KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

Virtual Site Visit
October 19, 2018
The Westin Buckhead Atlanta
Grand Ballroom A&B, Conference Level (4th Floor)

Agenda

Organization and Administration

7:30 - 8:00	Continental Breakfast	
8:00 - 8:05	Welcome	Russell Swerdlow, MD
8:05 - 8:10	Message from Vice Chancellor for Research	Richard Barohn, MD
8:10 - 8:50	Infrastructure, Theme and Progress	Russell Swerdlow, MD

Metabolism-Focused Research: From Bench to Bedside to Community

8:50 - 9:55	**Molecular and Cellular Studies in AD**	
	Overview and Infrastructure	Elias Michaelis, MD, PhD
	Targeting Mitochondria as a Potential Therapeutic Strategy for Alzheimer's Disease	Shidu Yan, MD
	Dark Amyloid and Mitochondrial Dysfunction	Michael Wolfe, PhD*
	Mitochondria and Alzheimer's Disease	Heather Wilkins, PhD*
	What Memories Are Made Of	Kausik Si, PhD*
9:55 - 10:10	***Break***	
10:10 - 11:10	**Clinical and Translational Research in AD**	
	Overview and Infrastructure	Jeffrey Burns, MD, MS
	Cells-to-Systems Metabolism	Jill Morris, PhD*
	Vascular Contributions to Brain Health	Sandra Billinger, PT, PhD*
	Nutrition and Brain Health	Debra Sullivan, PhD, RD*
11:10 - 11:55	**Empowering Community Through Science and Care**	
	Overview and Infrastructure	Eric Vidoni, PT, PhD*
	Becoming an Independent Researcher in Latino AD Disparities	Jaime Perales Puchalt, PhD
	MyAlliance for Cognitive Health: Shifting the Point of Care	Michelle Niedens, LSCSW
11:55 - 12:00	**Closing Remarks**	Russell Swerdlow, MD

*KU ADC Pilot awardees

#brainpower

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Message from Senator Jerry Moran

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Message from Richard Barohn, MD

Overview:
KU ADC Infrastructure, Theme, and Progress

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Russell Swerdlow, MD
PI, P30 AG035982

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Kansas City

Lawrence

KC VA
UMKC
KCU


Kansas City
Lawrence

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Pre 2004 **2004** **2007** **2011** **2016**

T

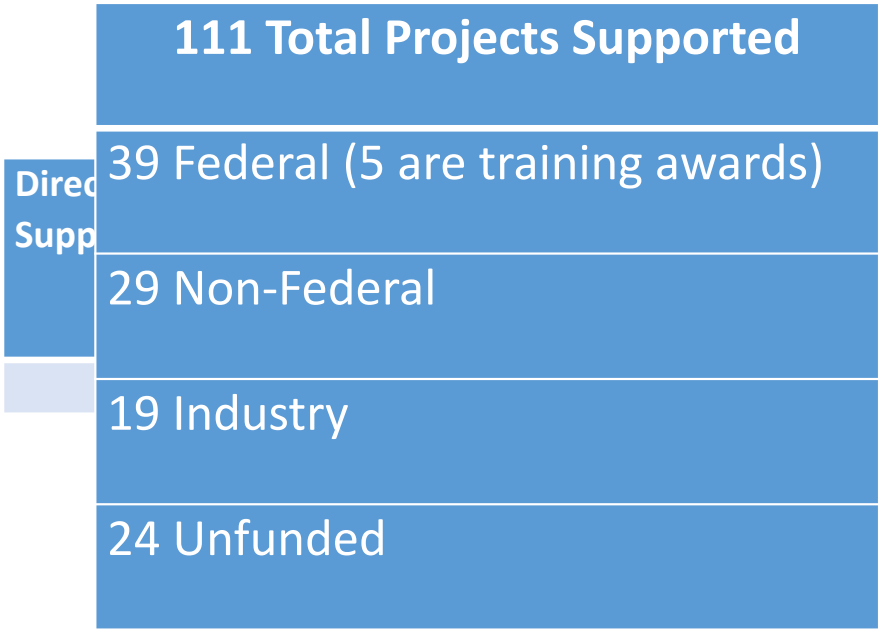
Jeff Burns

Anne Arthur

P30AG035982

Year 7 Overall Metrics

- Investigators: 150
  - 96 members, 54 users
  - 102 KU, 48 non-KU
- Projects Supported: 111
- Portfolio Value
  - $17.5 million in year 7
  - $65.8 million worth of grants
- Manuscripts Supported: 72



Aim 1: Advance AD and Brain Aging Research

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- Promote research into AD energy metabolism dysfunction
- Develop field-driving capabilities and initiatives
- Support innovative research into AD and related topics

Energy Metabolism Dysfunction: Causes, Consequences, Manipulations

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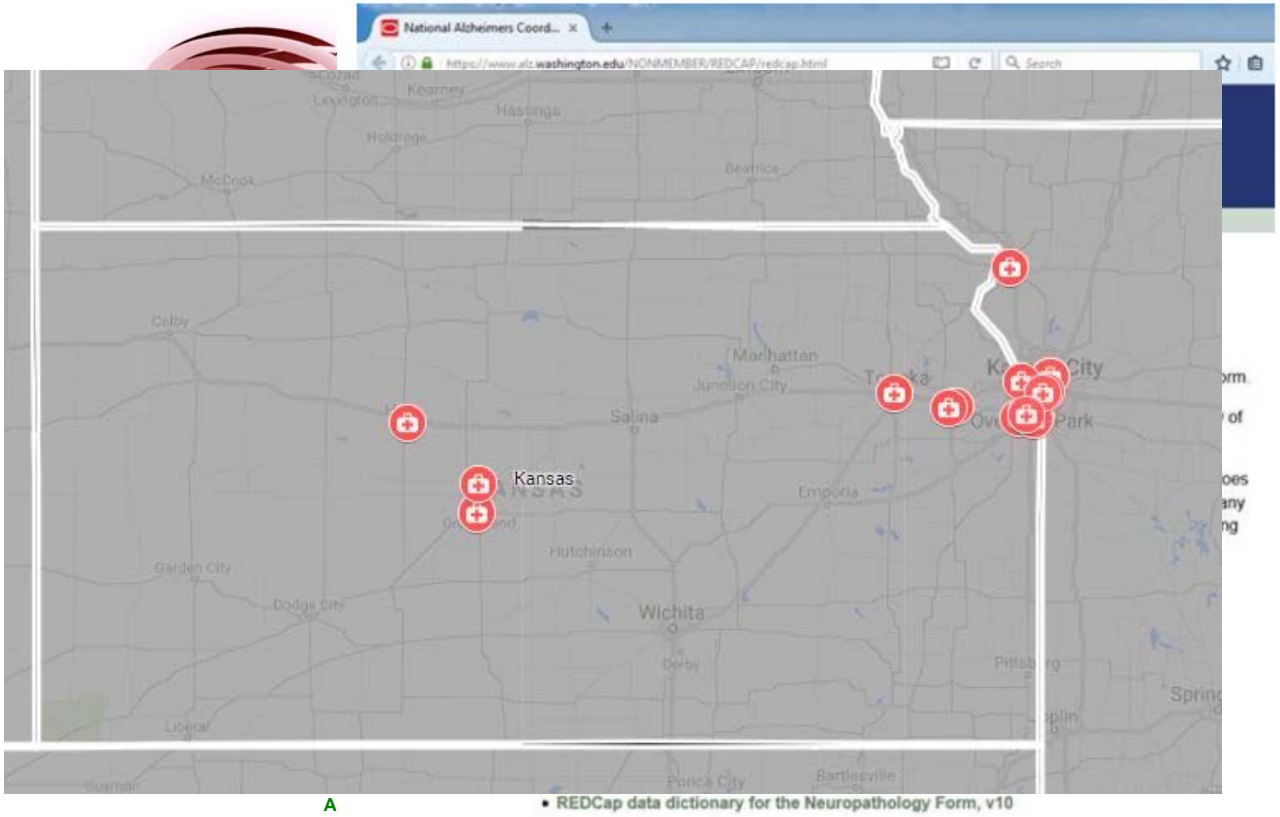
- Genetics
  - mtDNA associations
  - mtDNA-nDNA interactions
- Ketogenic Diet Clinical Stud
- Oxaloacetate Clinical Study
- S-equol Clinical Study
- Ongoing (APEX) and New (IGNITE, rrAD) Exercise Tria
- SGLT2 Study

KU ADC Cohort Haplogroup/APOE distributions

Haplogroup	Group	Frequency	Fisher's Exact P	AD APOE4 Frequency	CN APOE4 Frequency	Fisher's Exact P
H	AD	63/144=43.8%	0.755	38/62=61.3%	30/110=27.3%	0.0001
	Control	119/262=45.4%				
J	AD	23/144=16.0%	0.031	15/23=65.2%	5/22=22.7%	0.007
	Control	22/262=8.4%				
T	AD	11/144=7.6%	0.712	10/11=90.9%	5/24=20.8%	0.0001
	Control	24/262=9.2%				
U	AD	20/144=13.9%	0.185	11/19=57.9%	7/22=31.8%	0.122
	Control	25/262=9.5%				
K	AD	8/144=5.6%	0.138	3/8=37.5%	7/24=29.2%	0.681
	Control	27/262=10.3%				
UK	AD	28/144=19.4%	1.000	14/27=51.9	14/46=30.4	0.085
	Control	52/262=19.8%				

Field Driving Capabilities

- Biomarker Disclosure
- New Biomarkers
  - N-acetyl aspartate (MRS)
  - Glutathione (MRS)
  - Mito Protein Nitration
  - Platelet Cytochrome Oxidase
  - Annexin Binding
- Bioenergetic Medicine Drug Development
- Exercise Prescription
- Recruitment Approaches
- REDCap
- Service Delivery



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• REDCap data dictionary for the Neuropathology Form, v10

Enhance and Support Innovative Research

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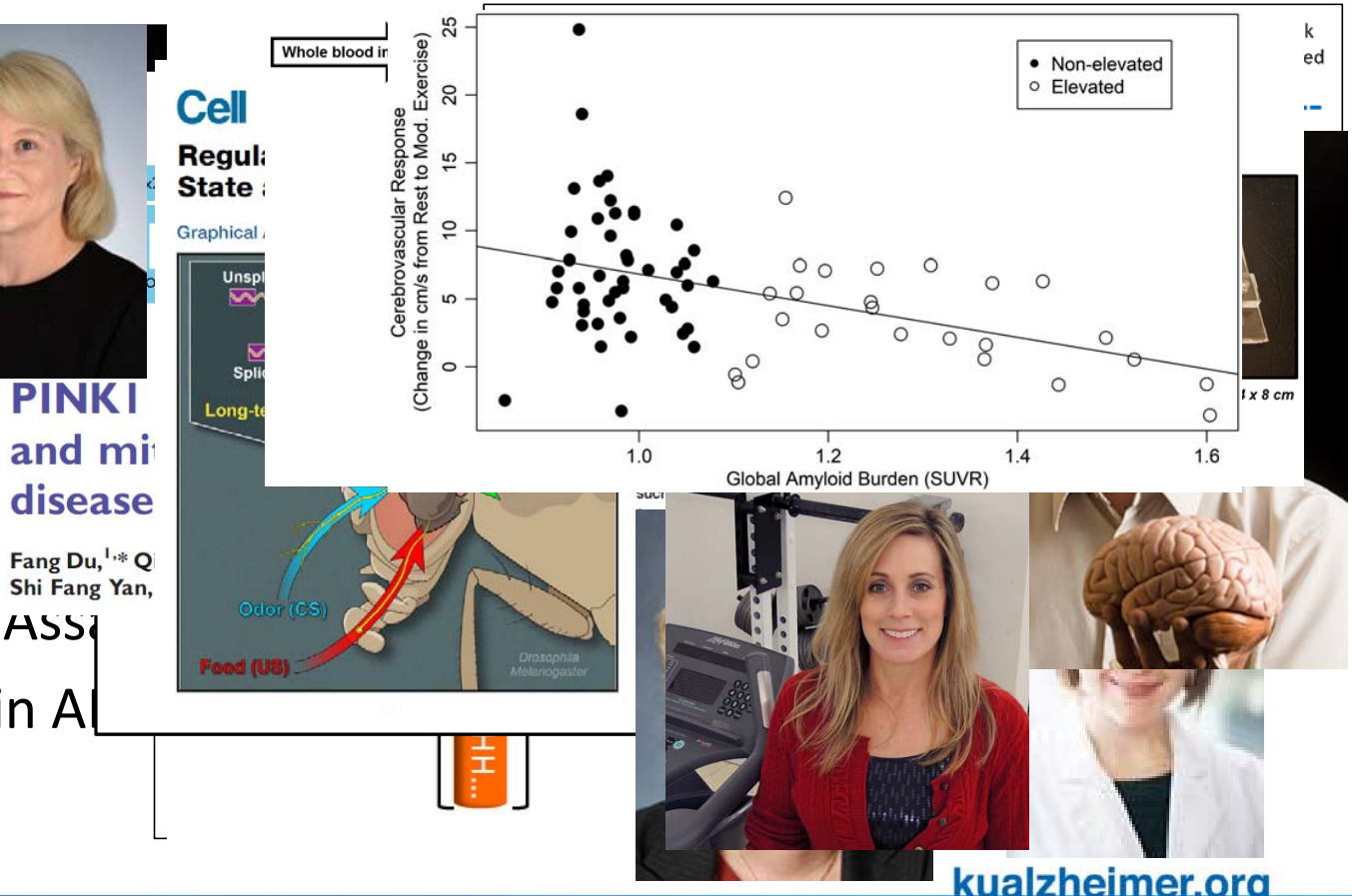
- IPSCs
- TBI-AD Connection
- "Dark Amyloid"
- O-GlycNAcylation
- Mitophagy
- Molecular Basis of Me
- Microfluidic Biomarker Ass
- Neurovascular Control in Al



kualzheimer.org

Aim 2: Serve as a Midwestern Hub for AD Research, Care, and Education

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- Bring together investigators
- Provide a rich training environment
- Provide well-characterized research participants and biospecimens

Aim 2: Serve as a Midwestern Hub for AD Research, Care, and Education

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- Bring together investigators
- Training environment
- Participants and biospecimens

Resources	
Resource	**Notes**
Blood Biospecimens	Q4 years; stored at KUMC BRCF
Genetic Data	mtDNA especially
Clinical Data	ADC-initiated and project-initiated
Imaging	ADC-initiated and project-initiated
Expertise	Study/Protocol development
Technical Support	
Clinical Trial Infrastructure	
Pilot Support	
Cybrid Cell Lines	
IPSCs	
Brain	
CSF	Project-driven; changing to ADC-initiated

Aim 3: Enhance the ADC Network

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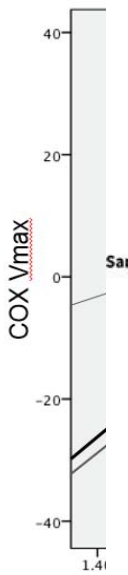
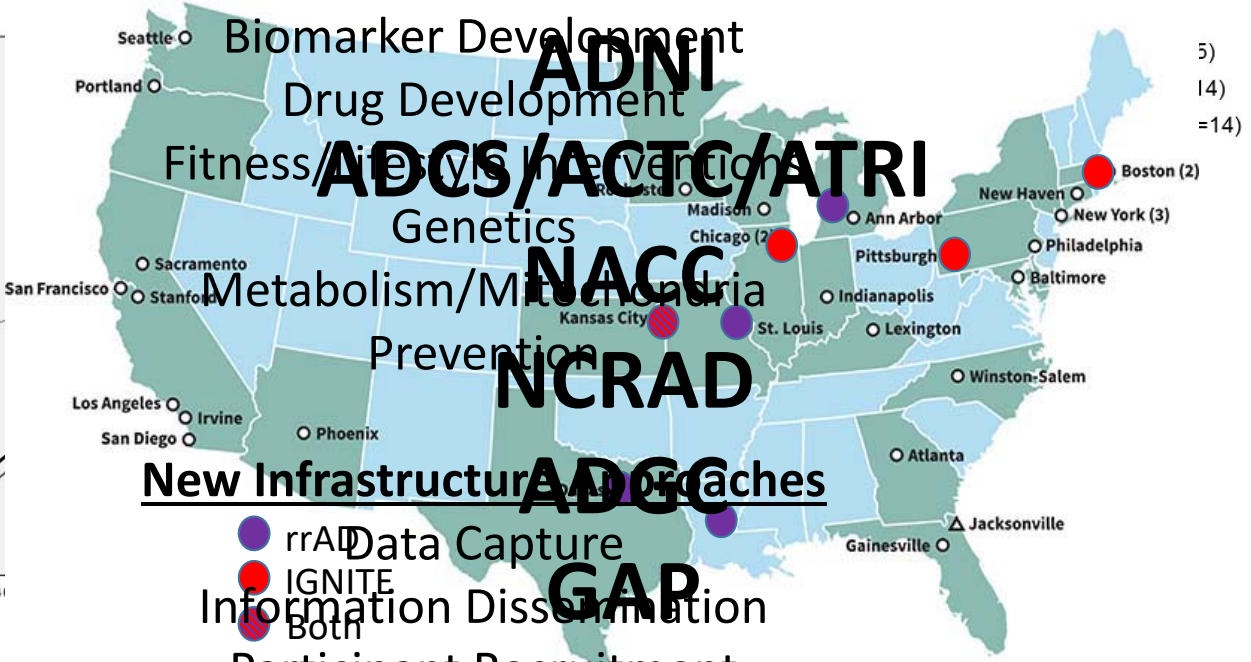
- Contribute to the national ADC network
- Foster new lines of research

Aim 3: Enhance the ADC Network

- National Network
- New Lines of Research





Novel Lines of Research

Biomarker Development

Drug Development

Fitness/Lifestyle Intervention

Genetics

Metabolism/Mitochondria

Prevention

New Infrastructure Approaches

Data Capture

Information Dissemination

Participant Recruitment

Service Delivery

rrAD

IGNITE

Both

ADNI

ADCS/ACTC/ATRI

NACC

NCRAD

ADGC

GAP

IDEAS

Administrative Core

Primary Affiliation	Department	Number
KCU	Biochemistry	1

Interaction with other KU Programs/Cores

What Others Seek Us Out For

- Investigator-Initiated Multicenter Trials (especially exercise)
- Recruitment Expertise
- Imaging Expertise (human and animal)
- Metabolism/Mitochondrial Expertise
- Metabolism/Mitochondrial Technical Abilities (including biomarkers)
- mtDNA/cybrids
- REDCap Data Capture

Heartland Center for Mitochondrial Medicine

Clinical Core

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- Formal "research" cohort of ~400 active participants
  - Skewed toward CN due to prevention interests
  - Rarely used for intervention studies
- Maintains clinical study infrastructure
  - Clinical Trials Unit
  - Study Coordinators
  - Regulatory support staff
  - 43 supported studies in year 7 (19 federally funded)

Data Management and Statistics Core

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- Electronic Data Capture
  - Boston University
  - Columbia University
  - Emory University
  - Indiana University
  - New York University
  - Northwestern University
  - Oregon Health and Science University
  - Stanford University
  - University of California, Irvine
  - University of California, San Francisco
  - University of Florida
  - University of Michigan
  - University of Pennsylvania
  - University of Southern California
  - University of Washington
  - University of Wisconsin
  - Wake Forest University
  - Washington University in St. Louis
  - Yale University

Outreach and Recruitment Core

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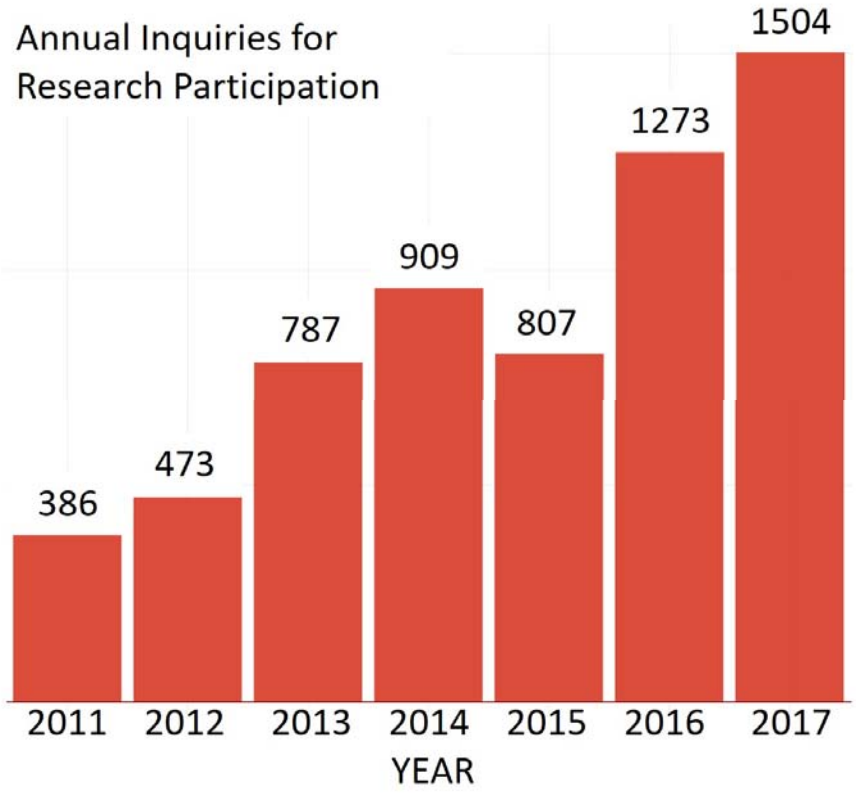
- Lifestyle Enhancement for Alzheimer's Prevention (LEAP)
  - Community based, culturally tailored education
- LEAP Physician Engagement
  - Stimulates referrals across regional health systems



Neuropathology Core

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- Cadaveric dural and fibroblast-derived iPSCs

REC: Training Program Structure

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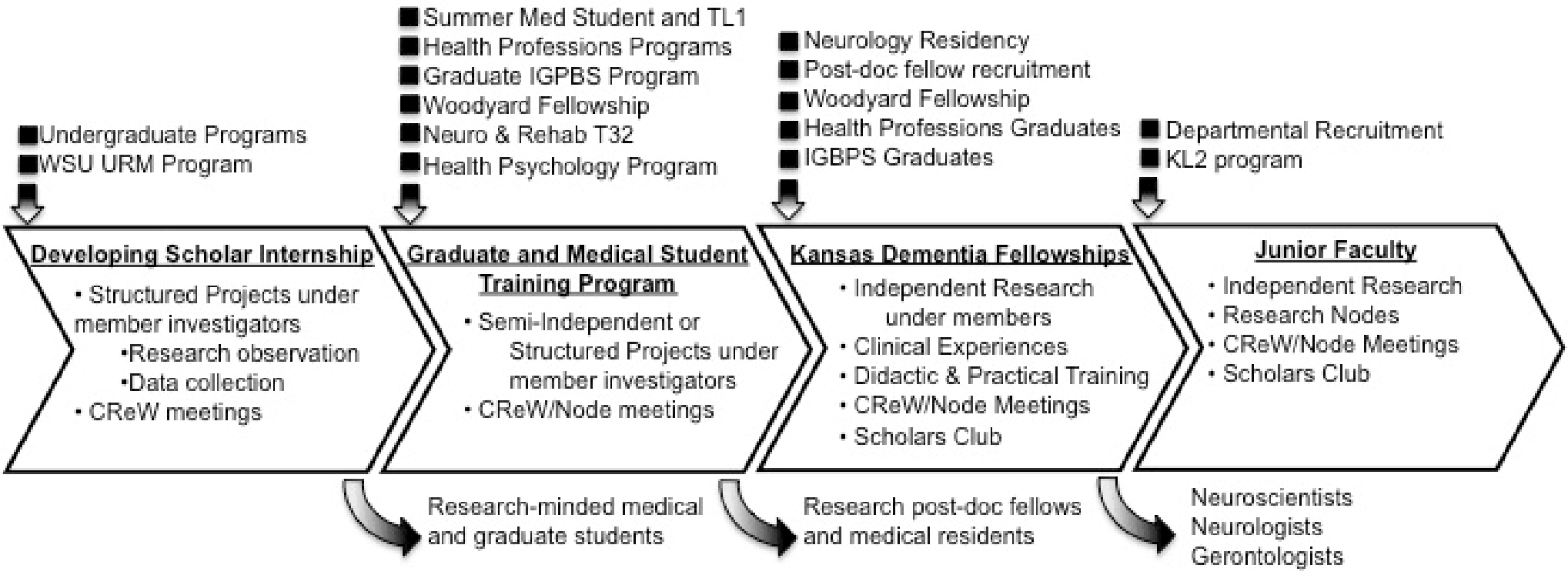

Year 7 Training Grant Applications

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Mentee	Mentor	Grant Type	Status
Wilkins, Heather	Swerdlow	K99-R00	Funded
Koppel, Scott	Swerdlow	F30	Funded
Gupta, Aditi	Burns/Brooks	K23	Funded
Devos, Hannes	Burns/Brooks	K01	Pending
Szabo-Reed, Amanda	Burns/Brooks	KL2	Pending
Perales, Jaime	Swerdlow/Vidoni	NIA Diversity Supplement; K01	Supplement Funded, K01 Pending

Neuroimaging Core

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- Investigator-Initiated Multisite Trial Support
  - Harmonization of imaging protocols
  - Development and deployment of novel sequences
- MRIs on 305 clinical cohort participants
  - Repeat scans on 120 participants
- Amyloid PET on 305
  - Repeat scans on 75

Mitochondrial Genomics and Metabolism Core

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- Complete mtDNA sequences for all Clinical Cohort participants
- Study consultation/design
  - Heavily utilized within and beyond KU
  - Year 2018: 15 of 21 pilot project applications would use the Core
- Biomarker and drug development

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Fairway, KS 66205
913-588-0555
kualzheimer.org

Molecular & Cellular Investigations: The Mitochondrial Genomics and Metabolism (MGM) Core

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KU ADC Kansas City and Lawrence

E. Michaelis, R. Swerdlow, M. Michaelis

D. Hui, H. Wilkins

MGM Core: Not mandated — A Core designed to take advantage of the scientific environment of the KU ADC

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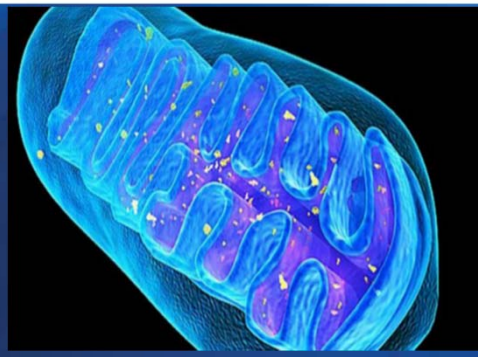
Scientific themes of the KU ADC:
Metabolism and Bioenergetics deficits in AD:
Molecular/Cellular to Clinical Approaches



Cellular & Genetic Focus on Mitochondrial Function and Structure in LOAD

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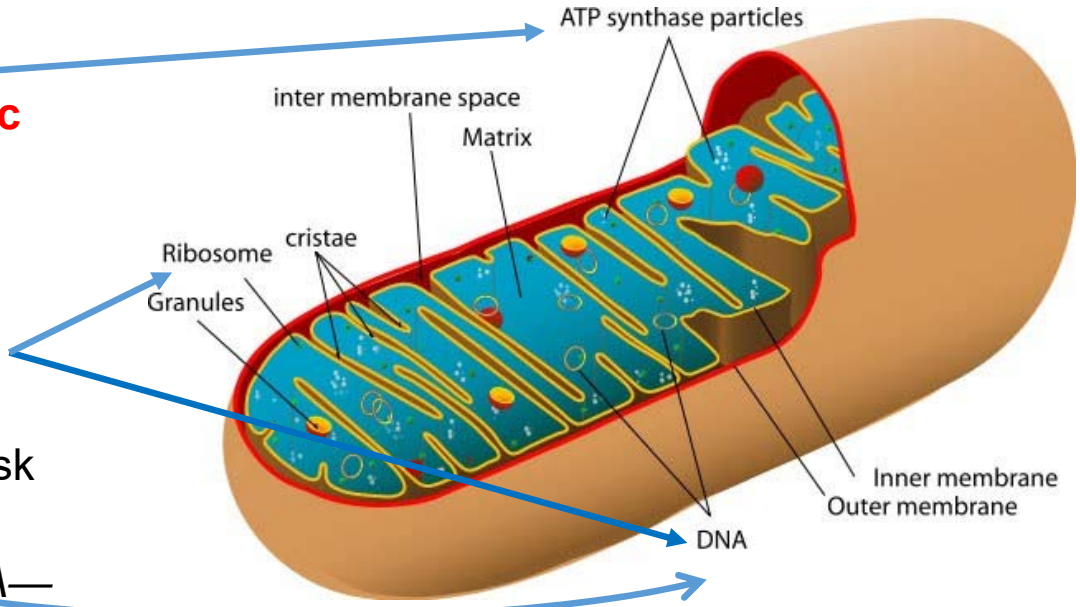
Rationale

- Decreases in activity of oxidative phosphorylation (OXPHOS)--**Systemic**
- Increases in reactive oxygen (ROS) / nitrogen species (RNS)
- ROS leading to mitochondrial DNA (mtDNA) mutations or protein modifications
- History of maternal LOAD— greater risk than paternal history of LOAD
- *Possible inherited mutations in mtDNA— single nucleotide variants (SNVs) in LOAD*



Mission of the MGM Core

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Provide investigators with information and the tools to conduct metabolism, genomic, and proteomic analyses of mitochondria and attract investigators interested in relating such measures to mitochondrial bioenergetics in aging and AD

Goals of the MGM Core

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a) Trans-Mitochondrial Cybrid Cell generation from AD/MCI/NL subjects

b) Mitochondrial bioenergetics measurements

c) Mitochondrial protein modification analyses

d) Exploratory bioenergetics drug testing (cells, animal models, humans)

e) mtDNA Next Generation Sequencing (NGS) and post-sequencing analyses on the entire cohort of the KU ADC

Developing cell models of AD

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Link between mitochondrial function and AD-related synaptic deficiencies and neuronal damage

- Generated 100 hybrid cell lines by inserting platelet mitochondria into $\rho 0$ SH-SY5Y neuroblastoma cells (*Cybrids—Drs*. *Swerdlow, Wilkins)*
- Cybrids derived from mitochondria of AD, MCI, and NL individuals
- Also from amyloid (+) and amyloid (-), cognitively normal individuals
- Shared cybrids with investigators of the ADC and others in the US and other countries

Cell models and mitochondrial metabolism measurements

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Cybrids used to probe:

- effectiveness of ROS scavengers in reversing effects of Aβ on neuronal structure and function –(*Dr. Yan*)
- relationship between systemic metabolism, neuroimaging measures, and mitochondrial function in 40 cybrid lines –*(Dr. Morris)*

Planned experiments to probe:

- effectiveness of activators of mitochondrial bioenergetics —(*Dr. Forrest, Pharmaceutical Chemist*)
- relationship between various forms of Aβ peptides and metabolism (*Dr. Wolfe*)

Mitochondrial Genomics—mtDNA NGS

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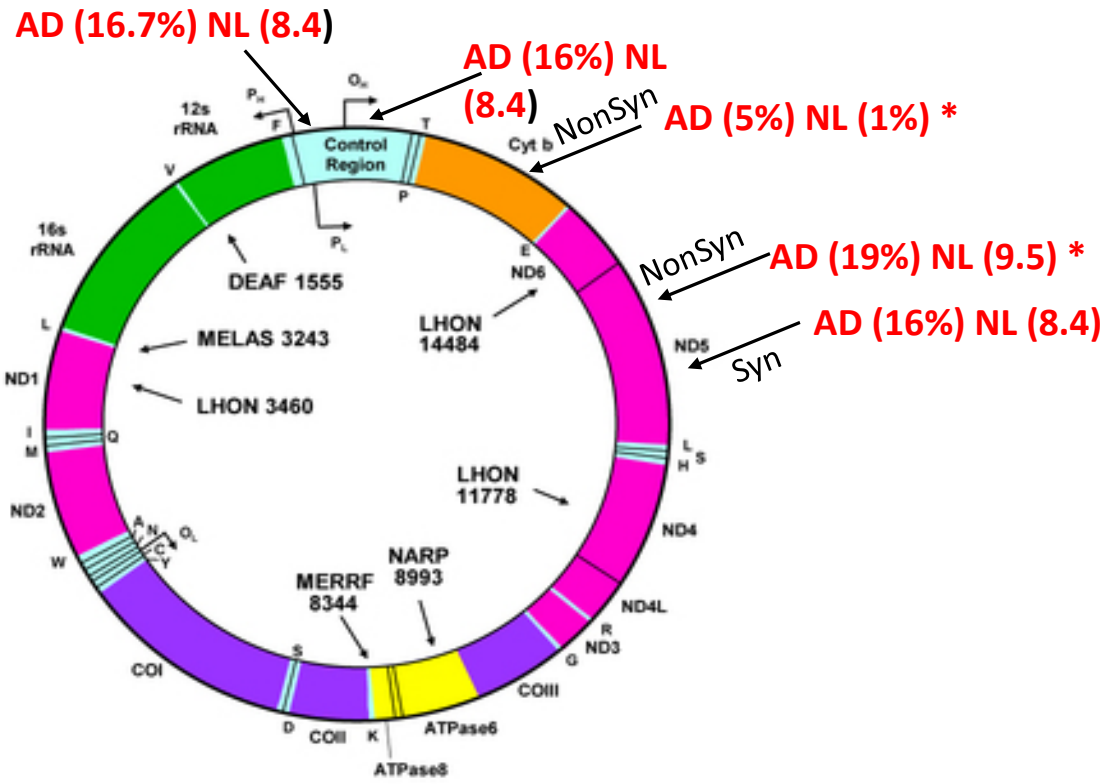
- Amplified, sequenced, curated, and analyzed mtDNA from 144 AD, 262 NL, and 37 MCI
- 19 SNVs only 1 SNV over-represented in NL
- AD-related SNVs: 4 non-synonymous mutations in OXPHOS enzyme subunits
- 3 SNVs in mt tRNA or rRNA



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Effect of MGM Core on Scientists at KU

- Year 2018:
  - 15 of 21 Pilot Project applications would use the MGM Core
  - 3 of 5 pilot projects approved use the MGM Core
- Years 2016/2017:
  - 3 of 4 projects funded were MGM Core related

Presentations from four individuals who have received support to explore new areas of research in molecular and cellular aspect of AD

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Heather Wilkins, PhD

- Postdoctoral fellow in the KU Alzheimer's Disease Center
- Expert in cell bioenergetics, cybrid cell studies, and the development of induced pluripotent cells into neuronal forms for the study of the effects of Aβ and tau on neuronal metabolism
- Recipient of a K99/R00 award from the NIA

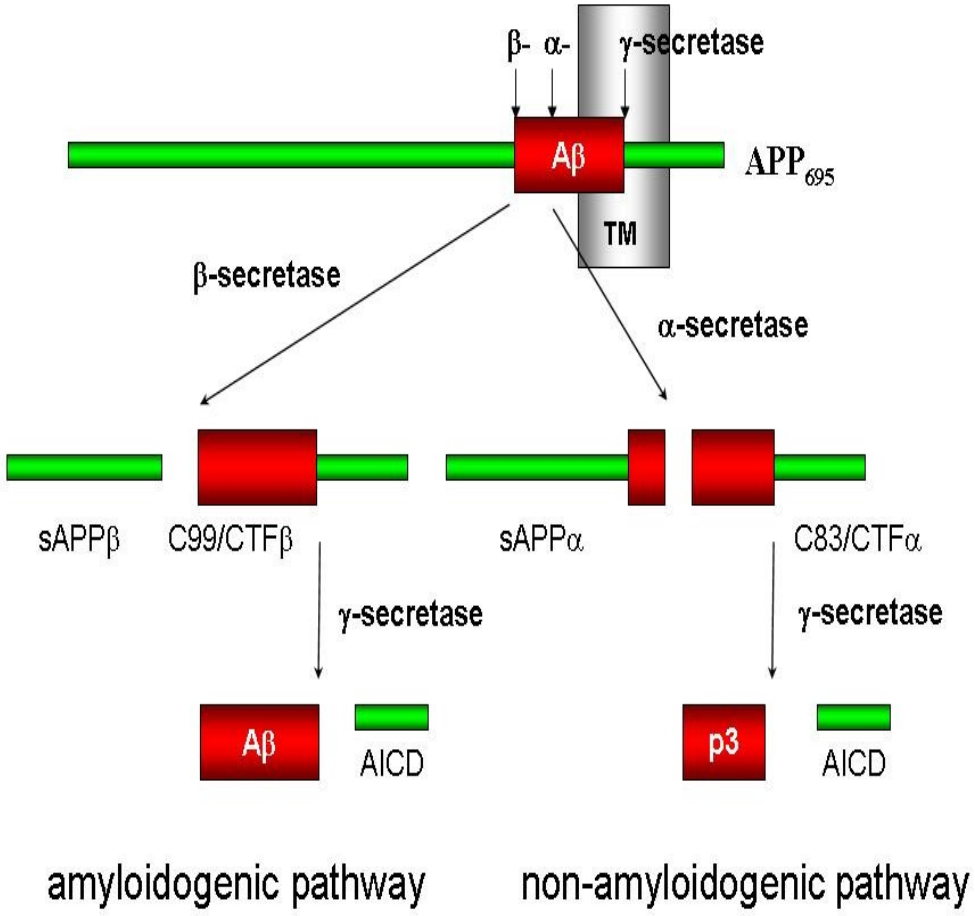
Mitochondria and Alzheimer's Disease

Heather Wilkins, PhD

Postdoctoral Fellow

University of Kansas Alzheimer's Disease Center

How do mitochondria affect Alzheimer's Disease Pathology?



http://www.irb.hr/eng/Research/Divisions-and-Centers/Division-of-Molecular-Medicine/Laboratory-of-Molecular-Neuropharmacology/Group-for-Neurodegenerative-Disease-Research

Several prior studies link mitochondrial function/bioenergetics to amyloid precursor protein (APP) processing and amyloid beta production

Gabuzda D et al. 1994. J Biol Chem.
Gasparini et al. 1997. Neurosci Letters.
Webster et al. 1998. J Neural Trasmission.
Gasparini et al. 1999.. Neurosci Letters.
Leuner et al. 2012. Antioxidants and Redox Sig.
Kukreia et al. 2014. Mol Neurodegener.

Mitochondrial Membrane Potential

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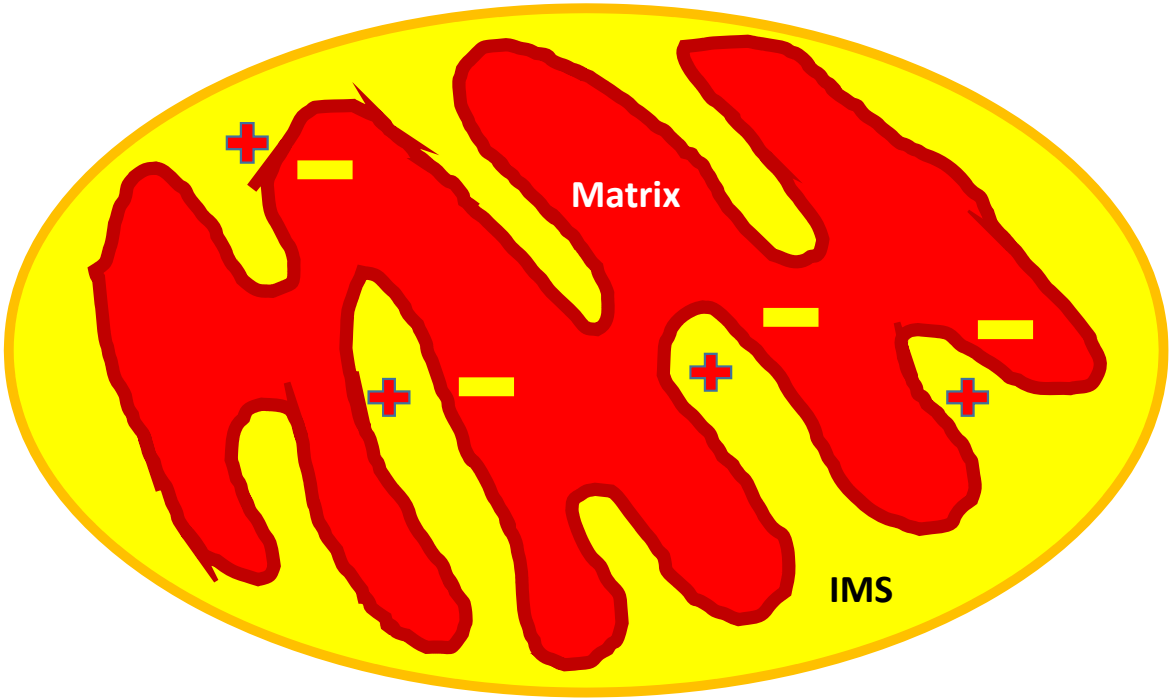

Mitochondrial Membrane Potential

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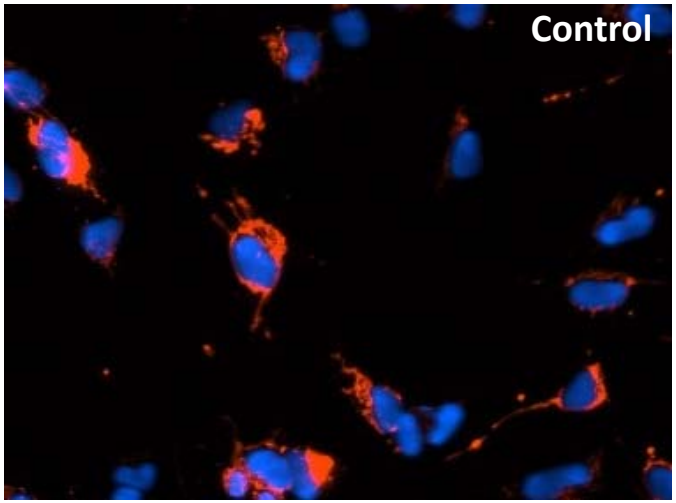
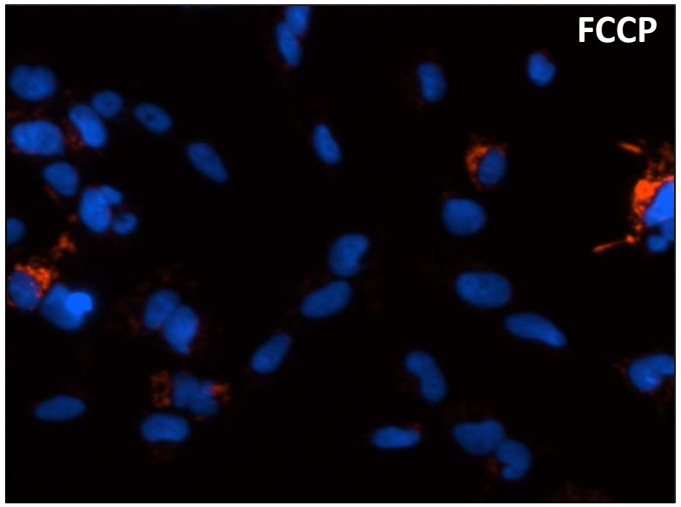
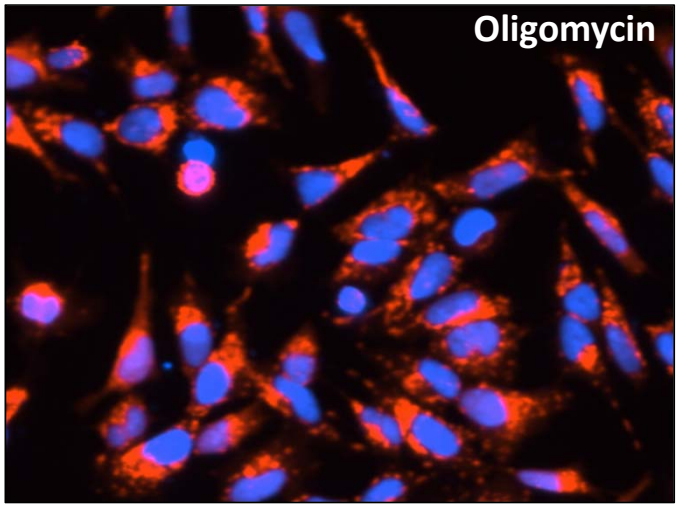
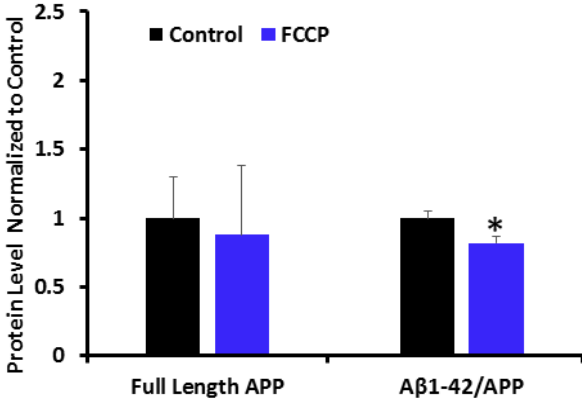


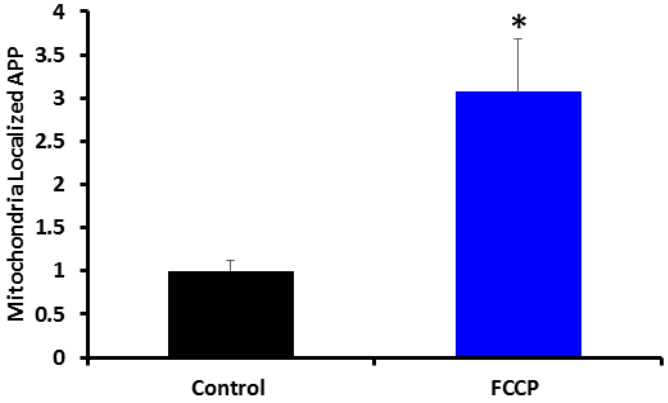


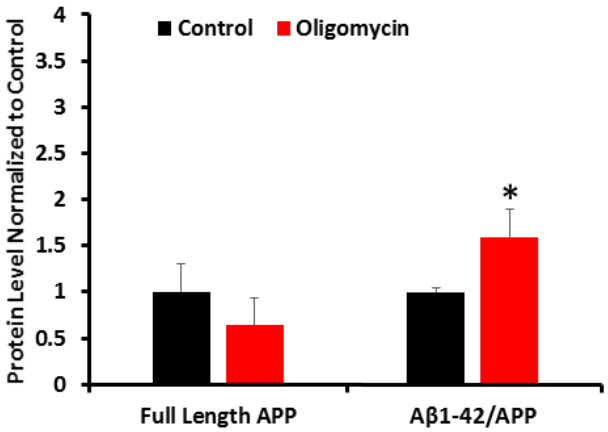


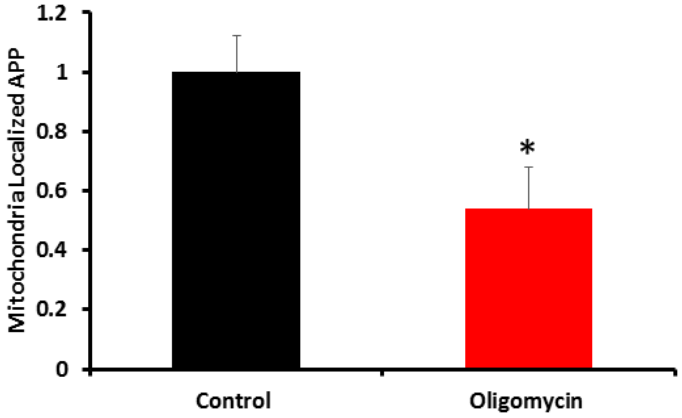
Supported by the KU ADC and MGM core

Mitochondrial Membrane Potential and APP/Amyloid









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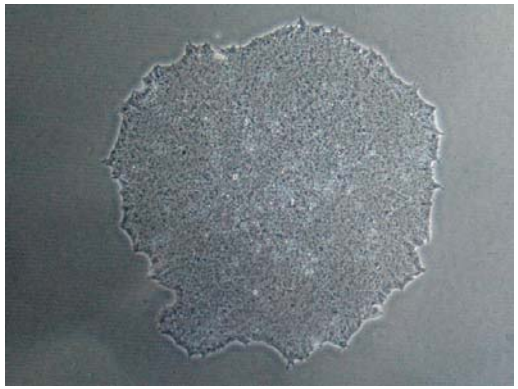
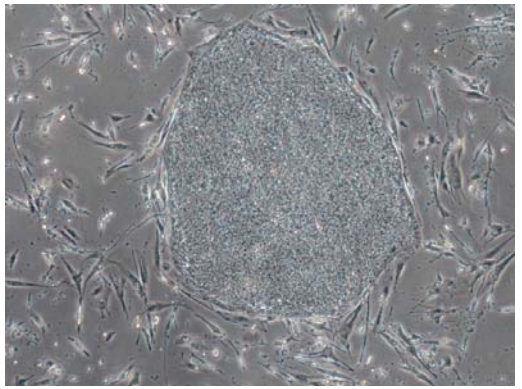
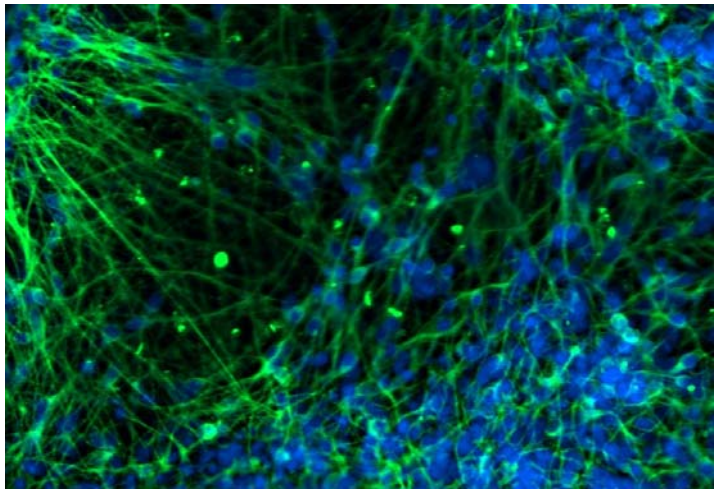
Induced Pluripotent Stem Cell Derived Neurons



ADC37, Alzheimer's disease



ADC25, Non-demented



Supported by the KU ADC, MGM core, neuropathology core, and NIA K99 AG056600

How does APOE influence mitochondria?

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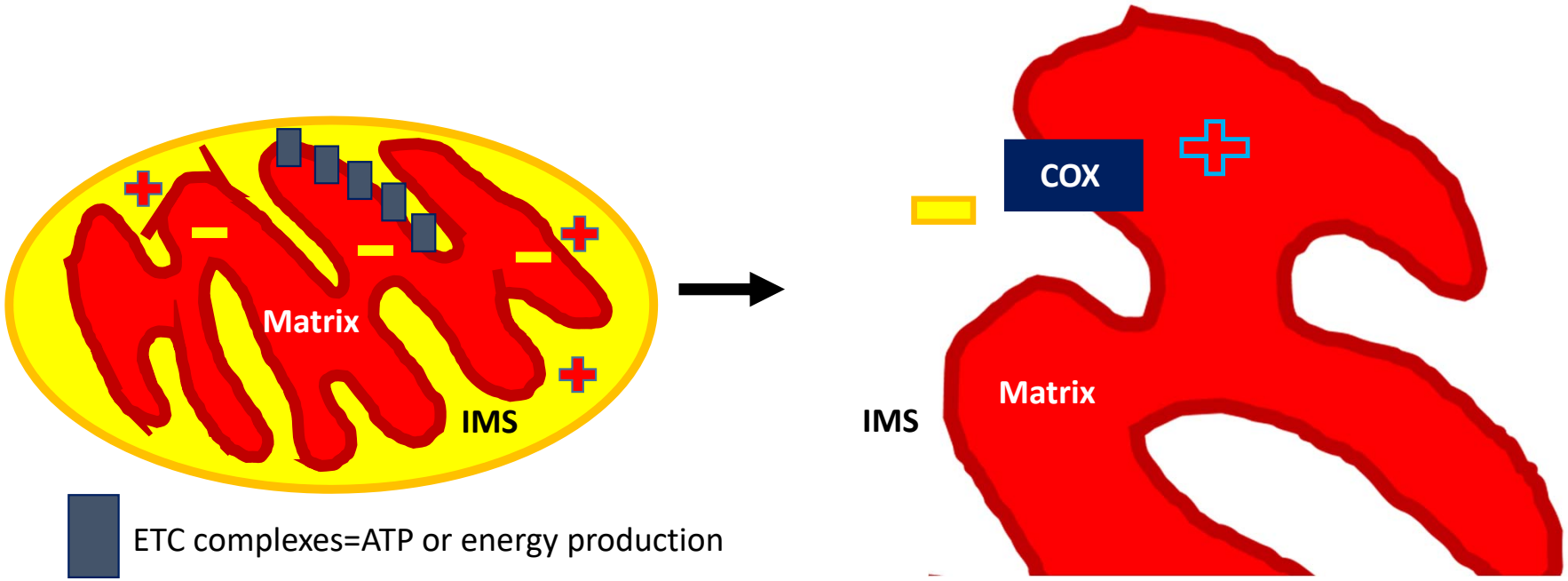
APOE ε4 carriers have reduced platelet mitochondrial cytochrome oxidase (COX) Vmax

(Wilkins et al. Redox Biology. 2017)

- **WHY?**



ETC complexes=ATP or energy production

APOE Genotype and Blood Mitochondrial Biomarkers

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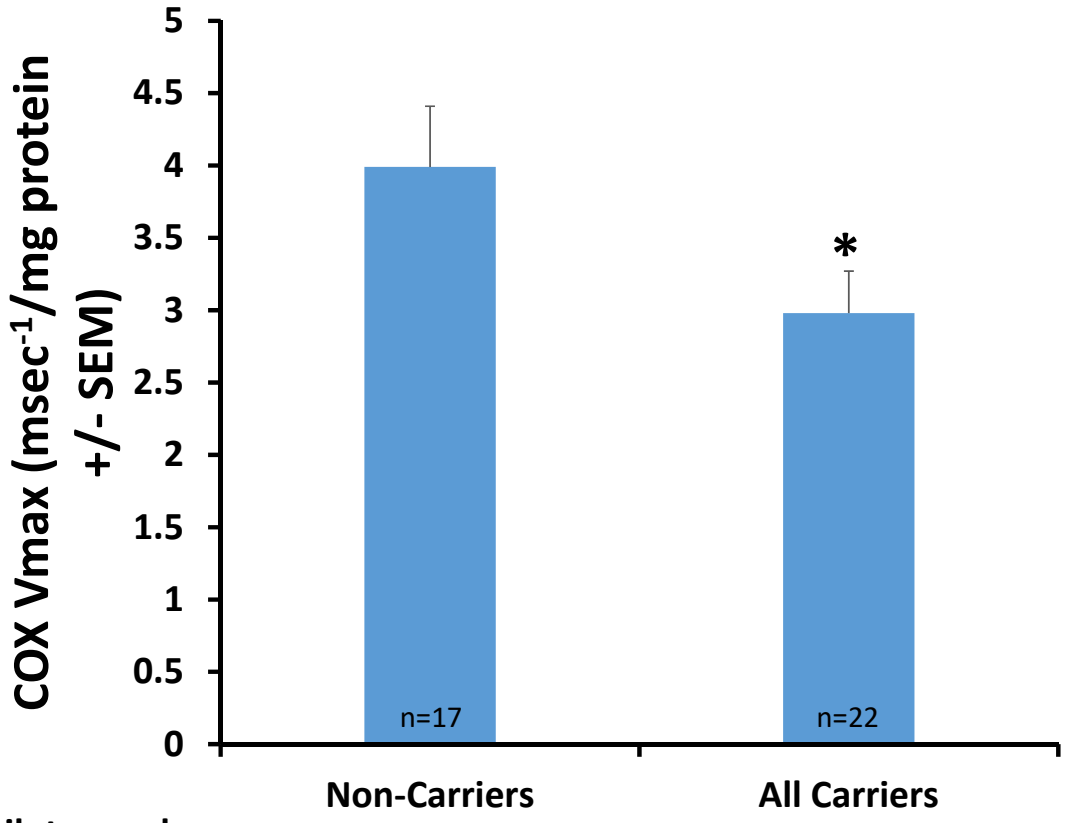

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APOE Genotype and Blood Mitochondrial Biomarkers

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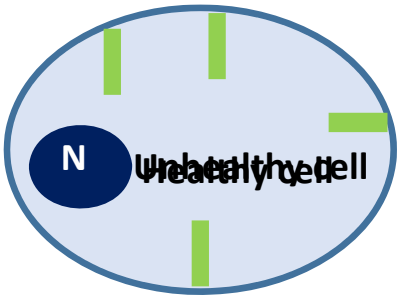

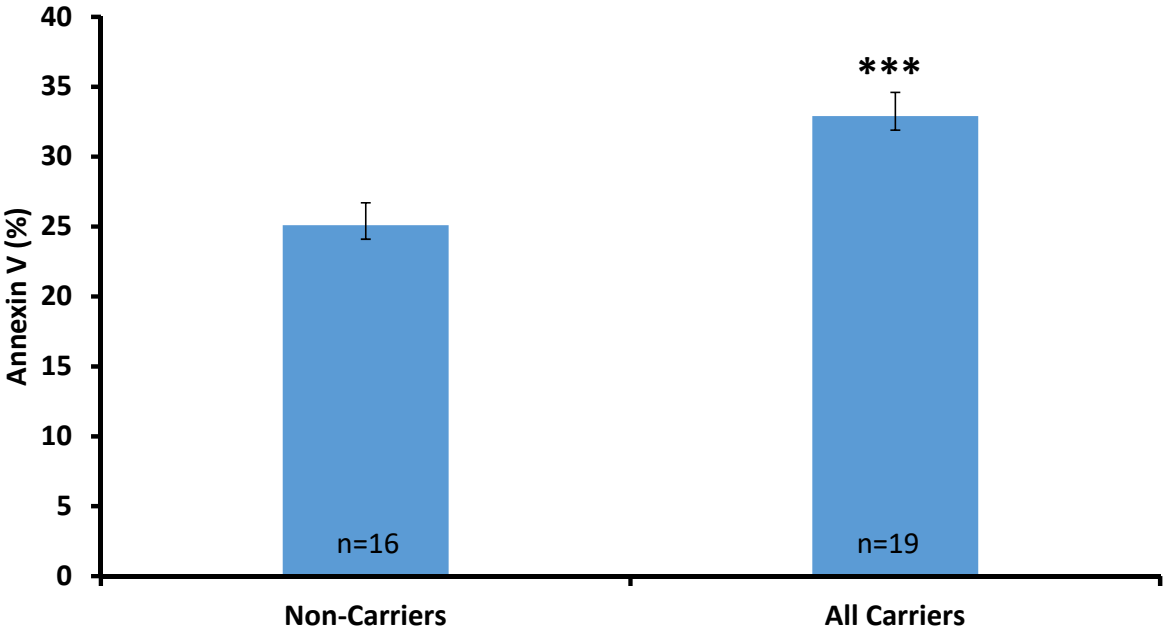

Phosphatidylserine

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Sex and Blood Mitochondrial Biomarkers

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Mean (SEM)	Male	Female	p value
Annexin V (%)	29.5 (1.9)	28.9 (2.1)	0.84
JC1	3 (.17)	3.65 (.25)	0.04
n	18	17	

Supported by a KU ADC pilot award

Future

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- **Mitochondrial membrane potential and secretase enzyme function**
- **Understand the effects of APOE ε4 on mitochondrial function**
- **Develop new mitochondrial and bioenergetic biomarkers**
- **Transition to an independent Alzheimer's Disease Scientific Career**

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Fairway, KS 66205
913-588-0555
kualzheimer.org

Clinical and Translational: Overview and Infrastructure

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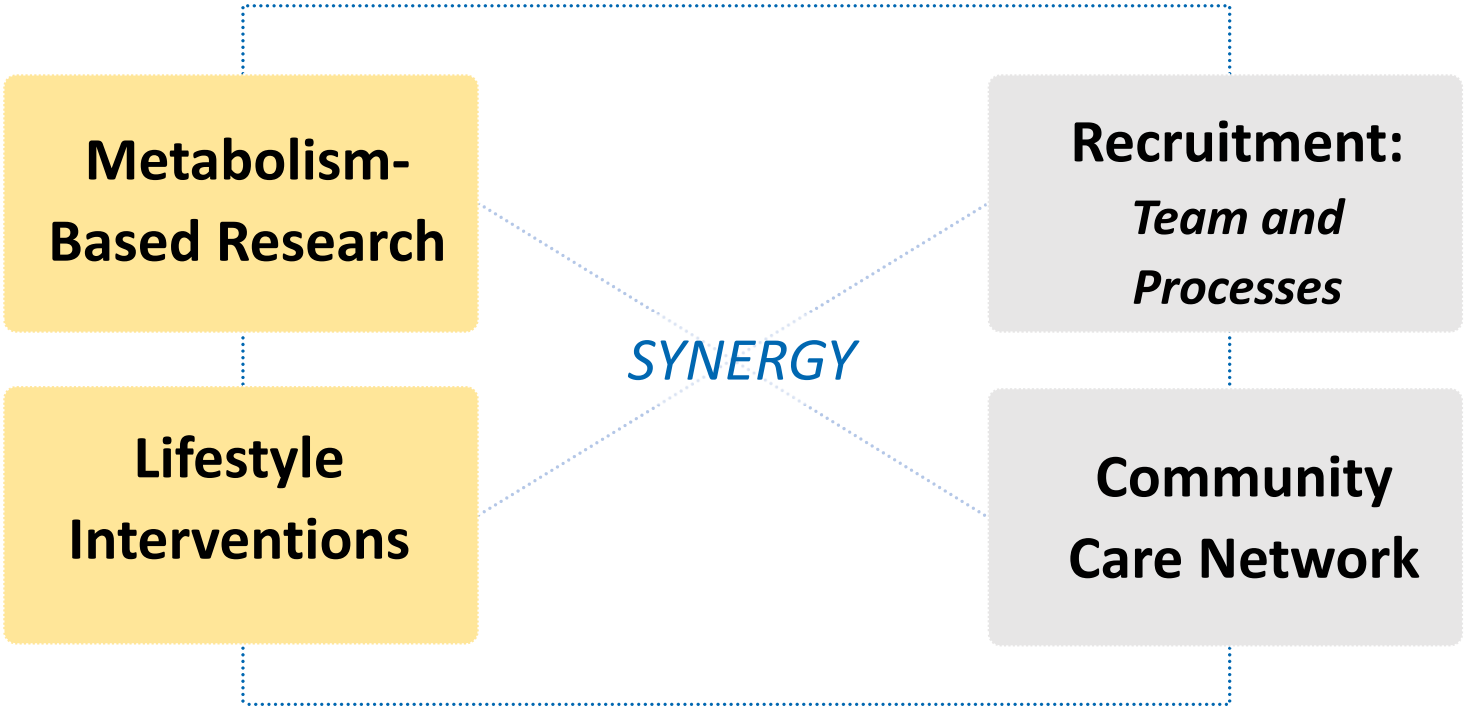
Jeffrey M. Burns, MD, MS
Co-Director and Clinical Core Leader
Edward H. Hashinger Professor of Neurology

“Product” and “Process” Innovation Drives Impact



Year 7: Clinical Core Productivity

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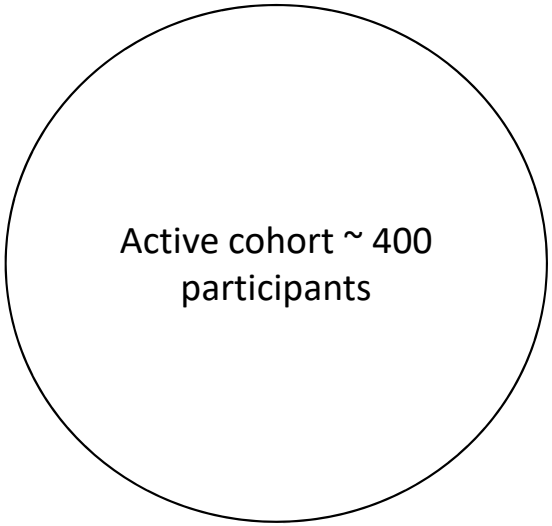
- 43 total studies supported
  - Data (15 studies), Biospecimens (10 studies), Participants (11 studies)
- 13 NIH multi-site collaborations
  - NACC, ADGC, ADNI, ADCS and ACTC
  - 3 Multi-site R01s
  - 5 NIH multi-site studies
    - ADNI3, A4, LEARN, ASPREE, and EXERT
- 23 externally funded grant awards (19 federal awards)

- Dramatic growth supported by
  - Clinical Cohort
  - Development of Other Cohorts
    - APEX (R01)
    - Registry (n > 7000)
  - Infrastructure creation: physical and team-based
    - CTSA
    - Trial teams (drug and exercise)
    - Recruitment

Clinical Cohort



ASSESSMENTS

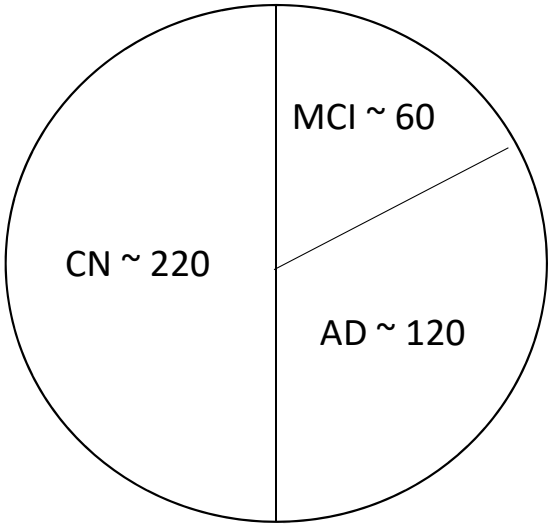
- Phlebotomy (every 4 years)
- MRI (every 2 years)

Mitochondrial genome

Other

- Accelerometry (every 2 years)
- VO2peak / Cardiorespiratory Fitness
- Neurovascular

Clinical Cohort



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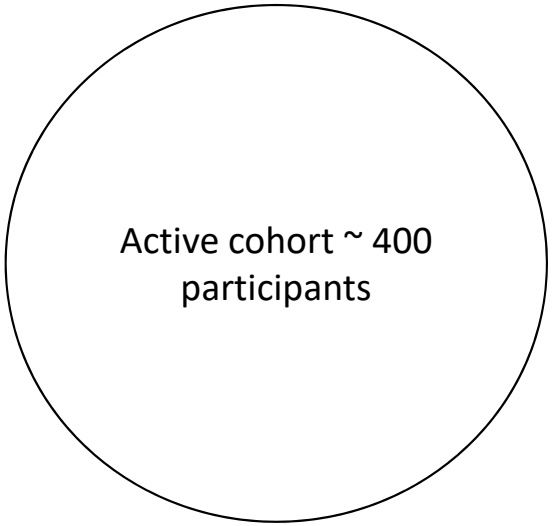
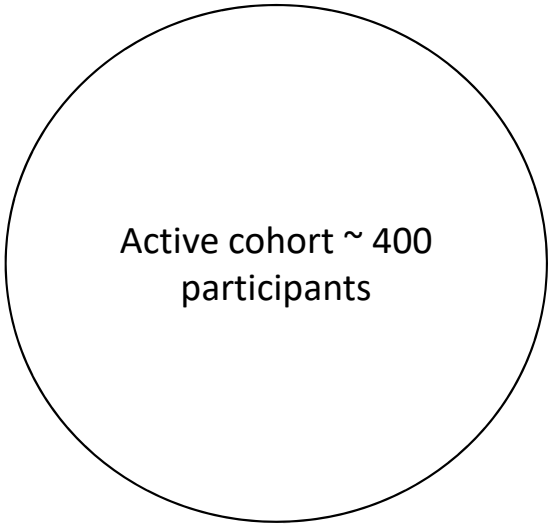
Clinical Cohort



Accomplishments

- Efficient processes
  - REDCap electronic data capture
    - Time to finalization 57 days (vs. 120d nationally)
  - Excellent retention
    - 11% discontinuation rate
    - Missed follow up 13% (vs. 20% nationally)
  - Autopsy Program
    - 63% consent rate
    - 59% autopsy rate (44 of 75 all time deaths)
- Imaging submitted to NACC
  - MRIs n=252
  - Amyloid PET n=294

Clinical Cohort = **“Innovation and Discovery Cohort”**



- Cohort not sufficient for our growing intervention studies
- Cohort “contaminated” by interventions

Re-defined Purpose: Natural history study to support longitudinal observational studies (biomarkers, imaging, risk factors, etc)

Clinical Cohort = **"Innovation and Discovery Cohort"**

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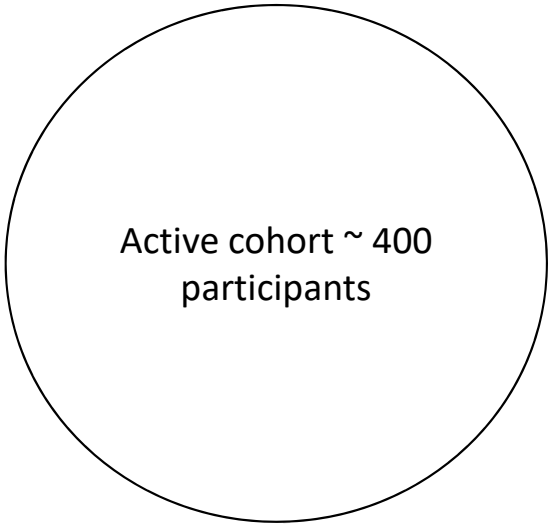
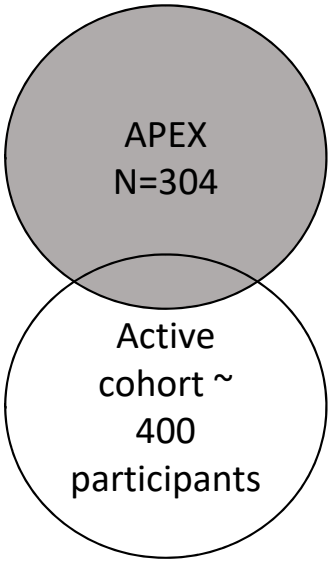


Studies Leveraging the Clinical Cohort

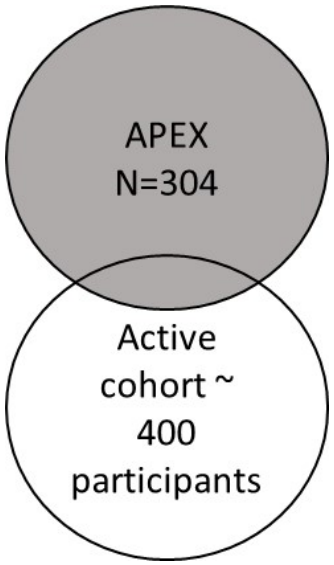
Study	Sponsor	Enrollment
Tech for Dementia Care (Williams)	R01	41
Functional Regulation (Johnson)	Internal Funds	61
Group exercise via iPad in AD (Vidoni/Ptomey)	ADC Pilot	8
Energetics and Cognition (Morris)	R00	52
TrACR (Billinger)	ADC Pilot & Am. Heart Assoc	107
Ketogenic Diet Feasibility (Sullivan)	ADC Pilot	15
Aging, AD and Mitochondrial Function (Morris)	R21	36
Neurovascular and Exercise Response (Vidoni)	Internal	39
KSU COBRE Neuroplasticity	P20	Pending
Neurophysiology in Preclinical AD (Devos)	KU ADC Pilot / K01	Pending
Neurovascular Impairment in Aging and AD	R01	Pending

Amyloid PET Cohort



- APEX R01 Exercise Trial
- N=304 Cognitively Normal (CDR 0 and neuropsych)
  - 28% elevated amyloid (n=86 vs. n=218 nonelevated)
- Projects supported
  - Billinger – Neurovascular program
  - Morris – Insulin resistance studies
  - Taylor / Sullivan – Diet studies
  - K awards (Morris and Devos)
  - F32 award (Perdomo)

Amyloid PET Cohort



Alzheimer's

ORIGINAL ARTICLE

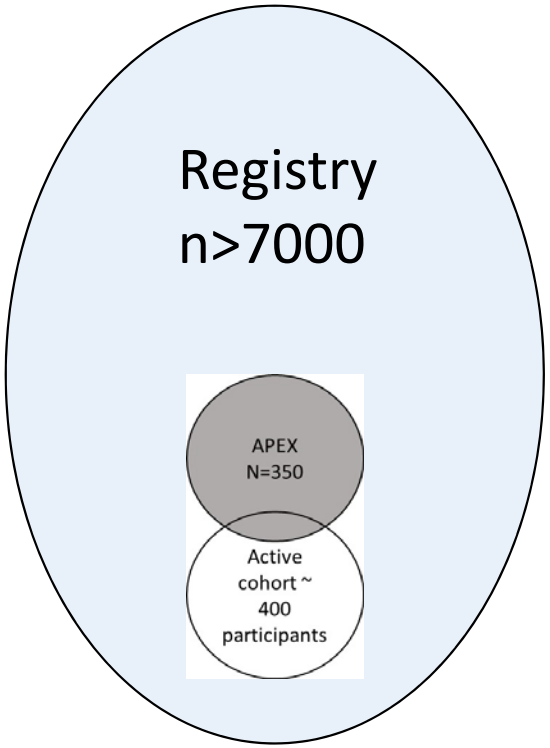
Augmenting Amyloid PET Interpretations With Quantitative Information Improves Consistency of Early Amyloid Detection

Nicholas R. Harn, MD, PhD, Suzanne L. Hunt, MS,† Jacqueline Hill, PhD,**
Eric Vidoni, PhD,‡ Mark Perry, MD, and Jeffrey M. Burns, MD‡*

[a]*Department of Neurology, University of Kansas Alzheimer's Disease Center, University of Kansas Medical Center, Kansas City, KS, USA*
[b]*Department of Psychology, University of Kansas, Lawrence, KS, USA*

Harn et al. Clin Nucl Med, 2017

Research Registry



Research Registry

- Enroll online, paper, phone
- Demographic, PMH, medications, cognitive issues
- Recruit for study opportunities
  - Clinical Cohort
  - Trials
  - Others (Genematch)

Leveraging Infrastructure to Scale Up

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Integrated with CTSA and CTSA Research Unit

Creating Infrastructure to Scale Up

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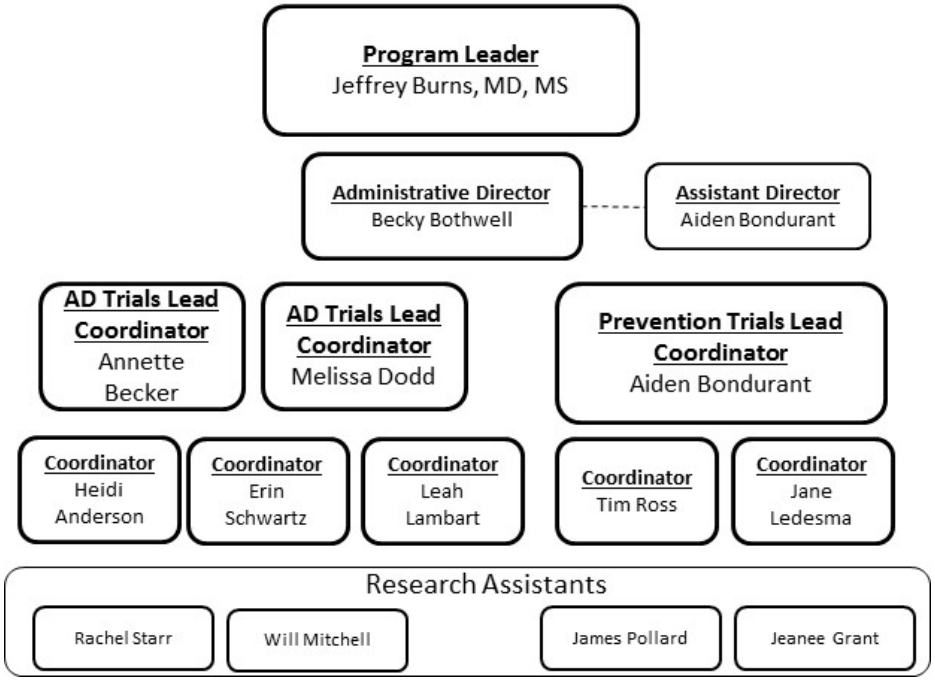
Support Teams

Physical Health Intervention Team	Clinical Trial Unit	Clinical Cohort

Recruitment	Neuropsych	Med Monitoring

Clinical Trial Unit



Study	Sponsor	Enrollment
Multi-Site Trials		
A4	NIH	20
ADNI3	NIH	13
GeneMatch	NIH	319
LEARN	NIH	15
ENGAGE	Biogen	8
M15-566 Anti-Tau Ab	AbbVie	7
Generation 1	Novartis	9
Generation 2	Novartis	1
GRADUATE II	Roche	Start up
Investigator-Initiated Trials		
Oxaloacetate	Alz Assoc	32
S-Equol in AD	Ausio	19
Dapa in AD	Astra-Zeneca	Start up
Closed		
ASPREE	NIH	41
LZAX	Eli Lilly	8
MK-8931	Merck	19
NEUROTROPE	Neurotrope	4
TCAD	Toyama	13
TTP	vTv Therapeutics	14
EARLY	Janssen	1
DAYBREAK	Eli Lilly	3

Clinical Trial Unit

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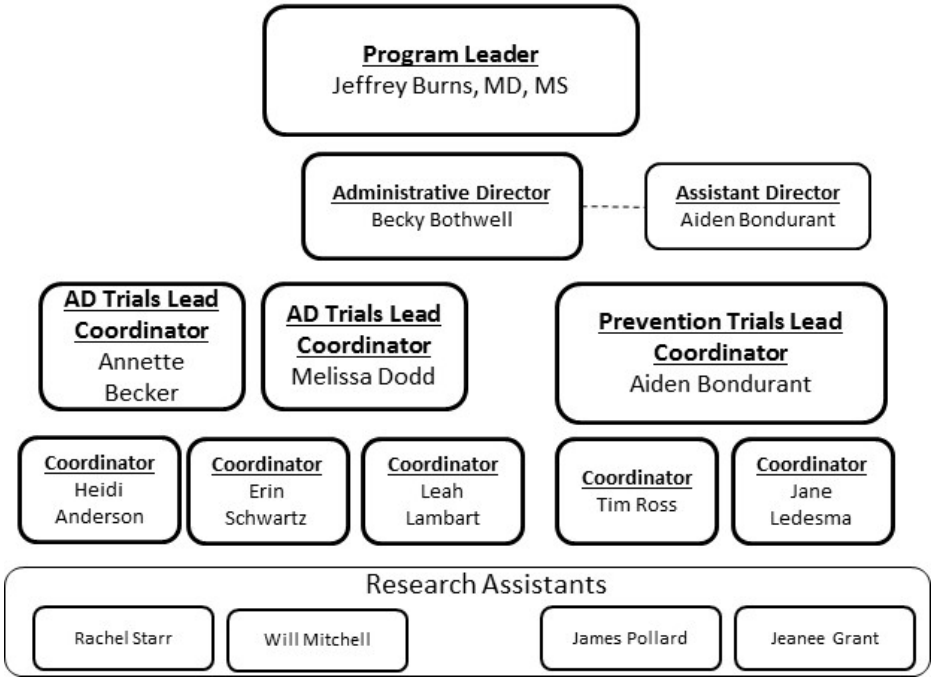
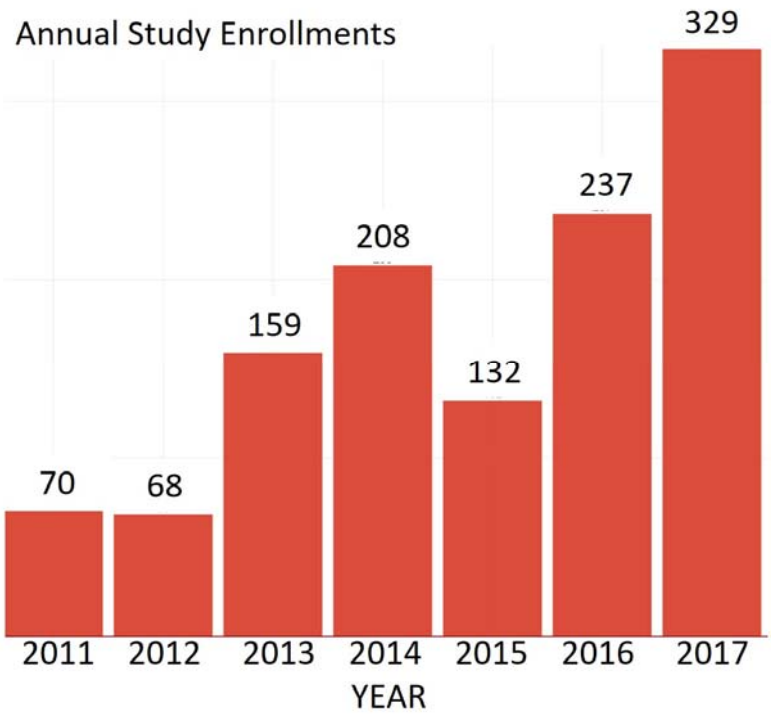
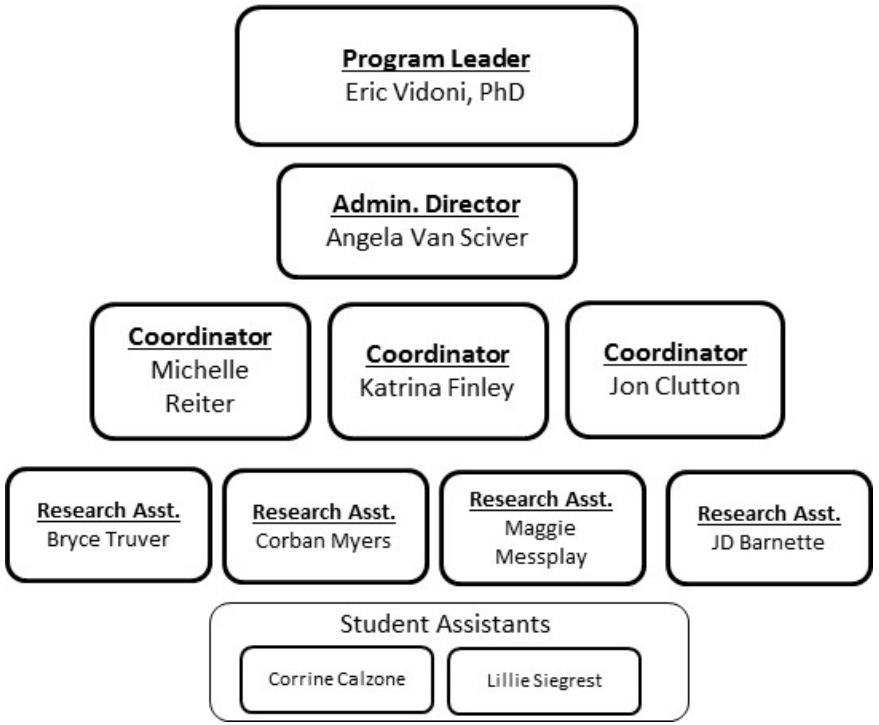




Physical Health Intervention Team



Current Exercise Studies

Study	Sponsor	Enrollment	Goal
APEX	R01	120	125
rrAD	R01	73	160
IGNITE	R01	55	213
EXERT	ADCS	5	10
LEAP! Rx	R01	2	220

Metabolic Approaches

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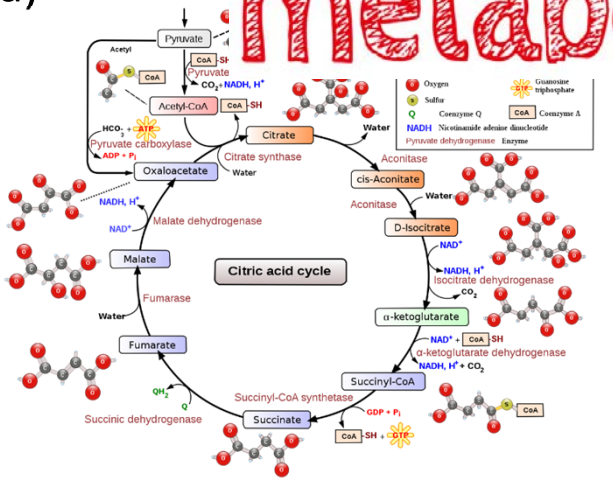
Investigator Initiated Drug Trials

- Oxalaoacetate for AD (Alzheimer's Association)
- S-Equol for AD (Ausio Pharmaceuticals)
- Pilot RCT of Dapagliflozin in AD (Astra Zeneca)

Exercise / Diet

- Diet Studies
  - NICE Study (R01)
  - Ketogenic Diet for AD
- Exercise Trials (4 R01s supported)



Exercise in the Fight Against AD

Our studies suggest

1. Exercise has brain benefits, even at low doses
2. Exercise may slow AD (disease modification)
3. Optimal target is to increase CR Fitness

But, we still need rigorous scientific data to

1. Definitively prove brain benefits
2. Understand magnitude of effects
   - What kind and how much is best?
3. Understand mechanisms

Lifestyle Empowerment for Alzheimer's Prevention

LEAP!

LIFESTYLE EMPOWERMENT FOR ALZHEIMER'S PREVENTION

Translating biomedical research findings into everyday strategies for Alzheimer's prevention and brain health.

Evidence-based lifestyle program for risk reduction

- LEAP! book: Brainpower Blueprint
- Interactive education programs in community

LEAP! accomplishments

- Rural outreach program established in Emporia, KS
- LEAP! Rx program funded by NIH
  - Goal: to scale program nationally

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Poised for Growth: New Studies

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Funded in 2017 and 2018

- R21: Thyfault / Morris – Skeletal Muscle Abnormalities in AD
- R01: Ptomey – Remote Delivery of Weight Loss in older IDD
- R01: Burns – Prescribing Smart Aging (LEAP! Rx)
- K23: Gupta – Cognitive Impairment in Renal Disease
- P20 COBRE (KSU) – Cognitive Approaches to Neuroplasticity
- Diversity Supplement: Perales – Cognitive Impairment in Latinos
- K99: Wilkins – iPSC studies in AD
- KL2: Szabo-Reed – Executive Control and Exercise Adherence
- R01: Billinger – Neurovascular Impairment in Aging and AD
- R01: Sullivan – Mediterranean Diet in Aging
- IIT (Astra Zeneca): Burns/Swerdlow – Dapa in AD

New Industry / NIH Multi-site

- ADNI 3
- AbbVie
- EARLY
- Generation 2
- Pegasus (Amylyx)
- Graduate (Roche)

Pending Grants

- R01: Lee – Glutathione MRS in Exercise
- R01: Swerdlow – Ketogenic Diet in AD
- R01 Siengsukon – Insomnia and Cognitive Impairment
- K01 Devos – Neurophysiology in Preclinical AD
- K01 Szabo-Reed – Correlates of Exercise Adherence
- R01 Swerdlow – Mito DNA / Haplogroup J and AD

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kualzheimer.org

Jill Morris, PhD

KU ALZHEIMER'S DISEASE CENTER
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- Assistant Professor of Neurology
- Director of the KU ADC Pilot Grant Program
- Chair of Biospecimen Committee
- Researching energy metabolism and cognitive decline

Cells-to-systems metabolism

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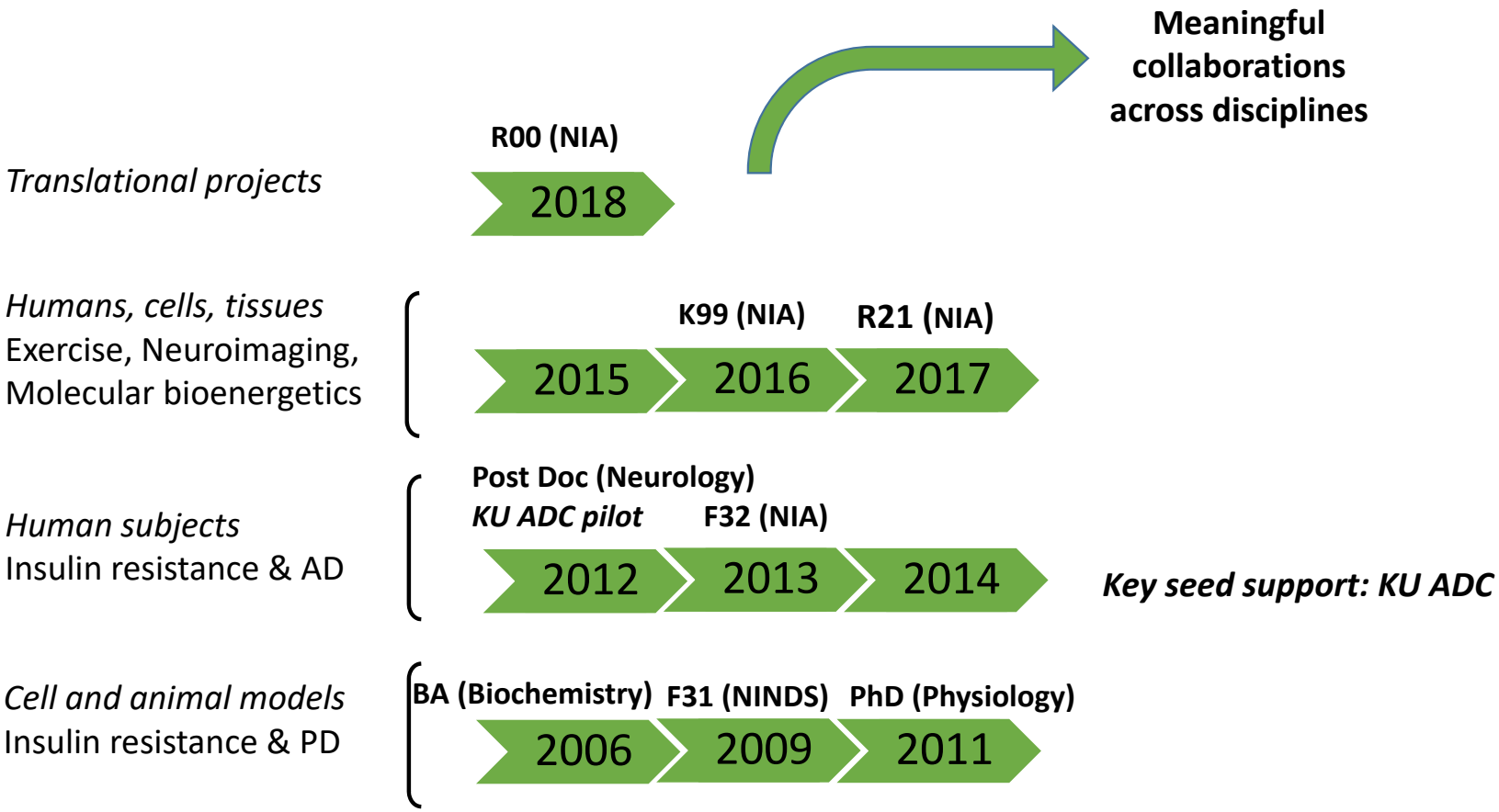
Jill K. Morris, PhD
Assistant Professor
Department of Neurology

Growing as a translational researcher

Growing as a translational researcher



Increased neuropathology and disease progression in prediabetic subjects

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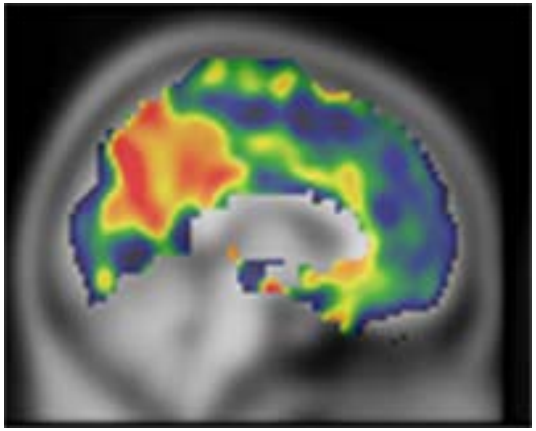
Cognitively Normal



Prediabetes increases regional cerebral amyloid

MCI

Measure	Timepoint	Normoglycemia	Impaired Glycemia	p-value (2yr Δ)
MCI to AD converters	Baseline	N/A	N/A	0.015
	2yr Δ	32.7% (16.4%/yr)	47.9% (24.0%/yr)	
CDR-SB	Baseline	1.56 (0.86)	1.61 (0.84)	0.044
	2yr Δ	1.35 (1.9)	1.88 (1.9)	
Global Cognition	Baseline	-0.615 (0.55)	-0.761 (0.61)	0.019
	2yr Δ	-0.193 (0.55)	-0.366 (0.58)	
Whole Brain Volume	Baseline	0.677 (0.027)	0.672 (0.02)	0.024
	2yr Δ	-0.012 (0.007)	-0.0152 (0.009)	
Hippocampal Volume	Baseline	0.655 (0.90)	0.642 (0.08)	0.439
	2yr Δ	-0.0152 (-.016)	-0.0194 (0.019)	

Prediabetes increases disease progression in MCI

Morris et. al. 2016, NBA; Morris et. al. 2014, NBA

Peripheral IR tracks with decreased brain volume

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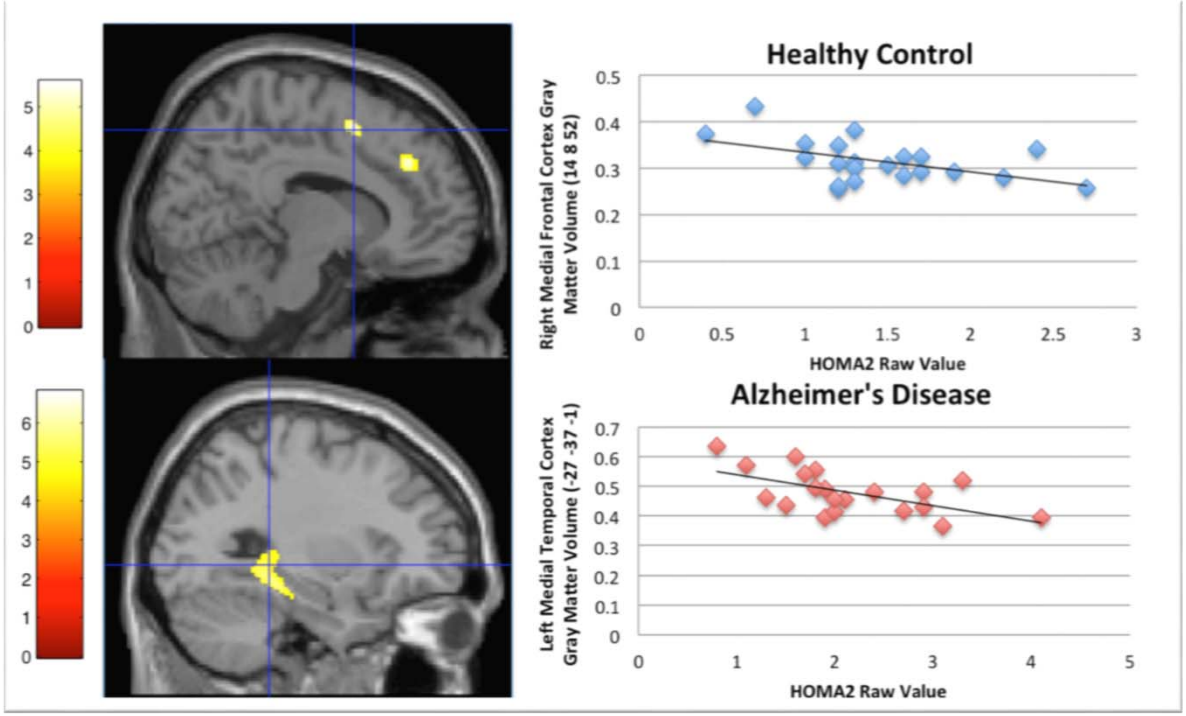

Morris et al 2014

AD subjects exhibit skeletal muscle insulin resistance

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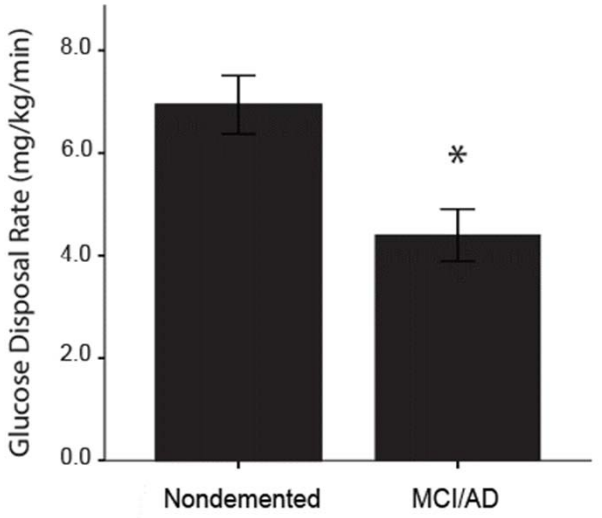
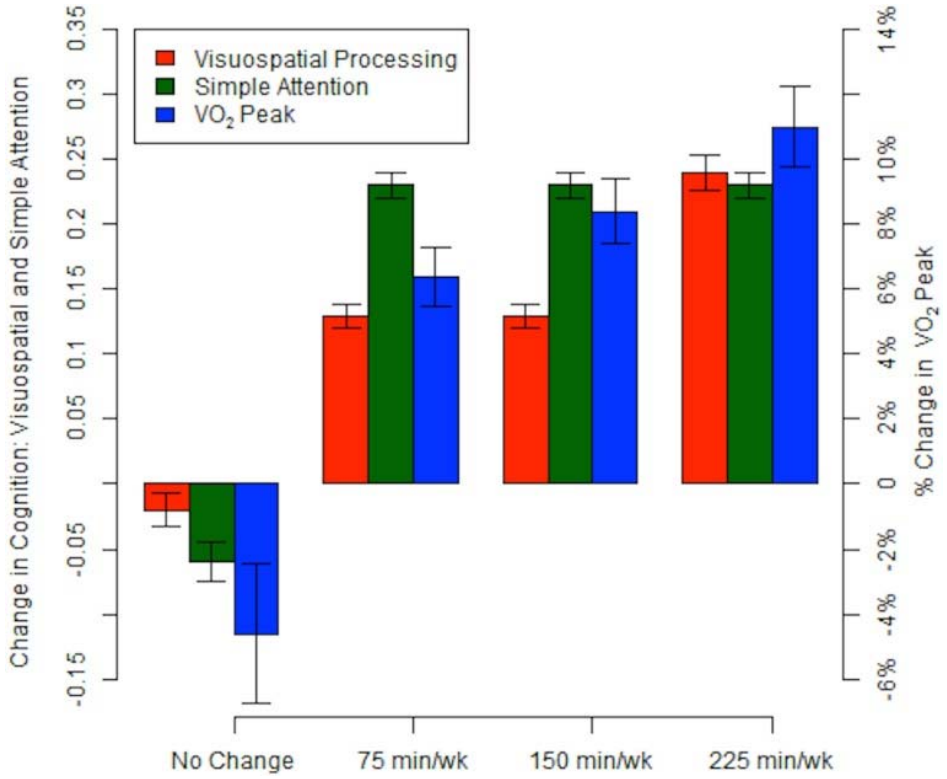


Morris et al 2016b, NBA

Exercise in Aging and AD

- BAP *(Brain Aging Project: 2006-2008)*
  - Longitudinal observational study, ND and AD
- TEAM *(Trial of Exercise on Aging and Memory: 2008-2013)*
  - Exercise trial, cognitively healthy elderly
- ADEPT *(Alzheimer's Disease Exercise Program Trial: 2010-2015)*
  - Exercise trial, probable AD
- APEX *(Alzheimer's Prevention through Exercise: 2014-ongoing)*
  - Exercise trial, cognitively healthy elderly "at risk" for AD

TEAM (Cognitively healthy elderly)



Vidoni et. al. 2015, Plos ONE

ADEPT (Alzheimer's Disease)

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	Timepoint	Stretching and Toning Control	Aerobic Exercise	Arm by Timepoint Interaction
Memory Composite	Baseline	-2.8 (1.4)	-2.5 (1.4)	$X^2 = 0.82$ (2) p = 0.66
	Week 13	-2.8 (1.5)	-2.3 (1.5)	
	Week 26	-2.7 (1.7)	-2.3 (1.7)	
Executive Function Composite	Baseline	-1.34 (0.85)	-1.12 (0.82)	$X^2 = 2.6(2)$, p = 0.27
	Week 13	-1.25 (0.94)	-1.09 (0.86)	
	Week 26	-1.33 (0.97)	-1.20 (0.90)	
Disability Assessment for Dementia	Baseline	91.2 (8.0)	88.0 (12.3)	$X^2 = 8.2(2)$, **p = 0.02**
	Week 13	89.5 (12.8)	89.8 (12.5)	
	Week 26	86.7 (13.3)	89.5 (13.7)	
Cornell Scale for Depression in Dementia	Baseline	7.4 (3.8)	8.6 (5.1)	$X^2 = 1.3(2)$, p = 0.51
	Week 13	8.1 (4.4)	8.4 (4.6)	
	Week 26	7.8 (4.4)	7.8 (5.2)	

Mean (standard deviation) unless otherwise noted.

doi:10.1371/journal.pone.0170547.t002

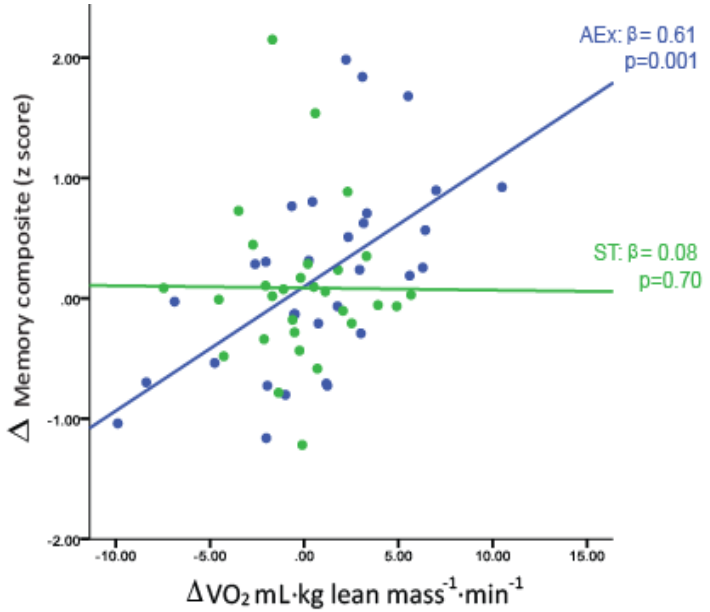
Morris, Vidoni et. al. 2017, PLOS One

AD subjects: fitness and memory/brain benefit are positively linked

Overall:

- Individuals who do improve fitness with AEx improve memory and hippocampal volume

- AD subjects: more variable response to exercise
  - Modest fitness gain (3% AD vs 8% in ND)



Do differences in cellular energy metabolism play a role?

Morris, Vidoni et. al. 2017, PLOS One

Next step: assess tissue mitochondrial function in early disease (MCI)

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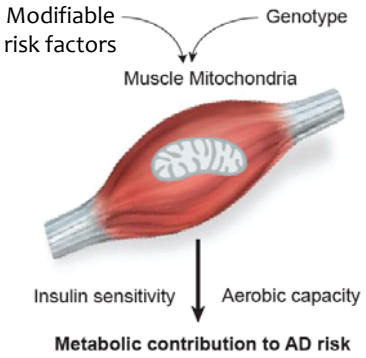
Aging and Disease Mitochondria (R21 AG056062)

Multidisciplinary collaboration: Dr. John Thyfault, Dr. Morris and Dr. Swerdlow

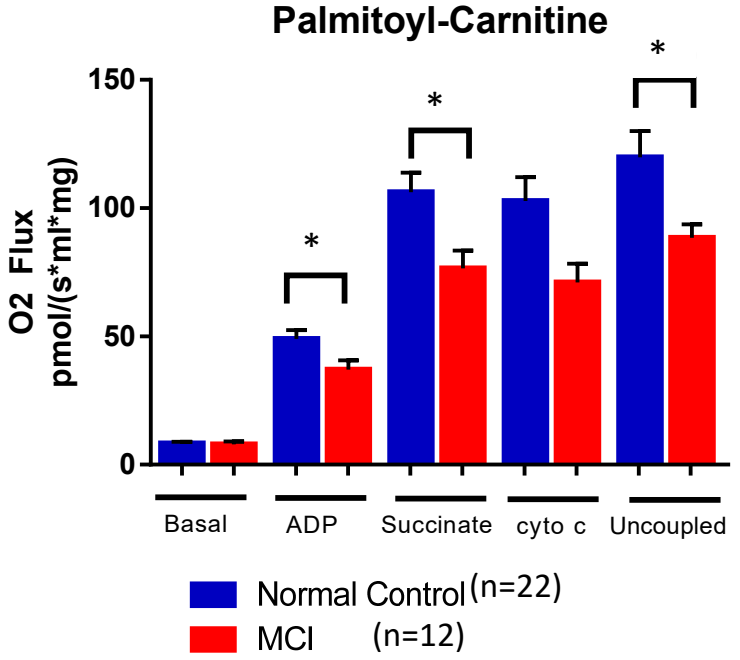


- **Non-brain targets may affect AD susceptibility** via lifestyle, genetics, or other factors
- Muscle mitochondrial function **has not been measured** in MCI or AD
- Fitness is partially dependent on muscle mitochondrial content and respiratory function, and declines in AD

MCI subjects exhibit impaired mitochondrial function in muscle

Muscle Biopsy Procedure

Muscle fiber bundle



No difference in activity levels

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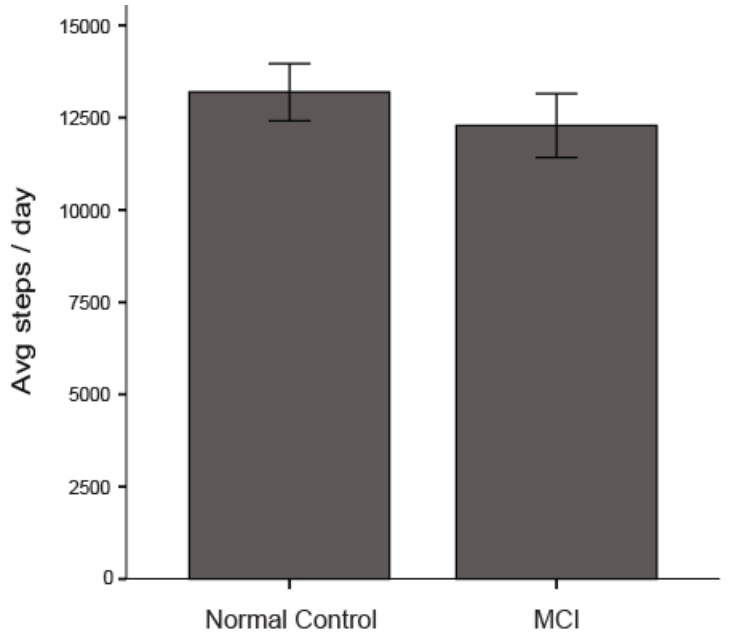

Future work

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- Cross sectional mitochondrial function + relationship with fitness
  - H_2O_2 emission, mitochondrial and respiratory chain content, transcriptional regulation of biogenesis, morphology, -omics, etc
  - Cells to systems relationships

- Exercise trials: bioenergetics, metabolism, vascular, neuroimaging
  - Mechanisms
  - Acute exercise
  - Better trial design

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Thank you to our team!!!!!

Morris Laboratory

Casey John, MS
Ashwini Kamat

KU ADC

Anne Arthur, ARNP
Ashley Thompson
Kayla Meyer
Angela Van Sciver
Ian Weidling
Arianna Christian, MS
Briana Bright
Mark McClellan

Students

Zachary Green
Nicole Burns
Alexis Aiman

KUMC Collaborators

Jeffrey Burns, MD
Eric Vidoni, PhD
John Thyfault, PhD
Russell Swerdlow, MD
Colin McCoin, PhD
Heather Wilkins, PhD
Xiaowan Wang, PhD
Jonathan Mahnken, PhD
Sandra Billinger, PhD
Matthew Taylor, PhD
Paige Geiger, PhD
William Brooks, PhD

External collaborators

Sid O'Bryant, PhD (UNT Health)
Sean Adams, PhD (UAMS)
Brian Piccolo, PhD (UAMS)
Ozioma Okonkwo, PhD (Wisconsin)
Jakob Haus (Michigan)

CTSU nursing support

FUNDING

NIA R00 AG050490
NIA R21 AG056062
NIA P30 AG035982

Research Volunteers

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The University of Kansas Medical Center

4350 Shawnee Mission Parkway
Fairway, KS 66205
913-588-0555
kualzheimer.org

Sandra Billinger, PT, PhD

KU ALZHEIMER'S DISEASE CENTER
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- Associate Professor in the Department of Physical Therapy and Rehabilitation Science
- Director of the Research in Exercise and Cardiovascular Health (REACH) lab
- Investigating vascular contributions to brain aging and neurologic conditions

Vascular Contributions to Brain Health

Sandra A Billinger, PhD, PT, FAHA

Associate Professor

KU Medical Center

Pathway to AD Research

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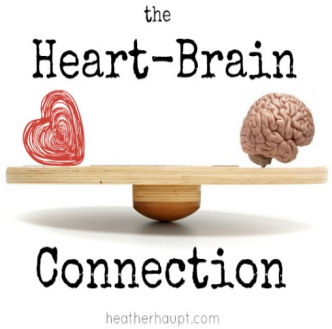

2002-2014

2014-2015

Pathway to AD Research

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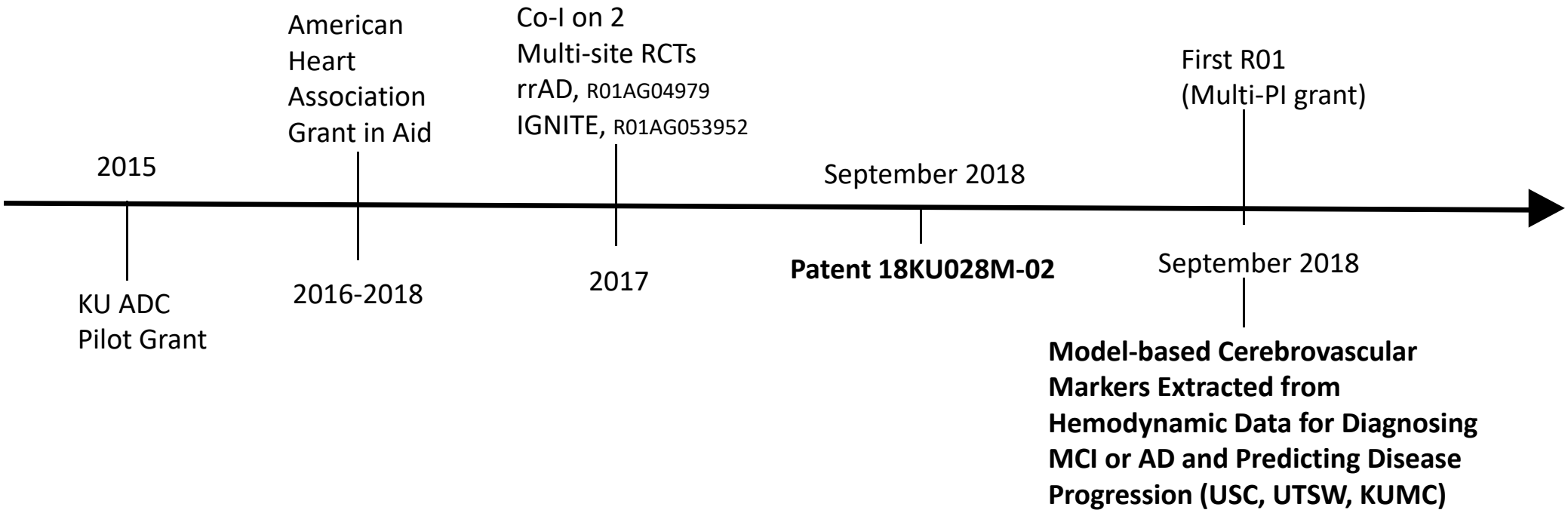

Brain Blood Flow Velocity to Exercise

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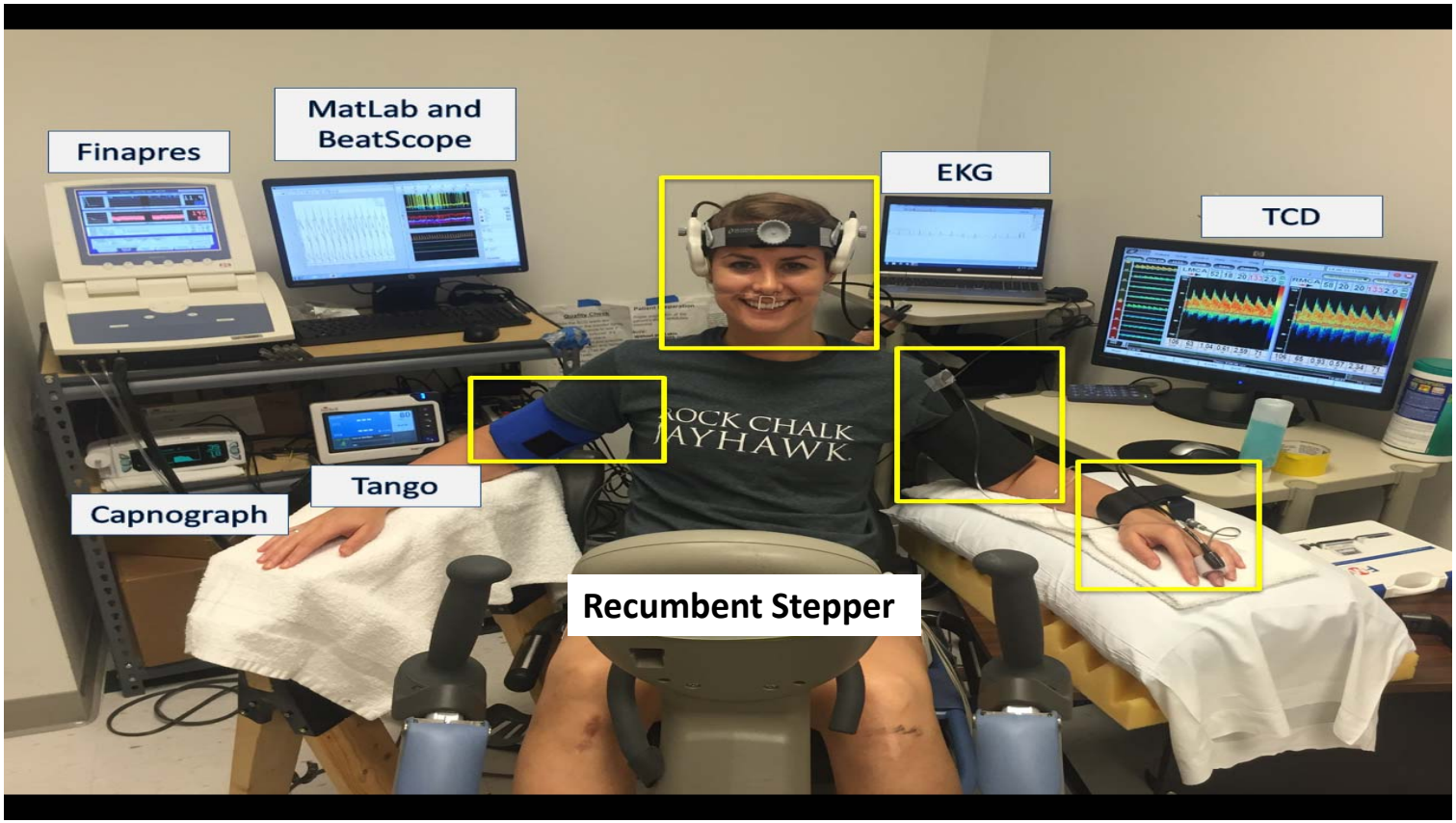
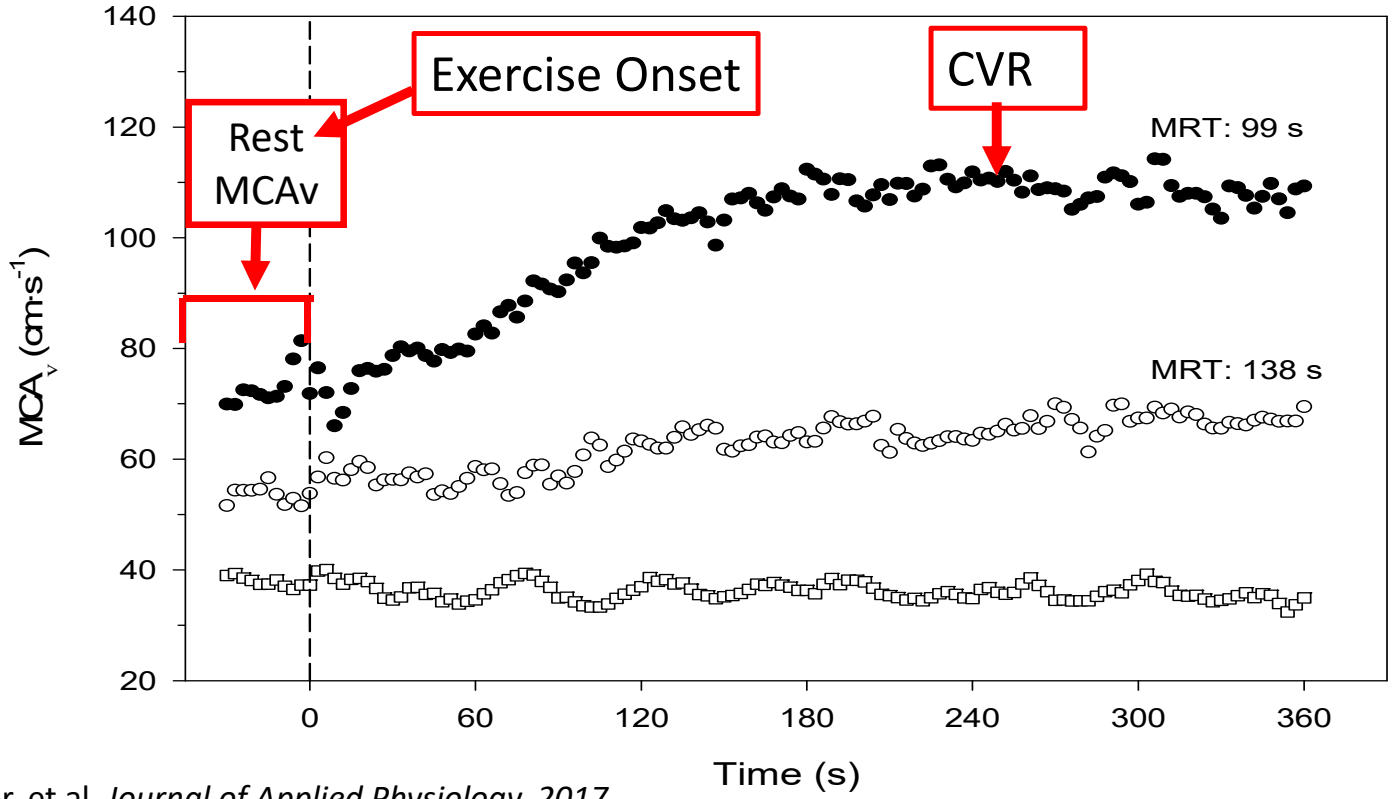


Brain Blood Flow Velocity Response to Exercise



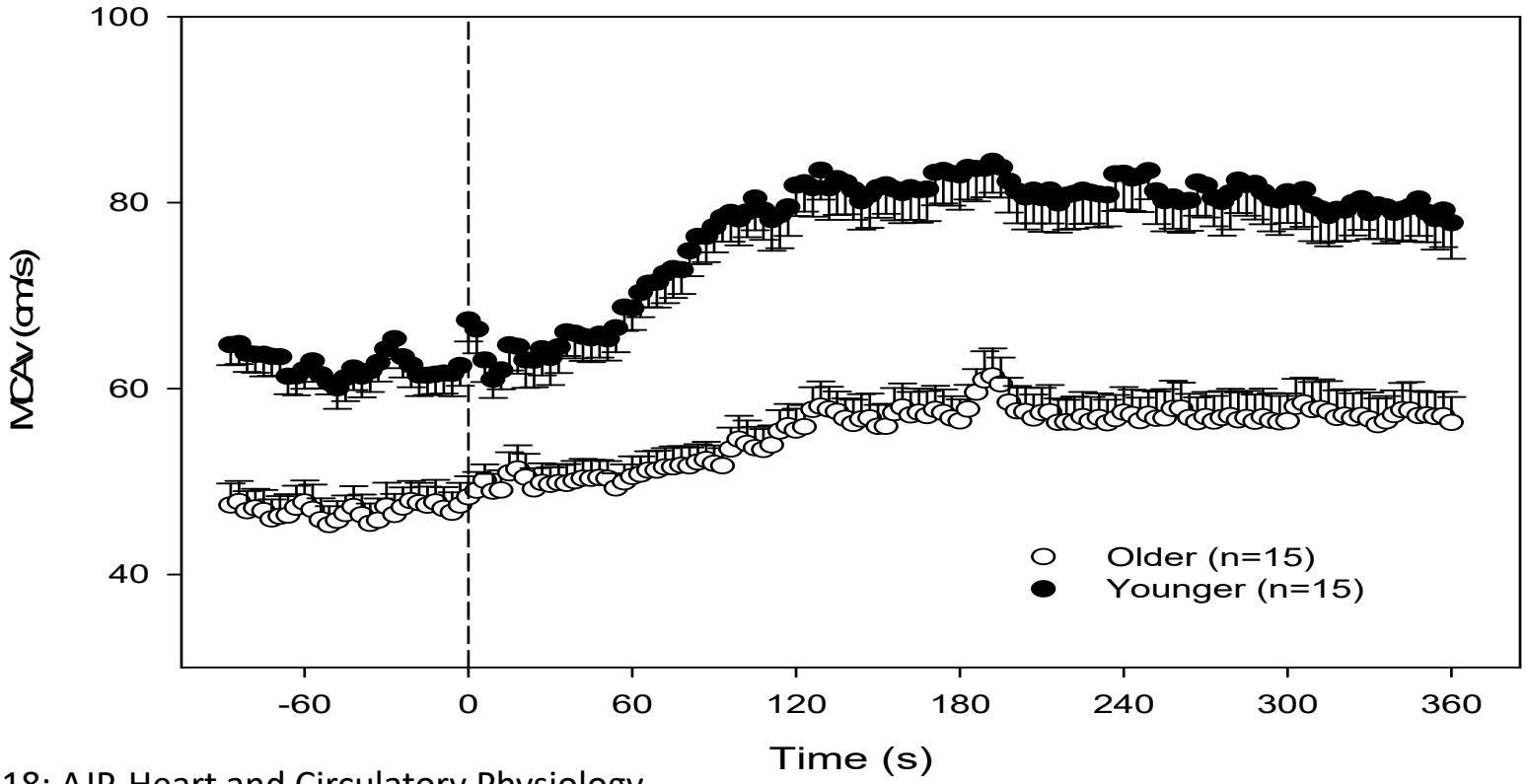
Active, Healthy Young Adult

Sedentary, Older Adult

Stroke (Age, Sex Matched)

Billinger, et al, *Journal of Applied Physiology, 2017*

Age and Brain Blood Flow Velocity Response to Exercise



Ward, 2018; AJP-Heart and Circulatory Physiology

A Brain “Exercise Stress Test”

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Trial for Assessing Cerebrovascular Regulation (TrACR) in Older Adults

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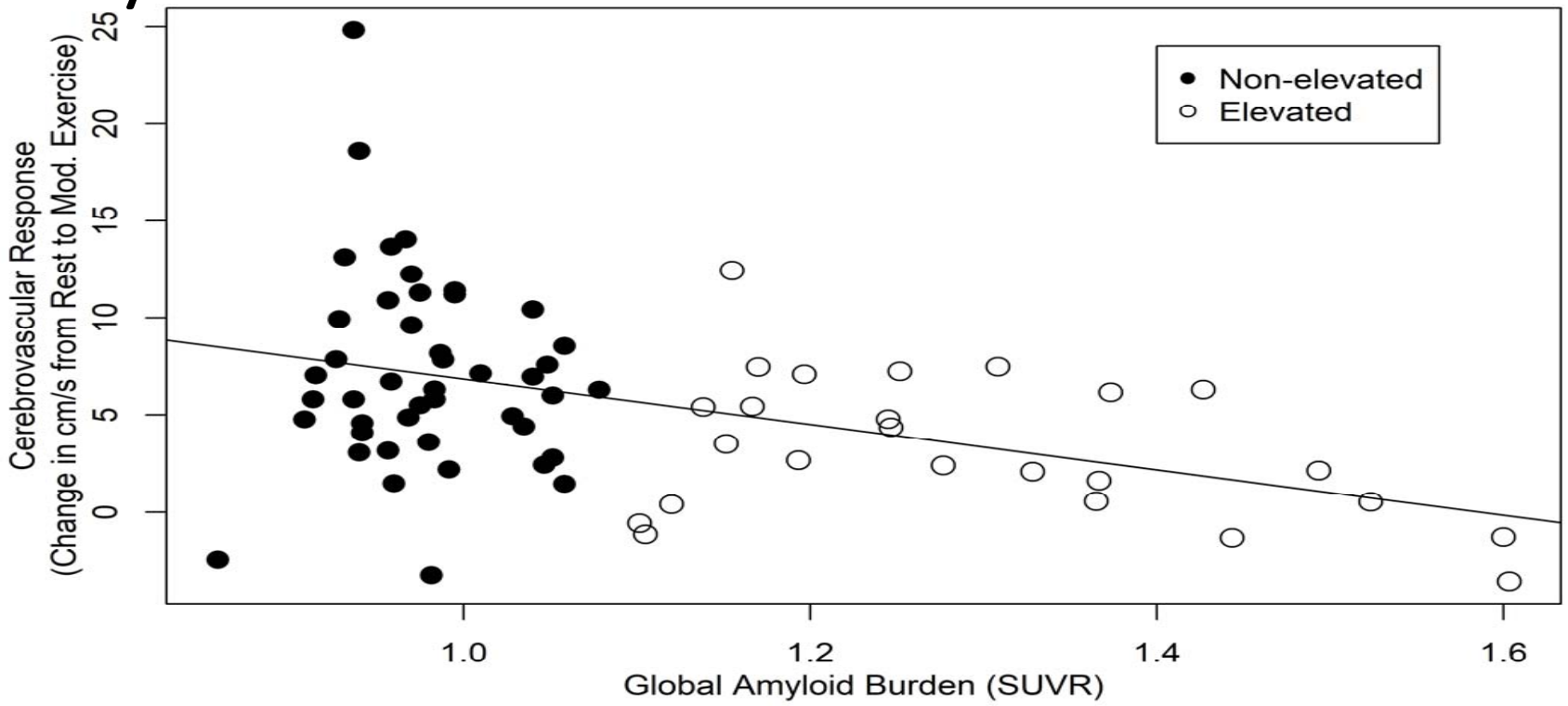
APEX (Burns: R01AG043962)

- Well characterized (cognitive, physical function)
- PET scan for Amyloid status (non-elevated/elevated)
- Neuroimaging core for MRI
  - White matter lesions (WML)

Billinger Lab (Billinger, KU ADC Pilot, 2015; AHA Grant-in Aid, 2016)

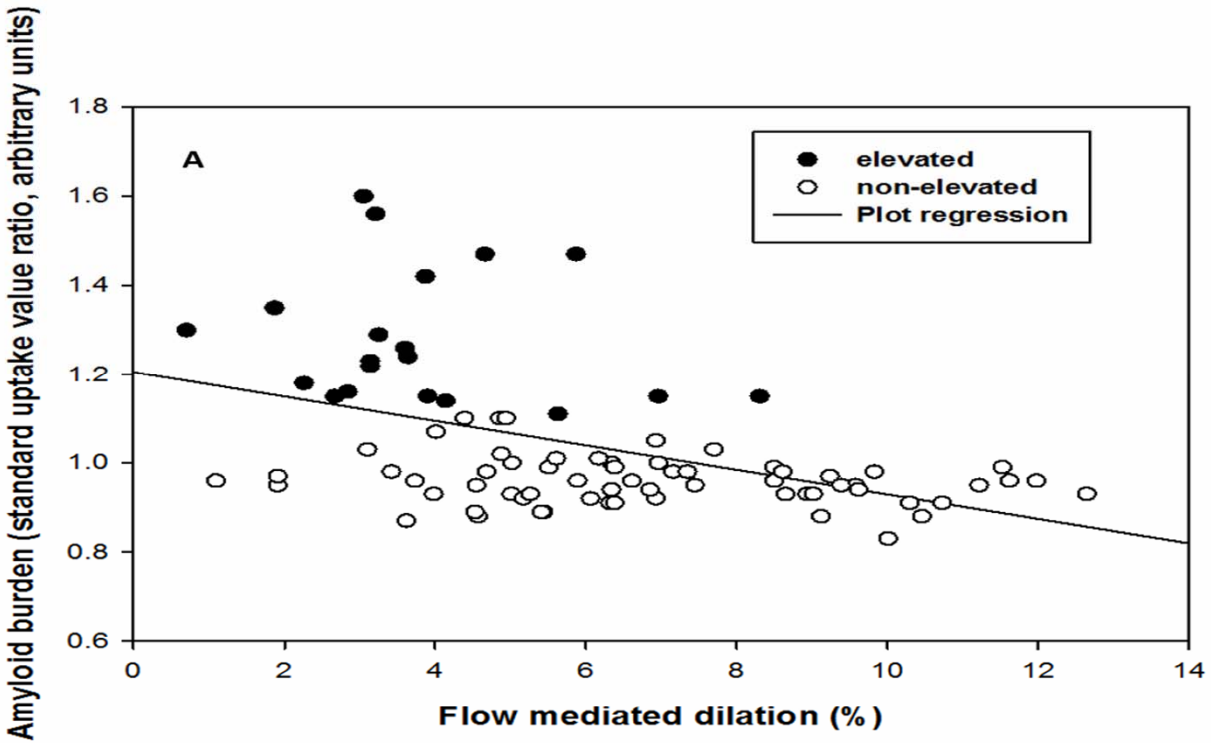
- Vascular risk
  - ASCVD score
  - Peripheral vascular measures (BP, Flow-mediated dilation, FMD)
  - Cerebrovascular regulation, CVR

Blunted CVR to Exercise with Increased Amyloid Load

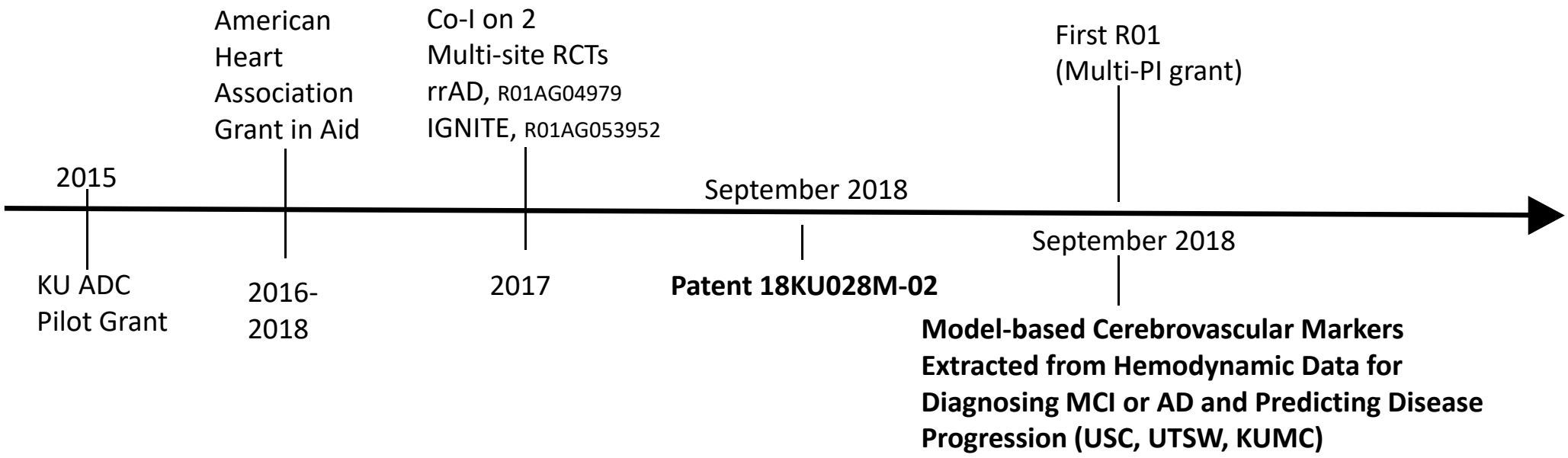


Sisante, et al, *J Cerebral Blood Flow and Metabolism, 2017*

Endothelial Function Diminished with Increased Amyloid Load



Forward Momentum in AD Research



Model-based Cerebrovascular Markers Extracted from Hemodynamic Data for Diagnosing MCI or AD and Predicting Disease Progression

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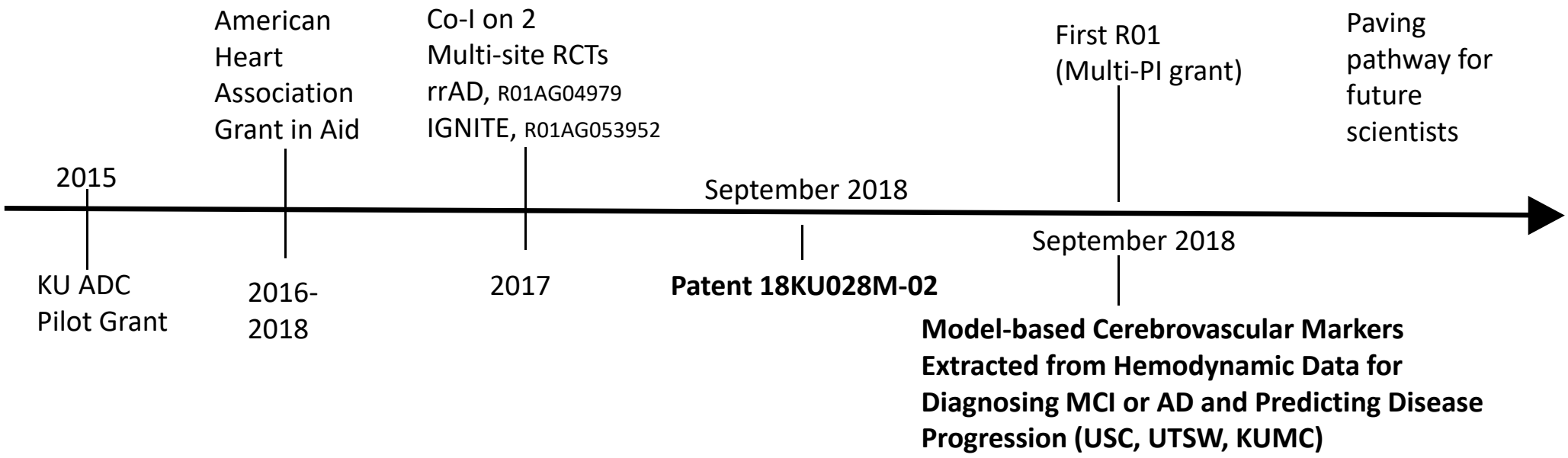
- Multi-site trial (USC, Vasilis Marmarelis; KU, Billinger; UTSW, Rhong Zhang)
- Leveraging existing infrastructure with P30/ADC
  - OR Core, Clinical Core, NeuroImaging Core
- Baseline Measures for 25 ND, 25 MCI, 25 Early AD
  - Neuropsych testing
  - PET Scan (Amyloid-Florbetaben)
  - WML
  - Vascular Hemodynamics (TCD, MAP, NIRS)
- Repeated yearly except PET (3-year follow up)

Forward Momentum in AD Research



Future AD Scientists

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The University of Kansas Medical Center

Post doctoral Fellows

Sophy Perdomo, PhD
University of Pittsburgh
Vascular Health
Arterial Stiffness
KU ADC REC (1 year fellowship)
F32 grant, December 2018

Andrea Freemyer, PhD
KU Medical Center
Neuroscience
Neuroplasticity
Cognition

PhD Student

Emily Witte, MS
Brain Health
Acute Exercise

KU

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4350 Shawnee Mission Parkway
Fairway, KS 66205
913-588-0555
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Debra Sullivan, PhD, RD

KU ALZHEIMER'S DISEASE CENTER
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- Chair of the Department of Dietetics and Nutrition
- Midwest Dairy Council Professor in Clinical Nutrition
- Understanding the impact of nutrition and weight loss on disease processes

Nutrition and Brain Health

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The University of Kansas Medical Center

Debra K. Sullivan, PhD, RD

Chair & Midwest Dairy Endowed Professor of Clinical Nutrition
Department of Dietetics and Nutrition

Nutrition at KU ADC

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- ~2008
  - Neuroimaging Core
    - In-Young Choi, PhD
    - Phil Lee, PhD
  - Measure cerebral glutathione
    - Potent antioxidant
  - Added food frequency questionnaire
    - Exploratory study

Am J Clin Nutr (2015) 287-293

See corresponding editorial on page 249.

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The University of Kansas Medical Center

Dairy intake is associated with brain glutathione concentration in older adults[1–3]

In-Young Choi, Phil Lee, Douglas R Denney, Kendra Spaeth, Olivia Nast, Lauren Ptomey, Alexandra K Roth, Jo Ann Lierman, and Debra K Sullivan

- Observational Study
- Funding: Dairy Research, Inc.
- n = 60 participants
- Cognitively normal older adults

Cerebral Glutathione Levels and Dairy Intake

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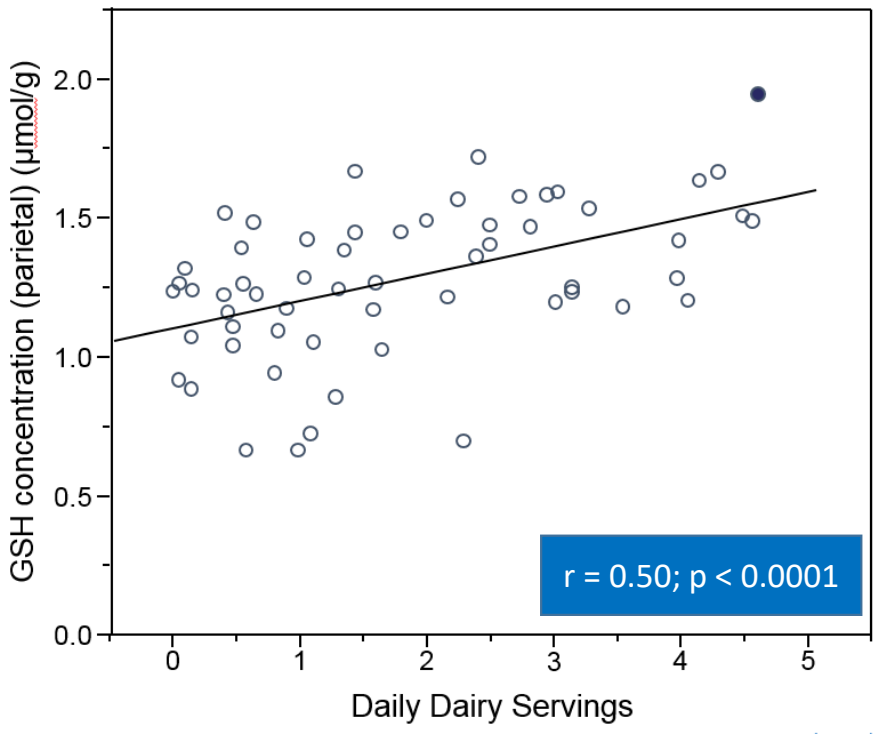
	GSH-frontal r_s	GSH-parietal r_s	GSH-fronto-parietal r_s
Dairy (servings/d)	**0.394**	**0.500**	**0.465**
Milk (servings/d)	**0.402**	**0.437**	**0.437**
Cheese (servings/d)	0.165	**0.374**	**0.275**
Yogurt (servings/d)	0.006	0.024	-0.025
Calcium (mg/d)	**0.280**	**0.328**	**0.328**
Riboflavin (mg/d)	0.245	0.230	**0.273**
Vitamin D (µg/d)	0.135	0.187	0.177

*** $p < 0.05$**



Ongoing RCT Milk Intervention. Funding: Dairy Research, Inc.

kualzheimer.org

Choi et al., *Am J Clin Nutr (2015) 287-293*

Nutrition at KU ADC

- ~2011
  - Added food frequency questionnaire to KU Alzheimer's Disease Center (ADC) APEX study

- 2013 Principal Investigator
  - Feasibility of the ketogenic diet in individuals with Alzheimer's disease.
  - Pilot Funding:
    - KU Alzheimer's Disease Center

A high-glycemic diet is associated with cerebral amyloid burden in cognitively normal older adults

Matthew K Taylor,[1,3] *Debra K Sullivan,*[1,3] *Russell H Swerdlow,*[3] *Eric D Vidoni,*[3] *Jill K Morris,*[3] *Jonathan D Mahnken,*[2,3] *and Jeffrey M Burns*[3]

Departments of [1]Dietetics and Nutrition and [2]Biostatistics, University of Kansas Medical Center, Kansas City, KS; and [3]University of Kansas Alzheimer's Disease Center, Fairway, KS

ABSTRACT

Background: Little is known about the relation between dietary intake and cerebral amyloid accumulation in aging.

Objective: We assessed the association of dietary glycemic measures with cerebral amyloid burden and cognitive performance in cognitively normal older adults.

Design: We performed cross-sectional analyses relating dietary glycemic measures [adherence to a high-glycemic-load diet (HGLDiet) pattern, intakes of sugar and carbohydrates, and glycemic load] with cerebral amyloid burden (measured by florbetapir F-18 positron emission tomography) and cognitive performance in 128 cognitively normal older adults who provided eligibility screening data for the University

Molecular imaging techniques with the use of positron emission tomography (PET) with an amyloid-specific ligand allow for the detection of cerebral amyloid in those with AD (2). This technique is increasingly used as a research tool to detect the molecular pathology of AD in cognitively unimpaired individuals, of whom 20–40% have evidence of cerebral amyloid deposits and are thus considered to be at higher risk of developing AD (3). These individuals are the target of interventional trials to prevent or delay the onset of AD, with an increasing interest in lifestyle behaviors, including dietary approaches (4).

Current studies show that impaired glucose metabolism and peripheral hyperglycemia are associated with a higher risk of

rnal of Clinical Nutrition

High Glycemic Load Diet Pattern associated with Cerebral Amyloid

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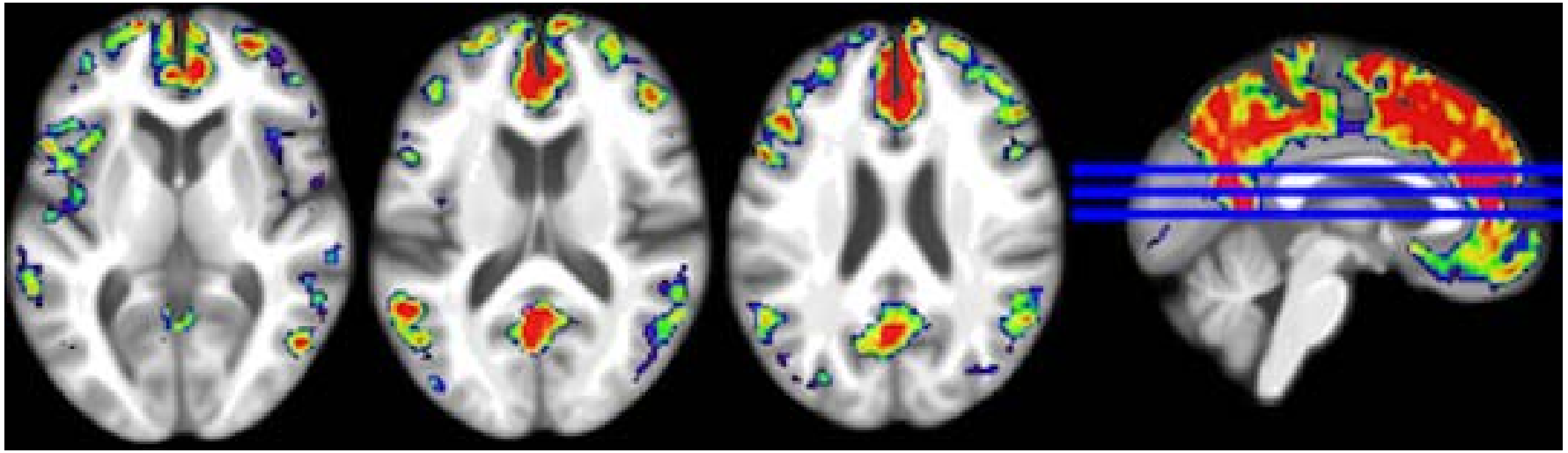
Visualization of Relationship between Amyloid & HGL Diet Pattern
n = 128



Standardized β values are projected on the MNI152 anatomical template, with warmer colors representing regions of greater association with HGLDiet.

ELSEVIER

CrossMark

Alzheimer's & Dementia: Translational Research & Clinical Interventions 4 (2018) 28-36

Alzheimer's & Dementia

Featured Article

Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease

Matthew K. Taylor[a,b], Debra K. Sullivan[a,b], Jonathan D. Mahnken[a,c], Jeffrey M. Burns[a,d,e], Russell H. Swerdlow[a,d,e,f,*]

[a]*University of Kansas Alzheimer's Disease Center, Fairway, KS, USA*
[b]*Department of Dietetics and Nutrition, University of Kansas Medical Center, Kansas City, KS, USA*
[c]*Department of Biostatistics, University of Kansas Medical Center, Kansas City, KS, USA*
[d]*Department of Neurology, University of Kansas Medical Center, Kansas City, KS, USA*
[e]*Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS, USA*
[f]*Department of Biochemistry and Molecular Biology, University of Kansas Medical Center, Kansas City, KS, USA*

Ketogenic Diet Participants and Study Design

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The University of Kansas Medical Center

- **Participants:** 15 individuals with AD + Study Partners enrolled
  - 7 CDR 0.5
  - 4 CDR 1
  - 4 CDR 2

All 4 CDR 2s dropped and 1 CDR 0.5 dropped due to caregiver burden

Design

Ketogenic Diet Cognitive Results

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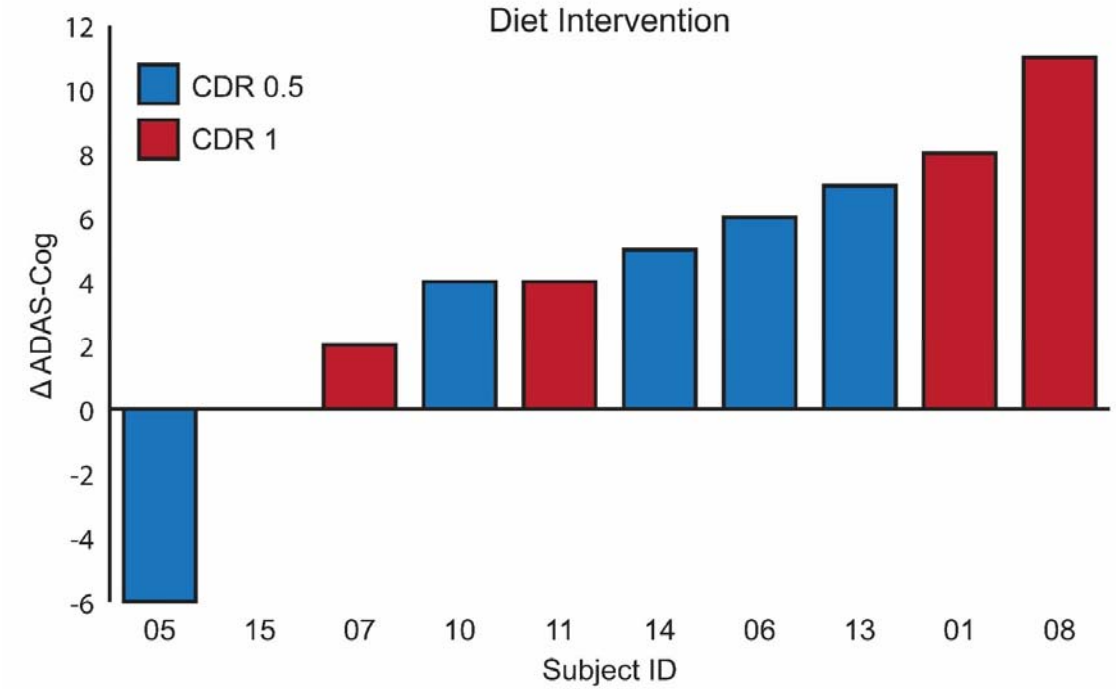
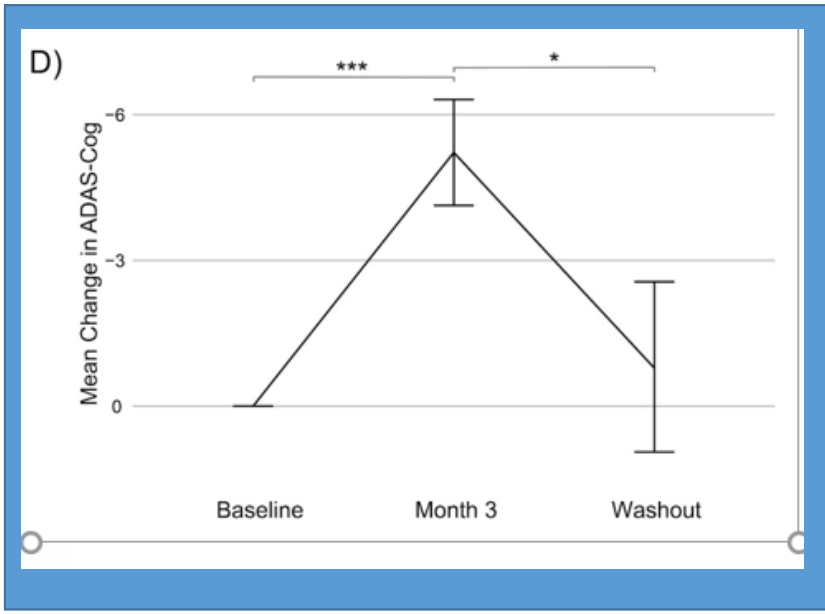
Individual Change in ADAS-Cog Scores from Baseline - 3 Months



Mean Change in ADAS-Cog Scores



*Participant 05 was diet intervention compliant, but not protocol compliant as cholinesterase inhibitor therapy was discontinued

Ketogenic Diet Status

KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

- 1 R01 AG060733-01A1
- Validation and Mechanistic Interrogation of Metabolism Targeting for AD
- MPI
  - Russell H. Swerdlow
  - Debra K. Sullivan
- RCT (n = 80)
  - MCT-supplemented Ketogenic diet
  - Therapeutic Lifestyles Diet
- 24th Percentile

Feasibility trial of a Mediterranean diet pattern to prevent cognitive decline

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- 2016 Pilot Funding: KU ADC
- Establish whether it is feasible for older adults with and without cognitive impairment to adopt and maintain a Mediterranean diet pattern for 6 weeks.
- Evaluate the acceptance and sustainability of the MedDiet pattern

Feasibility trial of a Mediterranean diet pattern to prevent cognitive decline (n=30)

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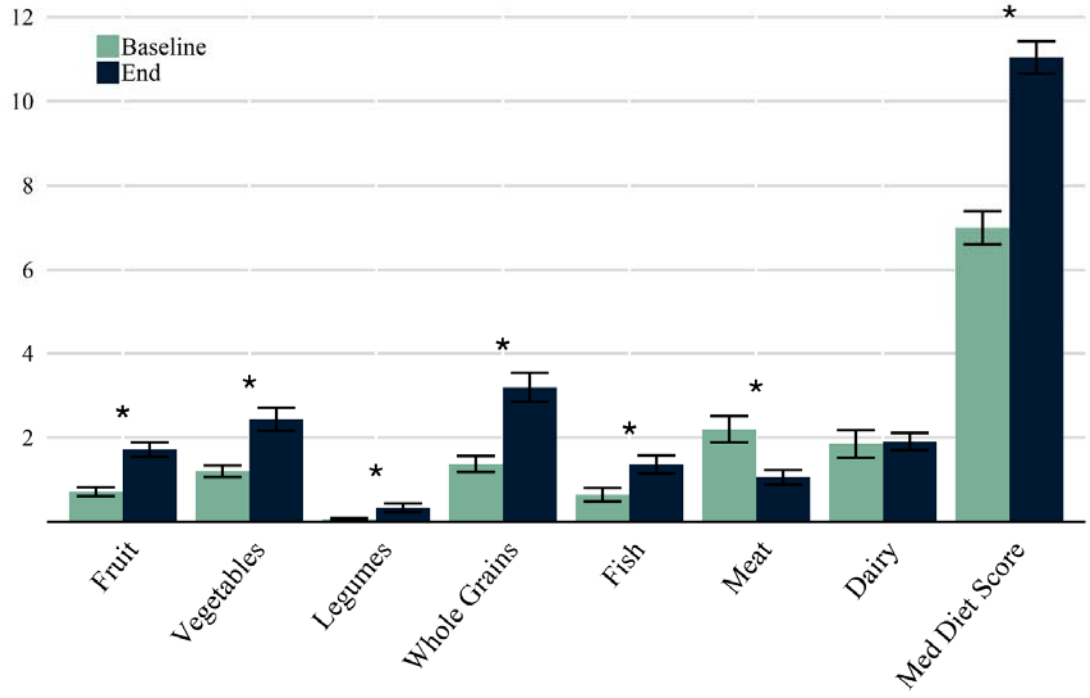
Demographics and Feasibility

	Probable AD N = 12	Cognitively Normal N = 18
Age (years)	77.4 ± 3.9	71.6 ± 5.2
Gender (%Male)	75%	29.4%
Completion Rate	80%	94%
Food box adherence	100	100

Reasons for attrition: change in health status and time burden.

Change in Diet Intake



Biomarker of Fruit/Vegetable Intake "Veggie Meter"

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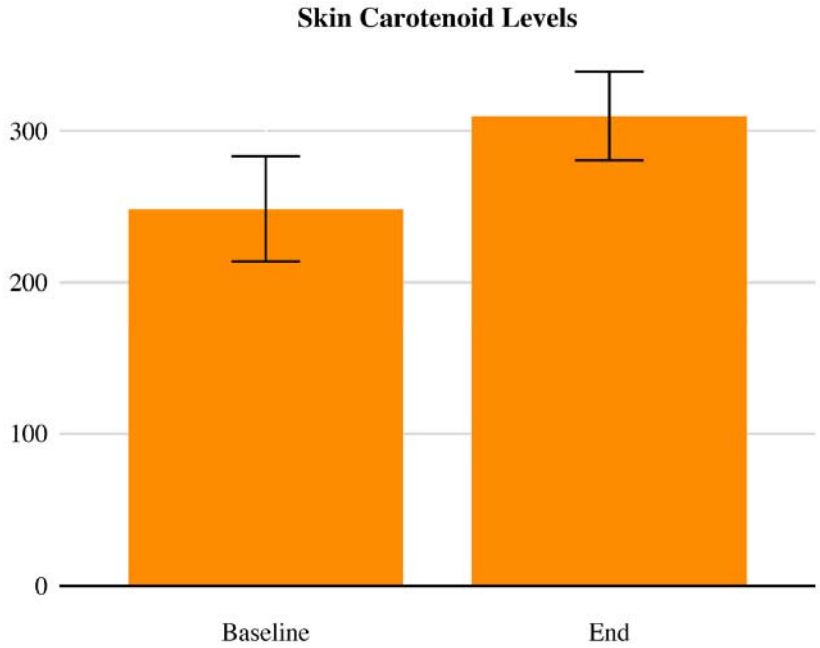
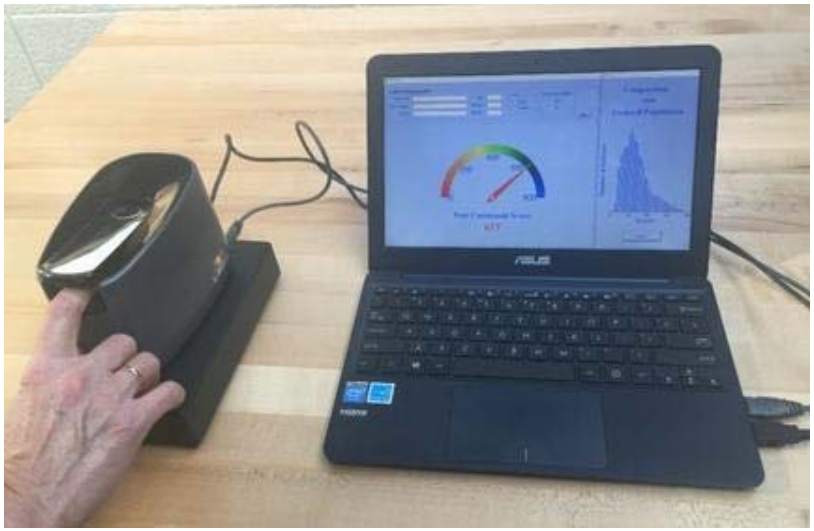
The University of Kansas Medical Center

Subset: Change in Skin Carotenoid Levels (n=12)



p = 0.006



NICE STUDY

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Nutrition Interventions for Cognitive Enhancement

"Enhanced Mediterranean Diet for Alzheimer's Disease Prevention"

- 1 R01 AG060157-01
- MPI
  - Debra K. Sullivan
  - Jeffrey M. Burns
- RCT (n = 200)
  - Enhanced Mediterranean diet pattern
  - Low Fat diet pattern
- Awarded 9/30/2018 – 5/31/2023

Training Future Researchers

KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

- Lauren Ptomey, PhD, RD
  - PhD Weight management in IDD
  - R01 Remote exercise in IDD
- Matthew Taylor, PhD, RD, LD
  - PhD ketogenic diet
  - Post doctoral fellow
  - K01 submission February 2019
- Sibelle Alhayek, MS
  - PhD student
- Brooke Noble, MS, RD
  - PhD student

- M.S., R.D. students

Emily Cope	Olivia Nast	Kristy Taylor
Randy Evans	Katherine O'Dell	Alyssa Klehr
Rachel Sandoval	Jordan Chen	Michelle Nussbaum
Katelynne Burghardt	Kayla Graves	Cassie McClellan

Debra K. Sullivan, PhD, RD
dsulliva@kumc.edu

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4350 Shawnee Mission Parkway
Fairway, KS 66205
913-588-0555
kualzheimer.org

Empowering Community Through Science and Care

KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

· Mission ·

To improve the lives of patients and families with Alzheimer's disease by eliminating the disease through research into its treatment and prevention

· Core Values ·

Meaningful Work

Always Improving
Driving Innovation
Empowering Community

Overview

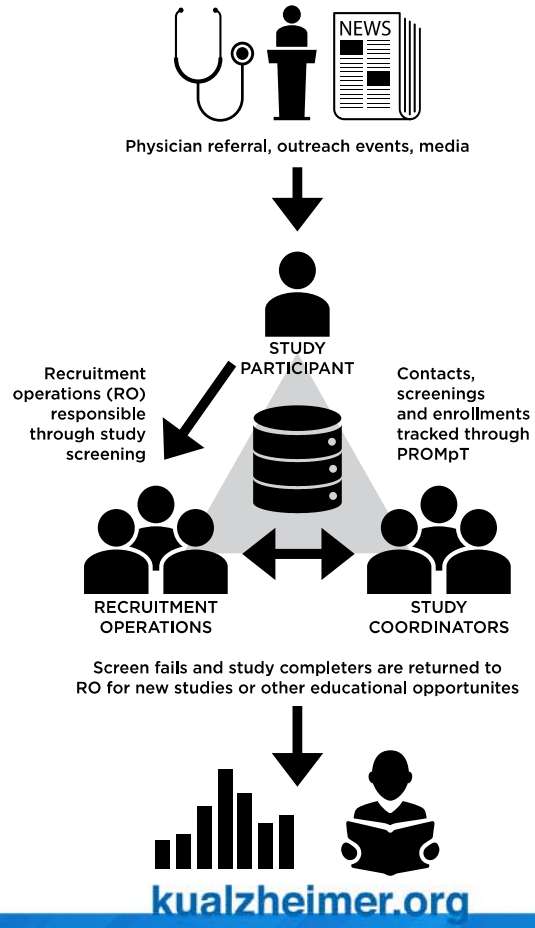
- Recruitment Innovation to Speed Trials and Improve Experience
  - Centralized model
  - Real-time recruitment metrics

- Translating Clinical Research to Lifestyle Modification Support
  - Aerobic exercise (TEAM, ADEPT, APEx), ketogenic (KDRAFT), and Med. diet (NICE)
  - Lifestyle Empowerment for Alzheimer's Prevention (LEAP! / LEAP!Rx)

- Engagement & Empowerment Through Knowledge
  - AD education developed and delivered with the community
  - Building collaborative care networks throughout KS

Adopted CRO-like model shifting burden off study coordinators

- Major investment in centralized recruitment infrastructure and personnel (Vidoni et al., 2018)
  - 4x increases in participation inquiries
  - 54% decrease in enrollment time
  - Real-time recruitment metrics via R/Shiny
  - EMR research referral and e-consent for medical record release



- Translational education program on AD-risk reduction through lifestyle modification
- Empowers successful behavior changes that promote brain health and overall wellness
- Provides evidence-based recommendations on nutrition, physical activity, and more for brain health
- 1300+ individuals have taken the LEAP!

Developing culturally appropriate versions of LEAP!

- African-Americans - *Aging With Grace*
  - 47 times to over 700 individuals
- Latinos - *¡Envejecimiento Digno!* (Perales, *Ethn Health*, 2018)
  - 12 times to 145 individuals
- Rural residents – *Wheat State LEAP!* for rural KS (Blocker, in prep)
  - 71 rural KS residents completed 12 week intervention
  - Increased steps and dementia knowledge


T. Weatherspoon


Jaime Perales


Erin Blocker

LEAP!
LIFESTYLE EMPOWERMENT FOR ALZHEIMER'S PREVENTION

LEAP!Rx
LIFESTYLE EMPOWERMENT FOR ALZHEIMER'S PREVENTION

- LEAP! Engagement methodology being tested in RCT (Burns: R01 AG052954)
- KU Health System physicians prescribe LEAP! through EMR
- YMCA delivers LEAP!Rx over 12 weeks
- 52-week follow-up


Amber Watts

Empowering a More Dementia Capable and Research Ready Community

KU ALZHEIMER'S DISEASE CENTER
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- Forget Me Not Play (in partnership with USAA/AAAA, GAP Foundation, and the KC Black Health Care Coalition)
  - Hosted two stagings (n=>500, n=311 completed post-performance surveys)
  - 93% agreed they had "a better sense of why African-Americans need to get involved in research"
  - 17 play attendees came to an *Aging With Grace*
  - 2 individuals enrolled in our Clinical Cohort

Transforming Dementia Capability in the Region

- Leading *Kansas City Collaborative for Dementia Capability* *(Ptomey/Vidoni ACL ALGG0009)*
  - Implementing RDAD-KC program in the region to support persons with dementia or IDD and their caregivers. (*adapted Teri et al., JAMA 2003*)


Lauren Ptomey

- Trained over 200 formal caregivers and professionals on dementia and dementia-capable care
  - Regional network of NTG Regional Affiliate Trainers (n=23)

- Enrolled 60 dyads in the RDAD-KC program
  - Reduced Unmet Needs and NPI-Q

Create a More Dementia Capable and Research Ready Community

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- We emphasize:
  - Collaboration with long-standing community organizations
  - Community-informed research and programs

Innovating New Models of Care

- Aligning Primary Care practices with early detection protocols
- Integrating dementia education and support into provider practice workflow
- Connection disease disclosure to a *wellness plan* that includes research

Community at the Core

KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

- Improving, Innovating, and Empowering so that our work is meaningful to our region.
- Stakeholders benefit from and inform our work.
- Energy and experience that is transforming recruitment and education, making our region more dementia capable and research ready.

Thanks to my great team!

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- Hit us up on SM:
  - @KUALZ
  - fb.com/KUADC

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kualzheimer.org

Jaime Perales Puchalt, PhD

KU ALZHEIMER'S DISEASE CENTER
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- Post-doctoral Fellow, KU ADC
- Expertise in epidemiology of aging and dementia
- Key architect and steward of community partnerships in the Latino community

Becoming an independent researcher in Latino AD disparities

Becoming an independent researcher in Latino AD disparities

Jaime Perales Puchalt, PhD, MPH

(NIA Diversity Supplement: P30AG035982)

Index

1. Previous experience
2. Long-term goal
3. Experience at the KU ADC
4. Conclusions and Next Steps

Index

1. **Previous experience**
2. Long-term goal
3. Experience at the KU ADC
4. Conclusions and Next Steps

My previous experience: 2006-2008

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The University of Kansas Medical Center

Universitat de València

Psychometrist and data manager, stress-related projects

My previous experience: 2009-2014

Site manager, COURAGE in Europe Project

- **Perales J**, Martin S, Ayuso-Mateos JL, Chatterji S, et al. Factors associated with active aging in Finland, Poland, and Spain. International psychogeriatrics. 2014 Aug;26(8):1363-75.
- Caballero FF, Miret M, Olaya B, **Perales J,** et al. Evaluation of affect in Mexico and Spain: psychometric properties and usefulness of an abbreviated version of the day reconstruction method. Journal of Happiness Studies. 2014 Aug 1;15(4):915-35.

My previous experience: 2011-2012

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UNIVERSITY OF CAMBRIDGE

Visiting PhD researcher, QoL in dementia research

- **Perales J**, Cosco TD, Stephan BC, Haro JM, Brayne C. Health-related quality-of-life instruments for Alzheimer's disease and mixed dementia. International Psychogeriatrics. 2013 May;25(5):691-706.
- **Perales J**, Cosco TD, Stephan BC, Fleming J, Martin S, Haro JM, Brayne C. Health-related quality of life in the Cambridge City over-75s Cohort (CC75C): development of a dementia-specific scale and descriptive analyses. BMC geriatrics. 2014 Dec;14(1):18.

My previous experience: 2014-2016

Postdoctoral fellow, Latino Kick Buts

- Cupertino AP, Cartujano-Barrera F, **Perales J**, Formagini T, Rodríguez-Bolaños R, Ellerbeck EF, Ponciano-Rodríguez G, Reynales-Shigematsu LM. "Vive Sin Tabaco… ¡Decídete!" Feasibility and Acceptability of an e-Health Smoking Cessation Informed Decision-Making Tool Integrated in Primary Healthcare in Mexico. Telemed J E Health. 2018 Jul

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1. Previous experience
2. **Long-term goal**
3. Experience at the KU ADC
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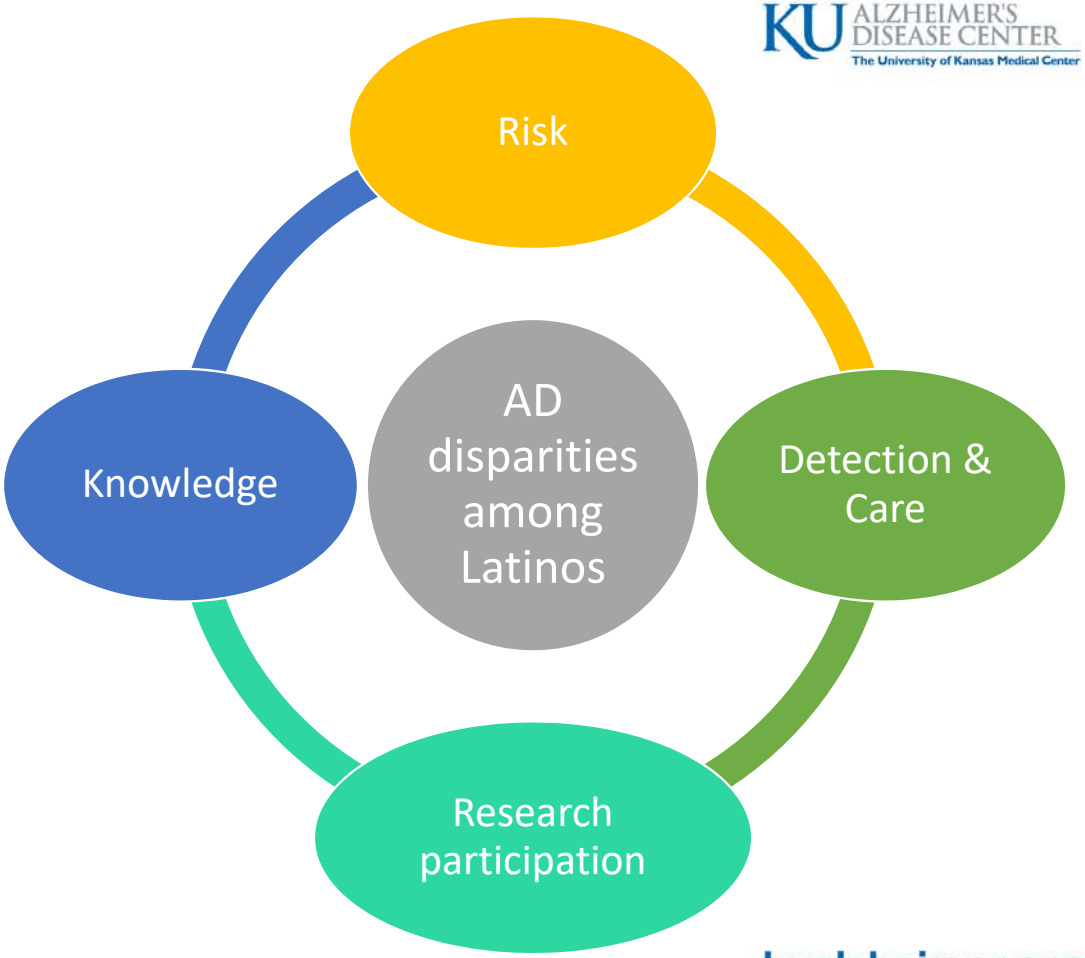
My long-term goal

- To become an independent dementia disparities researcher among Latinos



KU ADC is ideal for my goal

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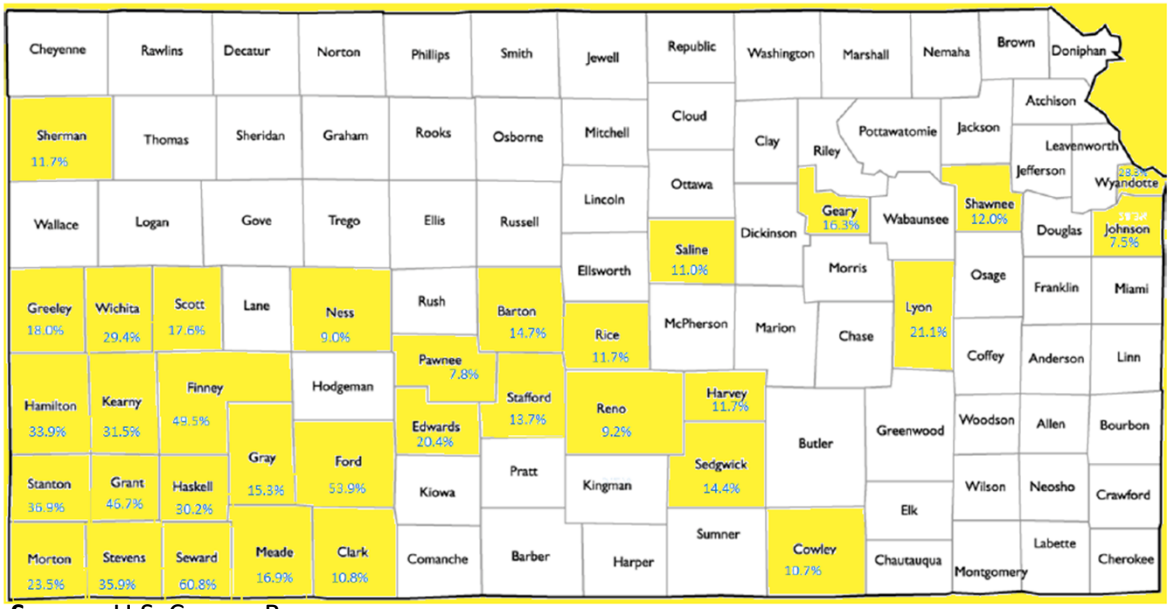
Latinos as Percent of County Population in the State of Kansas
Latino Percent Equal To or More than 7%



Source: U.S. Census Bureau
Map prepared by: Juntos Center KUMC Preventive Medicine and Public Health on June 9, 2018

KU ADC is ideal for my goal

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Latinos as Percent of County Population in the State of Kansas
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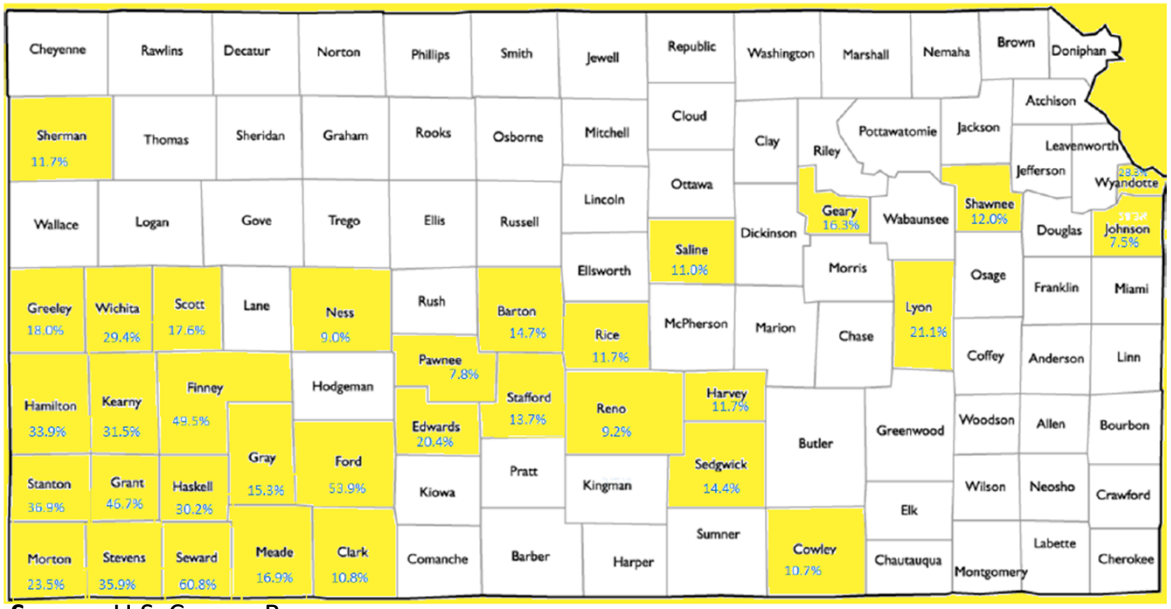

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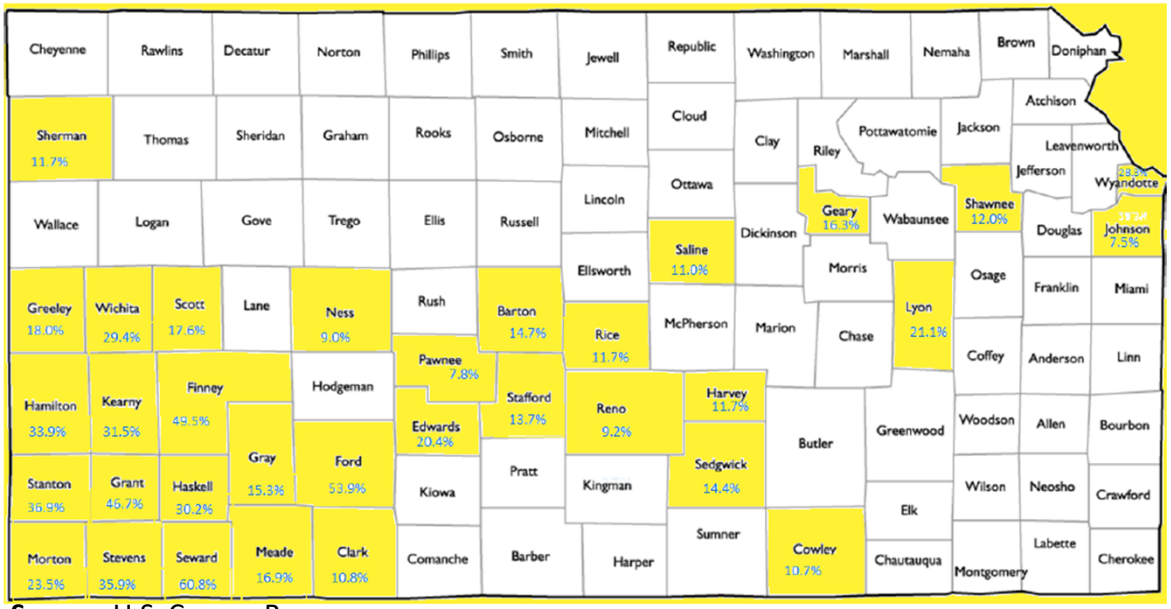
Map prepared by: Juntos Center KUMC Preventive Medicine and Public Health on June 9, 2018

KU ADC is ideal for my goal

Latinos as Percent of County Population in the State of Kansas
Latino Percent Equal To or More than 7%



Source: U.S. Census Bureau
Map prepared by: Juntos Center KUMC Preventive Medicine and Public Health on June 9, 2018

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ADC Goals:
1. Educate community on AD
2. Support recruitment
3. Coordinated care

Addressing gaps to reach my goal

NIA Diversity Supplement (P30)

Long term goal: Independent dementia disparities researcher among Latinos

Goal 1. AD clinical research methods

Goal 2. Collaborative networks

Goal 3. Skills to achieve research independence

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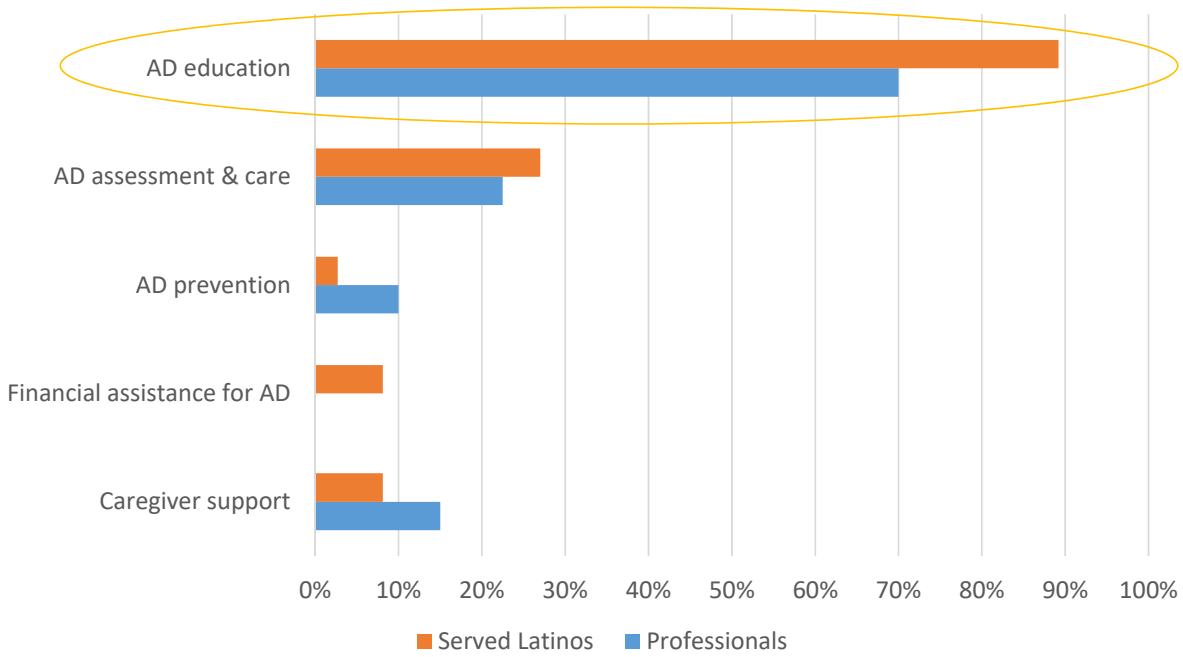
1. Previous experience
2. Long-term goal
3. **Experience at the KU ADC**
4. Conclusions and Next Steps

1. Our Latinos needed AD education

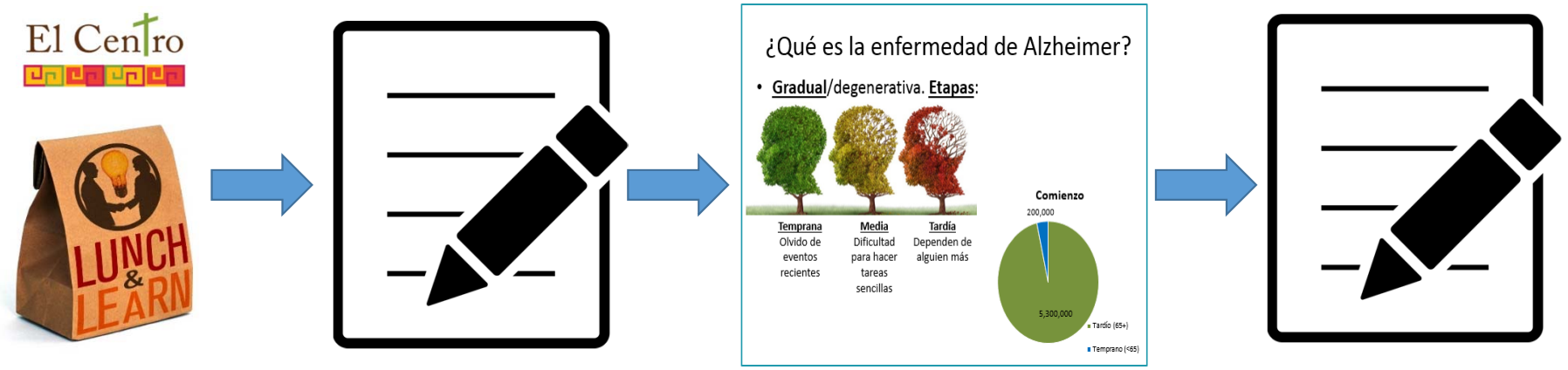


1. I developed an AD educational tool for Latinos

Envejecimiento Digno

- Borrow-Sanchez, 2011

1. Envejecimiento Digno increases AD knowledge



1. I harvested Envejecimiento Digno's success

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New amigos!

El Centro

LatinosAgainst Alzheimer's
A Network of *Us*AgainstAlzheimer's

GLOBAL ALZHEIMER'S PLATFORM FOUNDATION

Publication!

Taylor & Francis

Ethnicity & Health

ISSN: 1355-7858 (Print) 1465-3419 (Online) Journal homepage: http://www.tandfonline.com/loi/ceth20

Feasibility of an Alzheimer's disease knowledge intervention in the Latino community

Jaime Perales, W. Todd Moore, Cielo Fernandez, Daniel Chavez, Mariana Ramirez, David Johnson, Jason Resendez, Carolina Bueno & Eric D Vidoni

1. I have educated >60 Latinos ever since

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Guadalupe Centers

THE DONBOSCO CENTERS

THEO AND ALFRED M. LANDON CENTER ON AGING

Senior centers

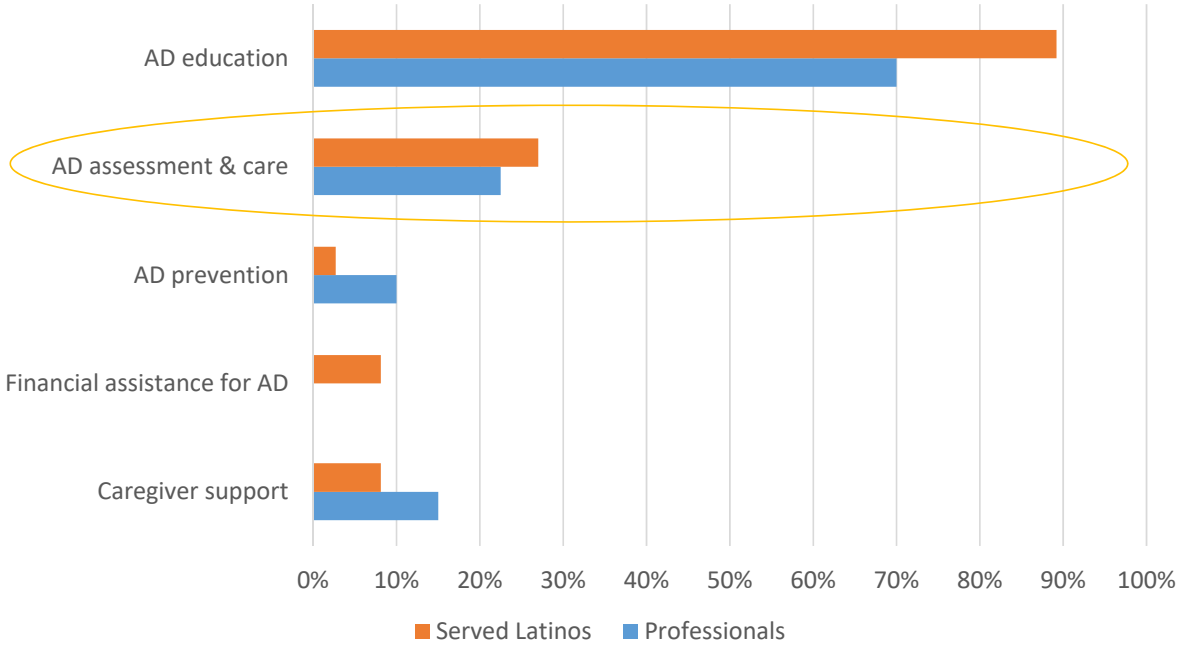
Holy Cross Parish

KEELER Women's CENTER

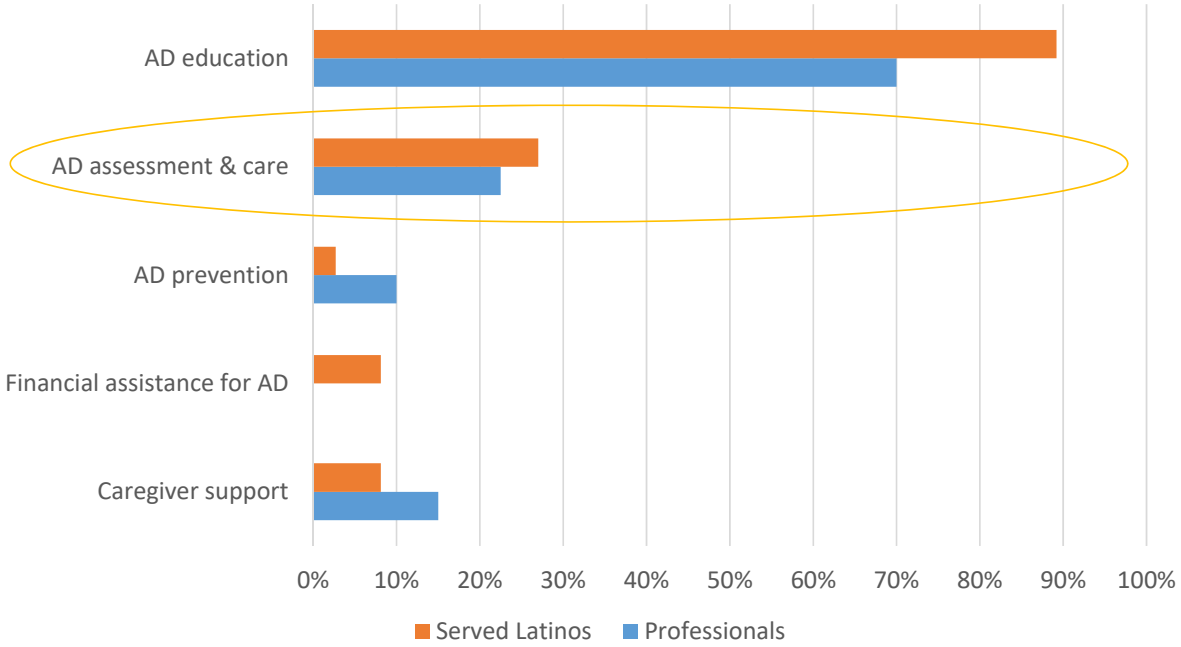
Religious centers

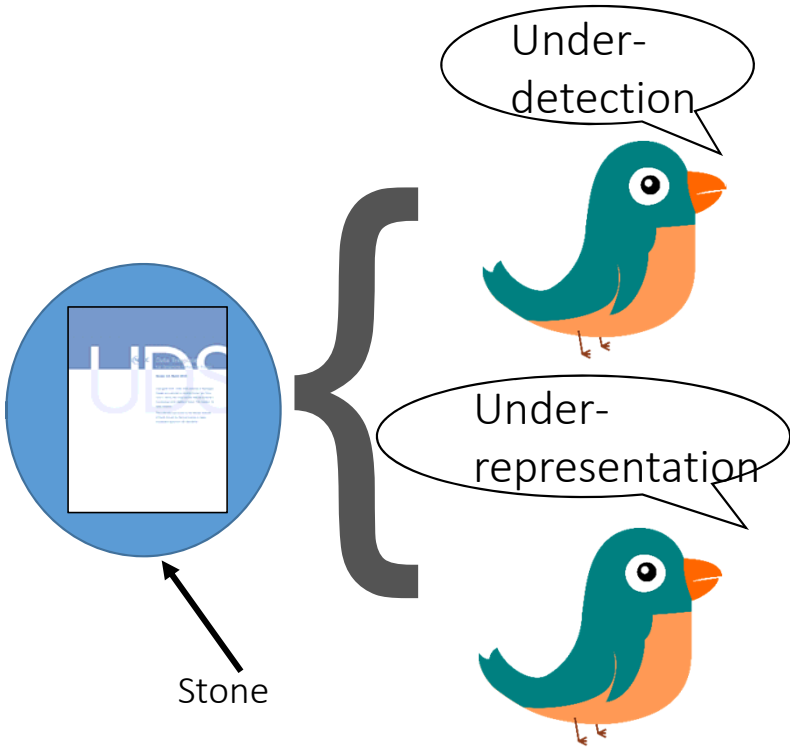
Latino Media

2. Our Latinos needed AD assessments



2. Our Latinos needed AD assessments





2. I trained in AD assessment

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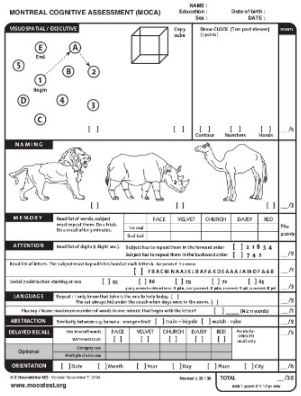

Cognitive testing

Clinical dementia rating

Consensus meetings

2. I led the integration of UDS 3.0-SP

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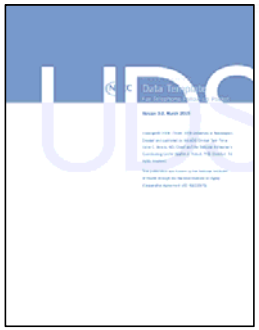
REDCap™



UF UNIVERSITY of FLORIDA

Banner Health®

2. I promoted UDS as a chance to assess memory

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Guadalupe Centers

THE DONBOSCO CENTERS

THEO AND ALFRED M. LANDON CENTER ON AGING

Senior centers

Holy Cross Parish

KEELER Women's CENTER

Religious centers

Latino media

2. I enrolled 30 Latinos in 10 months

Envejecimiento Digno increased research motivation

48 Latinos interested in Cohort

Recruited and assessed 30 Latinos in 10 months

Severe previous underscreening

Detected 3 undiagnosed individuals

Recent Publications

KU ALZHEIMER'S DISEASE CENTER
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Published

- Perales, et al. (2018): Feasibility of an Alzheimer's disease knowledge intervention in the Latino community; Ethnicity & Health
- Burns, Watts, Perales, et al. (2018): The Impact of Creative Arts in Alzheimer's Disease and Dementia Public Health Education; Journal of Alzheimer's Disease
- Perales et al. (2018): Cardiovascular health and cognitive function among Mexican older adults: cross-sectional results from the WHO Study on Global Ageing and Adult Health; International Psychogeriatrics
- Vidoni, Perales. (2017): Aerobic Exercise Sustains Performance of Instrumental Activities of Daily Living in Early-Stage Alzheimer Disease; Journal of Geriatric Physical Therapy

Under review

- Perales et al. (Submitted to Ethnicity & Health): Using a theater play as an Alzheimer's disease outreach strategy
- Perales et al. (Submitted to International Journal of Geriatric Psychiatry): Cardiovascular health and dementia incidence among older adults in Latin America: results from the 10/66 Study.
- Perales et al. (Submitted to International Journal of Geriatric Psychiatry): Risk of dementia and mild cognitive impairment among older adults in same-sex relationships

Index

1. Previous experience
2. Long-term goal
3. Experience at the KU ADC
4. **Conclusions and Next Steps**

Conclusions

KU ADC + Diversity Supplement = more independent AD disparities researcher

- Latino partnerships
- Clinical dementia assessment
- Leadership

We have been able to address some Latino AD disparities

- Knowledge
- Research participation
- Detection

Next steps

K01 on implementing AD services in primary care among Latinos (NIMHD)

- Training
  - Evidence-based AD care
  - Health systems research
  - Community based participatory research

Moltes gràcies!

¡Muchas gracias!

Thank you very much!

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4350 Shawnee Mission Parkway
Fairway, KS 66205
913-588-0555
kualzheimer.org

Michelle Niedens, LSCSW

KU ALZHEIMER'S DISEASE CENTER
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- Director, MyAlliance for Cognitive Health
- Premier regional resource for Alzheimer's care.
- 18 years with the Alzheimer's Assoc. Heart of America Chapter as Director of Education, Policy and Programming

MyAlliance for Cognitive Health: Shifting the Point of Care

Michelle Niedens, L.S.C.S.W.

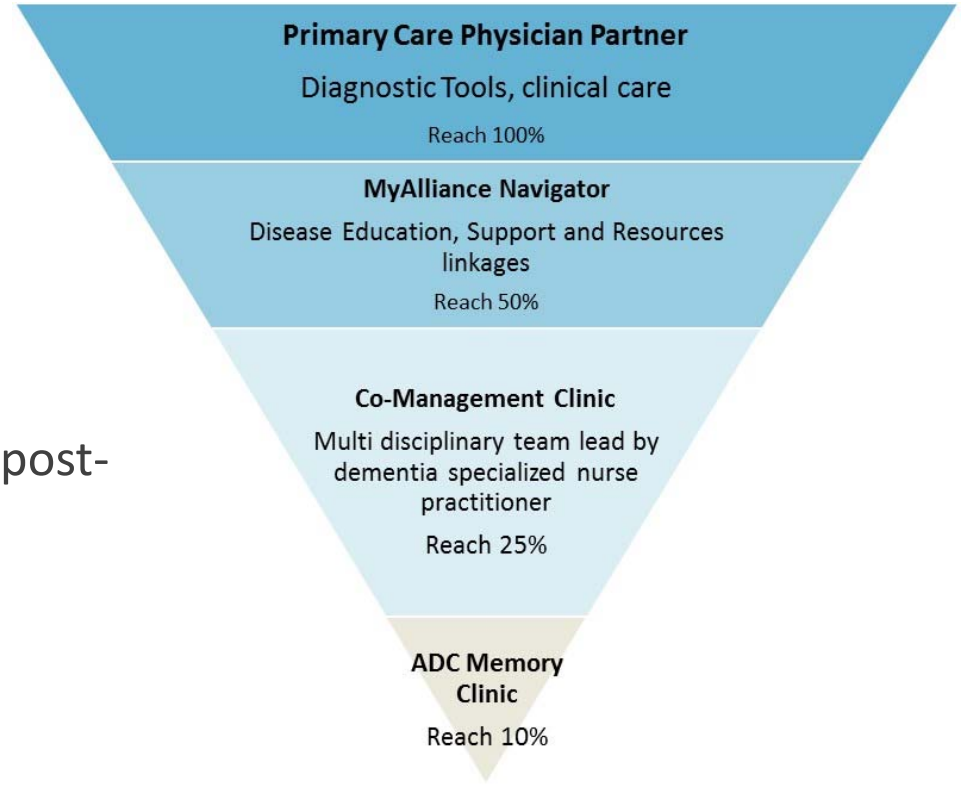
Statewide Community Care Network: MyAlliance for Cognitive Health

MyAlliance FOR COGNITIVE HEALTH

Mission: Improve the health of all Kansans at-risk or living with dementia

What is MyAlliance?

- Tiered approach to dementia management
- Partnership with PCPs
- Protocols for early detection
- Social Work Navigators embedded in clinic for post-diagnosis support



Towards a dementia-ready community

- Streamlines access to optimal care
- Delivers right care to right patients

kualzheim

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Key Features of MyAlliance

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Informed by

- Minnesota Act On Alzheimer's
- KU Heart and Stroke Collaborative
- Indiana Healthy Brain Aging Center
- Johns Hopkins MIND at Home Project
- Cleveland Managed Care Project
- North Central Texas REACH II Program
- Kansas Bridge Project

- Self-sustaining
  - CMS Chronic Care Management (CCM) billing
- Research Recruitment Mechanism
  - Change the culture of recruitment in the community
- Education / Workforce development
- Early Recognition
- Shift support to Patient Empowerment Model

Current Dementia Recognition in Primary Care

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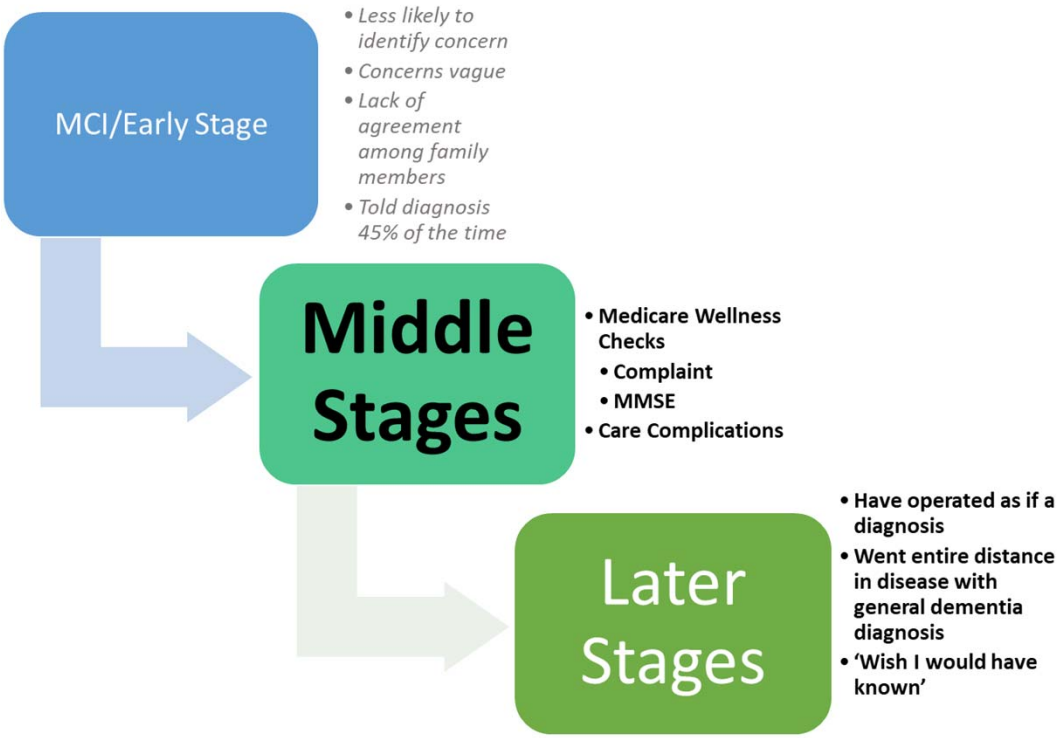

Current screening tools utilized:

Cognitive Screen used in Annual Medicare Wellness Visit	Providers = 204
MMSE	165 (81%)
General Question then MMSE	12 (6%)
MoCa	15 (8%)
Slums	11 (5%)
Other	0

Early Detection and Diagnosis of Memory Disorders by Primary Care

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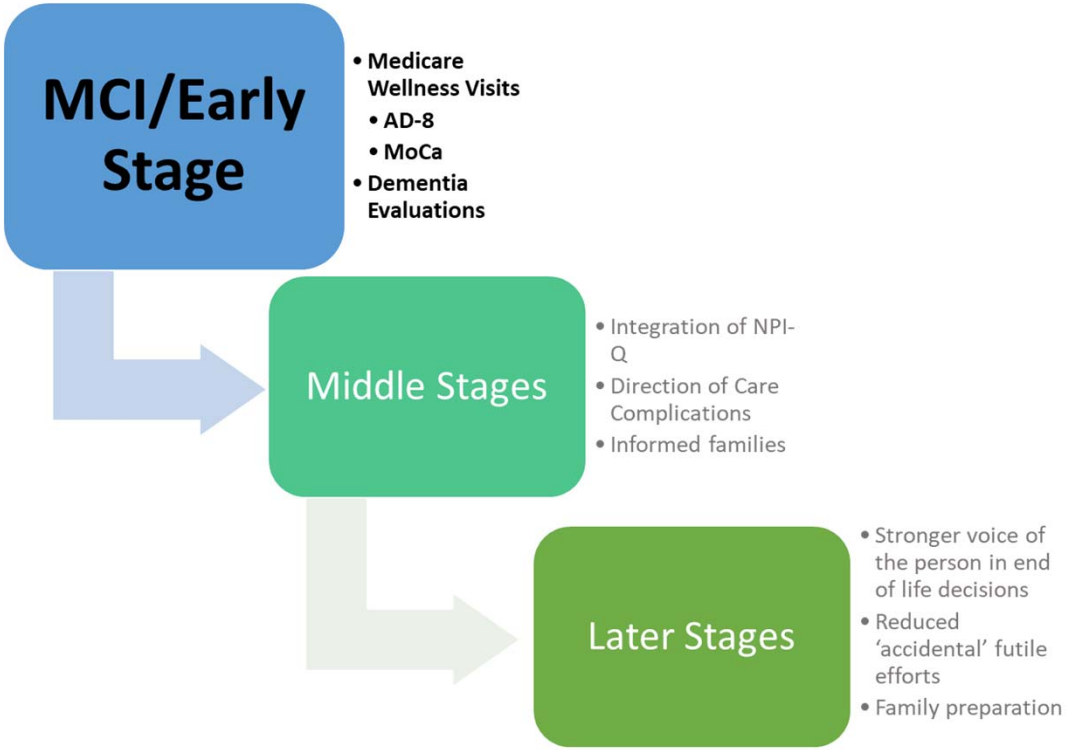

Users vs. Non-Users of Community Resources – Lessons in the Literature

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Users

- Care partners
  - More educated
  - Greater level of burden
- Patients
  - More cognitive and functional impairments
  - More behavioral problems
  - Reduced activities due to cognitive impairment

Non-Users

- Care Partners
  - > 70% of all care partners
  - Less depressed
  - More social supports
- Patients
  - Less cognitive and functional implications
  - Fewer behavioral problems

Practice Based Semi Structured Interviews on Use of Care Coordination/Support

- 59% had either embedded social workers or care coordination/health navigation staff.
- Vast majority of Social Workers/Navigators report little to no experience with dementia.
- Utilized for imminent need.
- Focus on limited range of chronic conditions.

Application of a patient empowerment model

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- Changing language from “care plans” to “wellness plans”

Navigator Roles
Care coordination
Disease Education
Post-diagnosis Emotional Support
Driving and Safety
Health Promotion
Access community resources
Self Advocacy including active role in decision making
Build support system capacity
Design compensatory systems
Access to research opportunities

Integration of Patient Empowerment Model

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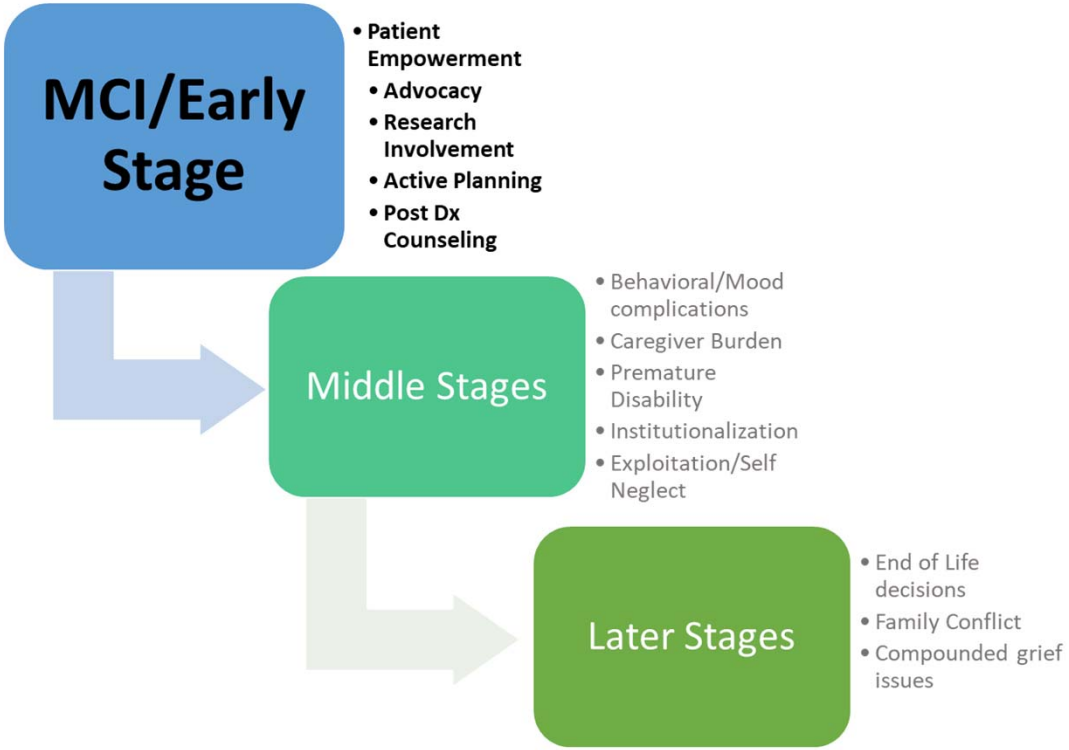

Research Recruitment Components

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- Sustainable research recruitment network
  - Built on a high-value clinical care program (funded via Medicare CCM codes)
- Increase access points to research
  - Patients
  - PCPs
  - Community Stakeholders
    - Black Health Care Coalition
    - El Centro
    - Expand research connections to community support networks
- Potential to change the culture of research participation for PCPs and Patients

Educational Components:

- Expand number of social workers with dementia specific focus.
  - Strengthen curriculum in social work programs in the region through partnership
    - Dementia Intensive (Joint effort of 8 Social Work Schools/Departments)
    - Participation in Integrated Health Scholars Project
  - MentorD
    - Provide year long dementia education and mentorship program for social workers
    - Modified version for adjunct navigators
    - Modified version for community health workers
- MyAlliance PCP partnerships
    - Use of Minnesota Act on Alzheimer's Provider Webinars
    - MyAlliance Provider Partners Program (Modified from Wash U curriculum)
    - Newsletter and Annual Dinners

Educational Components (continued)

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- PAIRS (Inspired by Northwestern Buddy Program)
  - 6th Year

Scott Koppel, MD, PhD Student

Summary

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- Develop a dementia capable community health system
- Increased opportunity to participate in research for patients and PCPs
- Proactive disease management
  - Early recognition, focus on wellness
  - Reduce health care costs
- Opportunity to train front line health care workers in dementia care

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