



Effective Translation of Alzheimer's Disease Research: Opportunities for Private Philanthropy

A report of a
multi-stakeholder
convening held
November 2015,
Marina del Rey,
California



Addressing the growing Alzheimer's epidemic

An estimated 5.2 million Americans age 65 and older have Alzheimer's disease (2016). By 2050, that number is projected to increase to 13.8 million.ⁱ The impact of a treatment that would halt, slow or modify the disease would have a tremendous impact.ⁱⁱ Although Alzheimer's disease research has made remarkable progress, and substantial efforts are underway to address the health and other costs of dementia, no therapies are in use today that will stop, slow, or prevent this disease. The enormous complexity of the human brain, the processes involved in development and progression, and animal models that do not accurately reflect the human disease, are recognized as some of the major barriers for successful translation of basic discoveries to effective therapies for Alzheimer's disease.

BACKGROUND

The dramatic increase in life expectancy in the United States has innumerable benefits—enhanced family and community contributions, greater economic productivity, and expanded opportunities for self-expression to name a few. Longer lives have also resulted in social, medical, and economic challenges of historic proportions. Alzheimer's disease, other dementias and cognitive problems—all of which become more common as we age—pose a particular challenge (See: *Addressing the growing Alzheimer's epidemic* sidebar).

In late 2015, The Rosalinde and Arthur Gilbert Foundation and the Santa Barbara Foundation in partnership with the American Federation for Aging Research (AFAR), took a deeper look at the challenges and opportunities associated with translational research in Alzheimer's disease. They gathered an esteemed group of stakeholders including philanthropic leaders, policymakers, and experts in Alzheimer's disease and aging research, representing a range of disciplines (See *Meeting Participants* on page 8).

This report summarizes the key learnings from this vibrant convening and provides guidance for philanthropic leaders considering how to invest most effectively in developing cures, treatments, and other interventions that reduce, and may even one day eliminate, the terrible toll that Alzheimer's disease exacts on our nation's families and communities.

STRATEGIC PHILANTHROPY

There are several ways that strategic foundations can make important contributions to Alzheimer's disease research. One such opportunity can be found in translational research—and specifically Type I translational research, which moves knowledge and discovery gained from the basic sciences into new drugs and treatments.

TRANSLATIONAL RESEARCH

Translational research is the conversion of basic research knowledge into practical applications to improve human health and well-being.

TRANSLATIONAL RESEARCH: A BRIEF OVERVIEW

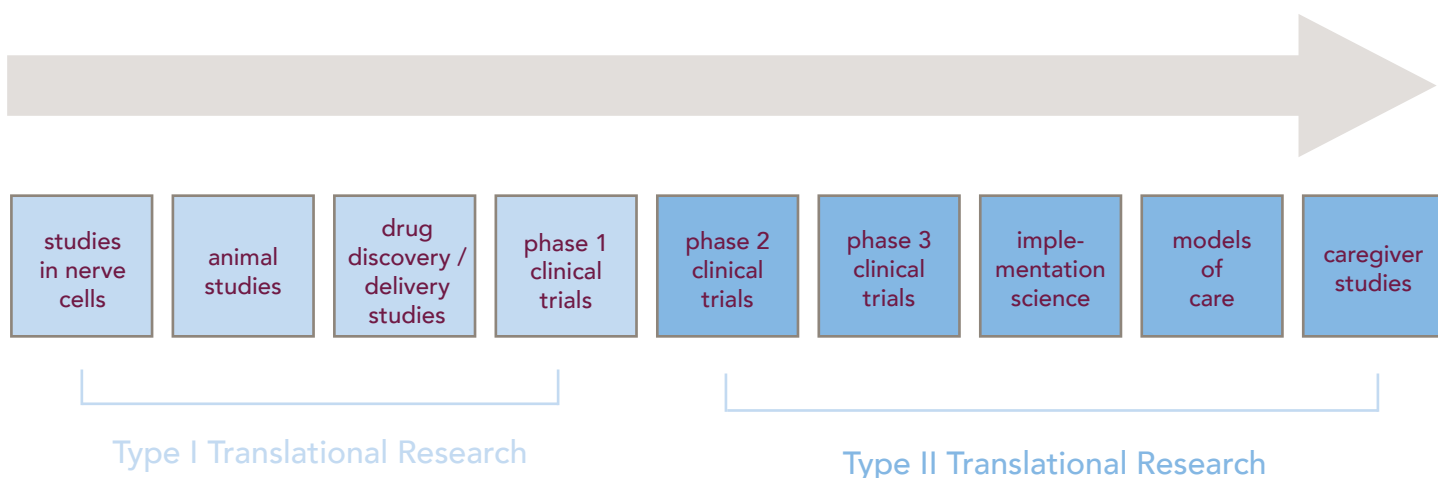
Translational research in Alzheimer's (and indeed all diseases) means different things to different people. In the broadest sense, translational research could be defined as a systematic effort to convert basic research knowledge into practical applications to improve human health and well-being. Translational research is often described in two broad phases of translation. Type I research is the movement of basic science discoveries into research that involves humans, while Type II is getting new clinical research findings adopted in the community (i.e., practitioners or the public).

Type I translational research includes studies in nerve cells or in animals, research into how a drug might be delivered, and what are called "Phase 1" clinical trials. These "Phase 1" studies test a new candidate drug or treatment in a small group of people for the first time to evaluate its safety, determine appropriate dosage, and identify side effects.

Type II translational research includes "Phase 2" trials that evaluate a drug in a larger group to assess its effectiveness, and "Phase 3" trials that study the drug in even large groups of people to confirm its effectiveness, monitor side effects, and compare it to commonly used treatments. This regulated process of drug development is a required component of the Food and Drug Administration review and evaluation of potential drugs and/or interventions for treatment. Beyond supporting drug development, translational research may also include "implementation science" that studies how care is delivered in hospitals and communities. In the case of Alzheimer's disease, this may also include studies of programs to help caregivers.

"Connecting research and patient care requires partnerships among a diverse group of stakeholders—researchers, clinicians, policymakers, funders, and representatives from academia, government and the private sector. Together we can bridge the bench-to-bedside gap."

- Martin H. Blank, Jr.,
The Rosalinde and Arthur
Gilbert Foundation



"How can we better package our science to make it accessible to the general public and to those who want to donate to the cause? What is the landscape? Who are our partners? We need to move together."

- Cynthia Carlson, MD, University of Wisconsin School of Medicine and Public Health

KEY CHALLENGES FACING TRANSLATIONAL RESEARCH

While there is a wide range of ways that philanthropy can participate in the translational research activities noted here, the meeting identified two major challenges:

Building the human capital necessary to enhance Alzheimer's research

The preponderance of NIH grants from 1995 through 2012 have gone to mid-career investigators (ages 41 through 50). The number of grants awarded to early-career scientists (ages 31 through 40) dropped significantly during that time. In sum, it is a challenging funding environment for new researchers in all areas of Alzheimer's research.ⁱⁱⁱ There are also struggles for physician-scientists, who combine clinical and traditional research training and may be particularly helpful in conducting translational research. Barriers for these researchers include a decreased emphasis on research methods in residency and lack of new alternative (and attractive) career paths available for these highly trained doctors.^{iv}

Limitations of the traditional design of translation targets and associated studies

The convening highlighted several critical limitations of translational research (which may also impact a broader range of studies) including:

- Failure to adhere to uniform guidelines for pre-clinical testing (that is, before Phase 1 trials).
- Lack of data sharing across laboratories studying similar compounds, which unnecessarily slows progress.
- Insufficient and inappropriate animal models that don't have the same characteristics older humans have (e.g., multiple co-existing diseases).
- Limited examination of the potential of new drug targets to make a difference in slowing or stopping the disease. In too many cases, research on these targets (generally molecules or disease pathways) doesn't ultimately lead to clinically relevant findings.
- Limited reproducible results prior to going into human studies.

"We need to convey to funders what the ecosystem of the science is, how each step drives toward the overarching need of the community."

- Ian Kremer, LEAD Coalition



OPPORTUNITIES FOR INVESTMENT

Given the broad landscape of public and private translational research initiatives currently underway and the challenges at hand, the convening sought to identify areas that need added focus and partnership, and identify ways that grantmakers, especially those new to the field, can think about and make important contributions to translational research in Alzheimer's disease.

Educate and engage funders

Funders need opportunities to come together and learn from experts in the field and from one another to build the knowledge, capacity, and most importantly, relationships needed to conduct effective grantmaking in translational research. Needs include convening funders to define translational research entry points, and bringing funders and scientists to the same table to discuss opportunities to fund research proposals where outcomes are clearly measurable. Meetings organized by Grantmakers in Aging, Grantmakers in Health, and the Health Research Alliance, for example, would provide opportunities for education and engagement around translational research.

Create a research agenda for grantmakers

The National Plan to Address Alzheimer's Disease includes a detailed listing of current federal activities and, as directed by the National Alzheimer's Project Act, initial recommendations for priority actions to expand, eliminate, condense, or coordinate programs. Under the National Plan's umbrella sits The International Alzheimer's Disease Research Portfolio ⁹, a database bringing together funded research supported by public and private organizations in the US and abroad. The database allows users to assess the portfolios of major organizations (currently 30+) for areas of overlap as well as opportunities to collaborate and coordinate in a collective effort to advance Alzheimer's research. While these broad and comprehensive research frameworks provide priority research directions, developing and communicating a specific, tailored agenda, including research areas needing funding at different levels, would help funders find the right translational research projects to support.

"Giving young investigators a couple of initial years to build their portfolios is essential...[It] keeps people in the field. The payoff is large for a small investment."

- Eileen Crimmins, PhD,
University of Southern California

Create opportunities for philanthropic collaboration and partnership

Philanthropies with a history of research grantmaking and/or experience with scientific advisory boards and review committees can play an important role in making sense of research opportunities for philanthropic peers who don't have these capacities. Funders may consider partnering to co-fund new initiatives or agree to co-invest in existing initiatives. Foundations can collaborate to drive more general information exchange, using funds to convene researchers and other stakeholders to explore under-attended-to scientific issues, such as publishing not only positive but also negative research results or facilitating data sharing among researchers.

Support early career investigators and team science

Many funders have a great deal of experience supporting individuals and their ideas. Young scientists face a variety of barriers to joining the Alzheimer's and translational research fields. Private support can sustain the research careers of new or junior investigators during challenging periods such as the transition from post-doctoral fellow to assistant professor. Solving the most important translational research challenges in Alzheimer's likely requires much larger teams of researchers and much greater cross-discipline collaboration. Private philanthropy can facilitate this team science and even promote collaborative, field-based competitions or prizes (such as an Alzheimer's Grand Challenge), dedicated to overcoming major technical hurdles or finding ways to diagnose, treat, delay, or even prevent the disease.

Make the field more welcoming to all stakeholders, including philanthropy

Broader societal stereotypes that associate aging with decline dampen many scientists' (and others') interest in the issue in the first place. Private funders can help support efforts to create a more positive story about Alzheimer's disease research—one that points to the tremendous possibilities for this science, and highlights the work of the best and brightest scientists devoting their careers to this work. This story would also serve to motivate a wider range of grantmakers to invest grant funds in translational and other kinds of related science in this area.

MOVING TO ACTION

In addition to the analysis of challenges and opportunities described in this report, the convening's final session produced several concrete "action steps" that would enable private grantmakers to move the Alzheimer's disease translational research field forward immediately.

Convening

- Create opportunities for direct communication between scientists and foundations, bringing together people from different "silos".
- Hold face-to-face meetings with grantmakers through organizations such as Grantmakers In Aging, Grantmakers In Health, and the Health Research Alliance, and invite diverse stakeholders including the NIA and NIH.

Information Sharing

- Streamline electronic information resources from the NIA and NIH, so they are lay-friendly and more useful to private philanthropy and other stakeholders.
- Craft a series of case stories attractive to potential funders/investors (on how Alzheimer's disease affects communities and promising research areas that merit more attention), and disseminate these through publications such as Philanthropy magazine and other channels.

Communications

- Alert the public to hopeful advances and promising research areas in the field through engaging stories in health magazines and the national media to stimulate public support for translational research in Alzheimer's disease.
- Partner with organizations such as the Alzheimer's Association and AARP, who have been successful in consumer education and awareness, and expand or build on these initiatives.
- Shape and conduct a positive public information campaign to counteract negative stereotypes and the fatalism surrounding Alzheimer's disease.

Training and Career Development

- Convey to funders what scholarships or early-career translational research support will actually do, particularly how this funding sustains an investigator's career and can lead to a lifetime of research and impact.
- Push for training programs to help investigators tell their stories in brief, lay-language presentations, videos, and articles.
- Identify career stages where researchers are most likely to leave the field; educate and engage funders about how they can support developing scientists at these critical junctures.
- Encourage foundations to invest in the career development of new investigators, funding cross-disciplinary teams under the supervision of a senior scientist or funding scholarships or postdoctoral fellowships. Ask institutions to match these funds and disseminate success stories.

New Grantmaking Models

- Consider "crowd funding," in which a project is funded by raising monetary contributions from a large number of people.
- Explore portfolio investment models to take advantage of so-called "investment philanthropy," which includes venture philanthropy and impact investing.^{vi}

"We need to take down the silos between scientists and direct service providers. Everything overlaps. We don't want to do this alone."

- Helen Ramon, Bader Philanthropies, Inc.

FINAL REFLECTIONS

Grantmakers can play critical roles in accelerating progress in Alzheimer's disease translational research. This means supporting new researchers to grow the intellectual capacity and workforce needed to build on the scientific knowledge now under development. Grantmakers can also prime the scientific pipeline itself. Private philanthropy can provide structures and supports to help promising compounds get through the regulatory system efficiently.

Private foundations have natural advantages over other private and public investors in this space. They are independent, and willing and able to take chances and move quickly to fill gaps. Given their standing, grantmakers can support communications and mobilize advocacy around ideas supporting the common good. With all of these advantages in mind, private philanthropy can—and should—make significant and meaningful contributions to facilitate the effective translation of basic discoveries into effective therapies for Alzheimer's disease.



"We were pleased to work with the American Federation for Aging Research and The Rosalinde and Arthur Gilbert Foundation to bring together this group to discuss the role philanthropy can play in translational research. As a result of this convening, we realized new opportunities to involve individuals and organizations in the important research work being done to combat Alzheimer's disease."

**- Phylene Wiggins,
Santa Barbara Foundation**

Information reviewed by Heather M. Snyder, PhD, Alzheimer's Association, Senior Director of Medical and Scientific Operations, Medical and Scientific Relations

- i. <http://www.alz.org/facts/>
- ii. http://www.alz.org/alzheimers_disease_trajectory.asp
- iii. Hinman presentation
- iv. http://acd.od.nih.gov/reports/PSW_Report_ACD_06042014.pdf
- v. <http://iadrp.nia.nih.gov/>
- vi. <http://stm.sciencemag.org/content/6/241/241cm5>

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Convened by The Rosalinde and Arthur Gilbert Foundation and the Santa Barbara Foundation in partnership with the American Federation for Aging Research.

The Rosalinde and Arthur Gilbert Foundation

The mission of The Rosalinde and Arthur Gilbert Foundation is to invest in programs that promote education, tolerance, social services, healthcare, and the arts. The Foundation builds on the ideals and pursuits of its founders, Rosalinde and Arthur Gilbert. In the area of Alzheimer's disease, The Rosalinde and Arthur Gilbert Foundation focuses its grant-making on advancing research by early career investigators in the United States and Israel and investments in Alzheimer's disease caregiving. For more information, please see:

www.thegilbertfoundation.org



THE ROSALINDE AND ARTHUR
GILBERT FOUNDATION

The Santa Barbara Foundation

The Santa Barbara Foundation was established in 1928 to enrich the lives of the people of Santa Barbara County through philanthropy. As the largest community foundation in Santa Barbara County, California, and a major source of funding for local nonprofits, the foundation is committed to building philanthropy, strengthening the nonprofit sector and solving community problems.

To learn more, please visit: **www.sbfoundation.org**



American Federation for Aging Research

The American Federation for Aging Research is devoted to helping people live longer, healthier lives. Since 1981, AFAR has played a major role in advancing knowledge of aging by providing grants to scientists, physicians, and students conducting aging-related research. These investigators are committed to understanding the basic mechanisms of aging, and finding the causes, cures, and treatments of many age-related diseases, such as cancer, Alzheimer's disease, and diabetes. AFAR is committed to nurturing the talent and brainpower in aging research and geriatric medicine to ensure the health of millions of older people. Learn more about AFAR's work at **www.afar.org**



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