alzheimer’s disease and next to nothing about the family beyond some background information I had been given in advance. When you’re a freelance journalist, you typically don’t pick and choose the topics you write about; there’s a lot of on-the-job learning involved. It’s actually one of my favorite things about my profession: I truly do learn something new every day.

But nothing in my experience could have prepared me for what that day would bring. I didn’t know how deep a dive I would take into the world of Alzheimer’s disease, one of the great medical mysteries of our time. I would trace the steps of doctors who rode through the mountains of Colombia and pored over church records in rural Italy. I would learn about the rogue geniuses—half-neuroscientists, half-antropologists—who lived among the people they studied to better understand their mysterious afflictions and of young scientists who dedicated their careers to understanding a disease of the old.

Karla, the de facto DeMoe family spokesperson, met me in the lobby and took me up to their suite. Inside were Karla’s mother, Gail; her sister, Lori; her brothers, Dean and Doug; her niece, Kassie; and Kassie’s husband and young daughter. I walked into the chaos and scribbled furiously as they talked:

Dean — memory testing.
Worst part.
Their dad had it. Autopsy confirmed it, but it was so rare.
Lori — “You know you’re going down eventually.”
Kassie has not been tested yet.
“I think about it every day anyway. I repeat things + wonder if I have it.”

And boy, did they hate the MRI scans they did as part of the study.

Dean — “The night before, you try to stay up as late as possible.”
Doug — “You just lay there like you’re dead.”

Their story was astonishing. Gail DeMoe and her husband, Galen, had six children: Brian, Karla, Lori, Doug, Dean, and Jamie. Galen died from early onset Alzheimer’s disease, but nobody thought much about the hereditary...
Food for Thought

If you follow the news on Alzheimer’s disease research, you may have noticed that various findings on the relationship between nutrition and cognition seem to be reported every day. Food for Thought is designed to help you keep pace with this rapidly expanding area of research.


WHAT THEY DID: Some evidence suggests that specific chemicals in soy, called isoflavones, may improve cognitive health in women. Soy isoflavones are a particular type of micronutrient that is found in a number of plants and vegetables and is thought to mimic the effects of estrogen in the body. To better understand the potential benefit of soy isoflavones, Henderson’s team conducted a trial of isoflavone-rich soy protein in 313 healthy postmenopausal women between the ages of 45 and 92. The study participants received either 25 g per day of isoflavone-rich soy protein, which contains 91 mg of isoflavones, or 25 g per day of milk protein for two and a half years. Participants underwent assessments of memory and thinking, known as cognitive tests, before and after the intervention.

WHAT THEY FOUND: There were no differences in the overall cognitive test performance between the participants who received isoflavone-rich soy protein and those who received milk protein. However, participants in the isoflavone-rich soy protein group had greater improvement on specific tests of one aspect of memory (called visual memory) than those in the milk protein group. Because isoflavones are thought to be the effective component (or active ingredient) of soy protein, these findings suggested that isoflavones may have no beneficial effect on overall brain functioning but may improve visual memory.

THE BOTTOM LINE: Henderson and his colleagues concluded, “For healthy postmenopausal women, long-term dietary soy isoflavone supplementation in a dose comparable to that of traditional Asian diets has no effect on global cognition but may improve visual memory.” The group also noted that its research found no evidence of risks or adverse events associated with consuming a high-soy diet.

By Chendi Cui and Akira Sekikawa, Department of Epidemiology, University of Pittsburgh Graduate School of Public Health

An Assignment, a Family, and a Journey

Continued from page 1

factors until 2004, when Brian and Doug began to struggle in their jobs in the North Dakota oil fields where they had worked all their lives.

Unbeknownst to any of them, Galen had carried an extremely rare genetic mutation that guaranteed he would develop Alzheimer’s disease in his 40s and die in his 50s. Worse yet, five of his six children—everyone except Karla—had inherited the gene. Those who had it bore a 50 percent chance of passing it on to their own children, and all had established families by the time they knew. Brian, the oldest sibling and Kassie’s father, was already in a nursing home.

What astonished me was their approach to what was happening to them. Instead of dwelling on the devastation of their predicament, they had made a collective choice: They would fight back. So they agreed to become test subjects—first at the National Institutes of Health, then later at the ADRC—to give science an unprecedented opportunity to watch Alzheimer’s disease unfold in real time in their brains.

Thanks to Pittsburgh Compound B (PiB), the radiotracer developed by Klunk and his Pitt colleague Chester Mathis, researchers were able to watch the development and proliferation of amyloid plaques, one of the signature proteins of AD, in living patients. Prior to the development of PiB, which took several years of trial and error, doctors could only look at amyloid under a microscope during autopsy.

Now, with the DeMoes, they could see amyloid growth in its earliest stages, years before any symptoms were apparent. In time, they also would be able to watch the growth of tau, another signature protein, as well as other brain changes related to the disease and line those up against a person’s cognitive tests to parse out which stages are associated with diminished brain function.

Continued from page 1
By better understanding the disease’s biological progression, science is more precisely able to develop treatments that focus on halting Alzheimer’s in its earliest stages, which is thought—as is the case with many complex diseases—to be the point at which an intervention is most likely to succeed.

By the time I walked out of that hotel room, hours had passed, but I felt as though I had only scratched the surface of the DeMoes’ story. I walked to the parking garage in a stupor, and when I went to unlock my car door, I realized I was shaking. All I kept thinking was, “The world needs to know what these people are doing.”

In that moment, I had a thought that was both exhilarating and terrifying: I should write a book about them. Only I didn’t really have any experience in the publishing world, which is different from the news business, where I had worked all my life. I had no contacts. I had no agent. What I had were two young children, bills to pay, and a job that required a lot of hustle. I put the idea on the back burner, where it simmered for another year and a half.

And then Brian DeMoe, a man I never had the chance to meet, forced my hand. He died in December 2010. The realization smacked me in the face: This was the only way I knew how to do it. I would be using their real names. I would not be fictionalizing anything. I would be talking to the people it was about still having the ability to talk to me. I called Karla.

Surprisingly, she remembered me. She agreed to take my proposal to the publishing world, which is different from the news business, where I had worked all my life. I had no contacts. I had no agent. What I had were two young children, bills to pay, and a job that required a lot of hustle. I put the idea on the back burner, where it simmered for another year and a half.

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Surprisingly, she remembered me. She agreed to take my proposal to the rest of her family. I outlined it up front: I would not be fictionalizing anything. I would be using their real names. I would be asking them hard questions. This was the only way I knew how to do it.

A few days later, Karla reported back to me with their answer. They were all in.

After that, everything seemed to fall into place. A former work colleague had written a book and walked me through the process, then offered to introduce me to his agent, who loved the idea and signed me. We pitched it to Simon & Schuster, Inc.; they bought it. And then I began writing the book that would become The Inheritance.

Five years passed before the book would finally become a reality, and not everyone who started that journey lived to see its end. I will never fully wrap my head around the trust that the DeMoes placed in me as I wrote their story. They became my family. We even coined a name for our relationship: I was their “author-in-law.”

At first, I tried to keep them at arm’s length, as I’d been trained to do. I didn’t tell them much about my personal life. I let them in on only the superficial details.

But, in time, that kind of distance became impossible. “They’re disarming,” Klunk would later say to me, and he was right.

When I began writing the first draft in December 2012, Gail DeMoe wrote me a letter of encouragement. “We are so very lucky to have you in our lives,” she wrote. “God knew what he was doing!” I tacked it up on the bulletin board over my desk. Every day, I strove to be worthy of her faith in me.

Six months later, the woman I had come to know as “Grandma Gail” died from a heart attack. In the years that followed, as I pored over draft after draft, trying to find the right words, I would look at that note and think of her. I felt a sometimes overwhelming sense of responsibility.

I danced at DeMoe family weddings. I held DeMoe babies. I sat quietly with my notebook as younger family members learned their fate. I crisscrossed the country learning everything I could about Alzheimer’s disease, about genetic mutations, about drug development and clinical trials and government funding. I watched researchers design their attack using the history of how other seemingly intractable diseases were solved.

In March 2016, I stood before a congregation in the church down the street from the DeMoe family home and gave a eulogy for Lori, who fought Alzheimer’s disease with everything she had until the day she died: You know you’re going down eventually. In April 2017, I stood in the same spot, in the same church, and gave a eulogy for Doug, who had wrapped me in a bear hug the day I left the William Penn Hotel.

I remembered what Lori had said the first time I met her about her sister Karla—that it was hard for to be the sibling who didn’t have the mutation because you had to watch the others die. “Imagine her,” Lori had said then, in that hotel suite. “How would you like to be her?”

Eight years later, I am beginning to understand the answer to that question. I have no doubt that, one day, science will solve Alzheimer’s disease. When that day comes, I hope the rest of us will remember the price that was paid for that singular achievement. And I hope I will be celebrating with the DeMoes.

The Inheritance: A Family on the Front Lines of the Battle Against Alzheimer’s Disease by Niki Kapsambelis, published by Simon & Schuster, is available for purchase in local bookstores and online.
As readers of the *Pathways* newsletter know, the Alzheimer Disease Research Center is committed to offering a wide range of programs that allow us to engage with local community members and heighten public awareness about Alzheimer’s disease (AD) and brain health. One of our flagship community outreach programs is the Walter Allen Memorial Lecture Series. Offering two lectures per year, this series brings researchers and clinical experts to community settings for interactive educational programs. It is named in honor of Allen, a prominent African American photographer who worked for *The Pittsburgh Courier* in the 1950s and ’60s and was later diagnosed with AD.

The spring 2017 lecture, cosponsored by the Alzheimer’s Association Greater Pennsylvania Chapter, was held on May 4 at the Hill House Association in Pittsburgh’s Hill District. Titled “Getting the Most Out of Health Care Visits,” this panel-style discussion featured four local experts who spoke on strategies to help caregivers of people with memory loss experience smoother and more effective communication with health care providers. The panel was composed of geriatric psychiatrist Lalith Solai, geriatrician Rollin Wright, occupational therapist Pamela Toto, and pharmacist Jennifer Pruskowski. We thank all of these experts for joining us and our partners at the Alzheimer’s Association for providing an informative and engaging discussion.

The next Walter Allen Memorial Lecture is scheduled for Thursday, September 28, 2017, at 2 p.m. in the Kaufmann Center at the Hill House Association. We are excited to have Dr. Goldie S. Byrd as the featured speaker. Dr. Byrd is the founding director of the Center for Outreach in Alzheimer’s, Aging, and Community Health (COAACH) and the Nathan F. Simms Endowed Professor at North Carolina A&T State University. Her research activities include studying genetic susceptibility to AD in African Americans and using tools to identify genetic variants that may contribute to AD in African Americans and Hispanics. Dr. Byrd also has performed several studies geared toward increasing research participation by African Americans and understanding barriers to recruitment within that population. She has successfully developed a statewide outreach program at COAACH to heighten awareness of AD and stimulate research participation among African Americans. She regularly speaks to the public about her personal connection to AD and her passion for eliminating AD-related health disparities. Please mark your calendars to attend this final Walter Allen Lecture of 2017.

For up-to-date information about the Alzheimer Disease Research Center, the Brain Donation Program, clinical trials, and community presentations, please visit [www.adrc.pitt.edu](http://www.adrc.pitt.edu).
Q: If I am taking a memory medication, like Aricept, can I still qualify for a clinical trial?

A: At the Alzheimer Disease Research Center, participants may have opportunities to join clinical trials. Most clinical trials allow for potential participants to continue taking certain medications that are currently approved for mild to moderate Alzheimer's disease (AD), including Aricept (donepezil), Exelon (rivastigmine), and Razadyne (galantamine), as well as treatments from a different category of AD medication, like Namenda (memantine).

It is most important that potential participants share all of the prescription medications, nutritional or other supplements, and over-the-counter medications they are taking with the research team when being evaluated for a clinical trial. Certain clinical trial treatments could be harmful to individuals if they are combined with particular medications. Some medications, if taken during a clinical trial, might give researchers inconclusive or false results about the treatment being tested. In addition to minimizing side effects and ensuring accurate trial results, it also is important that individuals entering a clinical trial are stable on their medications, meaning they should be taking the medications as directed on a regular basis for a period of time prior to the clinical trial. This will help researchers to understand how people are tolerating their current medication when they are in their usual state before beginning treatment as part of a clinical trial. Some trials will require certain timelines of stability, such as three months of stability on a memory medication, before being screened for a study. All of the information about stable medications that are or are not allowed to be used is fully discussed before a potential participant enters into a clinical trial.

Participation in clinical trials provides vitally important information for scientists and researchers as they search to identify new treatment options and, ultimately, a cure for AD.
Spending Quality Time with a Person with Alzheimer’s Disease

By Sarah Goldberg, MS

People do not often think of Alzheimer’s disease beyond those experiencing the symptoms of the disease, but caregivers, family members, and friends of all ages are trying to help their loved ones along the way, too. The estimated 5.5 million Americans with early or late-onset Alzheimer’s disease¹ are just the tip of the iceberg of those affected by the disease. Even teenagers and young adults witness parents, grandparents, other family members, and friends manage the symptoms of Alzheimer’s.

Despite the nature of your relationship or past experiences together, it can be a struggle to stay connected with someone with Alzheimer’s as the days pass. How do you spend quality time with someone who may not remember you, speak clearly, reason well, or behave as expected? How do you nurture your relationship when the disease is changing the person you care about?

Here are some ideas of things you can do to communicate or spend time together even as someone starts having trouble interacting with you. Remember that being with someone does not always require a lot of conversation (for example, you can look through photos or take a walk). Thoughts and feelings can be shared without speaking by making eye contact, using gestures (like thumbs up or thumbs down), giving hugs, holding hands, or giving a pat on the back. Still stumped? Brainstorm with family members, friends, information specialists at the Alzheimer’s Disease Education and Referral Center, or staff members at the Alzheimer’s Association on how to adapt activities you both enjoy together.

1 2017 Alzheimer’s Disease Facts and Figures, Alzheimer’s Association

Ten Tips on How to Stay Connected to a Person with Alzheimer’s Disease

By Amy Rubin

1) Don’t argue or reason. Get in touch with his or her current perception of life and how he or she is feeling.

2) It’s okay to laugh. Try to incorporate humor if you can.

3) Keep a two-way conversation going for as long as possible. Don’t just talk at him or her, talk with him or her.

4) Be patient. The person needs more time to process information and carry out activities.

5) Keep activities simple. Play easier versions of favorite games (for example, Crazy Eights rather than Bridge).

6) Talk about past memories and growing up. Use pictures and home videos to start conversations.

7) Use music. Listen, sing, dance, and talk about his or her favorite singers and performers.

8) Use art. Draw, paint, color, sculpt, and use all different types of mediums to develop simple projects.

9) Garden. Arrange colorful potted plants indoors and outdoors.

10) Dine out or cook food at home together. Make sure the person is safe if you are cooking. If you are going out to eat, help him or her by giving two or three meal choices rather than a larger menu.

Please contact the resources below for more activities and supportive materials.

Alzheimer’s Association 24/7 Helpline 1-800-272-3900 alz.org

National Institutes of Health Alzheimer’s Disease Education and Referral Center: 1-800-438-4380 www.nia.nih.gov/health/altzheimers
ADNI3 Research Study Expands and Seeks New Volunteers

The Alzheimer’s Disease Neuroimaging Initiative (ADNI)—the long-running National Institutes of Health-supported study—has entered a new phase of discovery with the launch of ADNI3. Expansion of the groundbreaking study, now in its 13th year, will further develop ways to speed up clinical trials by providing researchers with the biomarkers or measurable indicators needed to detect the onset and track the progression of Alzheimer’s disease (AD).

The study matches changes in clinical and cognitive test results with AD-related changes in biological markers detected in blood, cerebrospinal fluid (body fluid found in the brain and spine), and DNA samples donated by volunteers. Brain scans will identify specific brain changes such as changes in brain volume and the presence of amyloid plaques, which are a hallmark of the disease. ADNI3 will add brain scans that detect tau protein tangles, another indicator of the disease. These studies enable scientists to better understand AD-related chemical changes and how genes influence the disorder.

By identifying and validating such biomarkers as abnormal levels of amyloid protein, ADNI has led to insights into who may be at risk for the disease and how AD-related brain changes correspond to clinical findings. In recent years, these game-changing discoveries have advanced clinical trial design and led to the testing of promising interventions.

"ADNI3 will move the bar higher and add new excitement along the lines of early detection," said National Institute on Aging Director Richard J. Hodes. "These insights are vital to researchers and clinicians working worldwide in their selection of clinical trial volunteers and the testing of promising interventions."

The ADNI3 study will seek up to 1,200 volunteers over the age of 55 to join about 800 current participants at 60 sites in the United States and Canada. The volunteers will represent the full trajectory of the disease, including those with normal cognition, mild cognitive impairment (often a precursor to AD), and Alzheimer’s dementia.

New Blood Test Aids Pitt Alzheimer Research

By Alexis Carter, staff writer at The Pitt News

With a new blood test, ADRC researchers are hoping to determine whether the content of someone’s blood could indicate if their learning and memory abilities are in danger of diminishing.

In a recent study, ADRC researchers Oscar Lopez and James Becker—in collaboration with researchers from the University of Chile—found higher ratios of abnormal tau levels in patients diagnosed with Alzheimer’s compared to the control group. Tau is a protein that keeps the brain’s nerve cells healthy. The proteins bind to microtubules—tube-shaped structures that shuttle nutrients from one end of the brain nerve cells to the other—and allow them to communicate with one another.

In Alzheimer’s disease—which slowly destroys memory, thinking and the ability to perform simple daily tasks—abnormal tau proteins detach from the tube-like structures found inside the cell. The abnormal tau proteins become tangled, meaning nutrients cannot move among pathways between the brain and the body, and communication among surrounding nerve cells is severed.

These higher ratios are associated with lower brain volume in areas important for learning and memory. A blood test that can detect the ratio of tau in the blood stream could become a diagnostic tool for patients with Alzheimer’s—making it easier to identify the disease early on.

"The importance of the early diagnosis is that if the right measures are taken at the right time, that will save money, and the burden of the disease will be reduced," Lopez said.

"A lot of caregivers who are family members may think, 'Is this going to happen to me?'" Maryn Formley, volunteer support group facilitator at the Hill House for the past four years, said. "A mechanism for early detection is great as long as it's affordable and accessible."

This article is excerpted with permission from the story "New Blood Test Aids Pitt Alzheimer’s Research," which was first published in The Pitt News on February 15, 2017.

While the new blood test is an exciting development along the lines of early detection, it is important to note that this study’s findings are experimental—meaning they need to be replicated before any definite conclusions are drawn.
With Gratitude

The University of Pittsburgh Alzheimer Disease Research Center thanks the following individuals and organizations for their generous donations received between December 1, 2016, and June 6, 2017.

In Memory of

Tom Abbey
   Judith Abbey

James C. Belz
   Paul Belz and Kathryn Roark
   Patricia Crumrine
   Todd Derr and Amy March
   Dorothy J. Kelly
   Paul and Mildred Kovacik
   Annie Moran-Rue
   Charles A. Rexrode II

Michael A. Benedict
   Eugene Benedict

Jane Bevan
   Samuel and Beatrice Moore

Joanne P. Blair
   Edward Blair

Frances E. Bodnar
   Constance L. Davies-McFadden
   Kristin Gaydosh
   Deborah Holliday
   Wendy L. Roehrich Hall
   Thomas and Diane Sixsmith
   Carol Tabas

Donald Bredl
   Reynolds School District
   board members, administrators, and employees

Elaine Buettner
   William Buettner

Valentino Buttignol
   Carol Buttignol

Rose Cepits
   Edwin and Dorothy Mann
   The Team at Talbots

Mr. and Mrs. Larry Coffelt
   Louis R. Franzini Jr.

Marie Culp
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   Jamie Typovsky

Jack Hays
   Mary Jane Ellis

W. Arch Irvin Jr.
   Vincent Cisanti

Phyllis R. Johnston
   Robert, Gretchen, Preston, and Landon Bazala
   Grey D. and Debra Pratt
   Grey E. Pratt
   Thomas, Heather, Rylee, and Kassady Shrimp
   Charles and Nikki Turley

Major General Dennis Jones
   Tom and Marilyn Smith

Betty Louise Jordan
   C & E Sales, Inc.
   Lesa Kuebler
   The staff of the Student Financial Services Office at Clarion University of Pennsylvania

Elizabeth K. “Betty” Kenney
   John and Donna Abriola
   Albert Albrecht
   Alycon Wealth Partners
   Robert and Eileen Bametzrieder
   Adam and Lissa Broome
   Annette J. DeVito Dabbs
   Drs. Jonathon and Judith Erlen
   Martin Fellows
   Shaun L. Fleming
   Michelle Heller
   Lori A. Jockel
   Martine L. Kostanich

Sergio and Elena Lazzaris
Robert Lee
Kathy Sue Magdic, DNP
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Thank you!

Your contributions are greatly appreciated and help to support research and education in the area of Alzheimer’s disease. You can remember or honor a loved one by sending your donation to:

**University of Pittsburgh**
Alzheimer Disease Research Center
UPMC Montefiore, Suite 421 West
200 Lothrop Street
Pittsburgh, PA 15213-2582

If you no longer wish to receive issues of *Pathways*, please contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.
Volunteer!

Get involved! We are in constant need of participants for several research studies and invite anyone with interest to call the University of Pittsburgh Alzheimer Disease Research Center at 412-692-2721 or e-mail oakleym@upmc.edu.

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Alzheimer’s Disease Neuroimaging Initiative 3 (ADNI3) Study

**Description:** The overall goal of this study is to determine the relationships among the clinical, cognitive, imaging, genetic, and biochemical biomarker characteristics of the entire spectrum of Alzheimer’s disease (AD) from its earliest stages. Subjects will undergo longitudinal clinical and cognitive assessments, computerized cognitive batteries, biomarker and genetic tests, PET (FDG, amyloid, and tau) and MRI scans, and cerebrospinal fluid collection.

**Study Length:** Up to five years

**Study Requirements:**
- 55–90 years of age
- Normal cognition or a diagnosis of mild cognitive impairment or AD
- A study partner who will accompany you to all study visits

**Contact:** MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu

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A4 Study

**Description:** The Anti-Amyloid Treatment in Asymptomatic Alzheimer’s (or A4) Disease Study is among a new generation of clinical trials being developed to test therapies that might prevent, or at least delay, the onset of Alzheimer’s disease in cognitively normal people who may be at risk, as evidenced by a PET scan.

**Study Length:** Three years

**Study Requirements:**
- 65–85 years of age
- Normal thinking and memory abilities
- A study partner who has contact with you at least once a week and who can answer questions about you once a year (contact may be in person or by phone)
- Willingness and ability to receive intravenous infusions of the investigational treatment (solanezumab) or a placebo every four weeks for three years

**Contact:** MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu
Biogen (Engage-Emerge) Study

**Description:** This study will evaluate the efficacy and safety of an investigational drug (aducanumab) in individuals with early, mild Alzheimer’s disease or certain types of mild cognitive impairment (MCI). Study medication is administered by a once-a-month infusion.

**Study Length:** 18 months

**Study Requirements:**
- 55–85 years of age
- A diagnosis of AD or certain types of MCI
- A study partner who will accompany you to all study visits (once a month)

**Contact:** Carolyn Rickard at 412-692-2707 or mishlercj@upmc.edu or MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu

Connectomes in Brain Aging Study

**Description:** This study will determine how different parts of the brain are connected and how these connections allow people to think, behave, and feel. The study will involve two to three days of scanning and tests. Some participants will be asked to return after two years for additional tests.

**Study Length:** Two to three days for all participants; two years for some participants

**Study Requirements:**
- 50–89 years of age
- Normal cognition or a diagnosis of mild cognitive impairment or Alzheimer’s disease

**Contact:** MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu or Rebecca Roush at 412-586-9860

ADRC’s Collaboration with the Andy Warhol Museum: Eight Years Strong

2017 marks the eighth year that the Andy Warhol Museum has partnered with the University of Pittsburgh Alzheimer Disease Research Center (ADRC) to provide an innovative social engagement program for people with memory impairment and their families.

The program evolved from a collaboration among contemporary Brazilian artist José Rufino, the Warhol, and the ADRC in 2009. Rufino had first traveled to Pittsburgh in 2008 to participate in an artists’ conference. That visit led to a return trip in 2009 for an artist residency in conjunction with the Warhol Museum’s exhibition Flipping Pop: Roots and Practices of Brazilian Contemporary Art and then the collaboration with the ADRC.

Rufino distinguished himself as an artist by exploring the subject of memory and interpersonal loss through art. During his collaboration with the ADRC, Rufino used his work to encounter and explore the lives of those affected by Alzheimer’s disease. On April 24, 2010, he presented his exhibition at the Andy Warhol Museum. Following Rufino’s visit to the Warhol, the museum and the ADRC continued their partnership by creating the current social engagement program.

Memory-impaired individuals and their family members are invited to participate in an upcoming Warhol Museum tour and artistic expression activity. The next program will be held on September 21, 2017, from 10 a.m. to 1 p.m. For more information or to register for the September program, contact the ADRC at 412-692-2700.