

NAPA Research Progress Report

NAPA Advisory Council Meeting

Richard J. Hodes, M.D.
Director
National Institute on Aging

October 27, 2014

New Alzheimer's-related Initiatives

Biomarkers of Alzheimer's Disease in Down Syndrome (R01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-15-011.html>

- NIA & NICHD

Interdisciplinary Research to Understand the Vascular Contributions to Alzheimer's Disease (R01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-15-010.html>

- NIA & NINDS

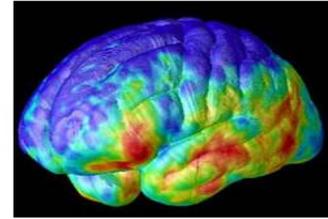
Immune and Inflammatory Mechanisms in Alzheimer's Disease (R01)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-15-018.html>

- NIA

2015 Summit Update

- February 9th-10th, 2015
- National and international participation anticipated
- Summit registration now open
<http://www.nia.nih.gov/about/events/2014/alzheimers-disease-research-summit-2015>
- G7 wrap-up on March 3-4, 2015, in Geneva, planned by the WHO



Progress on AD-Related Dementias

- Research recommendations from ADRD 2013 were published in *Neurology* on August 26, 2014.
- New Studies of FTD
 - FTD clinical research consortium to support the development of FTD therapies (NINDS & NCATS/ORDR)
 - Longitudinal natural history study of familial FTD (NIA & NINDS)
 - A large program project to understand the cellular disease processes that lead to ALS and FTD (NINDS)

Progress on AD-Related Dementias

- **Small Blood Vessels: Big Health Problems? Workshop**
 - Held September 18-19, 2014
 - Integrated research findings across organ systems, including the brain
 - Identified research gaps, which will be published in a white paper
 - Sponsored by NINDS, NHLBI, NEI, Office of Disease Prevention, Office of Research on Women's Health

IADRP 2.0 - <http://iadrp.nia.nih.gov/>



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INTERNATIONAL ALZHEIMER'S DISEASE RESEARCH PORTFOLIO

The International Alzheimer's Disease Research Portfolio (IADRP) database brings together funded research supported by public and private organizations both in the US and abroad all categorized using the [Common Alzheimer's Disease Research Ontology or CADRO](#). Launched in 2010 as a joint collaboration between the [National Institute on Aging \(NIH\)](#) and the [Alzheimer's Association](#), IADRP enables users the ability to assess the portfolios of major organizations (currently 30) for areas of overlap as well as areas of opportunities in which to collaborate and coordinate in a collective effort to advance AD research.

RESEARCH HIGHLIGHTS - NEW FUNDING ANNOUNCEMENTS

- [NIH – Alzheimer's Disease Pilot Clinical Trials \(R01\) PAR](#)
- [Alzheimer's Association – Biomarkers Across Neurodegenerative Diseases RFA](#)
- [Alzheimer's Research UK – Project Grants and Fellowships](#)
- [Alzheimer's Australia – Student and Early Career Investigators](#)
- [Alzheimer's Society of Canada – Young Investigator Awards](#)

HOW TO JOIN IADRP

The IADRP Project Team is currently seeking participation from public, private and international biomedical and public health organizations who fund Alzheimer's disease (AD) research. To find out more information about how your organization can contribute and help shape this effort, please contact **Charlene Liggins** (ligginsc@mail.nih.gov), **Nina Silverberg** (silverbergn@mail.nih.gov), or **Heather Snyder** (hsnyder@alz.org). [See [IADRP's Data Submission Process](#)]

IADRP QUICKSEARCH

Select CADRO Categories
<input type="text"/>
Funding Organization Name
<input type="text"/>
Funding Year
<input type="text"/>
_____ or _____
Fulltext Search
<input type="text"/>
<input type="button" value="Search Now"/>

IADRP – Current Members

US Organizations

- US Federal Government (6 agencies)
- Alzheimer’s Association
- Alzheimer’s Drug Discovery Foundation
- Ellison Medical Foundation
- Cure Alzheimer’s Fund
- Geoffrey Beene Foundation
- Patient-Centered Outcomes Research Institute
- State of Texas
- State of California
- State of Wisconsin
- State of Oregon
- State of Virginia

International Organizations

- Government of Poland
- Government of Australia
- Alzheimer’s Society of Canada
- Alzheimer’s Research UK
- Alzheimer’s Society of UK
- Alzheimer’s Australia Dementia Research Foundation
- UK Medical Research Council
- Federazione Alzheimer Italia
- Sao Paulo Research Foundation (FAPESP)

Currently coding and validating AD project data

- Brain Canada
- Canadian Institutes of Health Research

Using IADRP for Tracking and Reporting

The screenshot shows the IADRP website interface. At the top, the logo reads "IADRP International Alzheimer's Disease Research Portfolio" with the tagline "Communicate. Coordinate. Collaborate." Below the logo is a navigation bar with tabs: Home, Advanced Database Search, About IADRP, About CADRO, Visualize Data, Reports and Publications, and Help. The "Reports and Publications" tab is circled in blue, and a blue arrow points to it from the text below. The main content area features the heading "INTERNATIONAL ALZHEIMER'S DISEASE RESEARCH PORTFOLIO" followed by a paragraph describing the database. Below this is a section titled "RESEARCH HIGHLIGHTS - NEW FUNDING ANNOUNCEMENTS" with a list of links to various research projects. To the right, there is a "IADRP QUICK SEARCH" form with fields for "Select CADRO Categories", "Funding Organization Name", "Funding Year", and "Fulltext Search", along with a "Search Now" button.

REPORTS AND PUBLICATIONS

RECENT JOURNAL PUBLICATIONS

- [International Alzheimer's Disease Research Portfolio \(IADRP\) aims to capture global Alzheimer's disease research funding](#)
- [Common Alzheimer's Disease Research Ontology: National Institute on Aging and Alzheimer's Association Collaborative Project](#)

[NATIONAL ALZHEIMER'S PROJECT ACT \(NAPA\) STRATEGIC PLAN](#)

2012 AD RESEARCH SUMMIT RECOMMENDATIONS

- [Session 1: Interdisciplinary Approach to Discovering and Validating the Next Generation of Therapeutic Targets for Alzheimer's Disease](#)
- [Session 2: Challenges in Preclinical Therapy Development](#)
- [Session 3: Whom to Treat, When to Treat, and What Outcomes to Measure](#)
- [Session 4: Drug Repurposing and Combination Therapy](#)
- [Session 5: Nonpharmacological Interventions](#)
- [Session 6: New Models of Public Private Partnerships](#)

2012 AD RESEARCH SUMMIT RECOMMENDATIONS - IMPLEMENTATION MILESTONES (2014)

- [Drug Development: Repurposing and Combinations](#)
- [Drug Development: Currently Known Targets](#)
- [Drug Development: Novel Targets](#)
- [Development of Non-Pharmacological Interventions](#)
- [Biomarkers of Disease Progression](#)
- [Epidemiology](#)
- [Research Resources](#)
- [Partnerships to Accelerate AD Drug Development](#)
- [Infrastructure](#)
- [Study Recruitment and Participation](#)

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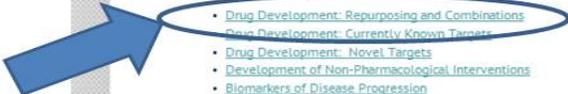
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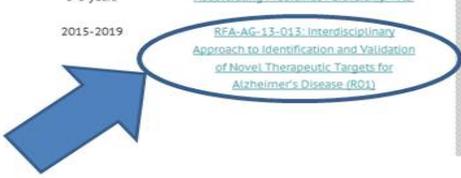


DRUG DEVELOPMENT: REPURPOSING AND COMBINATIONS

MILESTONE	SUCCESS CRITERIA	CADRO CODES	TIME REQUIRED	ACTIVITIES/PROGRESS
1.A: Convene an advisory meeting of experts from the pharmaceutical industry, government, academia, the FDA, and the non-profit sector to advance rational drug repositioning and combination therapy based on translational bioinformatics and network pharmacology approaches and to explore opportunities for new public-private partnerships to facilitate drug rescue/repurposing and combination therapy. [Summit 4.A, 4.B, 4.C, and 4.D]	Development of recommendations for rational repositioning and combination therapy development.		1 year	Accelerating Medicines Partnership - AD
	Development, negotiation, and implementation of appropriate agreements among the stakeholders involved in repositioning and combination therapy of drugs for AD. These agreements should address legal issues, intellectual property rights, and liability to expedite rigorous clinical testing of repurposed drugs.			2014
1.B: Initiate research programs for translational bioinformatics and network pharmacology to support rational drug repositioning and combination therapy from discovery through clinical development. [Summit 4.A, 4.B, 4.C, and 4.D]	Identification of at least 6 existing drugs suitable for repurposing and/or combination therapy for AD prevention or treatment.	Category C Translational Research and Clinical Interventions - 1 Drug Discovery	3-5 years	Accelerating Medicines Partnership - AD
	The drugs selected for repurposing or combination therapy will be prioritized based on...		2015-2019	RFA-AG-13-013: Interdisciplinary Approach to Identification and Validation of Novel Therapeutic Targets for Alzheimer's Disease (R01)

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Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Institute on Aging (NIA)
Funding Opportunity Title	Interdisciplinary Approach to Identification and Validation of Novel Therapeutic Targets for Alzheimer's Disease (R01)
Activity Code	R01 Research Project Grant
Announcement Type	New
Related Notices	<ul style="list-style-type: none"> December 12, 2012 - See Notice NDT-AG-12-020: Notice of Change in Due Date and Expiration Date.
Funding Opportunity Announcement (FOA) Number	RFA-AG-13-013
Companion Funding Opportunity	None
Number of Applications	See Section III.3, Additional Information on Eligibility.
Catalog of Federal Domestic Assistance (CFDA) Number(s)	93.956
Funding Opportunity Purpose	This funding opportunity supports integrative, interdisciplinary research focused on the identification and preclinical validation of novel therapeutic targets within molecular networks involved in different stages of Alzheimer's disease (AD) pathogenesis. The use of the multiple Program Director/Principal Investigator (PDI/PI) option aims to maximize the potential of team science efforts necessary to achieve the programmatic goals of this funding opportunity.

Key Dates

Posted Date	October 15, 2012
Open Date (Earliest Submission Date)	December 17, 2012
Letter of Intent Due Date	December 17, 2012
Application Due Date(s)	(New Date January 14, 2013 per NDT-AG-12-020). Originally January 13, 2013, by 5:00 PM local time of applicant organization.
AIDS Application Due Date(s)	Not Applicable
Scientific Merit Review	April/May 2013
Advisory Council Review	August 2013
Earliest Start Date(s)	September 2013
Expiration Date	(New Date January 15, 2013 per NDT-AG-12-020). Originally January 14, 2013
Due Dates for E.O. 12372	Not Applicable



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IADRP International Alzheimer's Disease Research Portfolio

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Category A. Molecular Pathogenesis and Physiology of Alzheimer's Disease (375)

Category B. Diagnosis, Assessment, and Disease Monitoring (1499)

Category C. Translational Research and Clinical Interventions

1. Drug Discovery (small molecules and biologics)

a. Amyloid (182)

b. Tau (52)

c. ApoE, Lipids, and Lipoprotein Receptors (44)

d. Neurotransmitter Receptors and Synaptic Plasticity (38)

e. Neurogenesis (11)

f. Inflammation (42)

g. Oxidative Stress (12)

l. Proteostasis (26)

FILTER BY FISCAL YEAR (FY)

2014 (3)

2013 (74)

2012 (374)

2011 (370)

2010 (370)

2009 (38)

2008 (38)

2007 (2)

2006 (2)

2005 (2)

FILTER BY FUNDING ORGANIZATION

Alzheimer's Association (35)

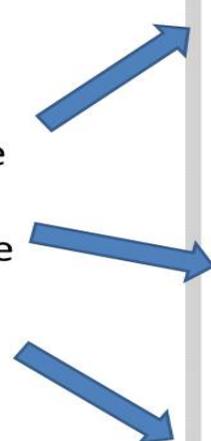
Alzheimer's Association Donor Research Foundation (2)

Alzheimer's Drug Discovery Foundation (2)

Project Number	Title	FY	PI Full Name
IRG-10-174897	_CSa Receptor as a Target to Slow Progression of Alzheimer's Disease_	2010	TENNER, ANDREA JOAN
3R21NS056911-01S2	A CELL-BASED SCREEN FOR INHIBITORS OF INTRACELLULAR BETA AGGREGATION	2008	DELISA, MATTHEW P
R21AG028462	A HIGH THROUGHPUT SCREEN FOR INHIBITORS OF AGGREGATION OF THE ALZHEIMER'S PEPTIDE	2008	HECHT, MICHAEL H
R21AG032405	A NEEDLE IN A HAYSTACK: NEW APPROACHES TO ALZHEIMER'S DRUG DISCOVERY FROM NATURAL	2009	WILLIAMS, PHILIP
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20110801	A New Treatment for Cognitive Disorders	2011	Costa-Mattioli, Mauro
1R03DA028852-01	A NONISOTOPIC HTS ASSAY TO ELUCIDATE CHOLINE TRANSPORTER (CHT) MODULATORS	2009	RUGGIERO, ALICIA M
261102.01	A novel apoE-derived therapeutic reduces AD pathology	2008	Laskowitz, Daniel
ART-PhD2007-5	A novel drug strategy for the treatment of Alzheimer's disease	2007	Gunn-Moore, Frank
20111012	A Novel Enantiomeric Diarylheptanoid Derived from Myrica cerifera as an Anti-Tau Therapeutic	2011	DICKEY, CHAD A
1 R43 AG044213-01	A Novel Small molecule TNF?? inhibitor as a disease-modifying AD drug treatment.	2012	GABBITA, SOMASUNDAR PRASAD
1 R21 AG040975-01A1	A Novel Strategy for Treating Memory Impairment in an Alzheimer's Disease Model	2012	HEGDGE, ASHOK N

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Home > RePORTER > Project Information

Project Information 5R21AG032405-02

Project Number: 5R21AG032405-02 Contact PI / Project Leader: WILLIAMS, PHILIP
 Title: A NEEDLE IN A HAYSTACK: NEW APPROACHES TO ALZHEIMER'S DRUG DISCOVERY FROM NATURAL Awardee Organization: UNIVERSITY OF HAWAII AT MANOA

Abstract Text:
 DESCRIPTION (provided by applicant): The long-term objectives of this research are to improve natural product drug discovery strategies and to use these improved strategies to discover new compounds that have the potential to be useful in treating Alzheimer's disease or as a tool for studying the biochemistry and physiology of Alzheimer's disease. The need for this research is substantial given the lack of any FDA approved drug therapies that have a significant effect on the progression of the disease. In that vein, the specific goals of this project are: 1. To develop an innovative BACE1 screening protocol that, for the first time, rapidly links a single compound within a mixture to the observed biological activity. This protocol combines a chemiluminescent assay, performed in 96-well plates, in series with a LC-MS homogeneous affinity assay. 2. To isolate and structurally characterize new substances from cyanobacteria and sponges testing positive in either screening assay, in order to test the hypothesis that natural products derived from these sources are a rational source of Alzheimer's drug leads. 3. To evaluate these compounds as potential BACE1 inhibitors. Compounds will be initially examined for potency, cellular activity, neuroprotective effect, BBB permeability, and P-gP interactions with further evaluations conducted as warranted. PUBLIC HEALTH RELEVANCE: The long-term objectives of this research are to improve natural product drug discovery strategies and to use these improved strategies to discover new compounds that have the potential to be useful in treating Alzheimer's disease or as a tool for studying the biochemistry and physiology of Alzheimer's disease. The need for this research is substantial given the lack of any FDA approved drug therapies that significantly affect the progression of the disease.

Public Health Relevance Statement:
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NIH Spending Category:
 Aging, Alzheimer's Disease, Brain Disorders, Neurodegenerative, Neurosciences

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Project Information

5R21AG032405-02

DESCRIPTION DETAILS RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS LINKS NEWS AND MORE

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5R21AG032405-02

DESCRIPTION DETAILS RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS LINKS NEWS AND MORE

Project Number: 5R21AG032405-02 Contact PI / Project Leader: WILLIAMS, PHILIP
 Title: A NEEDLE IN A HAYSTACK: NEW APPROACHES TO ALZHEIMER'S DRUG DISCOVERY FROM NATURAL Awardee Organization: UNIVERSITY OF HAWAII AT MANOA

ABOUT RePORTER RESULTS
 Publications: Publications missing? Principal investigators click here
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Title (Link to full-text in PubMed Central)	Journal (Link to PubMed abstract)	Authors	Similar Publications	Cited By
Isotriaroneol from <i>Ficus benjamina</i> and their inhibitory activity on BACE1	<i>Planta medica</i> , 2012 Aug; 78 (12): 1557-62	Dai, Jingqiu; Shen, Dal; Yoshida, Wesley Y.; Parrish, Stephen M.; Williams, Philip G		
Daidalosin A-C, fungal-derived BACE1 inhibitors	<i>Bioorganic & medicinal chemistry</i> , 2011 Nov 15; 19 (22): 6581-5	Sorribas, Analisa; Jimenez, Jorge I.; Yoshida, Wesley Y.; Williams, Philip G		
Stictamides A-C, MMP12 inhibitors containing 4-amino-3-hydroxy-5-phenylpentanoic acid subunits	<i>The Journal of organic chemistry</i> , 2011 Mar 20; 76 (10): 3635-43	Liang, Zhibin; Sorribas, Analisa; Sulzmaier, Florian J.; Jimenez, Jorge I.; Wang, Xin; Sauvage, Thomas; Yoshida, Wesley Y.; Wang, Guangji; Ramos, Jose W.; Williams, Philip G		
Diosponolides from a Guamanian Marine <i>Cyanobacterium</i> <i>Lynobia</i> sp. with selective inhibition of Serine Proteases	<i>Tetrahedron letters</i> , 2010 Dec 22; 51 (51): 6718-6721	Ruilo, Brent K.; Parrish, Stephen M.; Yoshida, Wesley Y.; Schupp, Peter J.; Schira, Tom; Williams, Philip G		
Sesosteroids A-D, BACE1 inhibitors from <i>Coniia sesostera</i>	<i>Phytochemistry</i> , 2010 Dec; 71 (17-18): 2165-73	Dai, Jingqiu; Sorribas, Analisa; Yoshida, Wesley Y.; Williams, Philip G		
Xestosaponins from the Indonesian marine sponge <i>Xestospongia</i> sp.	<i>Journal of natural products</i> , 2010 Jun 25; 73 (6): 1198-91	Dai, Jingqiu; Sorribas, Analisa; Yoshida, Wesley Y.; Kelly, Michelle; Williams, Philip G		
New methods to explore marine resources for Alzheimer's therapeutics	<i>Current Alzheimer research</i> , 2010 May; 7 (3): 210-3	Williams, P.; Sorribas, A.; Liang, Z		
Diclatolins, potential vinyl cyclooctane biosynthetic precursors to the diclatolins	<i>The Journal of organic chemistry</i> , 2010 Apr 2; 75 (7): 2399-402	Dai, Jingqiu; Jimenez, Jorge I.; Kelly, Michelle; Williams, Philip G		

Patents:
 Patent Number Patent Title
 No patents information available for 5R21AG032405-02

Publications

Patents