

TEXAS ALZHEIMER'S
RESEARCH CONSORTIUM

Overview & Update

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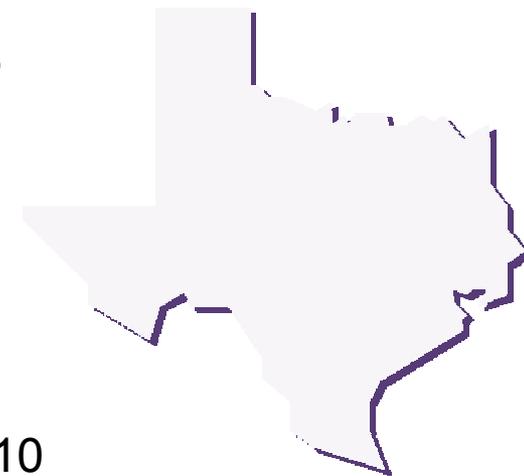
How Does Alzheimer's Disease Impact Texans?

Public Health Impact of Alzheimer's Disease Texas - 2010



Occurrence of AD in Texas

- Prevalence: 340,000 individuals with AD
- Incidence: >30,000 individuals with AD
- Annual Mortality: >4,200 deaths due to AD
- % cognitive impaired in NH (2005): 77%
- US rank in total number of cases: 3rd
- US rank in total number of deaths: 2nd



SOURCE: Alzheimer's Association Facts and Figures, 2010

Note: There are no formal studies published to date on the occurrence and cost of Alzheimer's disease in Texas. These estimates are extrapolated from studies of the total US population.

Public Health Impact of Alzheimer's Disease Texas - 2010



Annual costs to Texas

- Total economic burden \$14 billion
- Costs to businesses (coverage, loss of productivity) \$7 billion

Caregiver Challenges in Texas

- Number of caregivers >850,000
- Annual hours of unpaid care >950 million
- Annual value of unpaid care \$11.2 billion

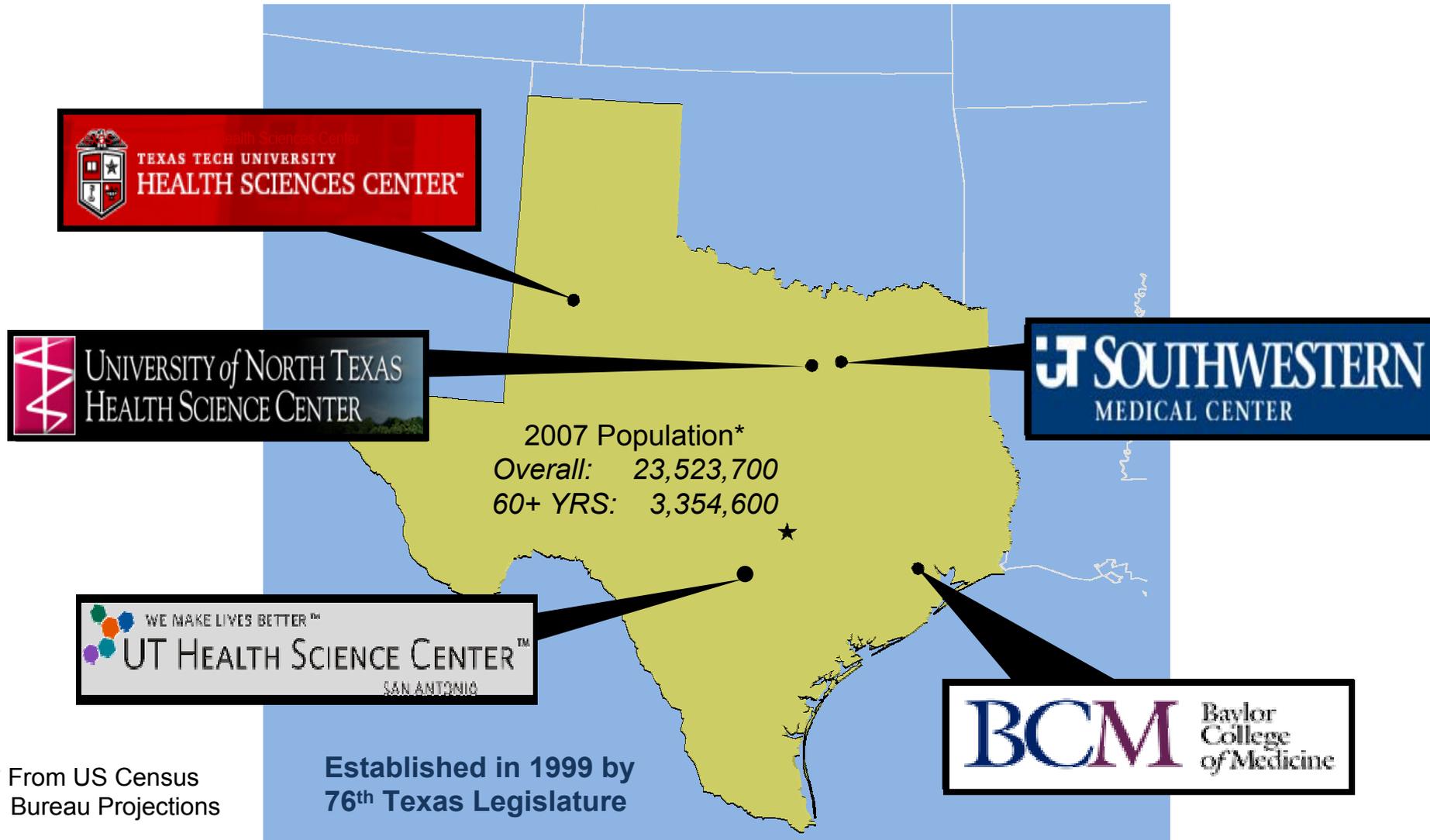
SOURCE: Alzheimer's Association Facts and Figures, 2010

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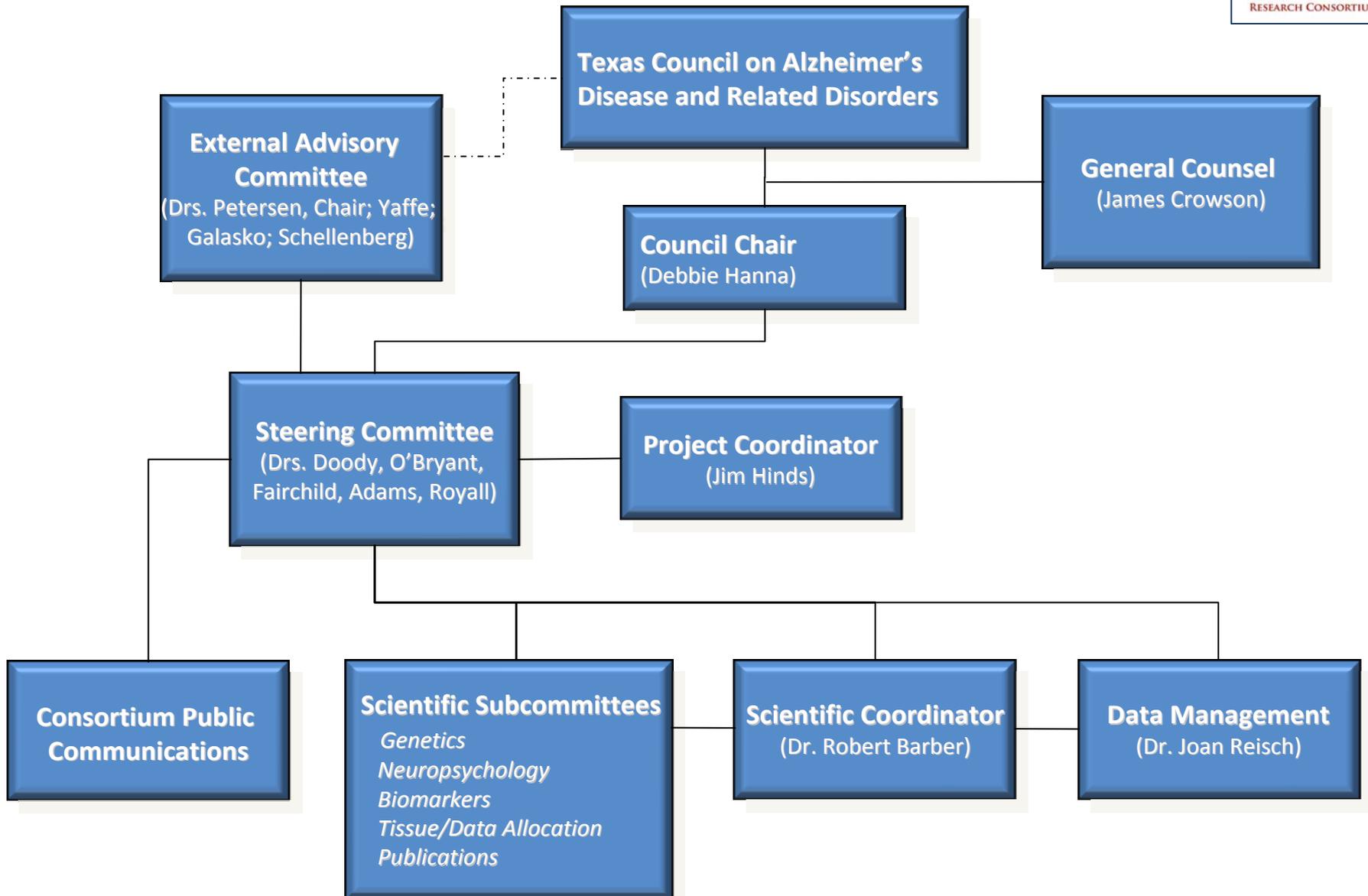
What is the Texas Alzheimer's Research Consortium?

Current TARC Sites



* From US Census Bureau Projections

Organizational Chart



Texas Alzheimer's Research Consortium

Timeline: September 2005 – August 2011



Biennium	Sep 05 – Aug 07		Sep 07 – Aug 09		Sep 09– Aug 11	
Funding	\$2 million		\$3.9 million		\$6.85 million	
Key dates	Jun 2006	Mar 2007	Jun 2007	Feb 2008	Jun 2009	Sep 2009
Research protocol development	Established goals and priorities	Recruitment begins	Expanded goals and priorities	Recruitment and follow up of research subjects	Amended recruitment goals; Added UTHSCSA, Hispanic and MCI subjects	Recruitment and follow up of research subjects
Recruitment goals		500 AD patients 100 Controls		200 new Controls		400 new Hispanic Controls; 80 new Hispanic AD patients; 125 MCI patients

Overview of Current Research



Study Design

- Construct an integrated centralized research database of clinical, neuropsychological, and biological data derived from baseline and annual follow-up examination

Overview of Current Research



Study Design

- Establish a longitudinal cohort of well-characterized individuals with AD, Mild Cognitive Impairment (MCI) and cognitively normal controls

- Enroll significant numbers of Mexican Americans to study how the disease process impacts this underserved ethnic group

Overview of Current Research



Research Objectives:

- Identify potential genetic factors associated with earlier age at onset among patients with AD

- Examine the role of biological and clinical markers for
inflammation
cardiovascular disease
cardiovascular risk factors
hyperinsulinemia

Current Research Methods



TARC Research Participants

- Recruitment – Completed
 - 500 Individuals with Probable AD
 - 300 Cognitively normal individuals

- Recruitment – Ongoing
 - Annual follow up of initial 800 subjects (incl. attrition replacement)
 - 125 Individuals with Mild Cognitive Impairment (25 Hispanic)
 - 80 Hispanic patients with AD
 - 300 Hispanic normal controls

Current Research Methods



TARC Examination procedures

- IRB approved informed consent obtained from all participants
- Standardized examination procedures across all five sites
- Comprehensive clinical, neurological, and neuropsychological evaluation
- Blood drawn for genetic, biomarker, and laboratory analysis and to biobank for future studies
- Complete annual follow-up examination
- Blood collected at annual follow-up examinations for biobank

*What Are Some Current and Emerging
Themes in Alzheimer's Disease
Research?*

Themes in Alzheimer's Disease Research

- ❑ Search for novel genes and biomarkers associated with Alzheimer's disease
- ❑ Identification of modifiable risk factors for Alzheimer's disease that may lead to preventative strategies
- ❑ Search for “at risk” groups who
 - a. Mild Cognitive Impairment (MCI)
 - b. At increased risk for developing MCI and AD
- ❑ How is Alzheimer's disease differentially manifest among diverse ethnic/racial groups?
- ❑ Are there subgroups of patients with Alzheimer's disease that may
 - a. Express Alzheimer's disease in a different manner
 - b. Respond better or worse to particular therapeutics



*How is the TARC Working to
Advance these Research Themes?*



Search for novel genes and biomarkers

- ❑ The TARC is collecting large-scale genetic and biomarker information on participants
- ❑ We have a biobank that is updated at each annual evaluation so change in biomarkers can be studied
- ❑ We are planning collaborations with other large-scale studies for combined analysis of pooled data
- ❑ TARC investigators are working to create a blood-test for Alzheimer's disease
- ❑ TARC investigators have data on novel genetic variations associated with the disease

Identification of modifiable risk factors that may lead to preventative strategies



- ❑ TARC investigators are studying diabetes, hyperinsulinemia, hypertension, among others
- ❑ We are investigating inflammation as a potential biological pathway for cardiovascular-induced cognitive decline/dysfunction
- ❑ Studying how these factors change over time
- ❑ We are now investigating how these factors may be differentially related to disease expression between non-Hispanics and Mexican Americans

Search for “at risk” groups



- The identification of Mild Cognitive Impairment as a prodrome for Alzheimer's disease was a major advancement to the field
 - TARC investigators have included MCI in the cohort to be followed over time
 - We are searching for novel genetic, biomarker, and clinical factors associated with progression of MCI to AD

- We are following non-AD controls over time to identify factors associated with the development of MCI and AD

Differential risk for Alzheimer's disease among various ethnic/racial groups



- ❑ The TARC recently added a 5th site, the University of Texas Health Sciences Center at San Antonio (UTHSC-SA) specifically for recruitment of Mexican Americans
 - UTHSC-SA is recruiting from a previously established longitudinal study, the San Antonio Heart Study
 - These Mexican American elders with and without MCI and AD will be followed over time to determine ethnic-specific risk factors for disease onset and progression

- ❑ TARC investigators are working towards collaborations with other ongoing Texas-based studies enrolling ethnic minorities

Identification of subgroups of patients with different disease mechanisms



- ❑ TARC investigators are searching for subgroups of Alzheimer's patients that are based on genetic, biomarker, and clinical information
- ❑ We are establishing a Translational Research Core specifically aimed at translating endophenotypes into targeted therapeutic trials



What Data Has the TARC Collected?

Texas Alzheimer's Research Consortium



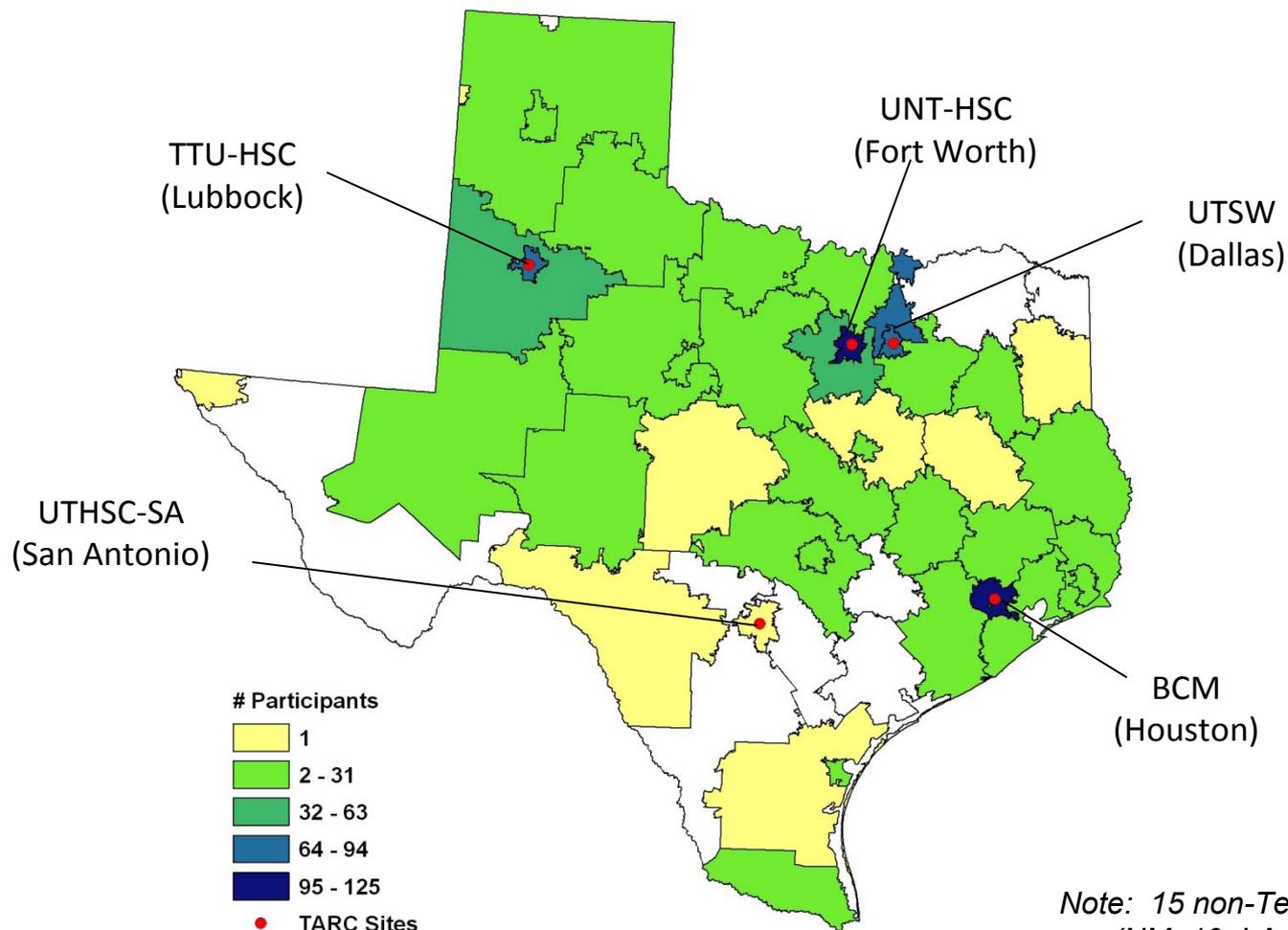
Number of Subjects by Diagnosis and Visit Number

Diagnosis	Visit Number			
	1	2	3	4
AD	685	419	246	28
Control	421	299	147	25
MCI	53	0	0	0
Total	1160	718	393	53

Distribution of participants by primary residence at baseline examination



Areas based on first 3 digits of zip code



Affymetrix Genome-Wide 6.0 Array

Nearly 2 million genetic markers

906,600 genetic polymorphisms

946,000 copy number variation probes

Completed

500 Alzheimer's disease patients

300 Cognitively normal individuals

Lipid and Diabetes Profile

Total cholesterol, Triglycerides, HDL, Cholesterol, LDL, VLDL, Homocysteine, Hemoglobin A1c, C-peptide, and Lipoprotein-associated phospholipase A2

Completed on

300 Alzheimer's disease patients

300 Cognitively normal individuals

Serum Proteins



Human Multi-Analyte Profile Panel

Measures concentrations of 190 blood proteins, including markers of infectious disease, autoimmunity, cardiovascular risk, hormones and growth factors

Completed on

300 Alzheimer's disease patients

300 Cognitively normal individuals

Publications



Peer-reviewed Manuscripts

1. O'Bryant, SE, Hobson, V, Hall, J, Massman, P, Diaz-Arrastia (in press). Decreased CRP in Alzheimer's Disease. *Journal of Geriatric Psychiatry and Neurology*
2. O'Bryant, SE, Hobson, V, Hall, J, Lacritz, L, Massman, P, Cullum, M, Diaz-Arrastia, R. (2009). Brain-derived neurotrophic factor (BDNF) in Alzheimer's disease. A project of the Texas Alzheimer's Research Consortium (TARC). *Journal of Alzheimer's Disease*, 17(2), 1051-1055.
3. O'Bryant SE, Waring SC, Cullum CM, Hall JR, Lacritz LH, Massman PJ, Doody RS, Lupo P, Reisch J and the TARC. Staging Dementia Severity with CDR Sum of Box Scores: An investigation by the Texas Alzheimer's Disease Research Consortium. *Arch Neurol* 2008;65:1091-1095
4. O'Bryant SE, Grammas P. A Case for the Creation of a Biomarker-Based Algorithm for the Detection of Alzheimer's Disease. *JTPHA* 2008;63(3):14-17
5. Waring SC, O'Bryant SE, Reisch J, Diaz-Arrastia R, Knebl J, Doody RS for the TARC. The Texas Alzheimer's Research Consortium Longitudinal Research Cohort: Study Design and Baseline Characteristics. *JTPHA* 2008;63(3):9-13
6. Hall JR, Schiffer RB, O'Bryant SE. Depression and Alzheimer's Disease. *JTPHA* 2008;63(3):25-29
7. O'Bryant SE, Hall JR, Waring SC, Humphreys JD, Hobson V, Schiffer RB. The Relationship Between Cardiovascular Disease and AD. *JTPHA* 2008;63(3):22-24
8. Rustfeld LO, Pavlik VN, Doody RS. Hyperinsulinemia Type-2 Diabetes Mellitus and Cognitive Decline. *JTPHA* 2008;63(3):17-22
9. Fairchild T. Economic impact of AD in Texas. *JTPHA* 2008;63(3):5-8

Abstracts

1. O'Bryant SE, Waring SC, Cullum CM, Hall JR, Lacritz LH, Massman PJ, Doody RS, Lupo P, Reisch J, and the TARC. Staging Dementia Severity with CDR Sum of Box Scores: An investigation by the Texas Alzheimer's Disease Research Consortium. *Arch Clin Neuropsychol* 2007;22:822
2. Hobson VL, O'Bryant SE, Hall J, Cullum M, Lacritz L, Massman P, Waring SC for the TARC. Serum BDNF and Alzheimer's Disease Severity: An investigation by the Texas Alzheimer's Disease Research Consortium. *Arch Clin Neuropsychol* (2008); 23(6), 674.
3. O'Bryant SE, Hobson VL, Hall J, Cullum M, Lacritz L, Massman P, Waring SC, Schiffer R for the TARC. Peripheral Inflammation and Neuropsychological Test Performance: An Investigation by the Texas Alzheimer's Disease Research Consortium. *Arch Clin Neuropsychol*. (2008); 23(6), 673.
4. Hobson, VL, Hall, J, Cullum, CM, Lacritz, L, Massman, P, Warring, S, O'Bryant, SE. The Boston Naming Test: Calculation and utilization of an "estimated" 60-item score from 30- and 15-item administrations. *Arch Clin Neuropsychol* (in press)

Summary



● TARC research focus

- novel genetic and biomarker studies
- longitudinal follow-up of subjects
- inclusion of MCI subjects
- inclusion of Hispanic individuals

● Multidisciplinary study

- a robust centralized research database of prospectively collected clinical, genetic, and biological data from subjects with sufficient follow-up to address an unlimited number of research questions now and into the future

Summary



TEXAS ALZHEIMER'S
RESEARCH CONSORTIUM

This unique longitudinal study could not feasibly be conducted at a single institution due to inherent budget, resource, and recruitment constraints and would not be possible without the vision and support of the Texas legislature