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Associations between Dentition Status, Nutritional Status, and the Eating Experience in Older Adults

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Sackler Institute for Nutritional Sciences

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Overarching Aim: To explore associations between nutritional status and dentition status in older adults AND explore the impact of impaired dentition on dietary intake and the eating experience

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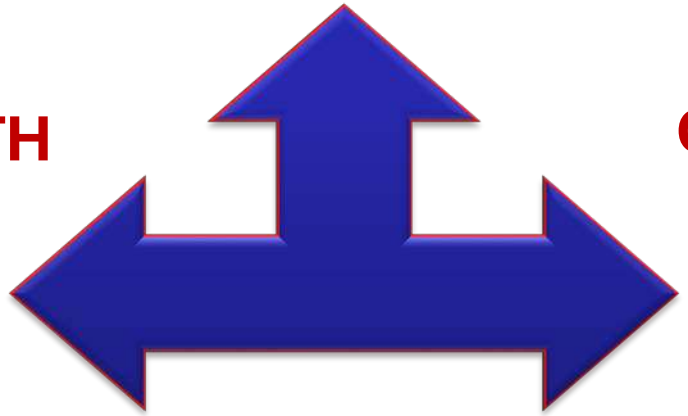
DIET AND NUTRITION

SYSTEMIC HEALTH & DISEASE



ORAL HEALTH & DISEASE

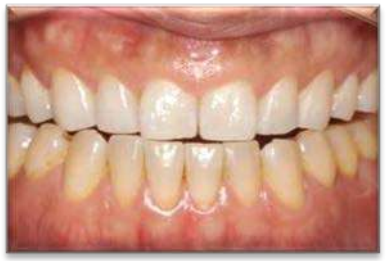
- Synergy between diet, nutrition, and integrity of the oral cavity in health and disease[1]
- Older adults are at high risk for both impaired oral health and suboptimal nutritional status
  - ~ 30% worldwide and ~ 20% in the US are edentulous[2,3]
  - ~ 50% malnourished or at risk of malnutrition (varies by setting)[4,5]

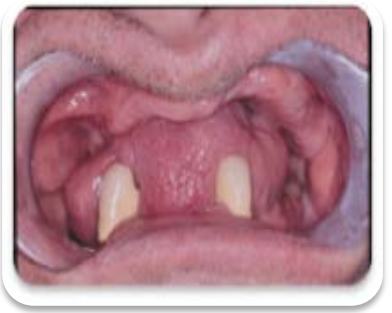
Tooth Loss and Dietary Intake

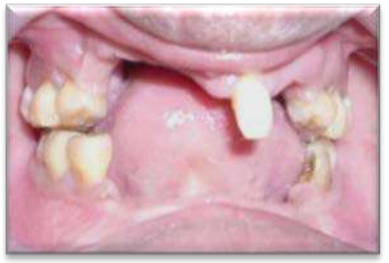
- Oral cavity is the gateway to nutrient intake
  - Biting– primarily with anterior teeth
  - Chewing – primarily with posterior teeth

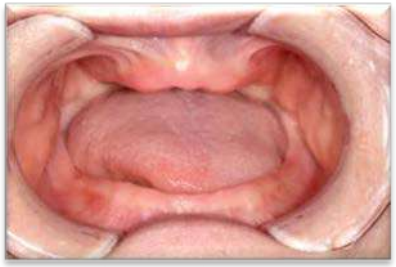
- Masticatory ability is influenced by:
  - Number and distribution of teeth
  - Occlusion (how the teeth fit together)

- Affects food choice and diet quality
  - Decreased consumption of fruit and vegetables, fiber, calcium, iron, and other vitamins.[6-10]









Systematic Review: Zelig et al, 2016[11]

Among community dwelling older adults what are the associations between tooth loss & malnutrition risk (as measured by the MNA)?

5 of 8 studies found significant associations:

- Fewer teeth and poorer occlusion were significantly associated with lower MNA score as compared to more teeth / better occlusion
- Complete denture wearers had higher MNA scores than those who were edentulous without dentures but lower MNA scores than dentate controls
- In partially dentate individuals, MNA scores improved with provision of removable partial dentures

PHASE 1: QUANTITATIVE RESEARCH

Phase 1 Aim: Explore associations between nutritional status (self-MNA), and tooth loss in older adults (=>65).

Hypothesis: Malnutrition risk be higher (lower Self-MNA scores) in those with fewer teeth / limited occlusion.[11]

[12] Zelig R, Byham-Gray L, Singer SR, Hoskin ER, Fleisch Marcus A, Verdino G, Rigassio Radler D, Touger-Decker R. Dentition and Malnutrition Risk in Community-Dwelling Older Adults. *Journal of Aging, Research and Clinical Practice (JARCP),* 2018;7:107-114.

Methodology

- Cross-sectional
- Conducted at the RSDM in Newark, New Jersey
- Sample: 107 adults aged =>65 years , who came for care between June 1, 2015 - June 30, 2016
- Variables:
  - Dental: Number and location of teeth
  - Nutrition: Self-MNA (validated tool to measure malnutrition risk)
  - Confounders: other clinical and demographic variables

Mini Nutrition Assessment (MNA)

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F1 Body Mass Index (BMI) (weight in kg) / (height in m^2) ☐
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

Screening score (max. 14 points)

12-14 : Normal
8-11 : At risk of malnutrition
0-7 : Malnourished

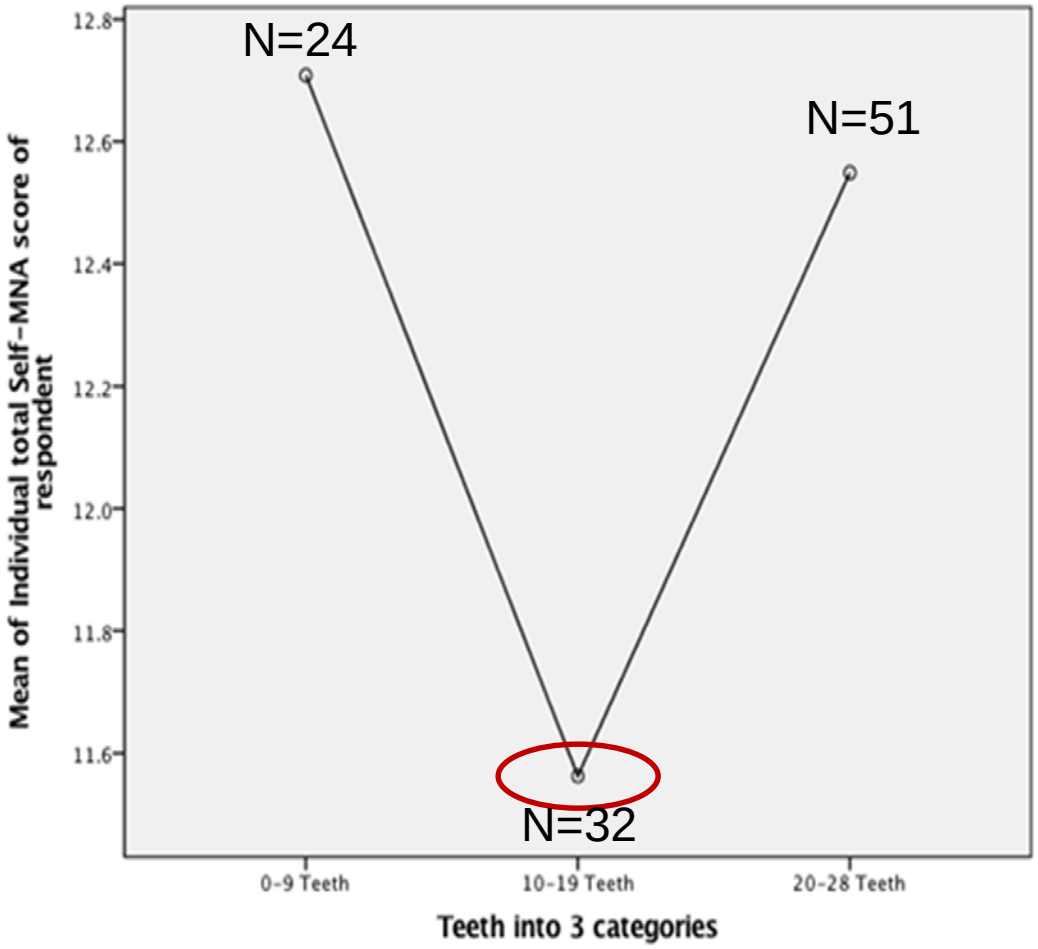
Subject Characteristics

~ 50% Male/Female
~ 37% Black or African American, ~ 32% White and 21% Hispanic

	Mean	SD	Range
Age	72.6	5.6	65.0 – 91.0
MNA Score	12.3	2.0	5.0 – 14.0
BMI	28.8	4.9	19.2 - 39.9
Number of Teeth	16.9	8.5	0.0 – 28.0

Associations

Figure 1: Mean Self-MNA Score in Relation to Dentition Categories



- No linear relationship between number of natural teeth and Self-MNA Score. (r=0.104, p=0.285)
- Those with 10-19 teeth had lower Self-MNA scores (mean=11.6, SD=2.5) than those with 0-9 teeth (mean=12.7, SD=1.3) or 20+ teeth (mean=12.6, SD=1.8), (p=0.116)
- Among those with 10-19 teeth the odds of being at risk for malnutrition/ malnourished were 2.5 X those with 20+ teeth (OR=2.5, p=0.076)

Phase 1 Conclusions:

Majority of this sample of older adults were:	• Partially edentulous • Overweight / obese • Normal nutritional status
Those with 10 – 19 teeth were more likely to be at risk for malnutrition:	• Not statistically significant but trend may have clinically meaningful implications
Limitations:	• Small sample size • Self reported MNA data
Future Research:	• Larger more heterogeneous sample • Better understand the eating experience

PHASE 2: QUALITATIVE RESEARCH

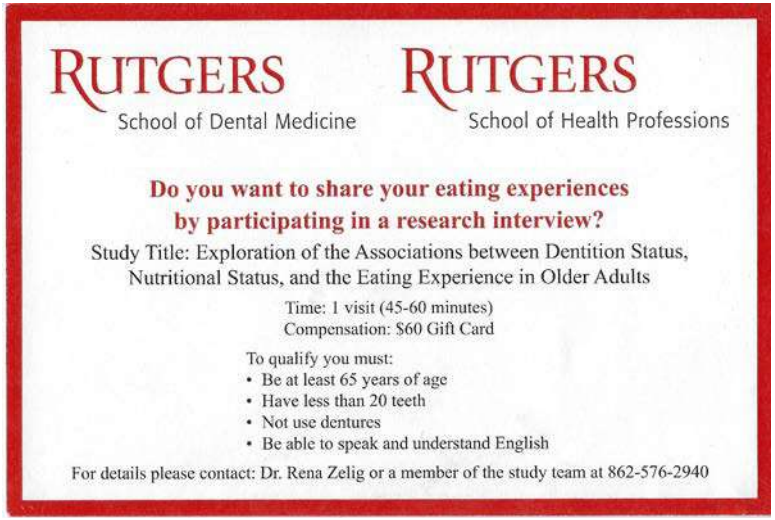
Phase 2 Aim: Qualitatively assess for themes from interviews about the impact of impaired dentition on dietary intake & the eating experience

Hypothesis: tooth loss leads to adaptive and maladaptive eating behaviors, particularly in consumption of fruits, vegetables & other high fiber foods.[13-14]

Methodology

- Convenience sample of RDSM patients

- Inclusion Criteria:
  - 65+ years of age
  - < 20 teeth
  - No dentures
  - Speak and understand English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Do you want to share your eating experiences by participating in a research interview?

Study Title: Exploration of the Associations between Dentition Status, Nutritional Status, and the Eating Experience in Older Adults

Time: 1 visit (45-60 minutes)
Compensation: $60 Gift Card

To qualify you must:
- Be at least 65 years of age
- Have less than 20 teeth
- Not use dentures
- Be able to speak and understand English

For details please contact: Dr. Rena Zelig or a member of the study team at 862-576-2940

- Recruitment:
  - Purposeful random sampling and direct marketing (postcards and calls)
  - Flyers hung at RSDM
  - Dental student and faculty referrals

Methodology

- In-depth semi-structured interviews conducted at RSDM
  - Interview guide was adapted from prior research[13,14,15] and focused on:
    - **Eating experience** (impact of missing teeth on food preparation and intake)
    - **Eating related quality of life** ERQOL (social/emotional impacts of missing teeth)
- Consent – verbal and written
- Data collection
  - Demographic characteristics (interview and EHR)
  - Mini Nutrition Assessment-Short Form (MNA-SF) score
  - Anthropometrics (height and weight measured)
  - Number and location of teeth (EHR)
- Compensation: $60
- Recorded and transcribed
- Thematic Analysis using NVivo 11

Demographic and Clinical Characteristics (N=19)

~ 52.6% Female
~ 63% Black or African American, ~ 32% White and 5% Hispanic

	Mean	SD	Range
Age	71.3	5.2	66.0 – 83.0
Number of Teeth	10.8	6.5	0.0 - 19.0
BMI	28.6	6.3	16.5 – 47.1
MNA-SF Score	12.1	2.4	4.0-14.0

- 15.8% (n=3) completely edentulous
- 31.6 % (n=6) at risk for malnutrition or malnourished

Eating Experience Themes

ADAPTATION (+)

Cooking Method / Texture Modification

- Choose softer foods
- Cook until soft, puree, liquify / blenderize
- Chop, mash, peel, shred, ground
- Add product to moisten

Chewing Strategies

- Time and location

MALADAPTATION (-)

Food Avoidance

- Vegetables (especially raw)
- Fruit (e.g.: apples)
- Nuts and seeds
- Meats (e.g.: steak, pork chops)
- Grains (e.g.: bread)

These foods are rich in fiber, vitamins and minerals

Participants on Eating Out

Limitations in Eating Out with Others

- “Because you know when you don't have teeth sometimes saliva sprays out. So it's probably not fun for other people either …Cover my mouth and don't go out to eat with people I don't know very well. So yeah. And I don't like going out anymore. To events or parties…So I guess yeah I'm self conscious for not having any teeth.”

Adaptation When Eating Out

- “When I go in there I tell them, “Listen I want something soft” and I explain to them why. If they cant do it, don’t take my money.”

Adaptation When Eating Out

- “People want to go out to dinner. I have to drink a smoothie before I go. And usually I’ll order fish and eat the fish and that’ll be it. Mashed potatoes, but I really don’t like mashed potatoes.”

Participants on Feeling Self-Conscious or Embarrassed

Affects Social Interactions

- “Yeah, I put my hand in front of my mouth a lot. I do it all the time. I find myself, even doing it, when I talk to my daughter. It's embarrassing. It's not like I can just go to the dentist and say, "Give me everything I need." Because the expense is so high.”

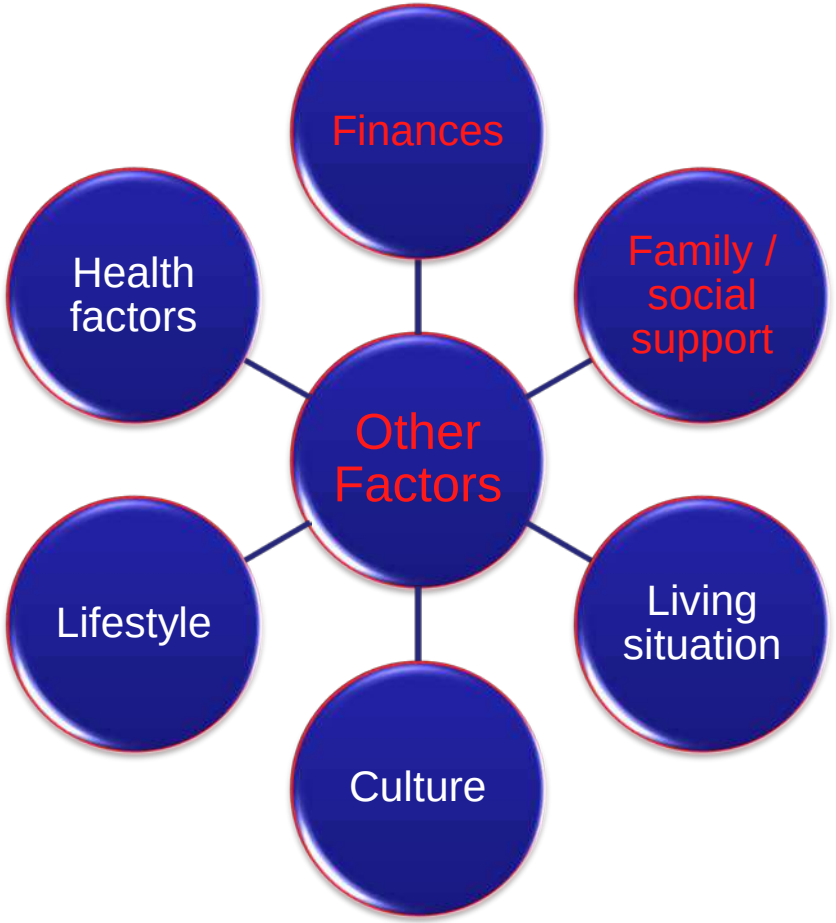
Affects Eating

- “Maybe a little self conscious. When you're out there in the public you feel a little odd ripping your sandwich up taking it piece by piece. But that's the way it goes.”

Affects Smiling & Talking

- “Yes! Of course! I can't smile, I can't talk. Especially in public. Somebody, made me laugh. Like if I was going shopping, somebody made me laugh. And then I forget about my teeth and then people be looking! Oh it's so embarrassing. I can't even open my mouth and talk. Sometimes when I'm in a group of people, we'll be talking but I don't want to say anything.”

Thematic Analysis: Other Factors



→ Lack of finances limited food choices

→ Support of family and friends enhanced ERQOL

Phase 2 Conclusions

- Adaptive coping strategies: adjusting chewing, food choices and preparation methods as eating become more difficult
- Maladaptive behaviors (food avoidance, limiting eating out and smiling in public) may lead to increased risk for malnutrition, social isolation and decreased quality of life
- Tooth loss may be compounded by multiple other psychosocial factors that affect ERQOL

Future Research

What We Know:

- Relationship may not be linear; 10-19 teeth are higher risk
- Tooth loss affects dietary intake and ERQOL
- Older adults use adaptive and maladaptive techniques to compensate when functional dentition is compromised

Future Research:

- Study the relationship between tooth loss, nutritional status (and overall health and wellbeing) using tools that measure diet quality and ERQOL in a larger more heterogeneous sample
- Design and tailor diet and nutritional interventions to meet the unique needs of older adults with tooth loss

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SUPPLEMENTAL SLIDES

Number of Natural or Restored Teeth by Nutrition Status Category (N=107)

Number of Natural or Restored Teeth	n	%
0 Teeth	5	4.7
1 – 9 Teeth	19	17.7
10 – 19 Teeth	32	29.9
20 – 28 Teeth	51	47.7

Nutritional Status Category	Mean number of natural or restored teeth	Standard Deviation	Range
Normal (n=80)	17.4	8.8	0 - 28
At Risk for Malnutrition (n=22)	16.2	8.3	0 - 28
Malnutrition (n=5)	14.4	4.3	10 - 21

Interview Guide: Eating Experience

The impact of missing teeth on food preparation and intake

- Have you changed your diet because of the condition of your mouth?
- Are there specific food or fluids you avoid? (PROBE into food groups)
- Are there any tricks that you use to help you eat? (PROBE into modification)
- Has eating become easier or harder over time?
- Are there any foods you would like to eat but cannot due to difficulty chewing them?
- Do you have any mouth pain? How does this affect your eating experience?

Interview Guide: Eating Experience

Eating Related Quality of Life / Social Emotional Implications

- Do you enjoy eating at this point in time?
- What affects your enjoyment of eating?
- Have your eating habits impacted your family/friends that you eat with?
- Do you eat the same foods as your family or is your food modified?
- Do you prepare meals at home? Have you adjusted or changed recipes?
- Do you eat meals outside of your home? Has this changed?
- Are you self-conscious or embarrassed because of your missing teeth?

Ethnogeriatric Imperative: Current and Implications: A Call for Action

Fred Kobylarz M.D., M.P.H
Associate Professor - Geriatrician
Rutgers – Robert Wood Johnson Medical School

Disclosures

- Horizon Healthcare Services, Inc. Pharmacy & Therapeutics Committee (P&T)
- Medicare Evidence Development & Coverage Advisory Committee (MEDCAC)

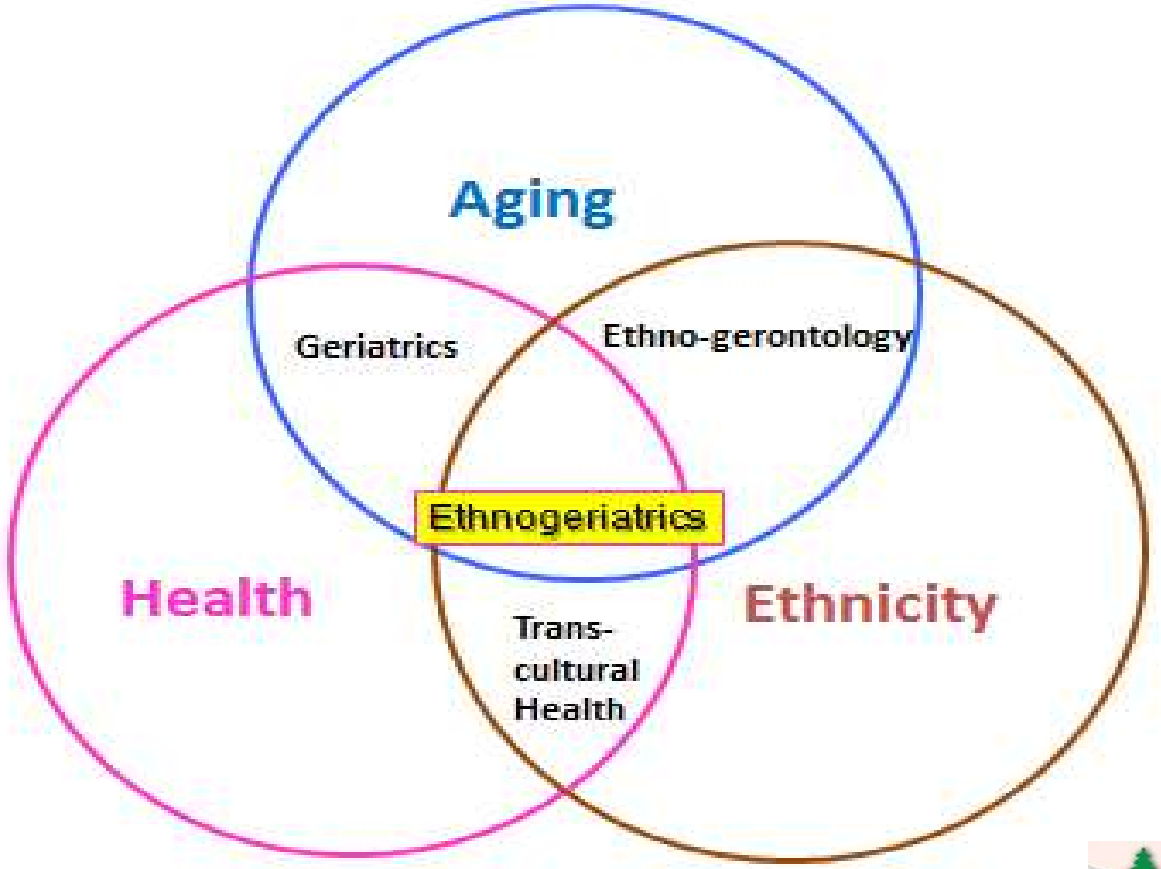
Questions to be discussed

- Why is ethnogeriatrics important?
- How does this relate to research on Healthy Aging, specifically the Medicare Annual Wellness Visit (AWV)?
- How dose this relate to the New Jersey Alzheimer's Disease Study Commission Report 2016?
- What are next steps?

Ethnogeriatrics & Demographics

- Definition:
  - A subspecialty in gerontology/geriatrics that focus on the interrelatedness of aging, health and culture particularly for older adults from diverse ethnic/racial communities.
- Demographics:
  - Increasing numbers of elders from diverse ethnic backgrounds
  - One-third of the U.S population 65+ are projected to be from one of the four minority categories
  - Vast diversity within ethnic minority and majority populations

Ethnogeriatrics
Sources of Scientific Knowledge



Stanford Geriatric Education Center

Challenges to High Quality Ethnogeriatrics care

- Disparities in health status and health care
- Differences in acculturation level and other characteristics within the populations
- Language and limited English proficiency
- Health literacy
- Culturally defined health beliefs
- Beliefs and preferences about long term care and end of life care

How will the U.S Healthcare System Meet the Challenge of the Ethnogeriatric Imperative? Yeo, G. J Am Geriatr Soc 57:1278-1285, 2009.

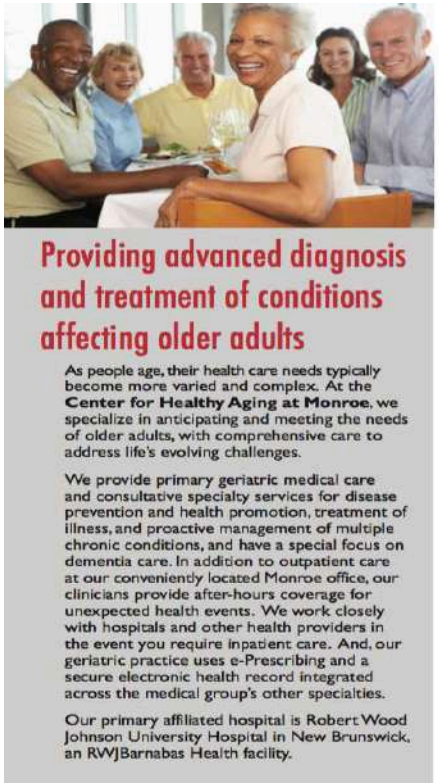
Improving High Quality Ethnogeriatics Care

- Incorporation of the 15 Culturally and Linguistically Appropriate Services (CLAS)
  - Ethnogeriatric training programs
  - Community health workers to increase access
  - Language services
  - Ethnic specific foods
  - Collection of race and ethnicity data
  - Communication in progress to stakeholders on implementation and sustaining

Rutgers Health- Center for Healthy Aging at Monroe (CHAM)

- Geriatricians: Department of Family Medicine and Community Health & Department of General Internal Medicine RWJMS
- Provide primary geriatric medical care and comprehensive geriatric assessments/consults
- Memory/Dementia Evaluations with Rutgers University Behavioral Health Care - Comprehensive Services on Aging (COPSA)
- Geriatric Fellowship Program
- Parker Nursing Home

Rutgers Health- Center for Healthy Aging at Monroe (CHAM)



Providing advanced diagnosis and treatment of conditions affecting older adults

As people age, their health care needs typically become more varied and complex. At the **Center for Healthy Aging at Monroe**, we specialize in anticipating and meeting the needs of older adults, with comprehensive care to address life's evolving challenges.

We provide primary geriatric medical care and consultative specialty services for disease prevention and health promotion, treatment of illness, and proactive management of multiple chronic conditions, and have a special focus on dementia care. In addition to outpatient care at our conveniently located Monroe office, our clinicians provide after-hours coverage for unexpected health events. We work closely with hospitals and other health providers in the event you require inpatient care. And, our geriatric practice uses e-Prescribing and a secure electronic health record integrated across the medical group's other specialties.

Our primary affiliated hospital is Robert Wood Johnson University Hospital in New Brunswick, an RWJBarnabas Health facility.

RUTGERS HEALTH

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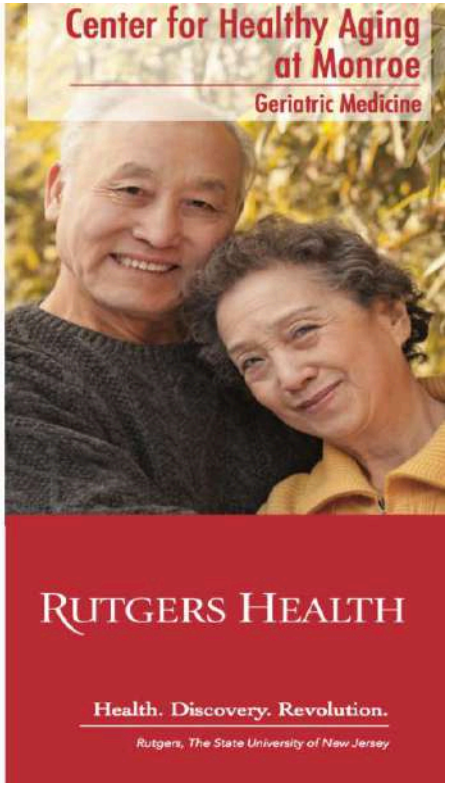
Our practice is a proud part of **Rutgers Health**, the clinical arm of Rutgers, The State University of New Jersey.

Rutgers Health is the most comprehensive academic health care provider in New Jersey, offering a breadth of accessible clinical care throughout the state supported by the latest in medical research and education. Rutgers Health connects health care providers across disciplines, including doctors, nurses, dentists, physician assistants, pharmacists, social workers, and behavioral health and addiction professionals, with a single focus: helping people and populations get well and stay well by delivering consistent, coordinated, value-based health care.



Rutgers Health- Center for Healthy Aging at Monroe (CHAM)

Healthy Aging Research: Medicare Annual Wellness Visit (AWV)

- Established by the The Patient Protection and Affordable Care Act (PPACA) of 2010
- **Purpose** is to create or update a Personalized Prevention Plan Service (PPPS)
- Medicare Beneficiaries know little about this new benefit and healthcare providers underutilize it.

AWV Elements

- Establishment of the beneficiary's medical and family history
- Establishment of a list of current providers, suppliers, and all prescribed medications
- Measurement of the beneficiary's height, weight, body mass index, and blood pressure
- Detection of any cognitive impairment
- Health risk assessment
- Screening for depression
- Review of functional ability and level of safety
- Establishment of a written screening schedule, such as a checklist for the next 5 to 10 years based on recommendations of the United States Preventive Task Force (USPSTF)
- Provision of personalized health advice to the beneficiary and a referral, as appropriate, to health education or preventive counseling services.
- Discussion of advance directive, upon agreement of the individual

https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/AWV_Chart_ICN905706.pdf

Few Studies – Many Gaps

- Most likely to receive AWV: White, urban, higher income, female, and 1-2 comorbidities
- Improved preventive screening rates
- Minimal impact on detection of cognitive impairment
- **Socioeconomic disparities in utilization**

- Trends in Use of the AWV 2011-2014 Ganguli, JAMA 2017
- Effectiveness of AWV Accessing Preventive Care 2011-2014 Camcho, J of Primary Care & Community Health 2018
- One-Year Effect of the Medicare Annual Wellness Visit on Detection of Cognitive Impairment: A Cohort Study, Nicole R. Fowler et al. *J of the American Geriatrics Society* 2018

Detection of Any Cognitive Impairment

- Assessment of an individual's cognitive function by direct observation, with due consideration of information obtained by way of patient reports and concerns raised by family members, friends, caretakers, and others

Federal Register / Vol. 75, No. 228 / Monday, November 29, 2010 / Rules and Regulation

Detection of Cognitive Impairment

- No data on operationalization
- Lack of understanding of tools used to assess cognitive function and potential lack of standardization
- Lack of knowledge and training
- Providers availability and time
- Incorporation of Health IT application

New Jersey Alzheimer's Disease Study Commission Report 2016

- Growing diversity among the aging population
- Served as Geriatrician member of the Commission
- Goal was to study the current issues in New Jersey associated with Alzheimer's disease and to comprehensively assess the needs of residents related to the state infrastructure of services for the disease.

https://www.state.nj.us/humanservices/news/reports/DAS%20-%20Alz%20Report%20-%20FINAL.pdf

New Jersey Alzheimer's Disease Study Commission Report 2016

- Methods:
  - Listening sessions, written input, and web based survey
- Results: common themes emerged
  - Increase awareness and reducing stigma
  - Need for a healthcare workforce trained in caring for patients with the disease
  - Importance of family members as caregivers
  - Public safety concerns
  - Financial challenges

New Jersey Alzheimer's Disease Study Commission Report 2016

- From a population health stand point
  - How important is it to address social determinants of health?
  - How important is it for us to address transitions of care and care coordination?
  - Which patients are most likely to be readmitted within the first 30 days after hospital readmissions?
  - Which patients are most likely to be readmitted in the next 12 months?
  - How many Emergency Department visits will these patients likely make in the next 12 months?

Next Steps & Opportunities for Collaboration

- Current research
  - Writing R21 NIA AWV Data Analysis Plan
    - Detailed patient and provider characteristics using claims data and Medicare Current Beneficiary Survey (MCBS) to elicit more information
    - Medical chart review on detection of cognitive impairment element
  - Other opportunities exist here to explore other elements; depression, preventive services, chronic diseases, advance directives, and others.

Next Steps & Opportunities for Collaboration

- New Jersey Alzheimer's Disease Study Commission Report 2016
  - Multiple goals/strategies proposed for future research
  - Potential Funding Sources
    - Foundation Grants
    - Alzheimer's Association

Questions and Comments

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Family Member Involvement in Older Adults' Diabetes Management: Considerations for Healthy Aging

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Healthy Aging Symposium
Institute for Health, Health Care Policy, and Aging
Rutgers University

Why Type 2 Diabetes?

- **A growing public health concern**

  1 in 4 older adults has diabetes (CDC)

- **A threat to healthy aging** (e.g., Kirkman et al., 2012)

- **Management is difficult, nonadherence is common** (Beverly et al., 2008; Broadbent et al., 2011)

- **Family members are involved in adherence to self-management behaviors** (Wiebe et al., 2016)

- **My research focus** = *The role of family and friends in helping and hindering diabetes self-management*

Social Relationships and Health

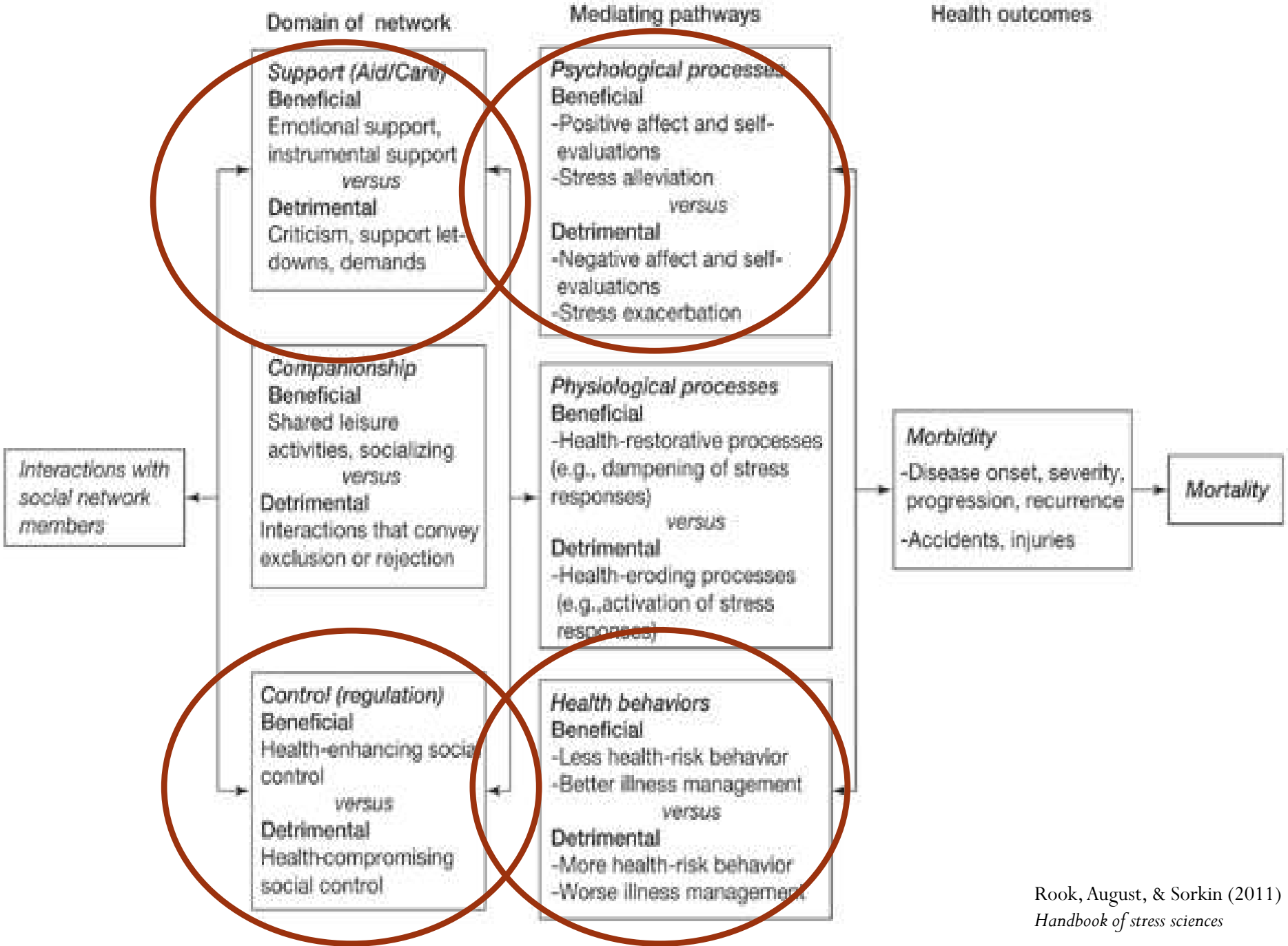
- Social relationships contribute to multiple aspects of health

↑ Healthy behaviors, positive physiological responses, better illness-related outcomes

↓ Disease onset and progression, mortality

- Evidence is strong
  - Different methods
  - Humans and animals

August & Rook, 2011; Berkman, Glass, Brissette & Seeman, 2000; Cohen, 2004



Rook, August, & Sorkin (2011)
Handbook of stress sciences

Family Member Involvement in Diabetes Management

Health-Promoting Involvement	Support	Control (positive & negative strategies)
Definition	Provision of *encouragement and positive feedback* on health behaviors	Efforts *to monitor and influence* health behaviors
Behavioral goals	Shared	Not shared
Patients' engagement in positive health behaviors		
Welcome		
Affirming		

BUT… Family members can also detract from adherence (*health-related undermining*).

Methodology

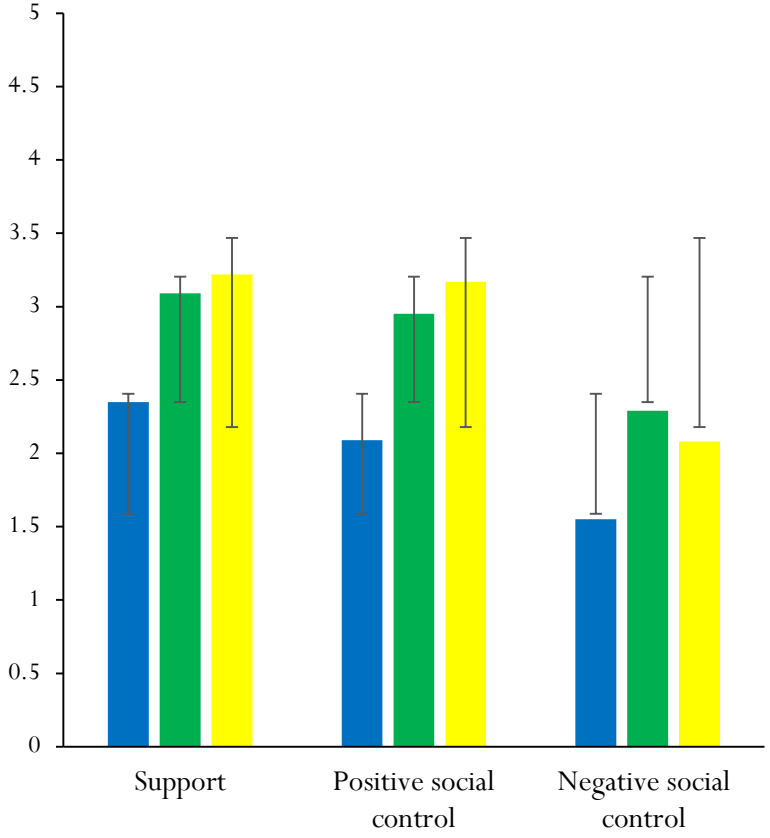
- **Participants***
  - Patients with type 2 diabetes
    - Community samples
    - Patients at primary care/endocrinology offices
  - Spouses of patients

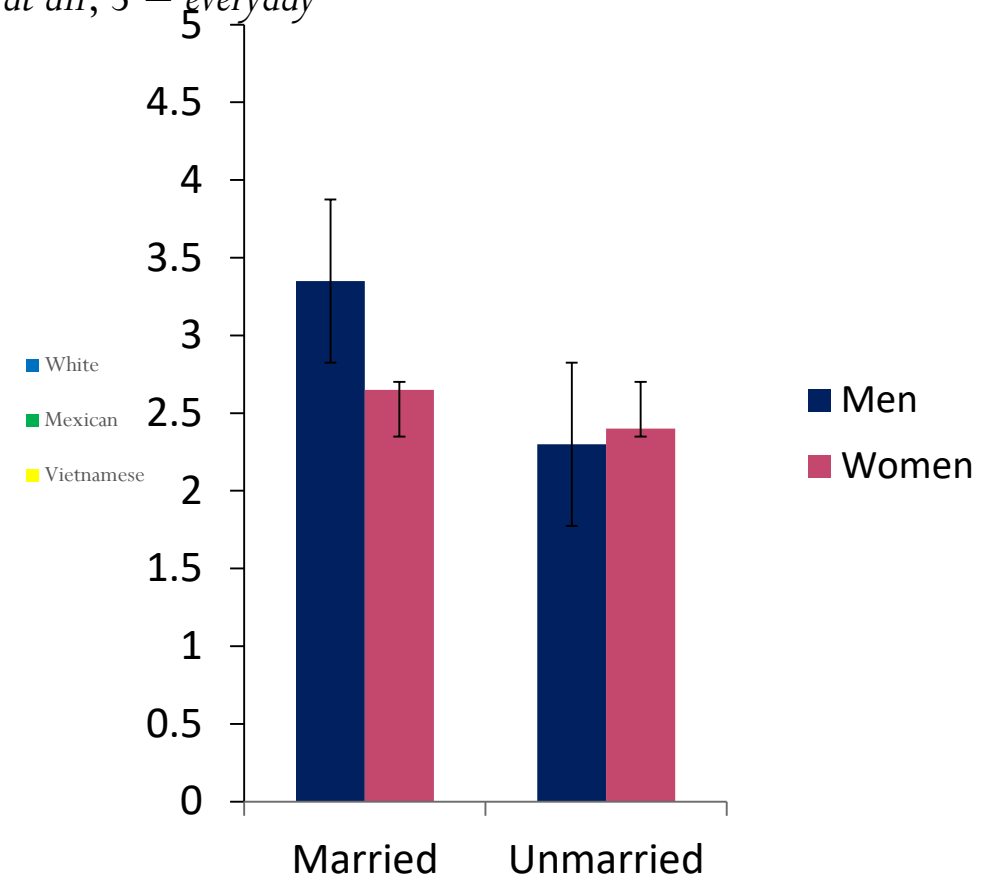
- **Procedures**
  - In-person interviews, self-administered questionnaires, daily electronic diaries, medical record abstraction

Data collected from 4 samples of 1,916 patients with type 2 diabetes

Frequency of Family Member Involvement in Diabetes

0 = *not at all*, 5 = *everyday*





- **# of days spouses reported being involved in their partners' diabetes management:**
  - Support (82%), positive control strategies (55%), negative control strategies (40%)

August & Sorkin, 2010; August & Sorkin, 2011; August et al., in prep

Sources of Family Member Involvement in Diabetes

	MARRIED		UNMARRIED	
	Men	Women	Men	Women
Spouse	78.1%[a]	63.1%[b]	N/A	N/A
Children	30.5%[a]	47.1%[b]	21.8%[a]	46.5%[b]
Sibling	8.5%[a]	16.1%[b]	20.3%[c]	15.3%[b]
Other relative	10.1%[a]	12.2%[a]	18.9%[b]	15.2%[b]
Friend/neighbor	5.1%[a]	12.1%[b]	25.5%[c]	15.1%[b]

Note. Superscripts that differ in the same row are significantly different at $p < .05$.

- **Racial/ethnic differences in number of family/friends involved in diabetes management (e.g., adult child, other relatives):**
  - **Racial/ethnic minorities > non-Hispanic Whites**

August & Sorkin, 2010; August & Sorkin, 2011

Family Members' Involvement in Diabetes: Implications for Patients

	Health behaviors	Emotions
Support	+	+
Positive control strategies	+ or 0	+ and -
Negative control strategies	- or 0	-
Undermining	-	unclear

- **Implications for patients depend on:**
  - **Gender, marital status, race/ethnicity, relationship quality, norms for involvement, appraisal of shared responsibility for diabetes management**

August & Sorkin, 2010; August & Sorkin, 2011; Henry et al., 2013; Khan et al., 2013; Rook et al., 2011; Stephens et al., 2010; Stephens et al., 2013; Tang et al., 2008

Family Members' Involvement in Diabetes: Implications for Spouses and Relationship Quality

- **Implications for spouses**
  - ***Support:*** ↓ stress
  - ***Control:*** ↑ stress and burden
    - Effects depend on patients' health characteristics

- **Implications for relationship quality**
  - ***Support:*** ↑ enjoyable marital interactions
  - ***Control:*** ↑ tense martial interactions

August et al., 2011; August et al., 2013

Potential *Reasons* for Spousal Involvement in Diabetes

- **Patient and disease factors**
  - Diabetes duration, perceptions of dietary behaviors, patients' worries
    - Findings differed by race/ethnicity and gender

- **Spouse factors**
  - Spouse awareness of anxiety about nonadherence
    - Related to more social control

- In progress:
  - Online dyadic study of patients and spouses
  - Comprehensive set of proximal and sociocultural factors posited to be reasons for spousal involvement

August et al, 2017; August et al, in prep

Preparing Family Members as Coaches for Patients with Types 2 Diabetes

- Multidisciplinary, community-based approach

- Coaching as a strategy to improve diabetes self-management

➡ Can *family members* taught to be coaches?

- Current stage: pre-testing
- Next steps: pilot testing feasibility and efficacy in patients & family members

Future Directions

- Further understanding of *how* and *why* social relationships influence health (and vice versa) in later life

- Expanding upon this work: Opportunities for collaboration
  - Other chronic conditions in later life
  - Considerations of sociodemographic factors
  - Interactions with formal social relationships (e.g., health care providers)

"Human behavior is likely to remain *sine qua non* of health care delivery for many years to come" (Christensen & Johnson, 2002, p. 97)

Facilitating Collaboration among Researchers Who Do Aging Research at Rutgers: Suggestions for the Future

- **Developing a network of faculty doing aging research**
  - Online social network (e.g., research interests, seeking collaborators, willingness to consult)
  - Research blitzes/meet-and-greets ~ once/year
  - Research on aging discussion group

- **Seed funding for multidisciplinary aging research**

Thank You

- Collaborators at Rutgers University and other universities

- Undergraduate and graduate student research assistants in the Relationships, Health, & Aging Lab @ Rutgers-Camden

- Funding: Rutgers Provost's Fund for Research, Rutgers Research Council, NSF RU FAIR ADVANCE, NIA, NIDDK, Anthony Marchionne Foundation, APA Division 20: Adult Development & Aging

Questions

RUTGERS
BIOMEDICAL AND HEALTH SCIENCES

Predictors of Survival after a Diagnosis of Dementia

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RUTGERS

Funding: AHRQ PCOR/CER R00 HS22406
"The Comparative Effectiveness of Home Care for Diverse Elders' Outcomes"
Rutgers-RBHS start-up funding

CHAO Laboratory
Community Health & Aging Outcomes

Graduate Research Assistants

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Seiichi Villalona, MA
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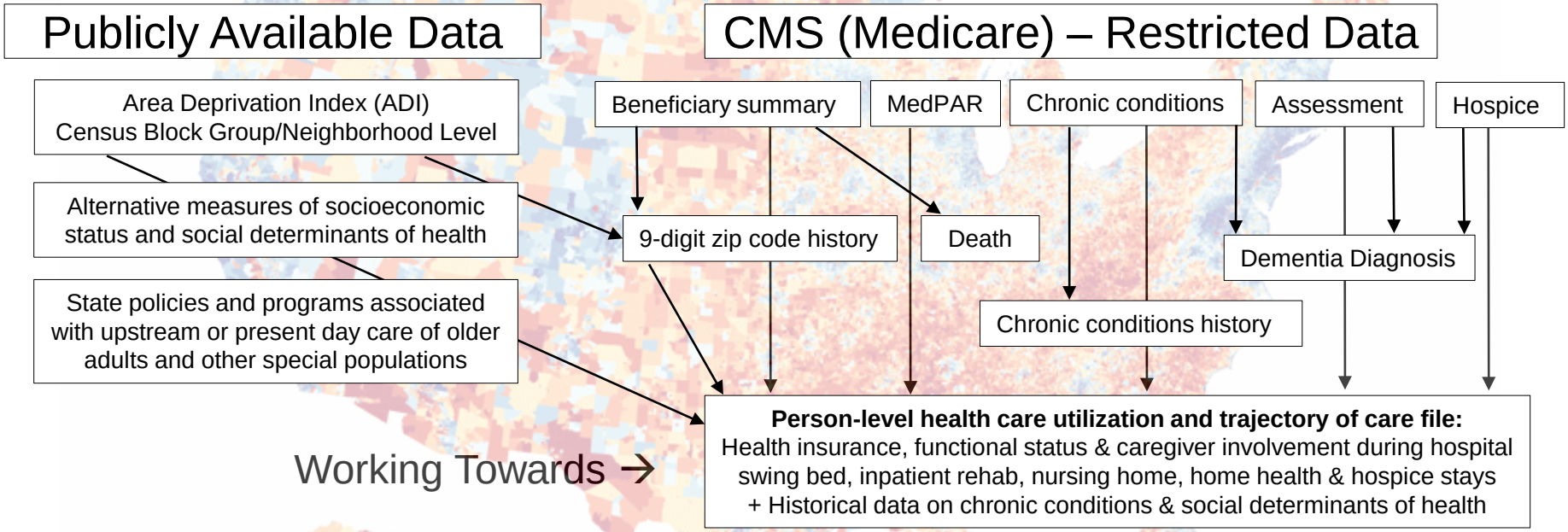
"Reflections" Photo Series

Tom Hussey (photographer)
https://www.tomhussey.com/

Data Sources and Linkages

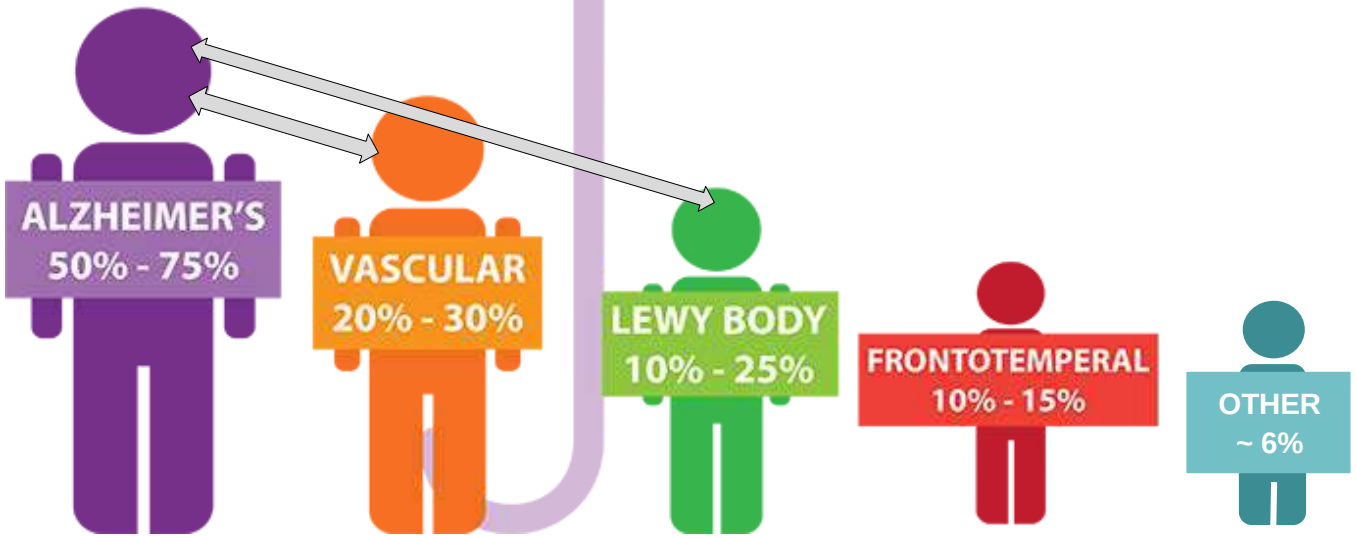


1 IN 3 SENIORS

dies with Alzheimer's or another dementia

DEMENTIA

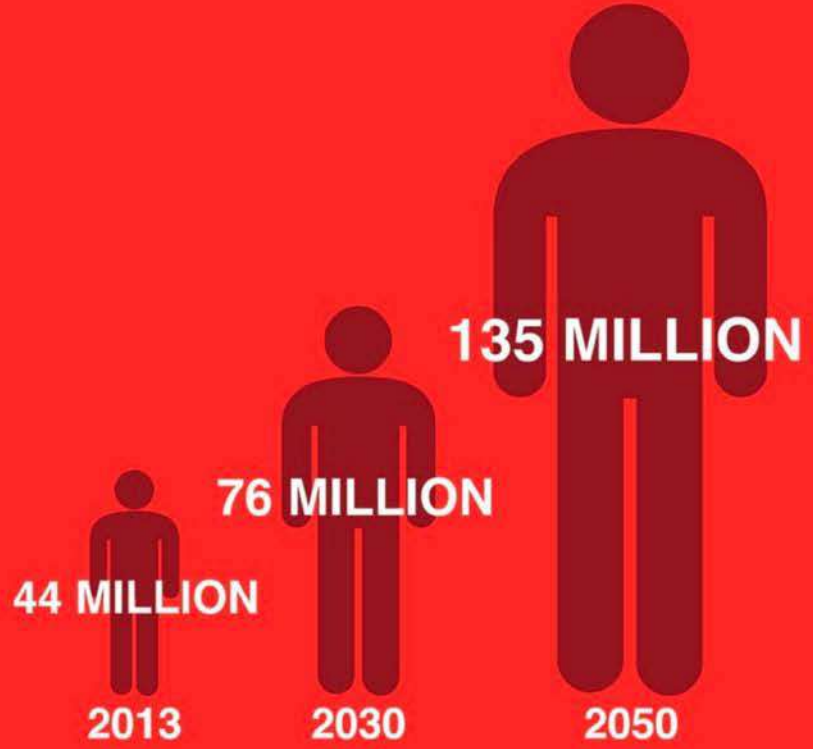
An "umbrella" term used to describe a range of symptoms associated with cognitive impairment.



Alzheimer's Disease International
The global voice on dementia

There is a new case of dementia somewhere in the world every

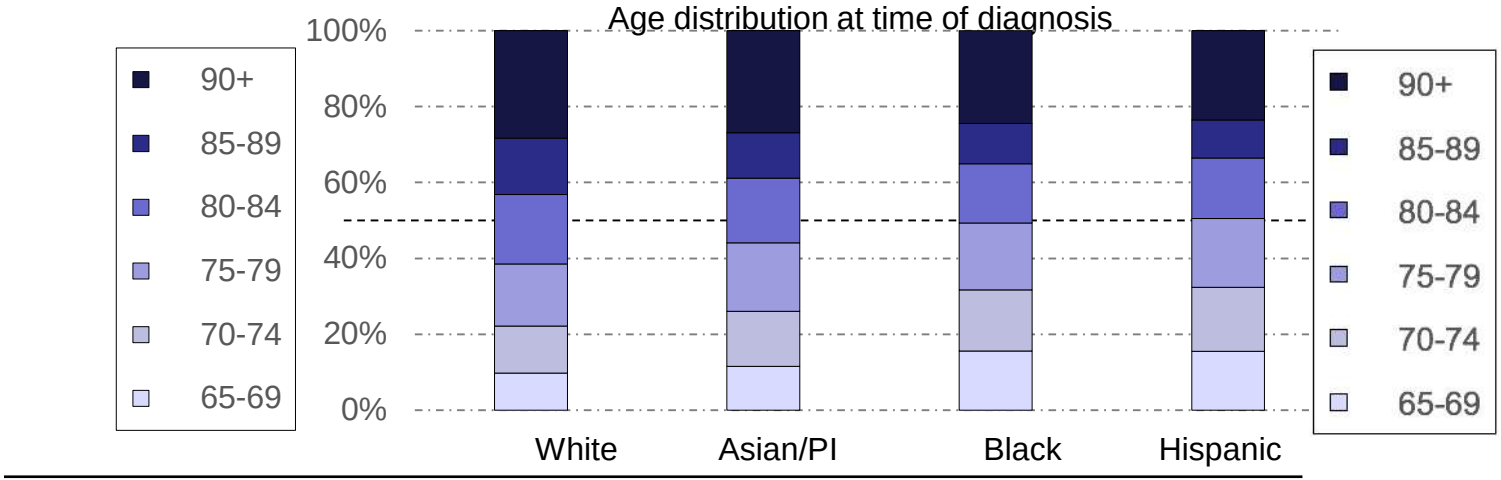
4 SECONDS



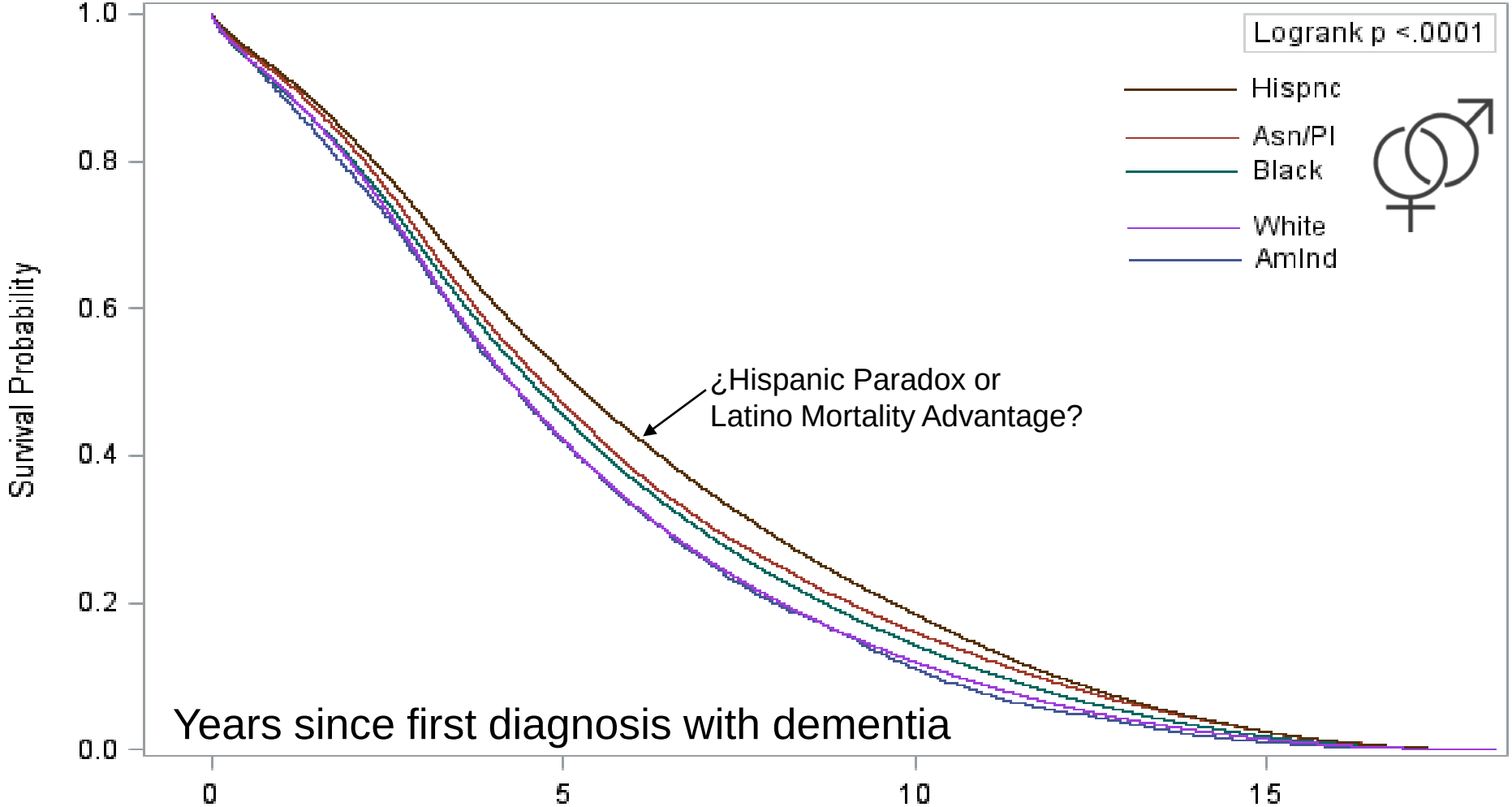
The number of people in the world with dementia will increase significantly by 2050.

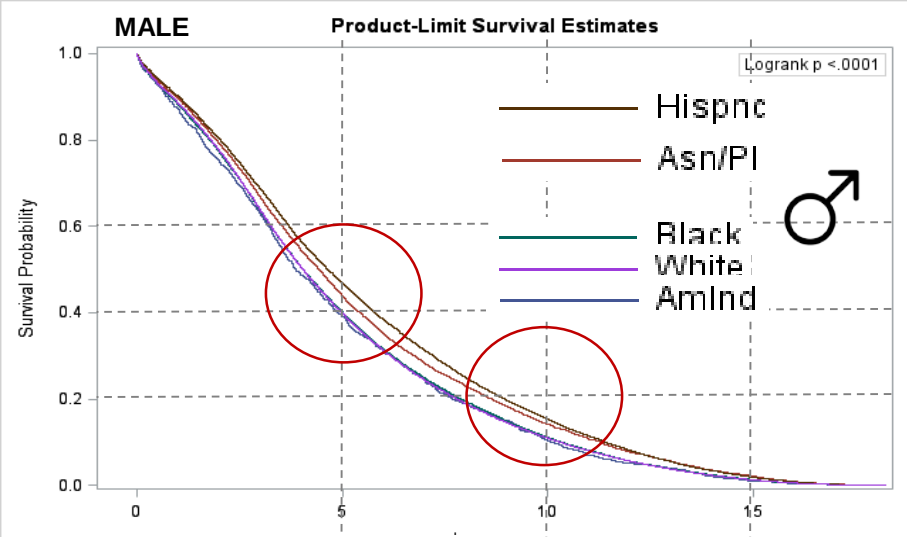
Study Population: U.S. Medicare 2013
65+ at time of first dementia diagnosis

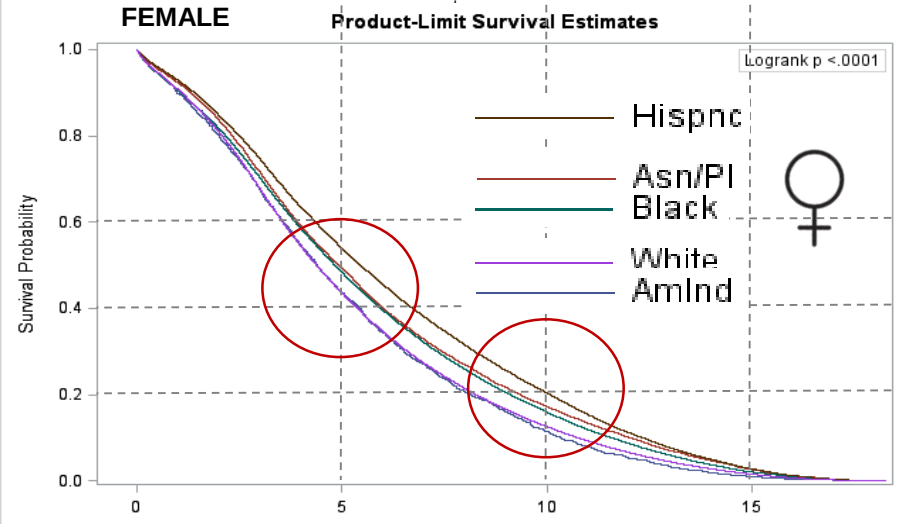
N = 4,349,565	White	Asian/PI	Black	Hispanic
Number (population)	3,456,373	125,944	442,402	324,846
Female, percent	65.2	64.2	66.8	65.2
Survival, years ($\bar{x}$, interquartile range)	5.3, 2.4-7.7	5.6, 2.3-7.6	5.7, 2.6-8.4	5.9, 2.7-8.7
Age at diagnosis ($\bar{x}$, s.d.)	80.0 (7.8)	78.8 (7.7)	77.8 (7.9)	77.5 (7.6)



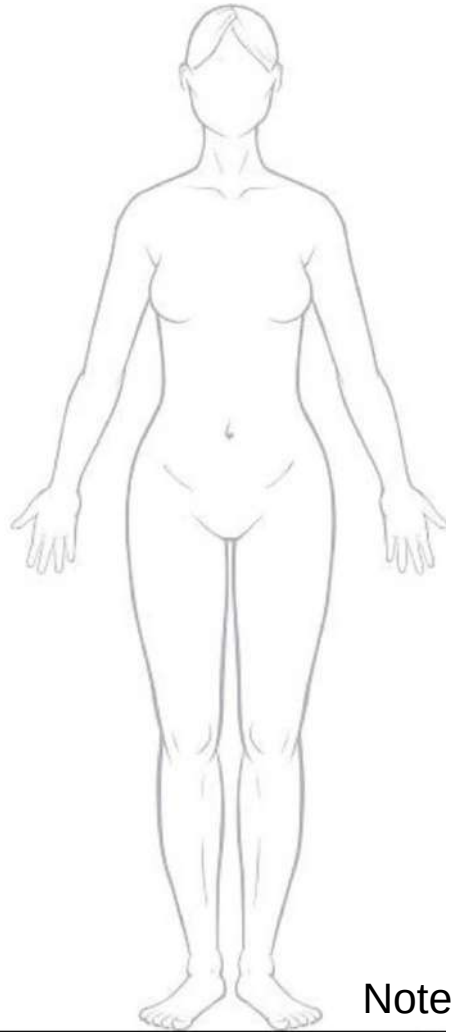
Survival Probability by Race/Ethnicity (RTI)





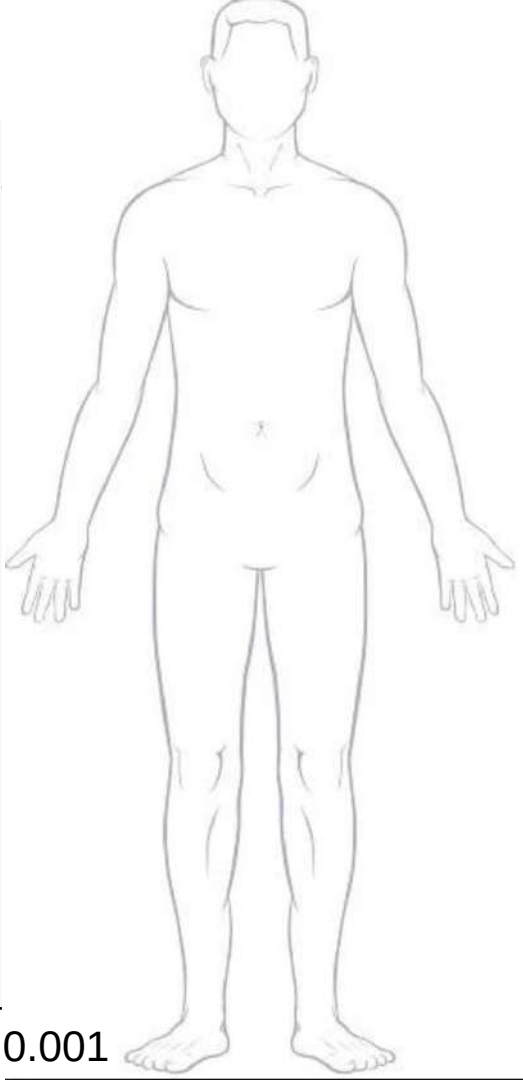


Can you spot the differences?



Hazard Ratios for Comorbidities

Stratified by Sex, Fully Adjusted Models (race, age, State, ADI)		
	Stroke/TIA	
	Cataract	
	Hypothyroid	
	Depression	
	Chronic Obstructive Pulmonary Disease	
	Acute Myocardial Infarction	
	Congestive Heart Failure	
	Hypertension	
	Chronic Kidney Disease	
	Anemia	
	Diabetes	
	Hyperlipidemia	
	Obesity	
	Peripheral Vascular Disease	



Note: 2013 national data, 10% random sample; ***p < 0.001

https://www.neighborhoodatlas.medicine.wisc.edu

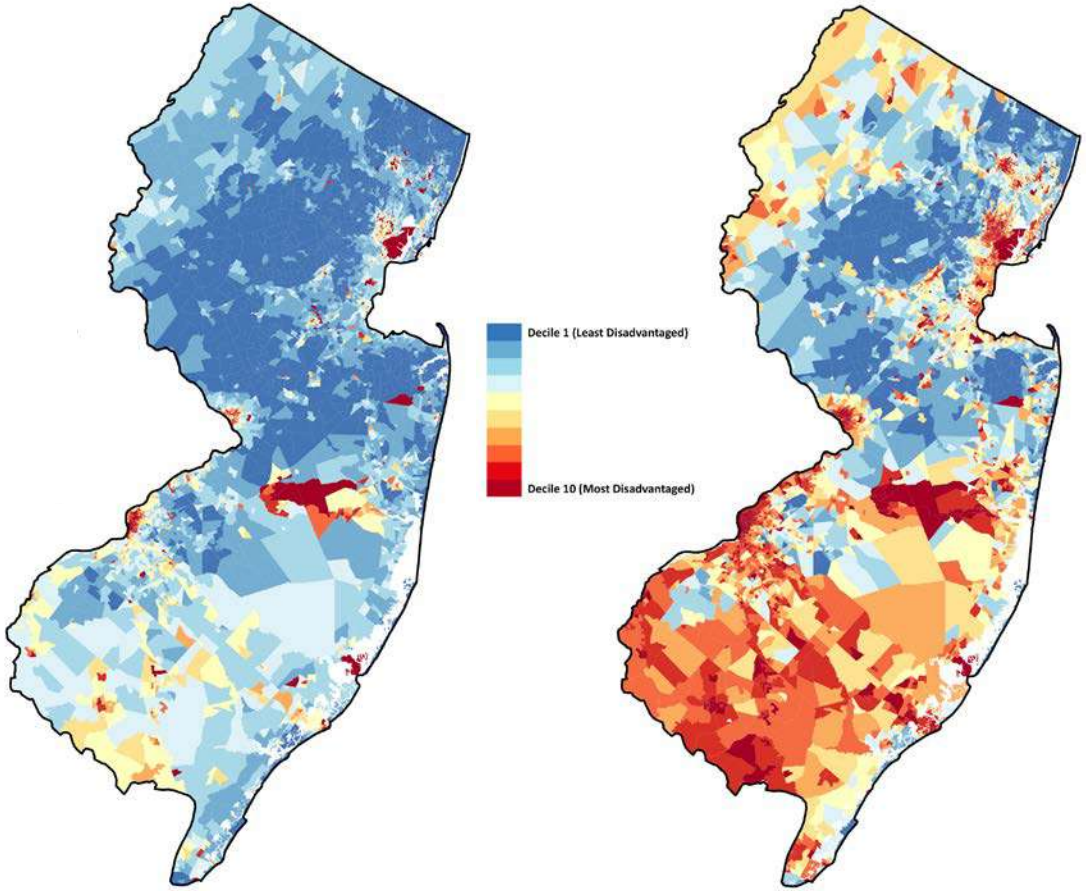
Neighborhood Atlas

Home Mapping Download Data Log In

About the 2013 Area Deprivation Index (ADI)

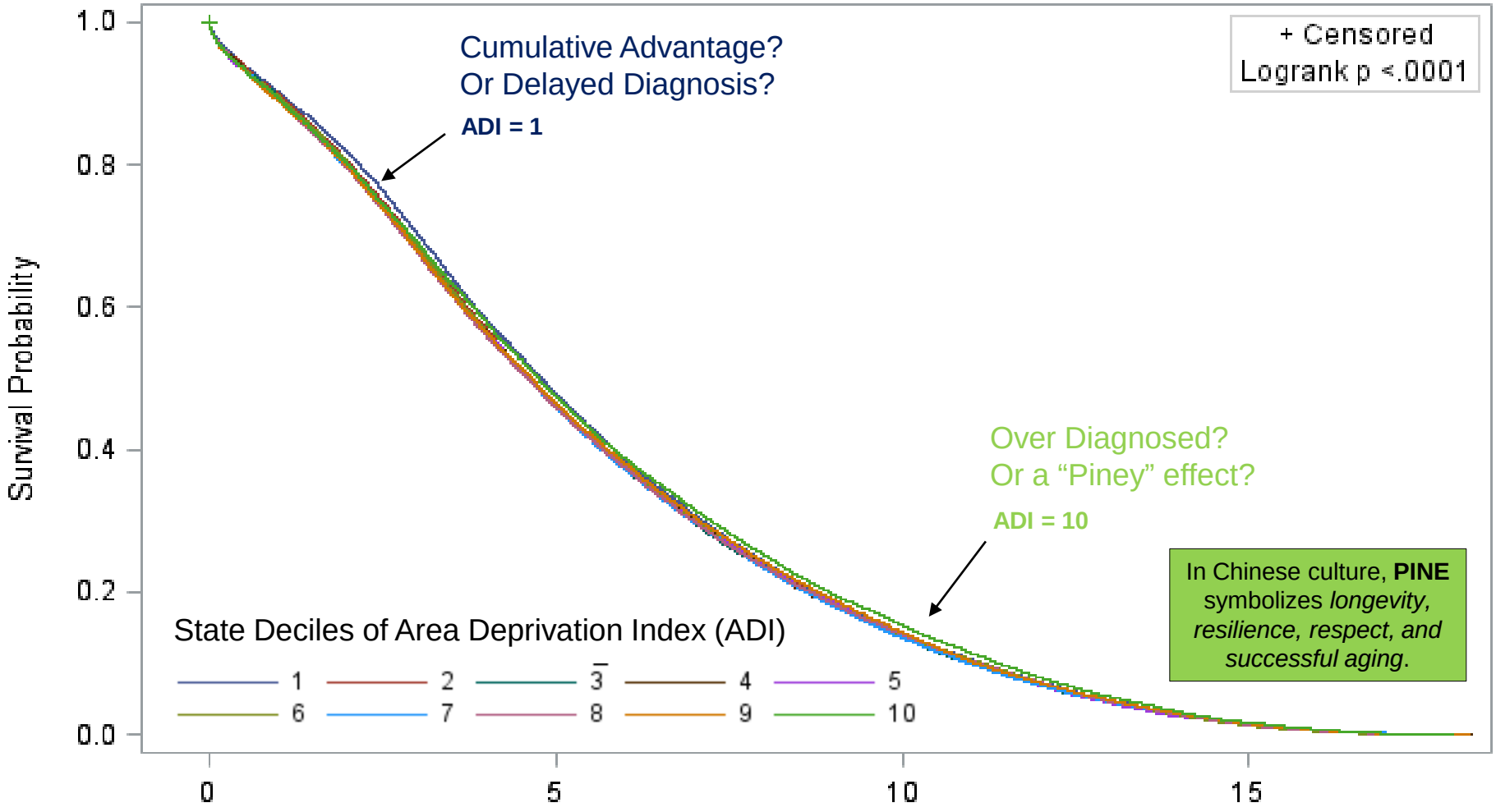
The Area Deprivation Index (ADI) is based on a measure created by the Health Resources & Services Administration (HRSA) over two decades ago for primarily county-level use, but refined, adapted, and validated to the Census block group/ neighborhood level by **Amy Kind, MD, PhD** and her research team at the University of Wisconsin-Madison. It allows for rankings of neighborhoods by socioeconomic status disadvantage in a region of interest (e.g. at the state or national level). It includes factors for the theoretical **domains of income, education, employment, and housing quality**. It can be used to inform health delivery and policy, especially for the most disadvantaged neighborhood groups.

2013 Area Deprivation Index (ADI) National vs. State Versions



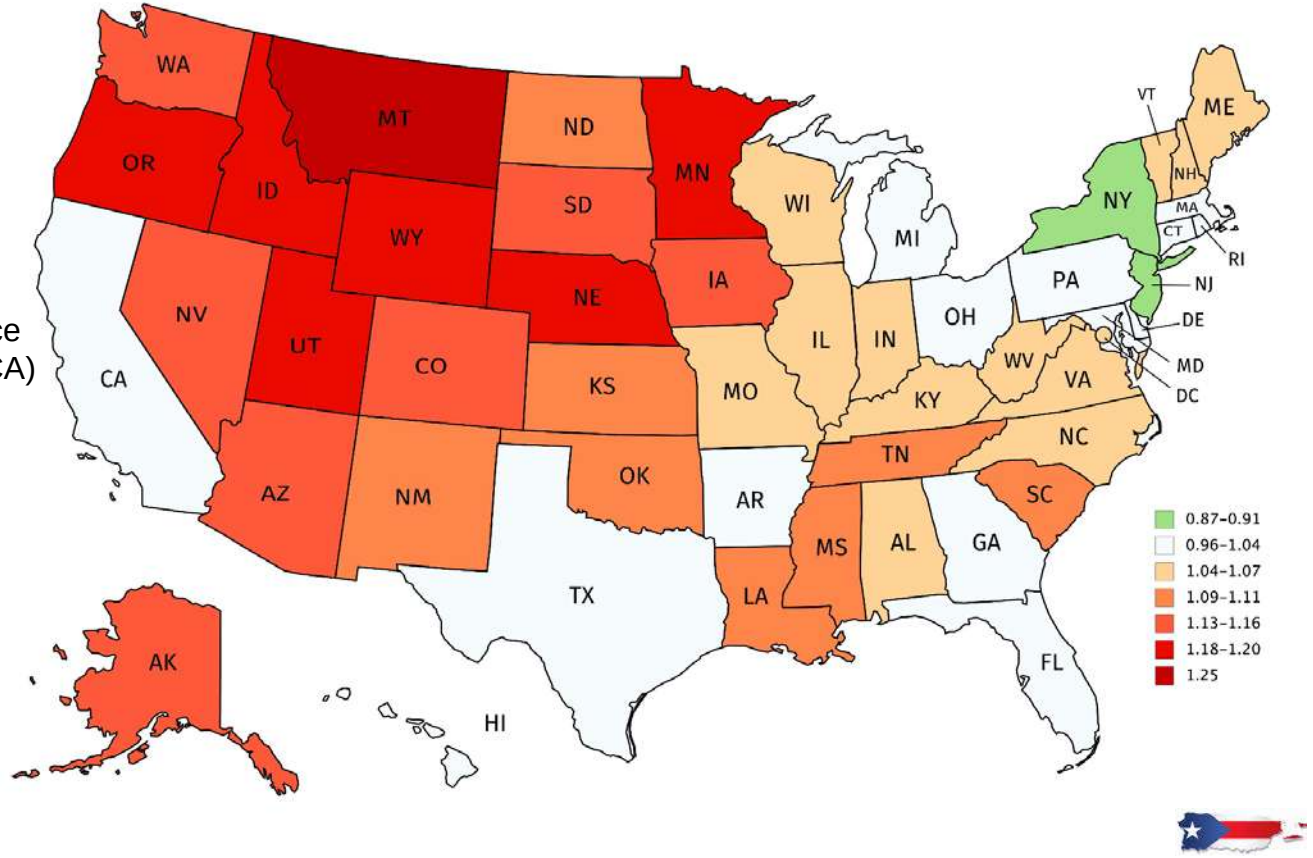
Is Central Jersey a Real Place?

Survival Probability across SES at time of Dementia Diagnosis



Hazard Ratios for State Effects – Fully Adjusted Models

Reference Group (CA)



Variation in Survival across Race & Ethnicity (RTI)

Hazard Ratios, Fully Adjusted Models (demographics, comorbidities, ADI, State)					
	Race	+Sex, Age	+CCW	+ADI^2	+State
Black	0.90***	0.94***	0.92***	0.92***	0.92***
Hispanic	0.86***	0.89***	0.83***	0.83***	0.83***
Asian	0.91***	0.90***	0.91***	0.91***	0.91***
Male		1.27***	1.24***	1.24***	1.24***
AIC (Model Fit)					

Note: 2013 national data, 10% random sample; *p < 0.05, **p < 0.01, ***p < 0.001

Variation in Survival across Sex, Race & Ethnicity (RTI) Stratified by Age at Diagnosis with Dementia

Hazard Ratios, Fully Adjusted Models (comorbidities, State, ADI)					
Age	**Male**	White	**Black**	**Hispanic**	**Asian**
65-69	1.20***	(ref)	1.00	0.925*	1.02
70-74	1.28***	(ref)	1.05*	0.908***	0.91
75-79	1.32***	(ref)	1.02	0.919***	0.95
80-84	1.34***	(ref)	0.95**	0.967	0.92*
85-89	1.35***	(ref)	0.85***	0.896***	0.92*
90+	1.14***	(ref)	0.87***	0.839***	0.92**

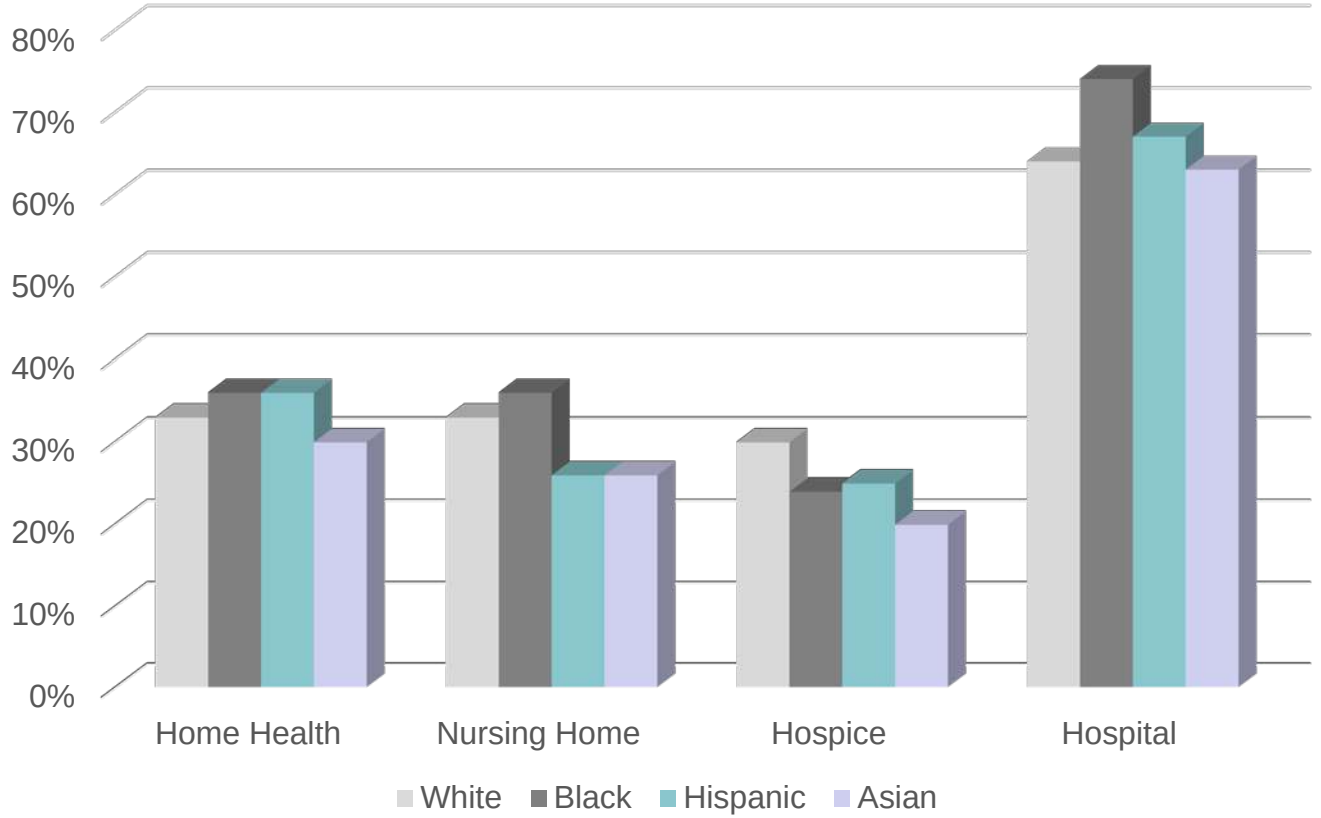
Note: 2013 national data, 10% random sample; *p < 0.05, **p < 0.01, ***p < 0.001

Variation in Survival across Race & Ethnicity, Stratified by Sex

Hazard Ratios, Stepped Models (demographics, +++)				
	+Comorbidities	+ADI^2	+State	
Black Male	0.97*	0.97*	0.97*	
Black Female	0.90***	0.90***	0.91***	
Hispanic Male	0.91***	0.91***	0.91***	
Hispanic Female	0.88***	0.88***	0.88***	
Asian Male	0.89***	0.89***	0.89***	
Asian Female	0.86*	0.96*	0.96*	

Note: 2013 national data, 10% random sample; *p < 0.05, **p < 0.01, ***p < 0.001

Variation in Health Services Utilization, Last Year of Life by Race/Ethnicity for People Living with Dementia



Variation in Survival across Use of Home Health, Stratified by Sex

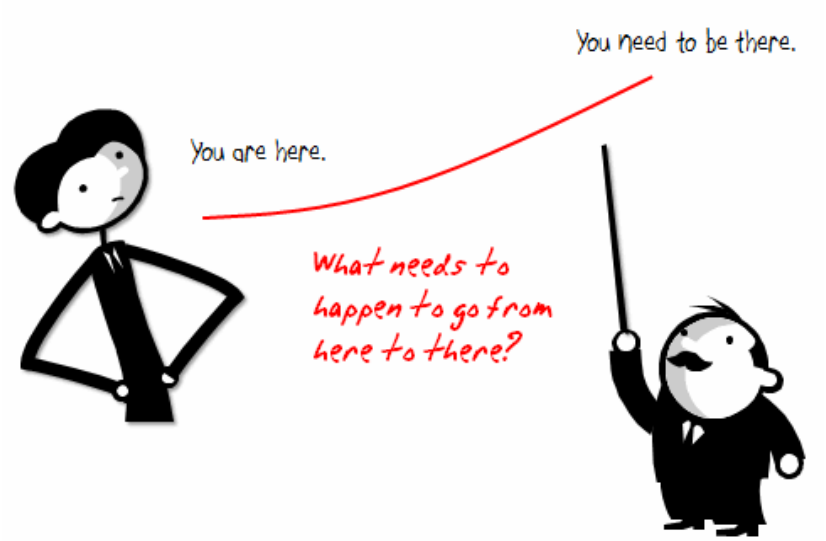
	+Comorbidities	+ADI^2	+State	+Home Health
Black Male	0.97*	0.97*	0.97*	
Black Female	0.90***	0.90***	0.91***	
Hispanic Male	0.91***	0.91***	0.91***	
Hispanic Female	0.88***	0.88***	0.88***	
Asian Male	0.89***	0.89***	0.89***	
Asian Female	0.86*	0.96*	0.96*	
Home Health (Males)				
Home Health (Females)				

Note: 2013 national data, 10% random sample; *p < 0.05, **p < 0.01, ***p < 0.001

Variation in Survival across Sex & Age at time of Diagnosis, Stratified by Race & Use of Home Health Care

Hazard Ratios, Fully Adjusted Models (comorbidities, State, ADI) (+ Home Health)								
	White	+HH	Black	+HH	Hispanic	+HH	Asian	+HH
Male	1.29***		1.36***		1.29***		1.17***	
70-74	0.88***		0.91***		0.89***		0.85***	
75-79	0.96***		0.97***		1.00		0.90***	
80-84	1.21***		1.14***		1.26***		1.13***	
85-89	1.66***		1.47***		1.70***		1.59***	
90+	1.63***		1.36***		1.48***		1.51***	

Next Steps



1. Build person-level trajectory files of health service utilization over multiple years for people living with dementia

2. Complete supplemental work to build state health policy library database related to healthy aging
(data enrichment at state level)

3. Complete supplemental work to impute ethnicity detail based on residential history & self-reported race
(data enrichment at person level)

4. Complete supplemental work on social determinants of health
(contextual data enrichment at person level)

Next Leaps – Seeking Collaborators

Adding focus on people living with dementia and HIV/AIDS (long time survivors and people diagnosed after age 65) *team forming now

Your Ideas - What else could we do? (with you!)

Wish List

1. Assessments to complete trajectory file (Hospital Swing Beds & Inpatient Rehabilitation) ($10K/yr x 4 years= $40K)
2. National Death Index Data ($10K/yr x 10 years = $100K)
3. Funding for Trajectories of Dementia Care Project ($750K/yr x 4 years = $3M)
4. Funding for Trajectories of Care Center *Multi-Project* ($3M/yr x 5 years = $15M)

Thank you!

Follow Olga Jarrín Montaner and the Community Health and Aging Outcomes Laboratory on Twitter

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Brain Network Mechanisms of Aging-Related Cognitive Decline

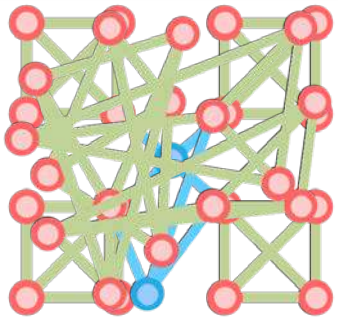
Michael W. Cole

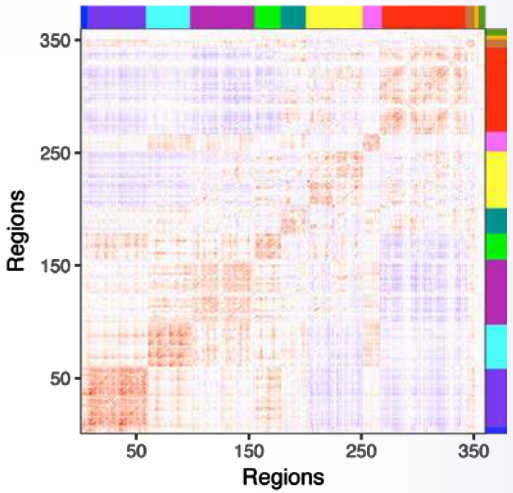
Center for Molecular & Behavioral Neuroscience

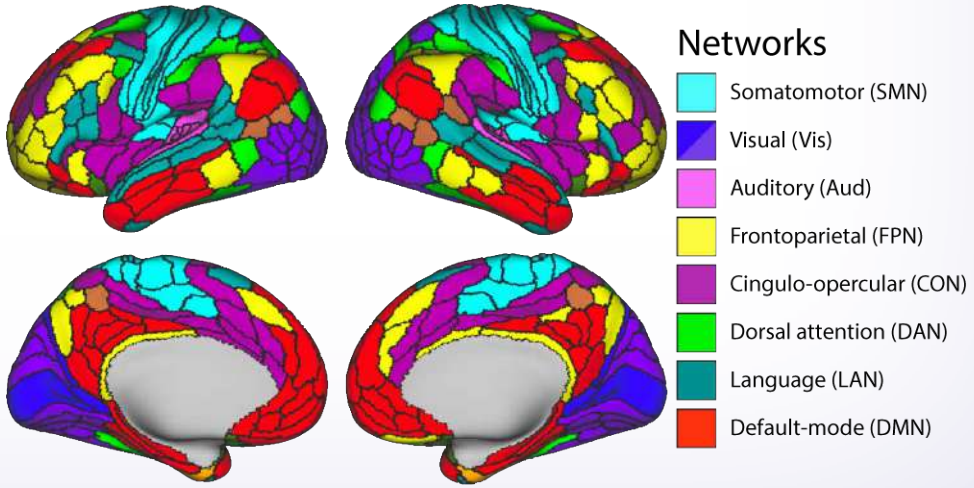
Rutgers University – Newark

What is the brain's large-scale functional architecture?

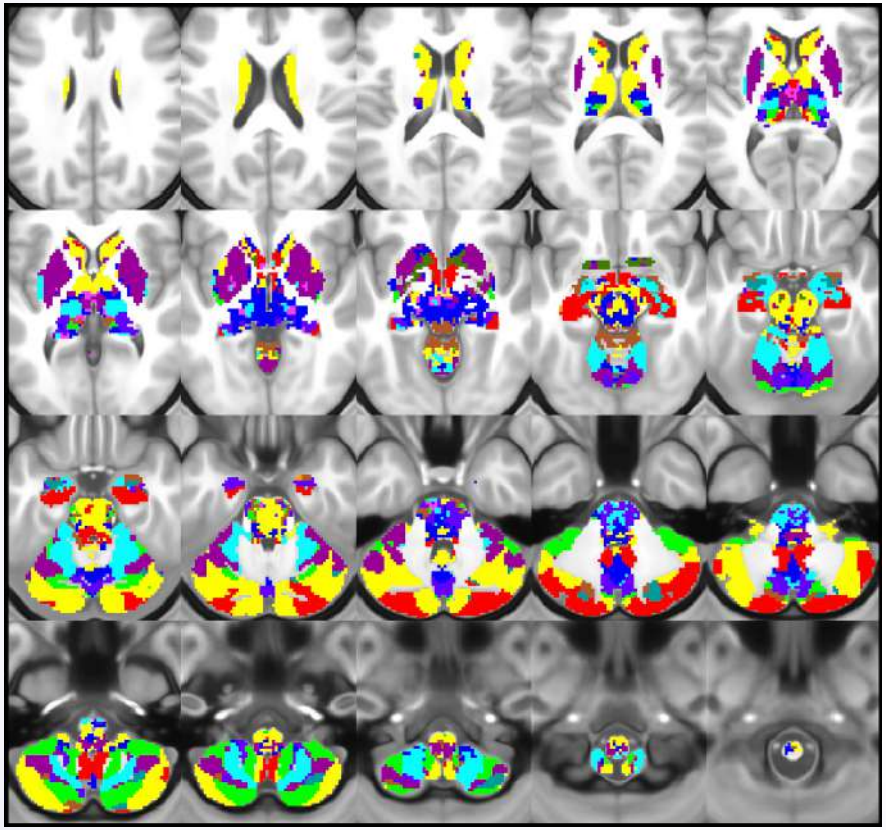
- Systems as graph communities
  - Clusters of highly interconnected nodes
- "Community detection" algorithms
- Applied to whole-brain resting-state fMRI graphs (Ji et al., in press)
  - Regions defined by Glasser et al., 2016

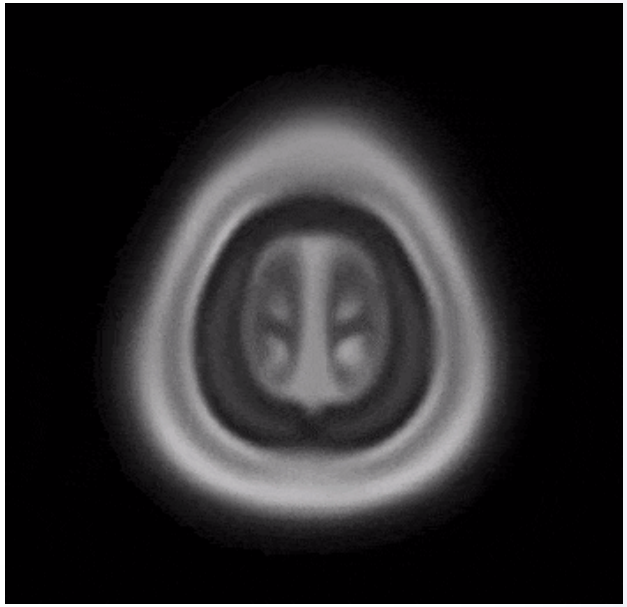






Subcortical extension of cortical networks





Available for download:
www.colelab.org/#resources

Ji et al. (In Press), *NeuroImage*

What is functional connectivity, why does it matter?

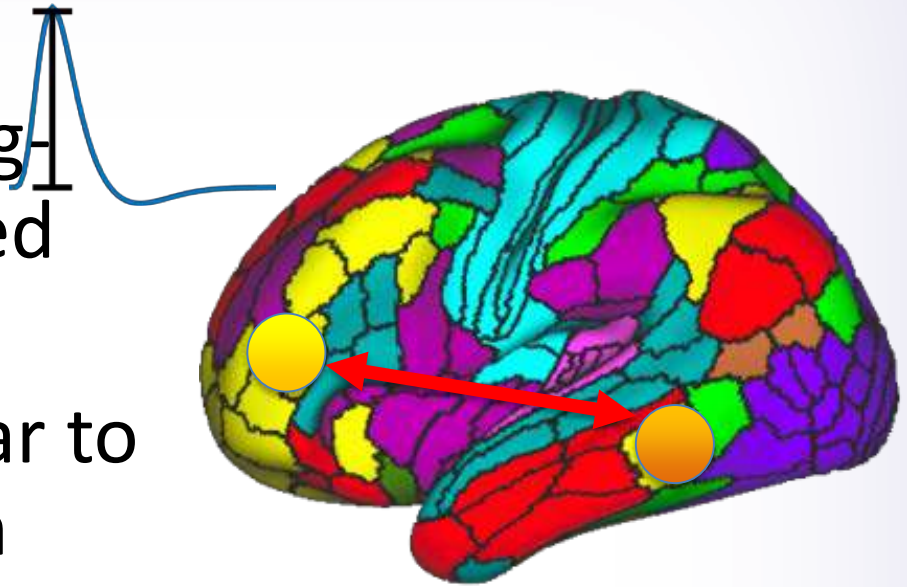
- Typical FC definition:
  "Statistical association between neural time series"
  - *What does this mean, mechanistically?*
- To the extent that FC = causal interaction between neural entities…
  - **Central to neural function, computation**
  - Neurons compute based on input **patterns**
  - No neuron acts alone
  - No million-neuron circuit acts alone
- How to make sense of large-scale FC? Analyze **patterns**
  - Graph theory (e.g., hubs, communities),
    machine learning (link activity/FC patterns to cognition)

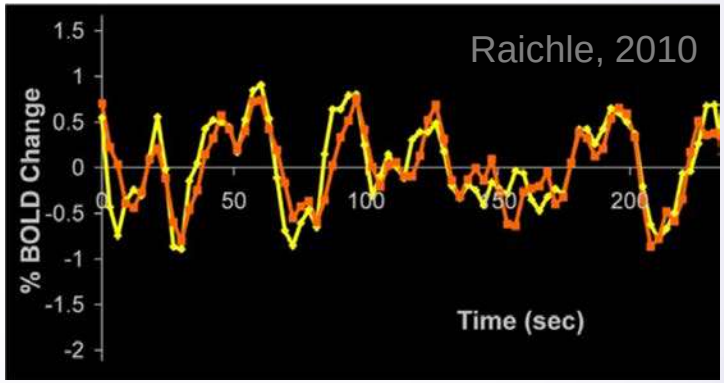
Overview

1. Cognitive activations spread via resting-state FC topology
2. Predicting unhealthy aging-related cognitive activation changes

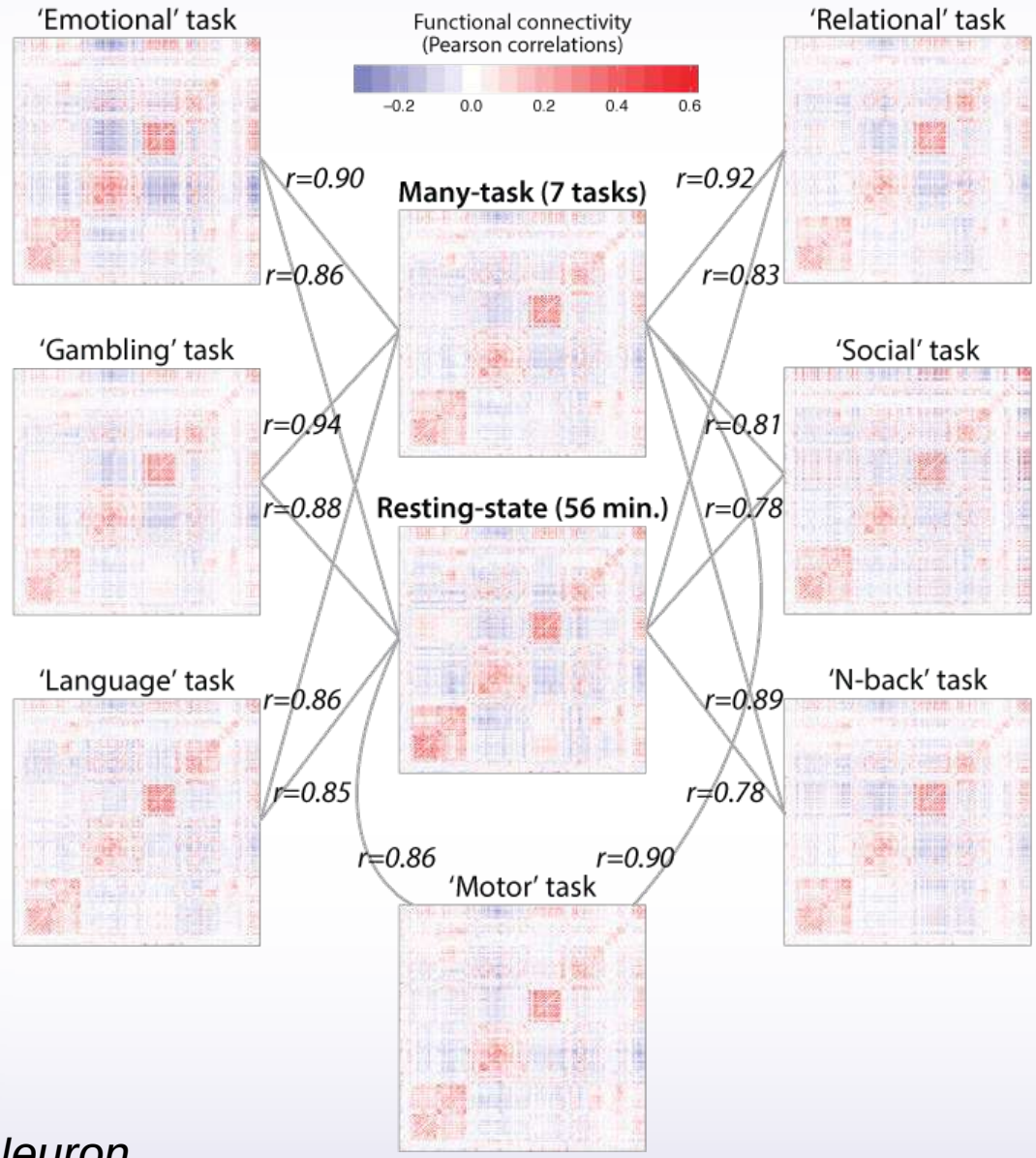
Resting-state FC and cognition

- Bifurcation into resting-state FC vs. task-evoked activation studies
- Rest FC patterns similar to task-evoked activation patterns
(Smith et al., 2009)
- But ***why***?
  - Need mechanism linking rest FC and activations



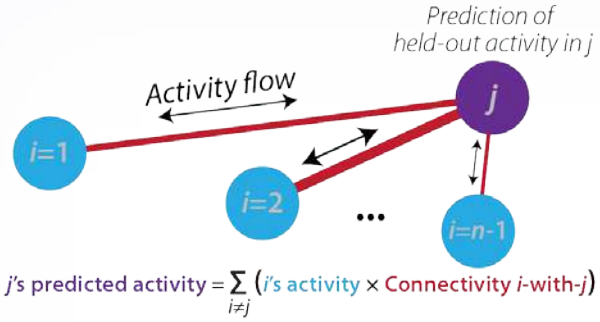


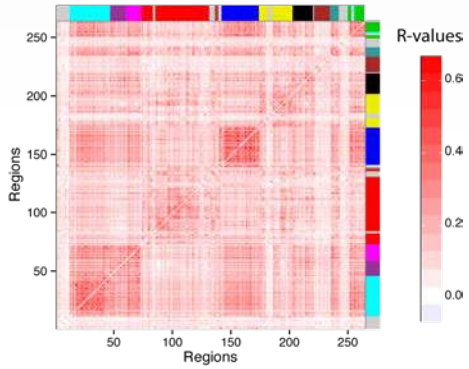
Highly similar FC patterns across mental states

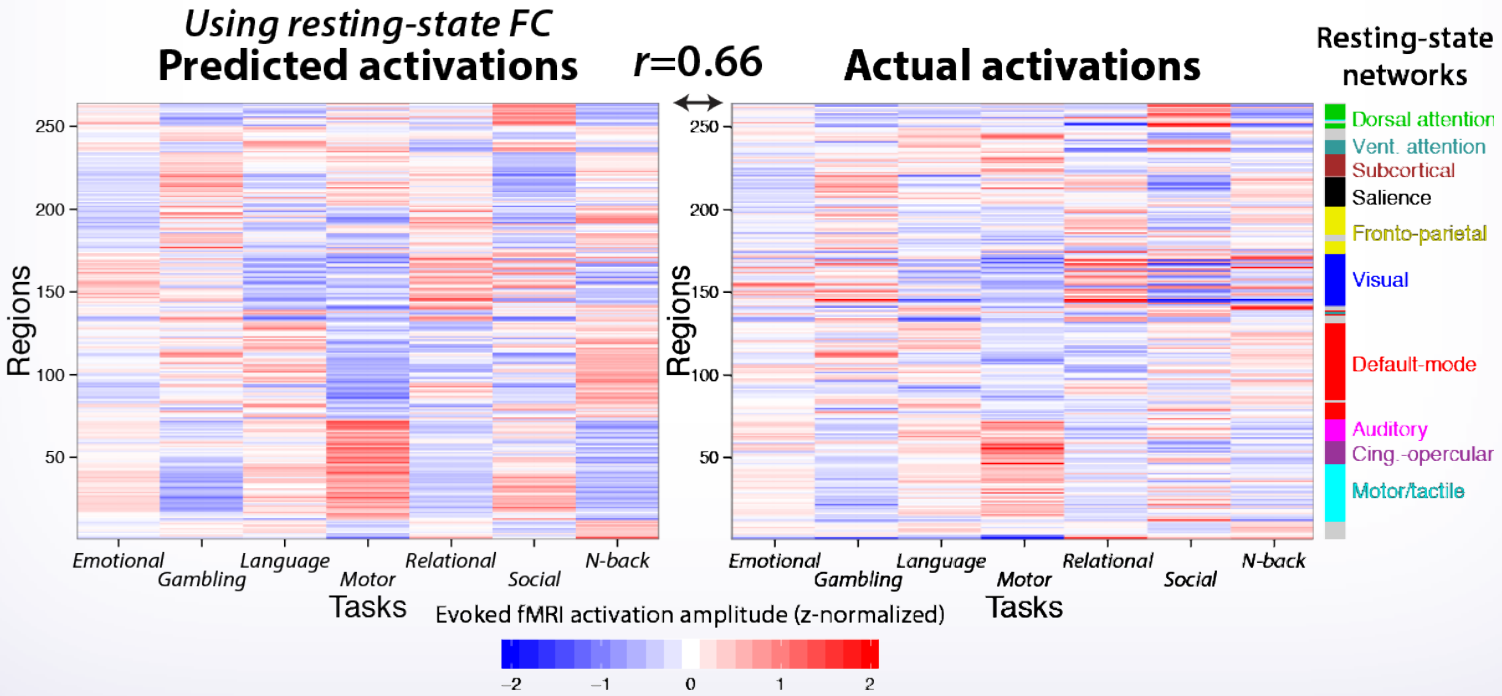


Cole et al., 2014; *Neuron*

Activity flow mapping

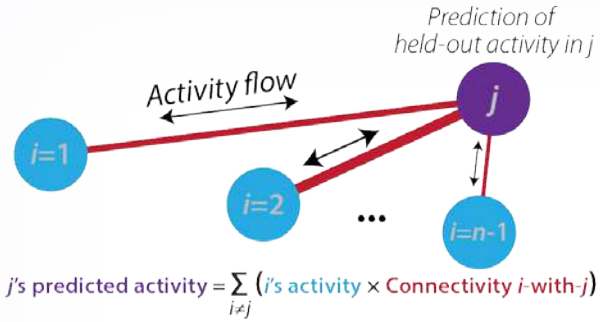


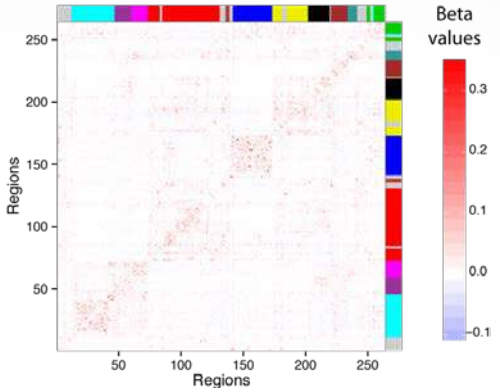


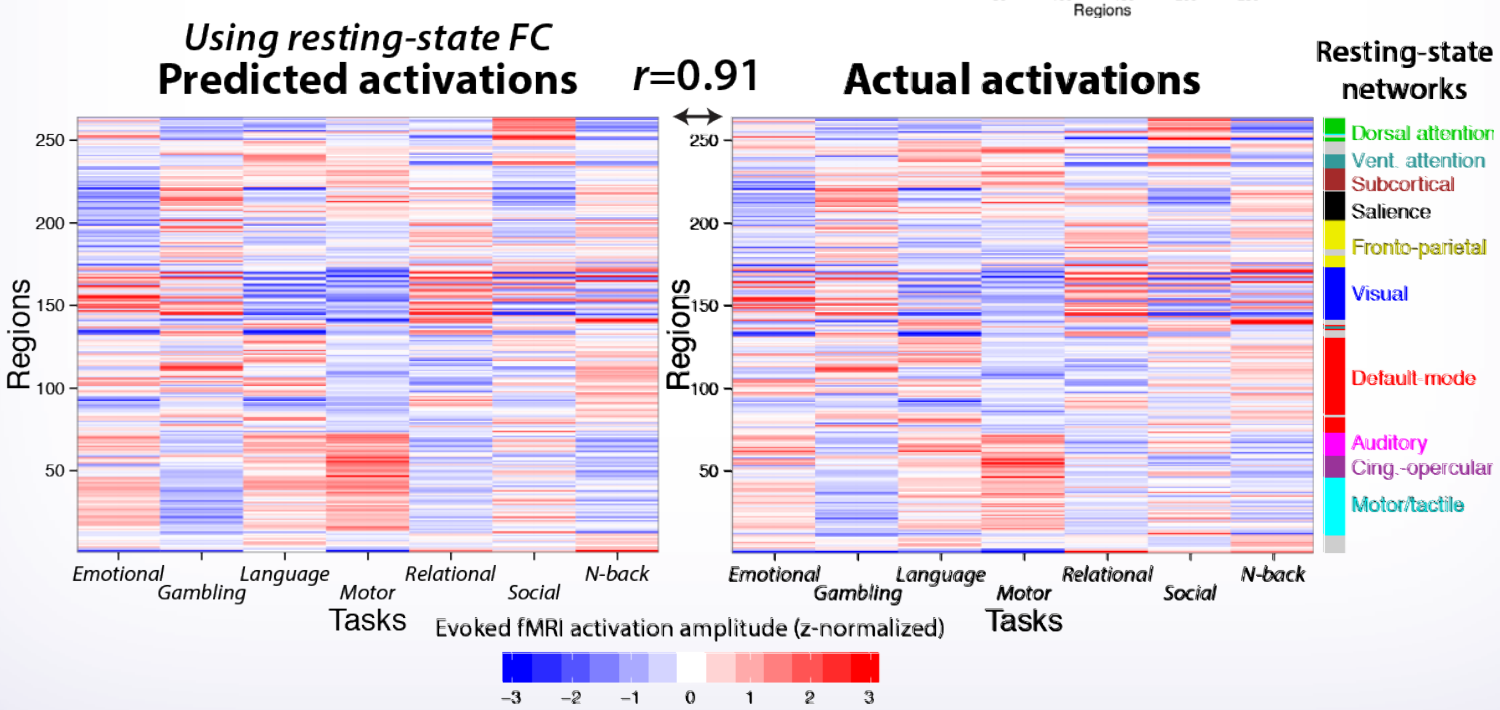


Cole et al., 2016; *Nature Neuroscience*

Activity flow mapping with multiple regression FC

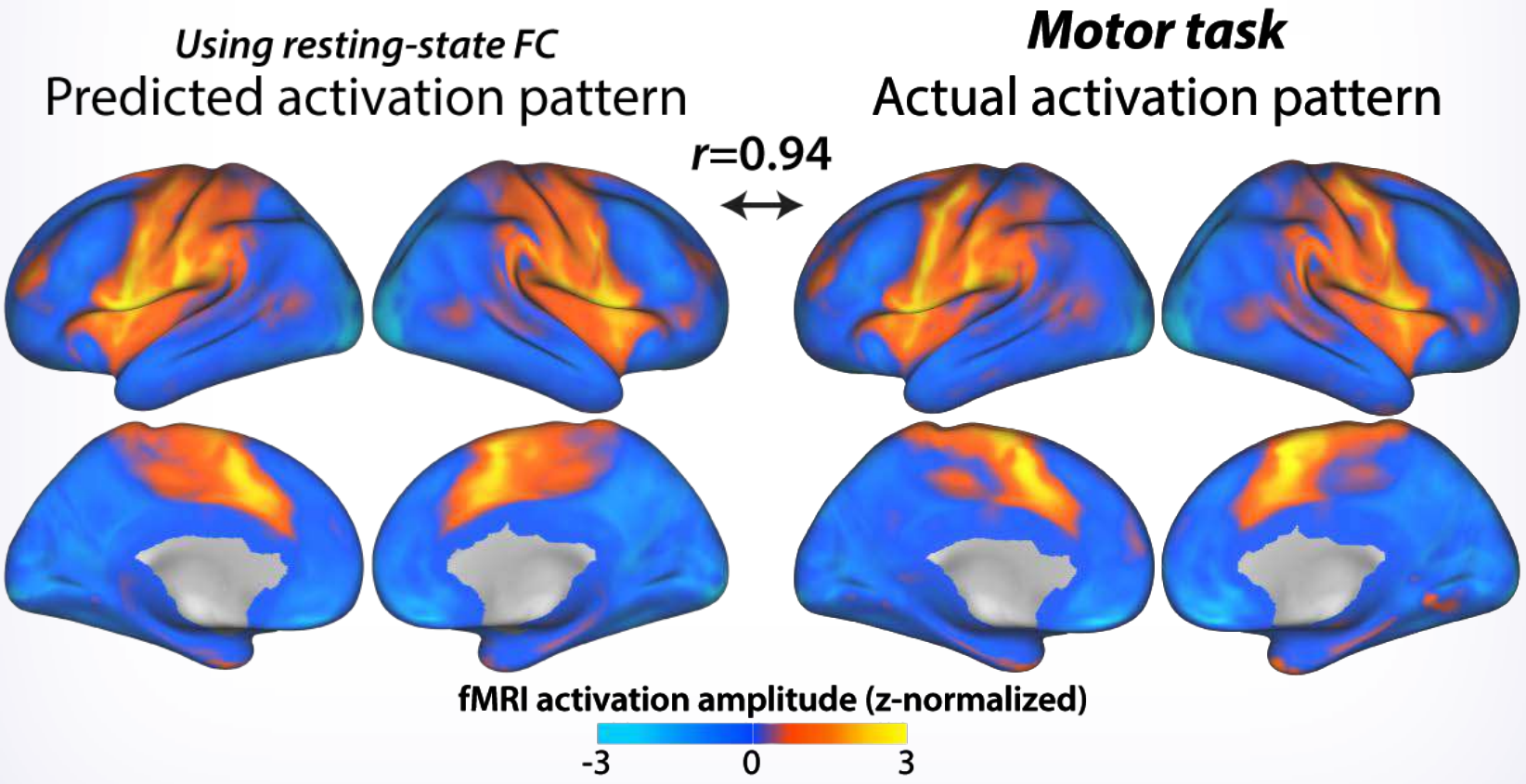






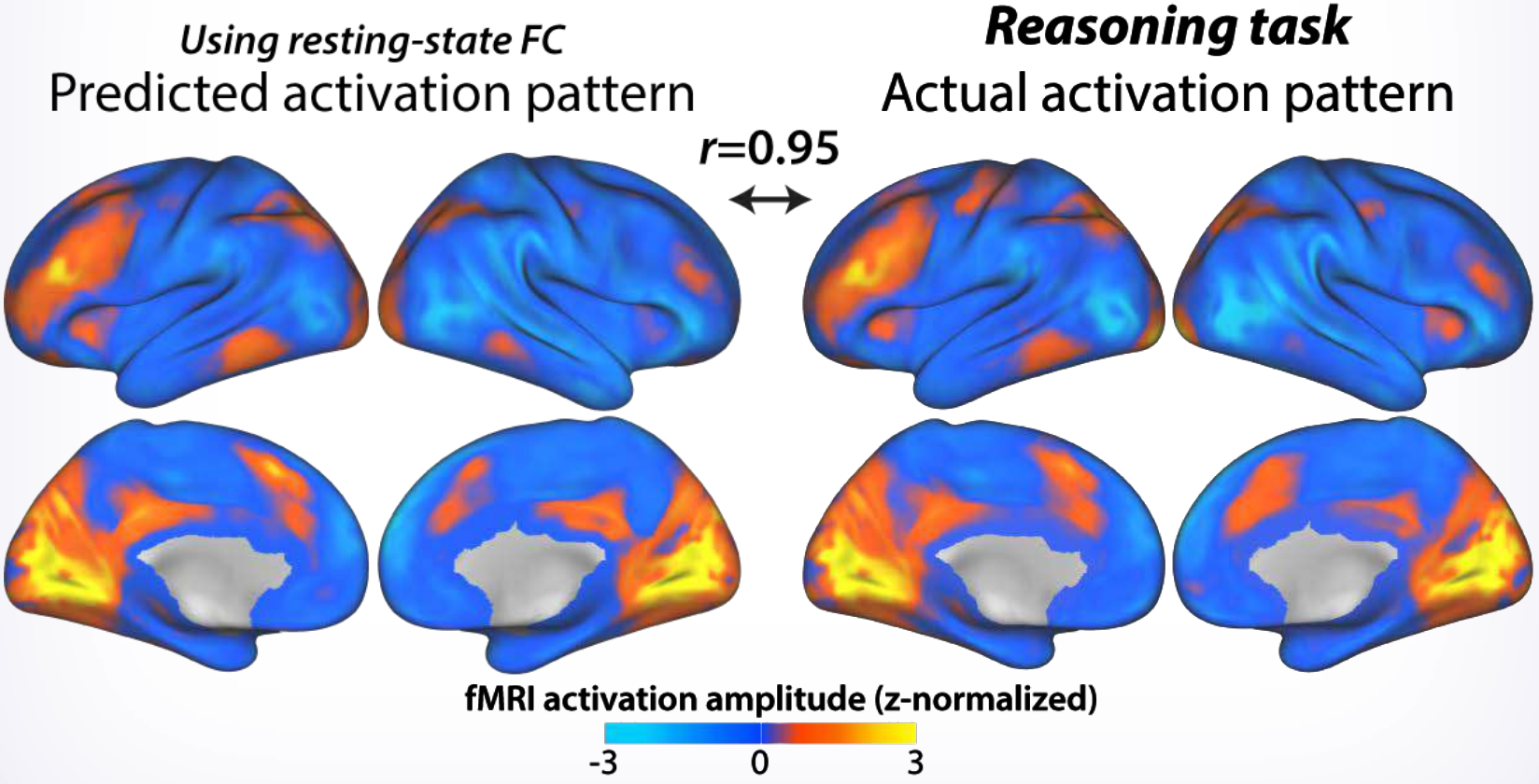
Cole et al., 2016; *Nature Neuroscience*

Activity flow mapping using multiple regression



Cole et al., 2016; *Nature Neuroscience*

Activity flow mapping using multiple regression



Cole et al., 2016; *Nature Neuroscience*

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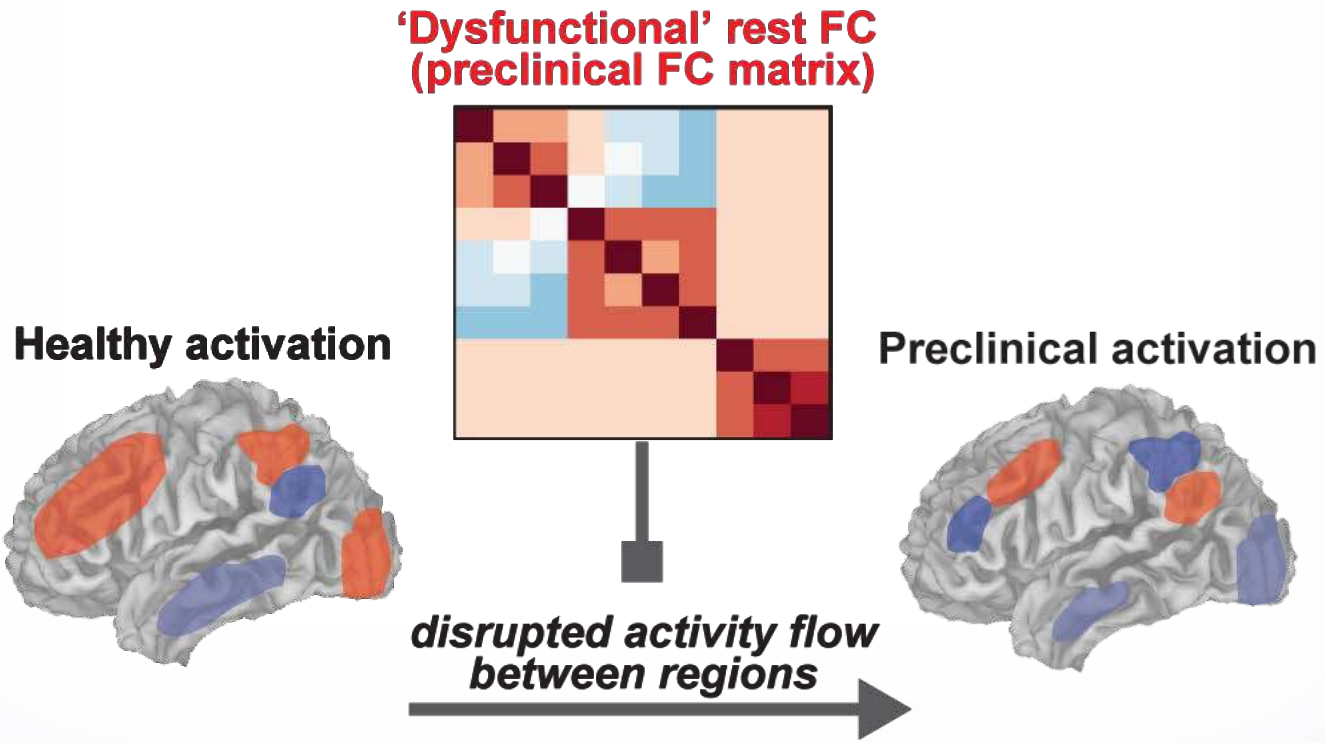
2. Predicting unhealthy aging-related cognitive activation changes

Predicting unhealthy aging-related cognitive activations

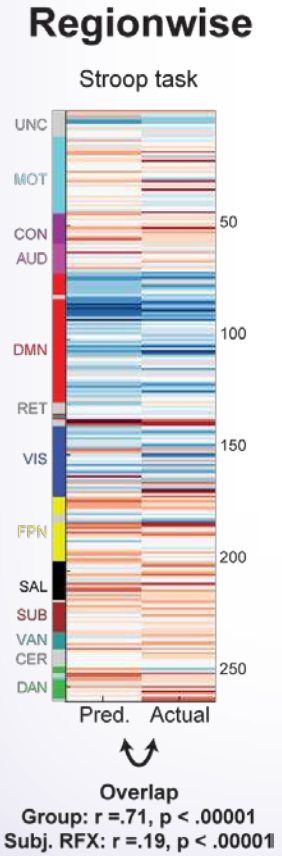


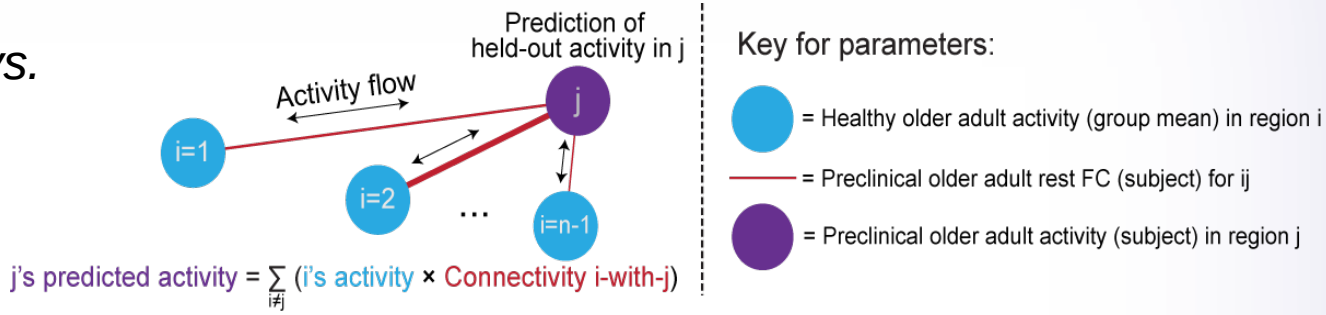
Subject characteristics: 101 cognitively-typical older adults, preclinical based on beta amyloid deposits or APOE genetic status

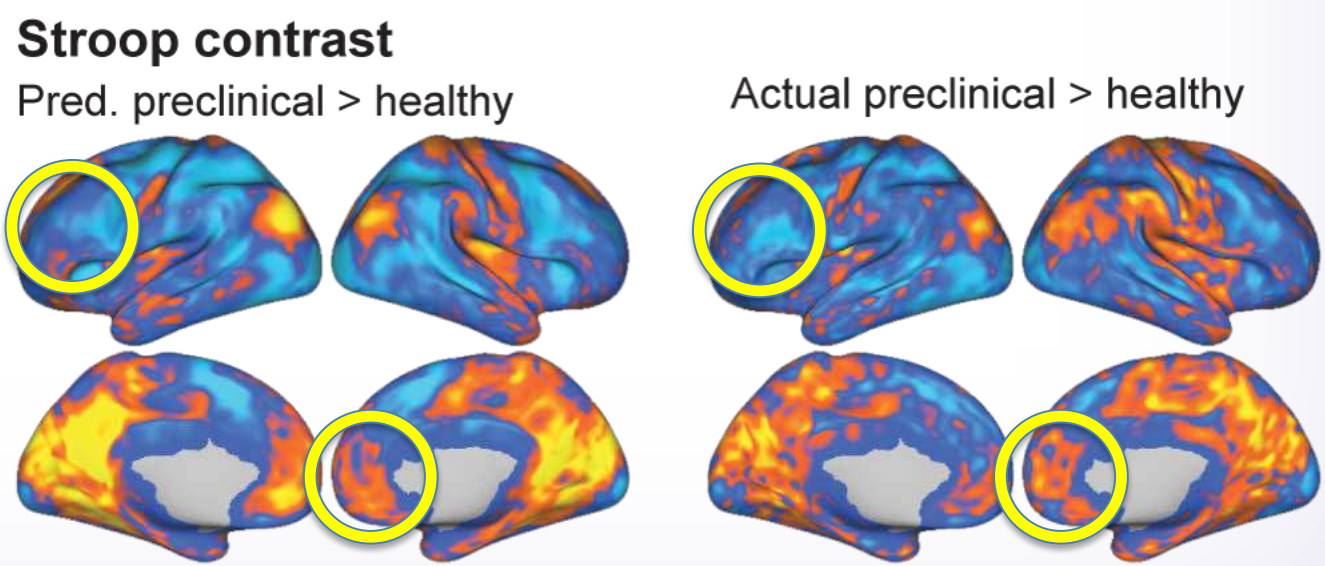
Mill et al., *in preparation*

Predicting unhealthy aging-related cognitive activations

Preclinical (APOE) vs. healthy older adults







Mill et al., *in preparation*

Take-home messages

- Large-scale FC provides insights into the neural mechanisms of cognition
- Activity flow mapping helps determine role of connectivity in cognitive task activations
  - Resting-state FC highly relevant to cognition
- Applied to aging research, activity flow provides insights & useful predictions


Integrative idea


- Rutgers-wide “big data” database for older adult recruitment and assessment
  - Include younger adults for matched aging controls, longitudinal studies (eventually they will be older!)
  - Healthy & unhealthy aging
  - State-wide practical: NJ most densely-populated state
- Study recruitment highly efficient, more valid
- *More studies possible*:
  Special subpopulations identifiable
- *More comprehensive assessment*:
  Pool data across studies for same individuals
- **Substantial advantage to Rutgers aging research**

Acknowledgements

RUTGERS
NEWARK

- My lab at the Center for Molecular & Behavioral Neuroscience (CMBN), Rutgers University-Newark
- Collaborators:
  Alan Anticevic, Todd Braver, Steve Petersen, Walter Schneider, & others
- *Funding*:
  - K99-R00 & R01 from National Institute of Mental Health (NIMH)
  - R01 from National Institute on Aging (NIA)

More information: **www.colelab.org**

RUTGERS

Rutgers Catalyst: Healthy Aging Symposium
October 18, 2018

Micronutrient Supplementation and the Aging Brain

Can Supplements Prevent Age-Related Cognitive Decline?

Joshua W. Miller, PhD
Professor and Chair
Dept. of Nutritional Sciences
School of Environmental and Biological Sciences
Rutgers, The State University of New Jersey

AN EVERYDAY HEALTH INFOGRAM

7 WAYS TO CUT YOUR ALZHEIMER'S DISEASE RISK

Research suggests that certain diet and exercise habits may lower Alzheimer's disease risk by more than half.

Steps to Prevent Alzheimer's

#1 Avoid saturated fats and trans fats.
Dairy products, meats, and certain oils (coconut and palm oils – listed on labels as "partially hydrogenated oils") contain saturated fat. Many snacks, pastries, and fried foods are filled with trans fats.

#2 Eat a healthy diet.
Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should be staples in your diet.

#3 Go nuts for nuts.
One ounce of nuts or seeds – a small handful – is a great source of vitamin E.

#4 Make vitamin B12 a priority.
Eat fortified foods or take a supplement to get at least the recommended daily allowance (2.4 mcg per day for adults).

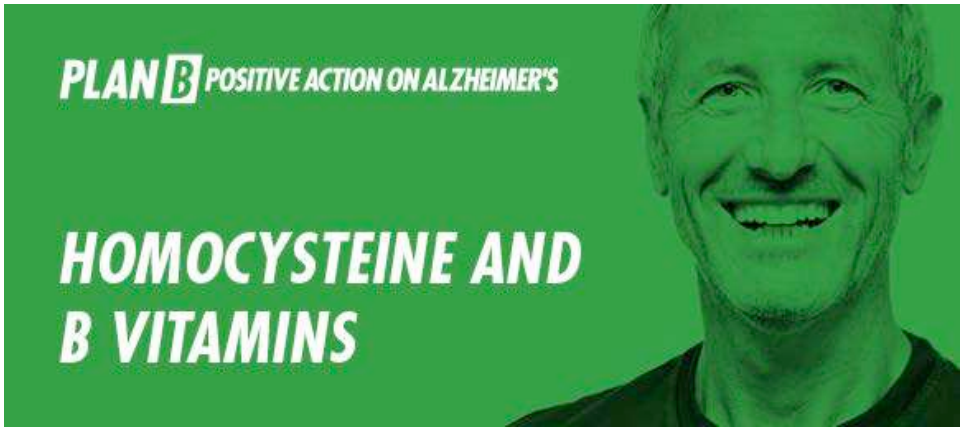
#5 Choose your multivitamin wisely.
Avoid multivitamins with iron and copper, and take iron supplements only when directed by your doctor.

#6 Cook with caution.
Avoid aluminum cookware, which has been linked to Alzheimer's-related dementia. Instead choose stainless steel or cast iron pots and pans.

#7 Keep moving.
Get at least 40 minutes of aerobic exercise three times a week – such as brisk walking, running, or cycling.

Source: Dietary Guidelines for Alzheimer's Prevention 2013, Physicians Committee for Responsible Medicine

everydayHEALTH



Press Release – July 16, 2014

UNIVERSITY OF OXFORD

Taking B vitamins won't prevent Alzheimer's disease

HEALTH (/NEWS-LISTING?CATEGORY=249) RESEARCH (/NEWS-LISTING?CATEGORY=228)

Taking B vitamins doesn't slow mental decline as we age, nor is it likely to prevent Alzheimer's disease, conclude Oxford University researchers who have assembled all the best clinical trial data involving 22,000 people to offer a final answer on this debate.

Clarke et al, Am J Clin Nutr, 2014

Effects of homocysteine lowering with B vitamins on cognitive aging: meta-analysis of 11 trials with cognitive data on 22,000 individuals[1–5]

Robert Clarke, Derrick Bennett, Sarah Parish, Sarah Lewington, Murray Skeaff, Simone JPM Eussen, Catharina Lewerin, David J Stott, Jane Armitage, Graeme J Hankey, Eva Lonn, David Spence, Pilar Galan, Lisette C de Groot, Jim Halsey, Alan D Dangour, Rory Collins, and Francine Grodstein on behalf of the B-Vitamin Treatment Trialists' Collaboration

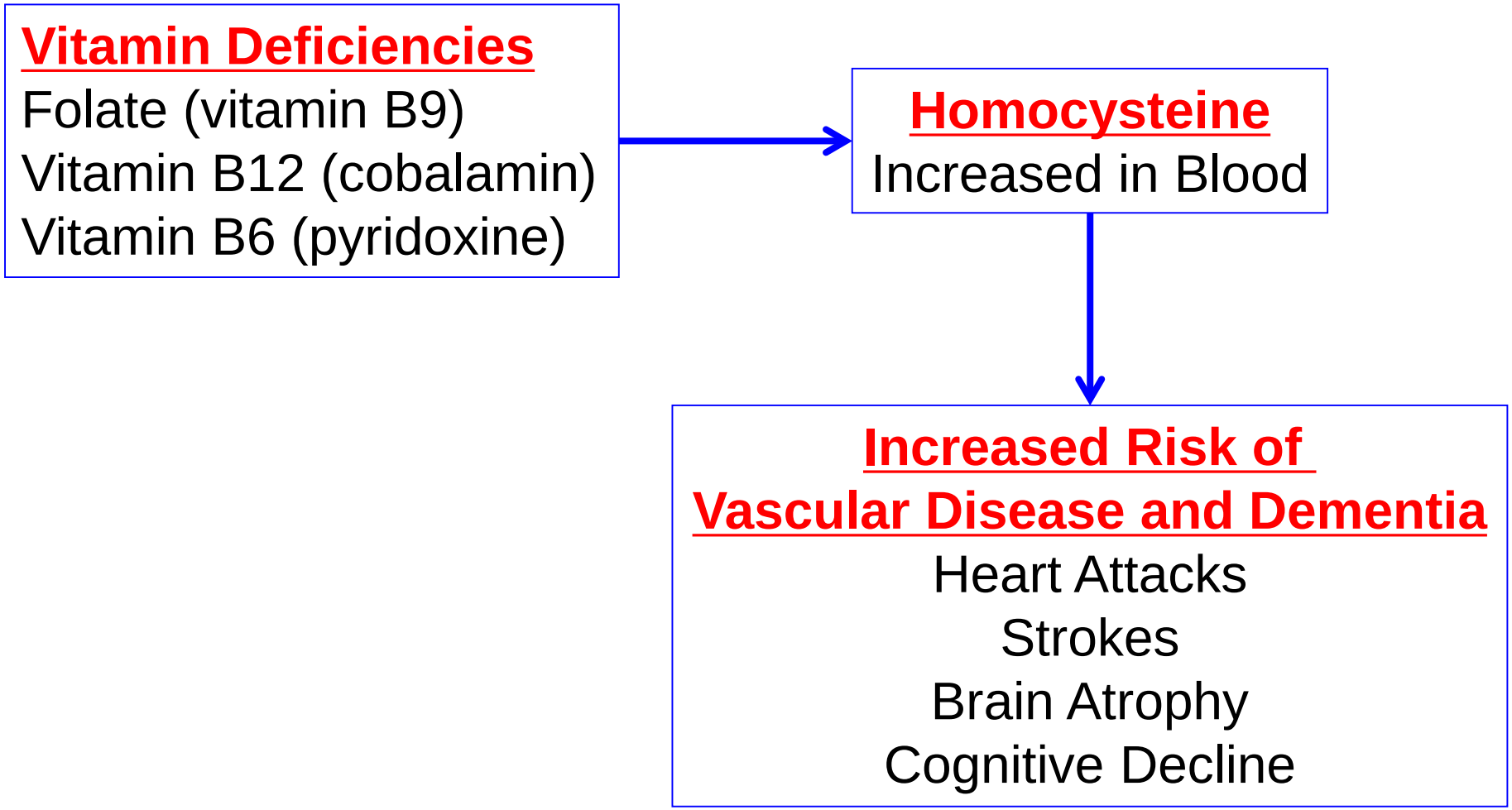
Do Supplements Prevent Cognitive Decline?

Answer…

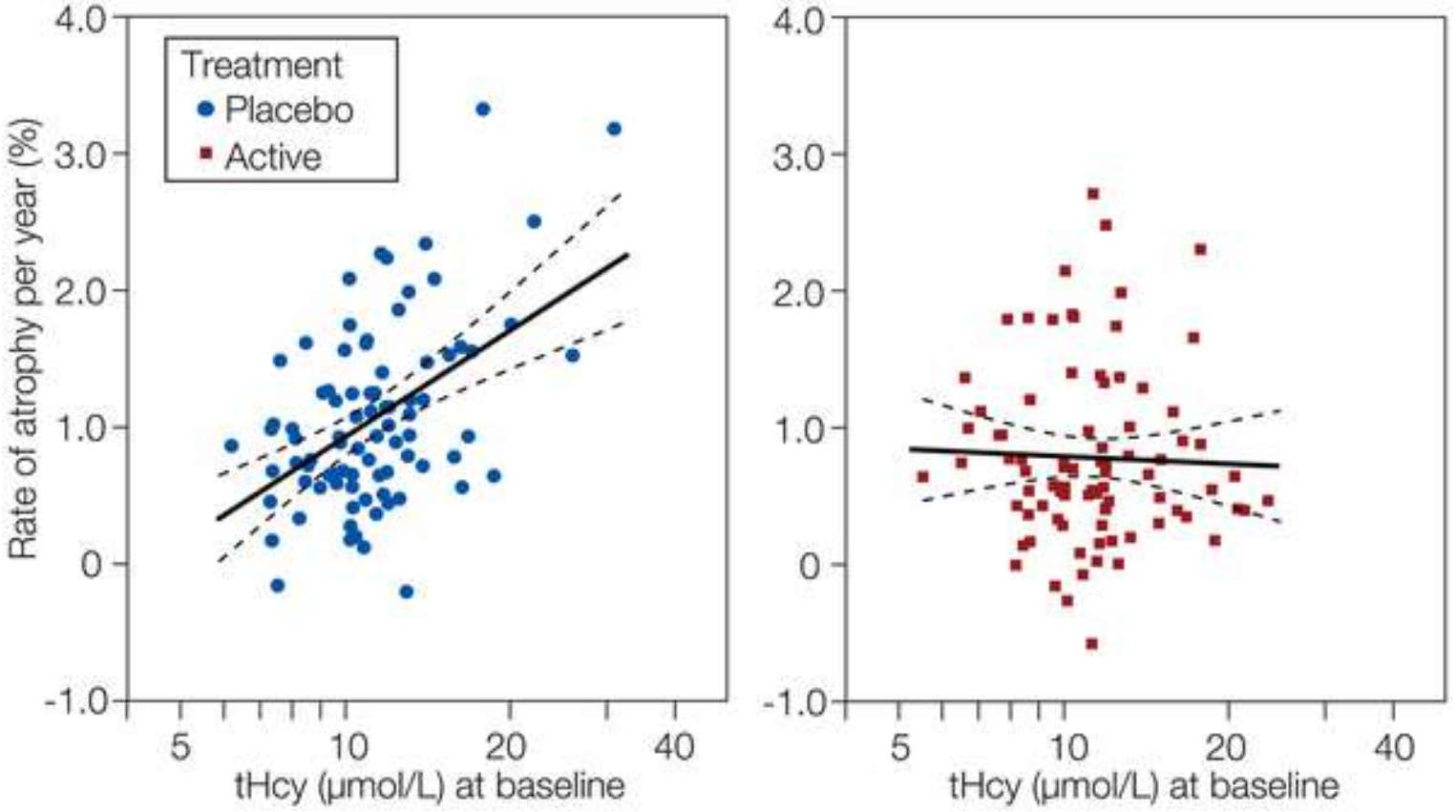
Probably, but...

The devil is in the details

B Vitamins, Homocysteine, and Vascular Disease



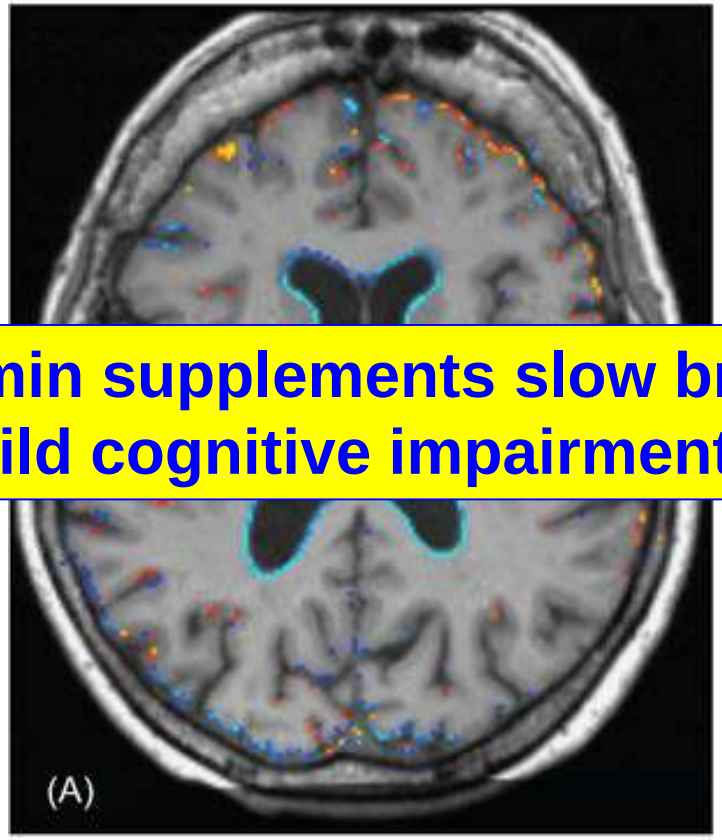
Effect of B Vitamin Supplements on Brain Atrophy in Older Adults with MCI



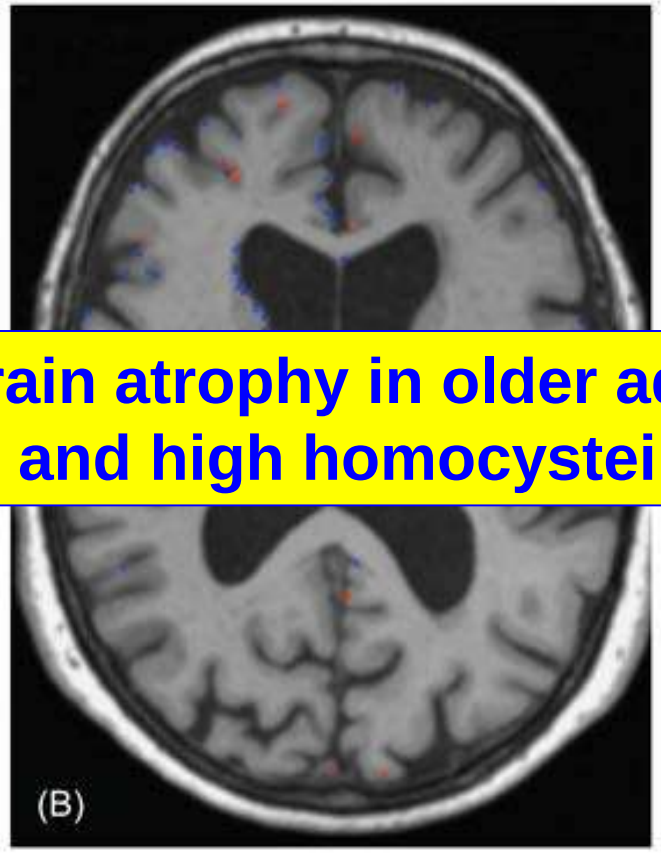
Smith et al, PLoS One, 2010

Effect of B Vitamin Supplements on Total Brain Atrophy

Placebo



B Vitamins



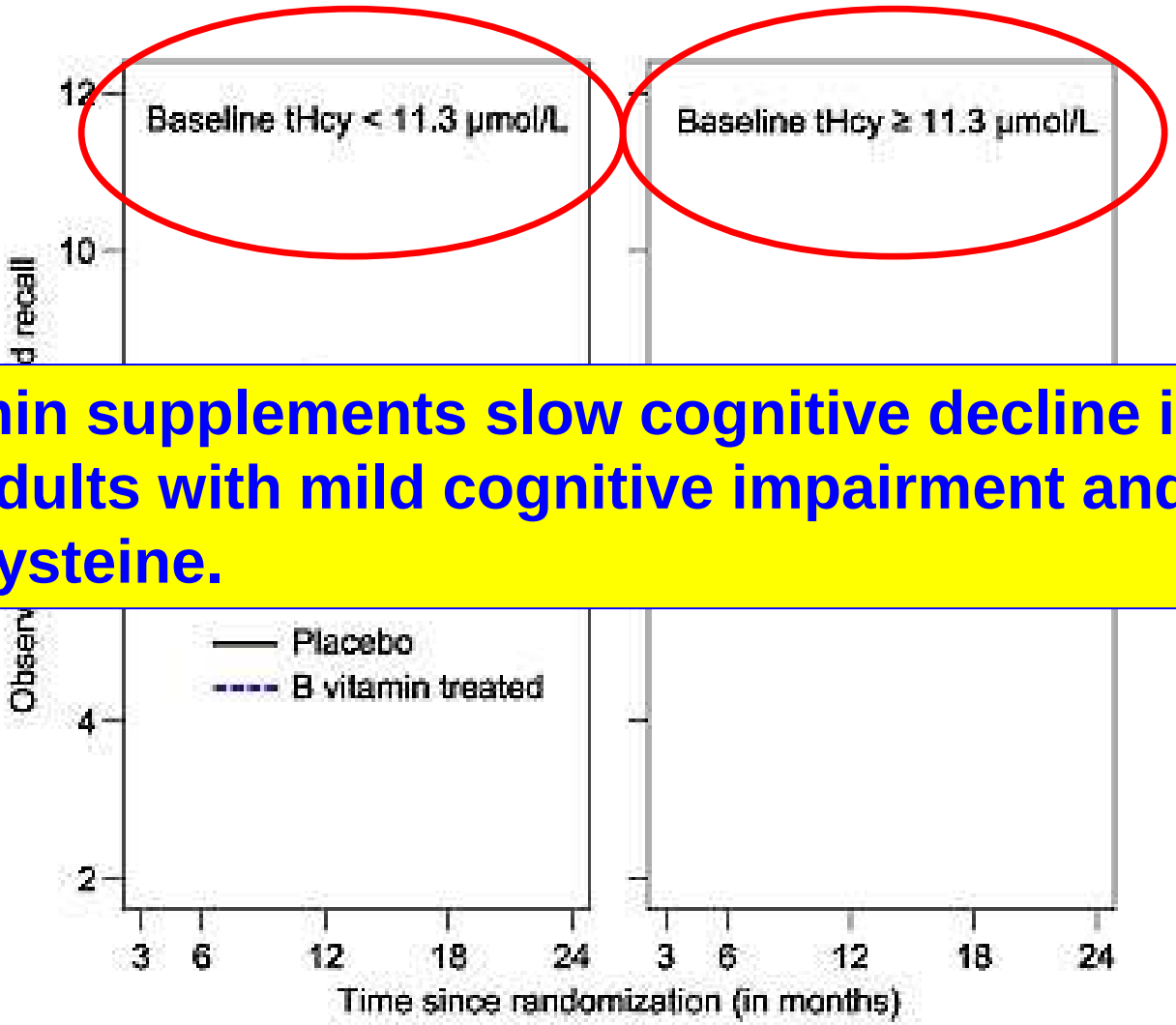
B vitamin supplements slow brain atrophy in older adults with mild cognitive impairment and high homocysteine.

∆Hcy: 22 to 30 µmol/L
Atrophy Rate: 2.5%/yr

∆Hcy: 24 to 12 µmol/L
Atrophy Rate: 0.46%/yr

Smith et al, PLoS One, 2010

Effect of B Vitamin Supplements on Delayed Recall (Short-Term Memory)



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De Jager et al, Int J Geriatr Psychiatry, 2011

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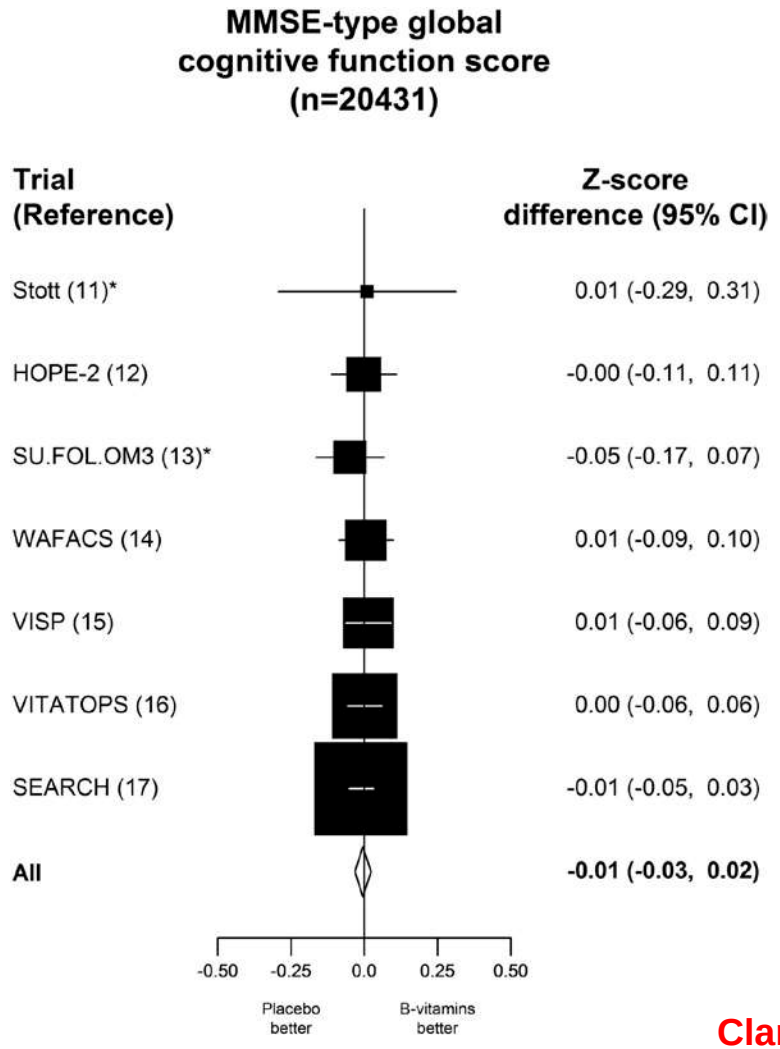
Effects of B Vitamins and Homocysteine Lowering on Global Cognitive Function

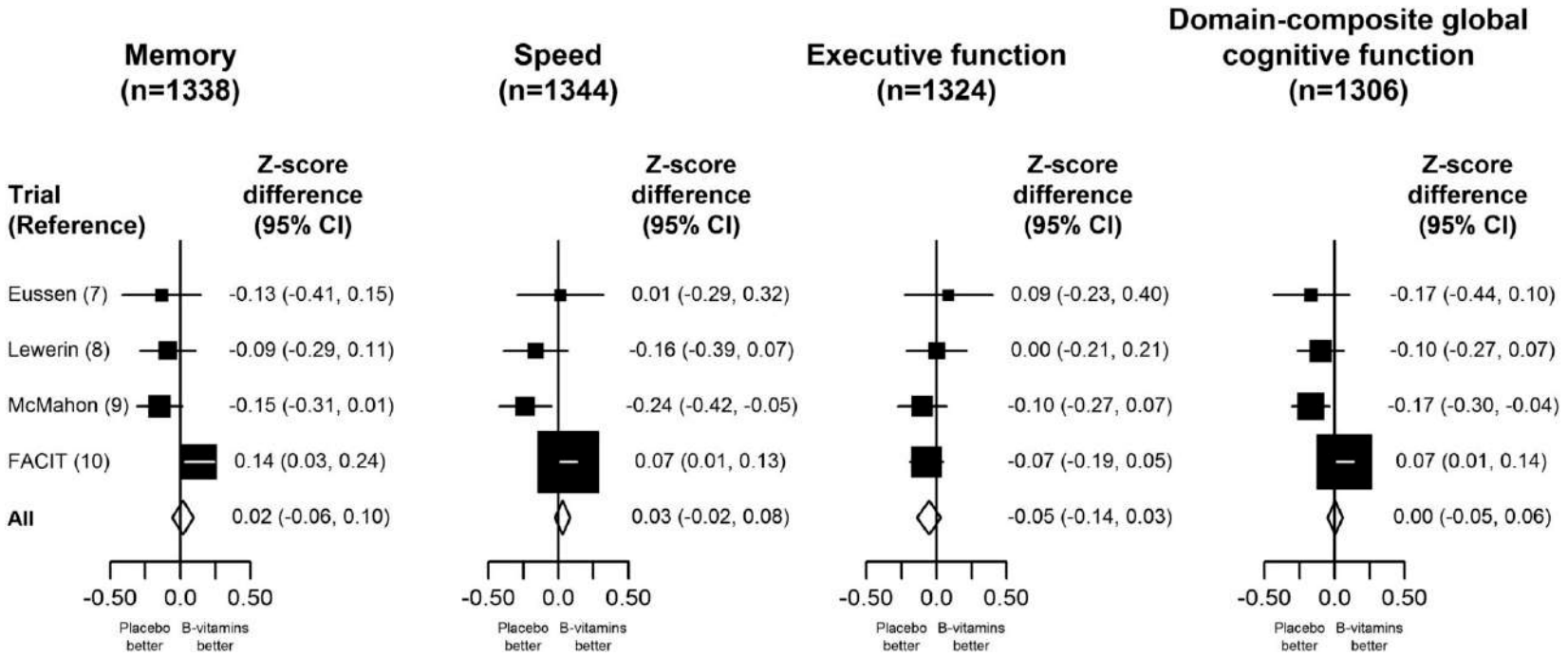
Meta-Analysis of RCTs



Clarke et al, Am J Clin Nutr, 2014

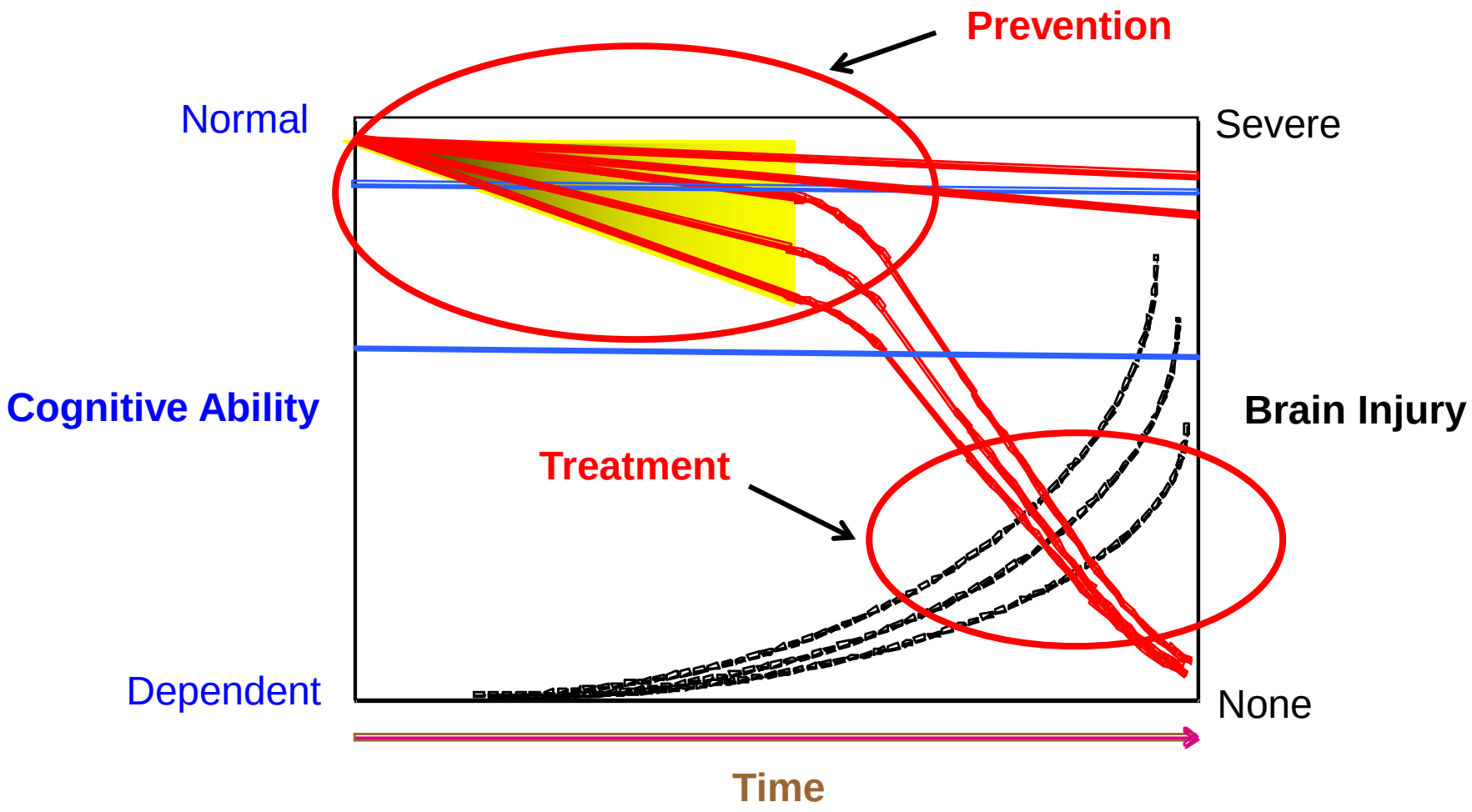
Effects of B Vitamins and Homocysteine Lowering on Domains of Cognitive Function

Meta-Analysis of RCTs



Clarke et al, Am J Clin Nutr, 2014

Trajectories of Cognitive Change



Charles DeCarli (unpublished)

Nutrition Reviews 73:723-35, 2015

Special Article

Assessing the association between homocysteine and cognition: reflections on Bradford Hill, meta-analyses, and causality

Andrew McCaddon and Joshua W. Miller

Hyperhomocysteinemia is a recognized risk factor for cognitive decline and incident dementia in older adults. Two recent reports addressed the cumulative epidemiological evidence for this association but expressed conflicting opinions. Here, the evidence is reviewed in relation to Sir Austin Bradford Hill's criteria for assessing "causality," and the latest meta-analysis of the effects of homocysteine-lowering on cognitive function is critically examined. The meta-analysis included 11 trials, collectively assessing 22 000 individuals, that examined the effects of B vitamin supplements (folic acid, vitamin B_{12}, vitamin B_6) on global or domain-specific cognitive decline. It concluded that homocysteine-lowering with B vitamin supplements has no significant effect on cognitive function. However, careful examination of the trials in the meta-analysis indicates that no conclusion can be made regarding the effects of homocysteine-lowering on cognitive decline, since the trials typically did not include individuals who were experiencing such decline. Further definitive trials in older adults experiencing cognitive decline are still urgently needed.

Change in Cognition in Healthy Older Adults

You can't prevent something that isn't happening...

Table 2 Changes in cognitive domain scores of elderly people (only participants with baseline and 2-year data)

	Unadjusted mean (SD)				
	Baseline	2 y	Change (95% CI)	Model 1, *p* value	Model 2, *p* value
Episodic memory (n = 2,467)[a]					
Placebo	0.04 (0.69)	0.13 (0.75)	0.08 (0.05 to 0.12)	0.27	0.42
B vitamins	0.05 (0.69)	0.16 (0.75)	0.11 (0.07 to 0.14)		
Attention and working memory (n = 759)					
Placebo	0.02 (0.86)	−0.04 (0.88)	−0.06 (−0.12 to 0.01)	0.38	0.37
B vitamins	−0.01 (0.84)	−0.10 (0.82)	−0.09 (−0.16 to −0.02)		
Information processing speed (n = 731)					
Placebo	0.08 (0.75)	0.06 (0.79)	−0.02 (−0.06 to 0.01)	0.65	0.51
B vitamins	0.04 (0.75)	0.01 (0.77)	−0.03 (−0.07 to 0.00)		
Executive functioning (n = 720)					
Placebo	0.04 (0.54)	0.10 (0.68)	0.06 (−0.00 to 0.12)	0.20	0.26
B vitamins	−0.01 (0.52)	0.13 (0.66)	0.13 (0.07 to 0.19)		

Abbreviation: CI = confidence interval.
Differences between the 2 groups over time were measured using analyses of covariance. Model 1: adjusted for baseline domain scores. Model 2: adjusted for baseline domain scores, age, sex.
[a] Model 2 additionally adjusted for study center.

Van der Zwaluw et al, Neurology, 2014

Key Considerations

- **What is the cognitive status of the subjects?**
  - Cognitively normal?
  - Mild cognitive impairment?
  - Dementia?
- **What are the cognitive outcomes?**
  - Improve cognitive function?
  - Slow or prevent cognitive decline?
- **What cognitive function tests are used?**
  - MMSE (global)?
  - Subdomains?
- **What is the B vitamin/homocysteine status of the subjects?**
  - Is homocysteine elevated?
- **How long is the intervention?**
  - Months?
  - Years?

Challenge and Opportunity

Challenge

- **Applying what we've learned from population-based studies to inform personalized medicine and personalized nutrition.**

Opportunity

- **To design and implement smarter intervention trials with nutritional supplements to determine if age-related cognitive decline can be slowed or prevented.**

Molecular Pathogenesis of Parkinson's Disease and Therapeutic Strategies

M. Maral Mouradian, M.D.

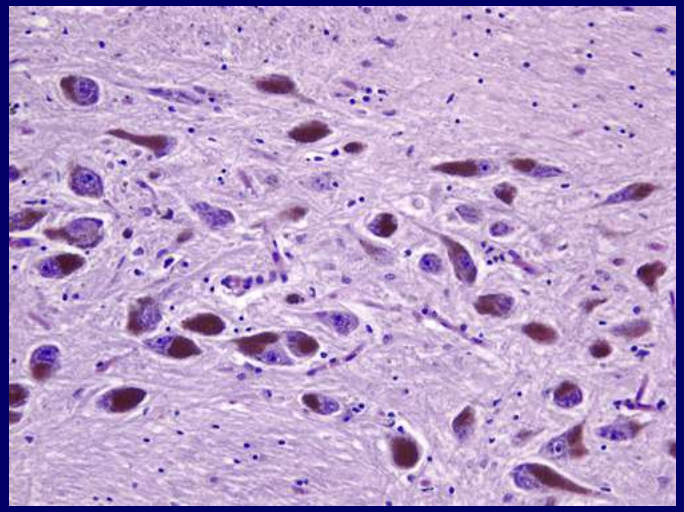
William Dow Lovett Professor of Neurology
Vice Chancellor for Faculty Development
Director, RWJMS Institute for Neurological Therapeutics
Chief, Division of Translational Neuroscience
Robert Wood Johnson Medical School
Rutgers Biomedical and Health Sciences

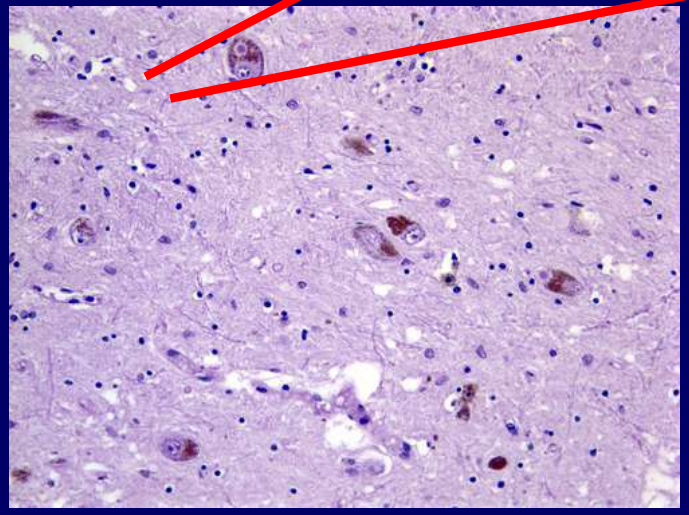
Institute for Health, Health Care Policy and Aging Research, RBHS
October 18, 2018

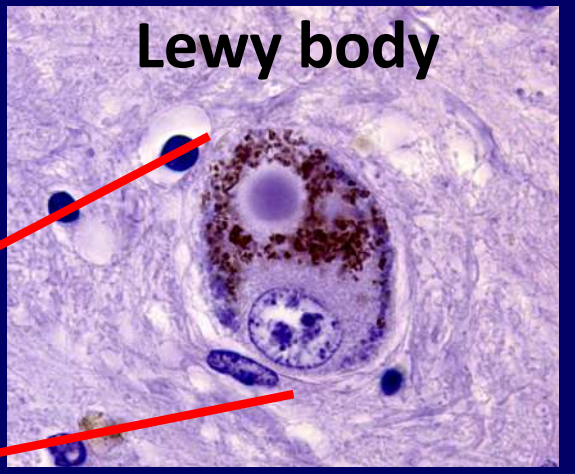
Pathology of Parkinson's Disease

Control

Parkinson





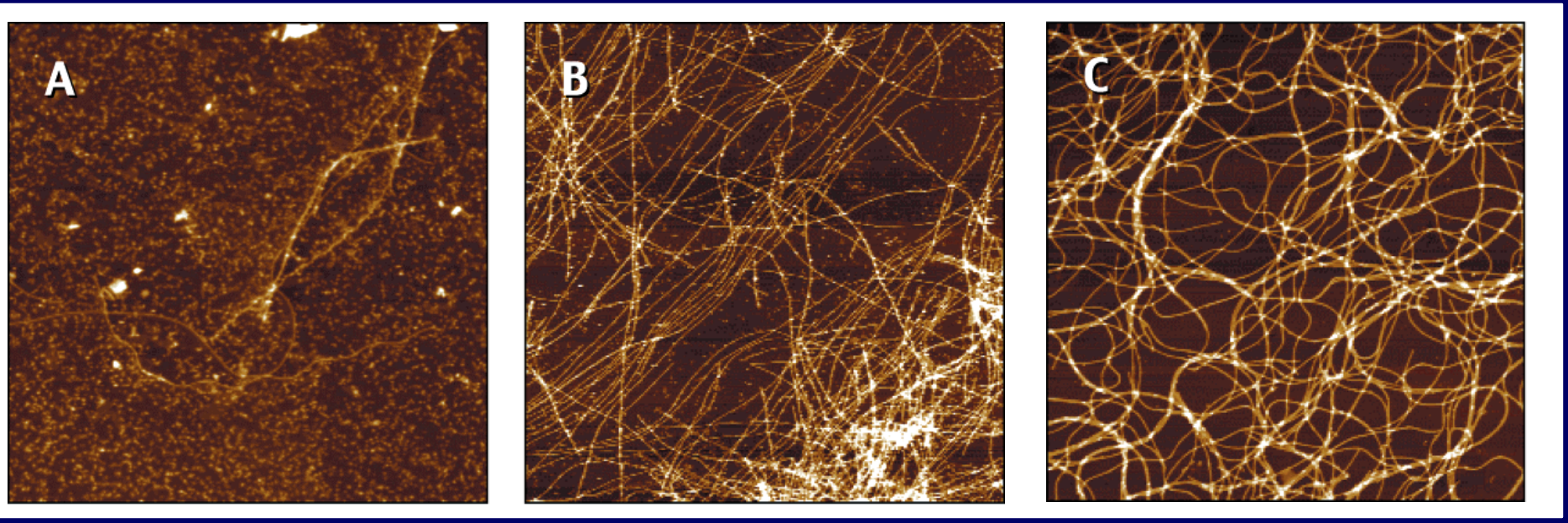


In Vitro Fibrillization of α-Synuclein

WT 300 μM
4 months

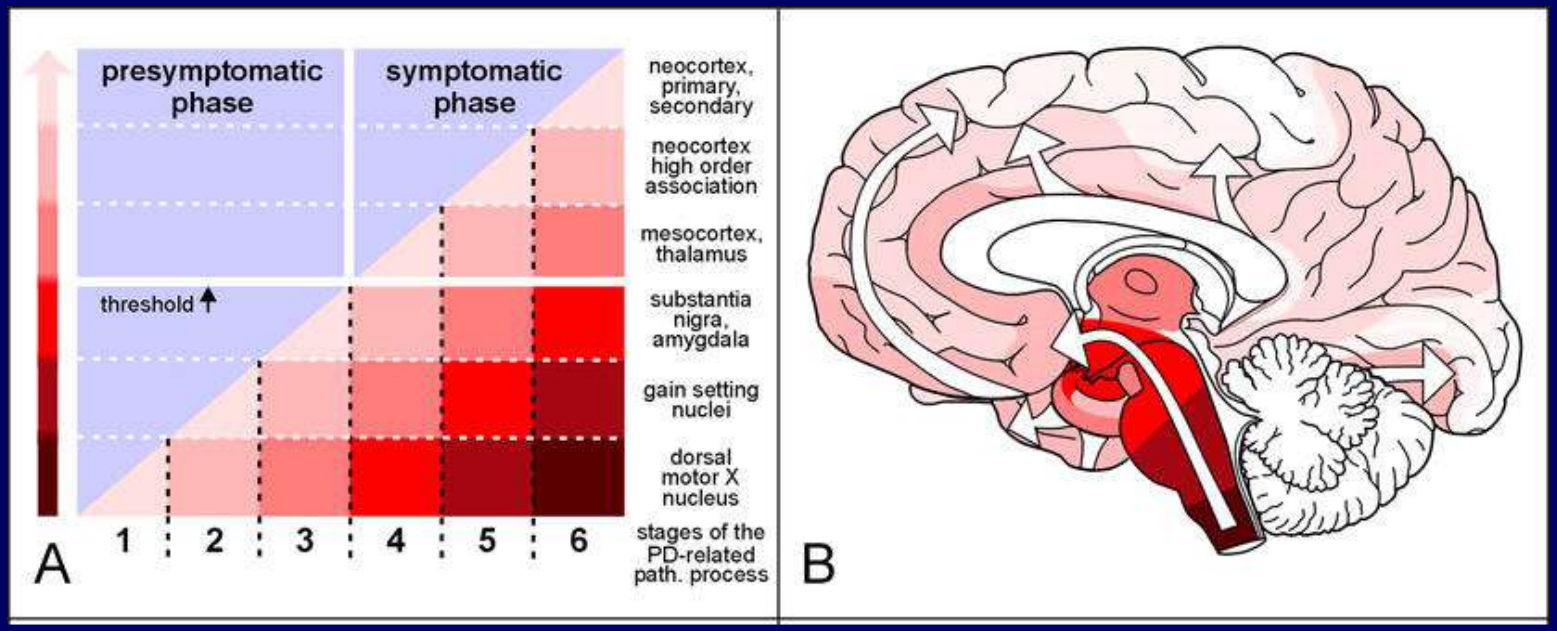
A53T 100 μM
1 month

A30P 300 μM
4 months



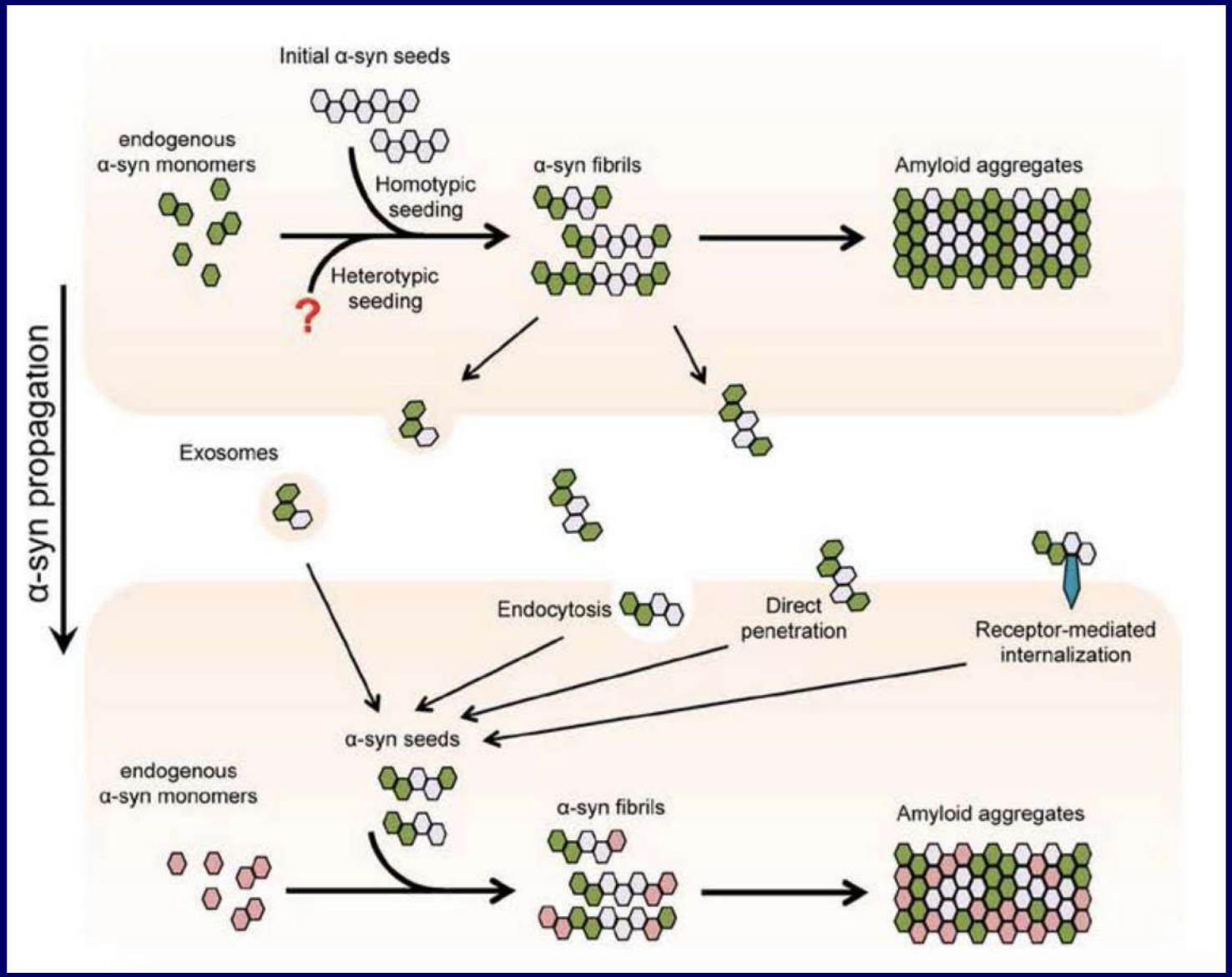
Conway, Biochemistry 39:2552, 2000

Staging PD: Pre-Symptomatic and Symptomatic Phases



Braak et al, Cell Tissue Res. 318:121, 2004

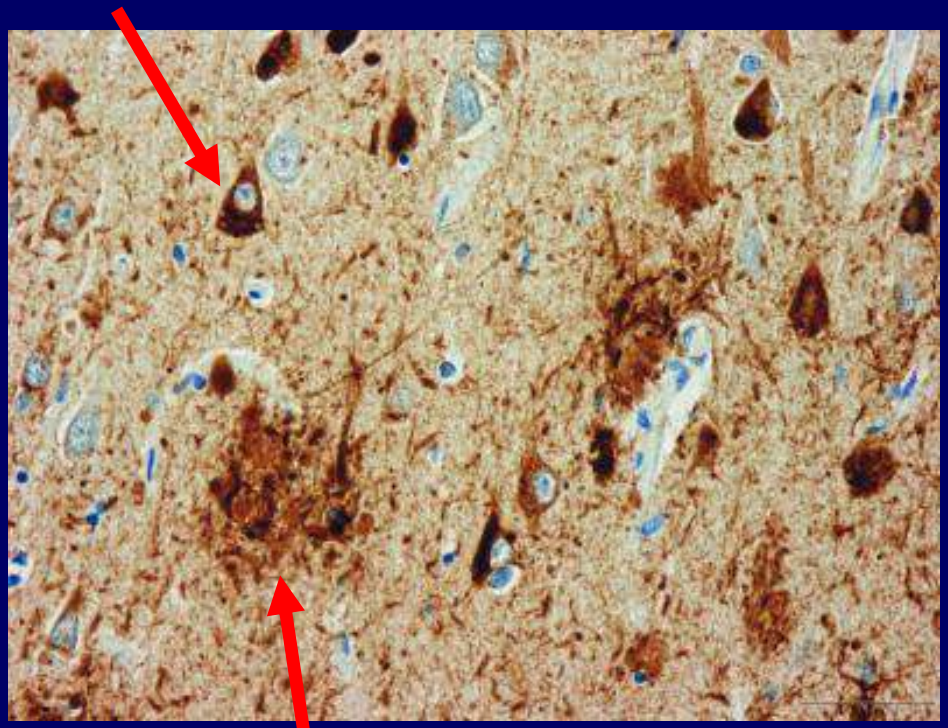
α-Synuclein Seeding and Propagation



Oueslati et al, Exp. Neurobiol. 2014

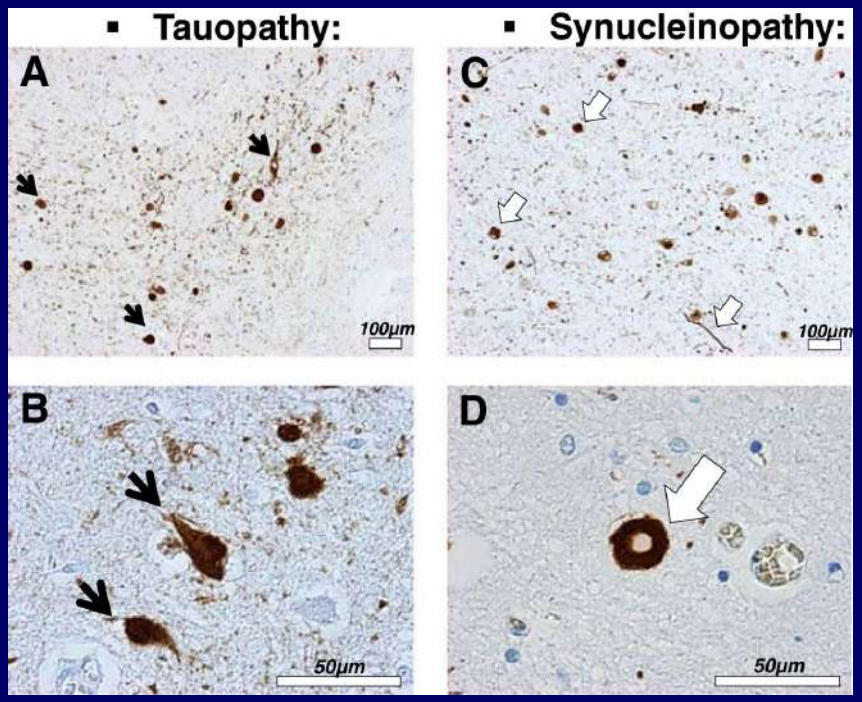
Commonalities of Misfolded Proteins and Hyper-phosphorylated Aggregates in Synucleinopathies and Taupathies

Tau
Neurofibrillary tangles



Amyloid
plaque

p-tau p-α-synuclein



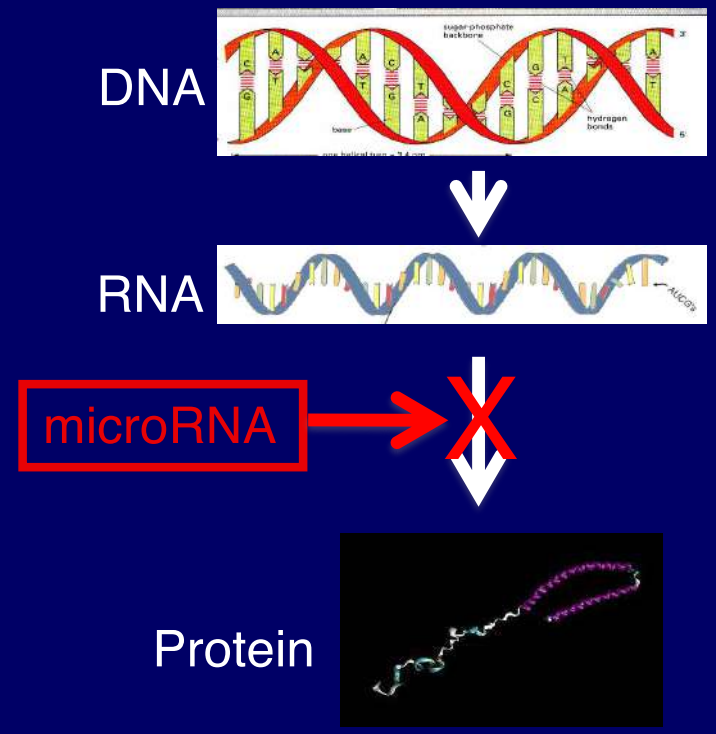
Consequences of Increased α-Synuclein Levels in Neurons

- Misfolding and aggregation
- Permeabilization of synaptic vesicles leading to dopamine leakage
- Oxidative stress
- Disruption of vesicular trafficking between the endoplasmic reticulum (ER) and the Golgi, causing ER stress
- Interference with autophagy
- Impaired proteasome function
- Interaction with other proteins

Reducing α-synuclein levels can be beneficial

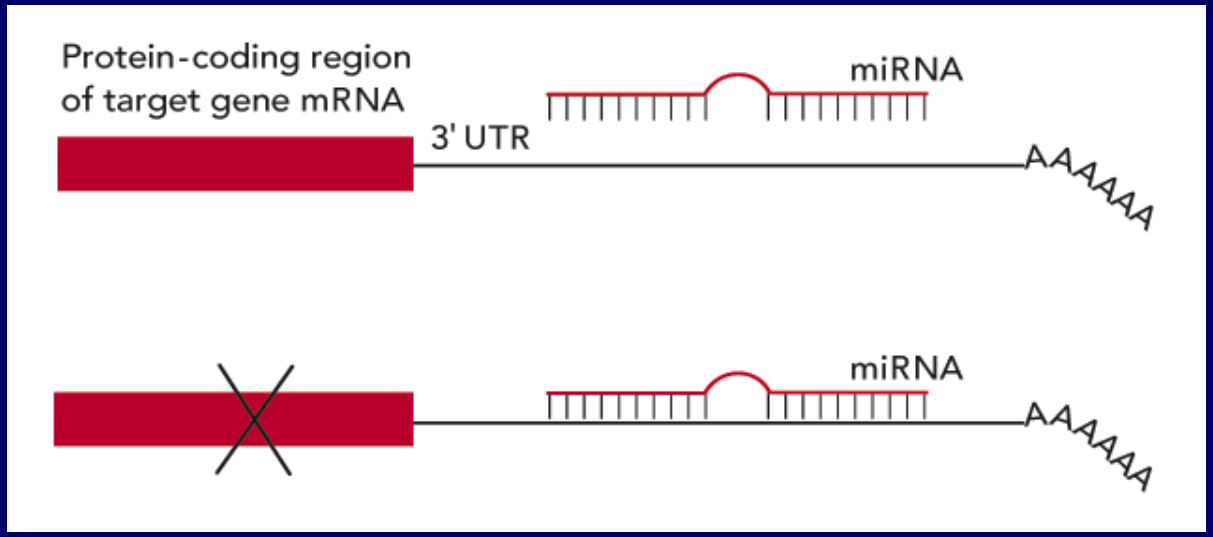
Reducing α-Synuclein Levels as a Therapeutic Strategy

- **Reduce production**
  - Inhibit transcription
  - Inhibit translation
- **Enhance clearance**
  - Autophagy
  - Proteasome

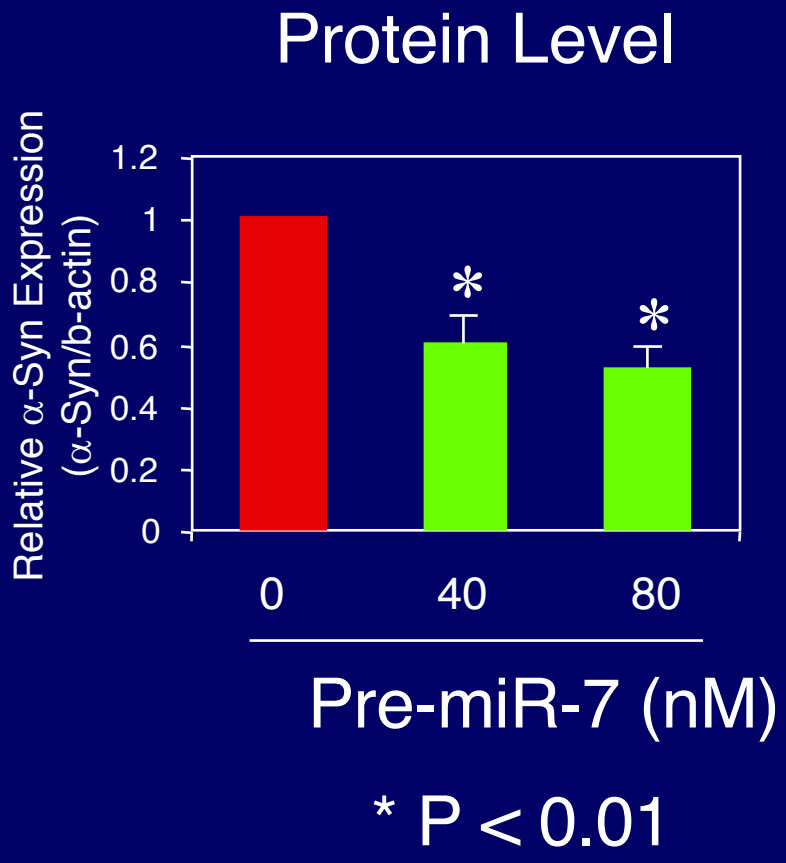


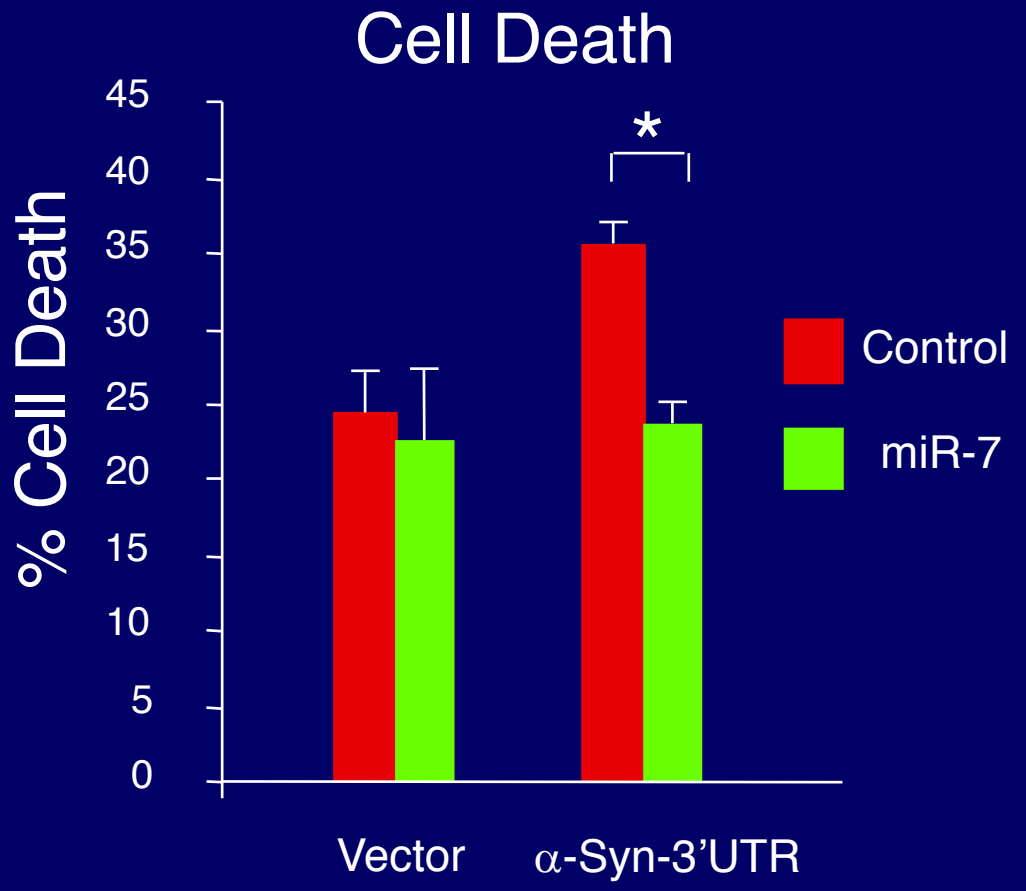
MicroRNA

- Small noncoding RNA molecules
- Regulate gene expression post-transcriptionally



MicroRNA-7 Reduces α-Synuclein Protein Levels and Protects against its Toxicity



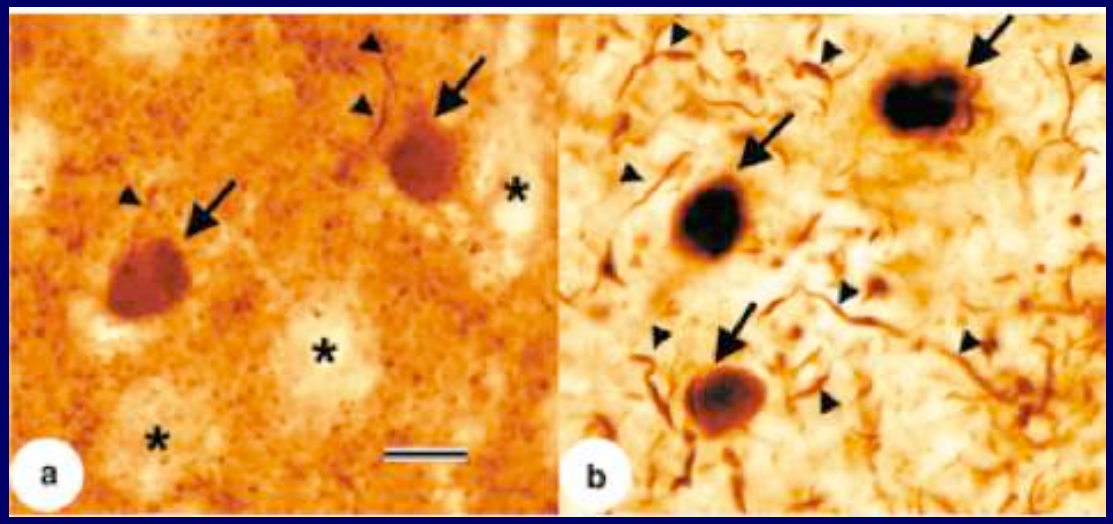


Junn et al, PNAS,106(31): 13052, 2009

α-Synuclein Phosphorylation as a Therapeutic Target in PD and DLB

Misfolded α-Synuclein is Phosphorylated in α-Synucleinopathies

Human DLB

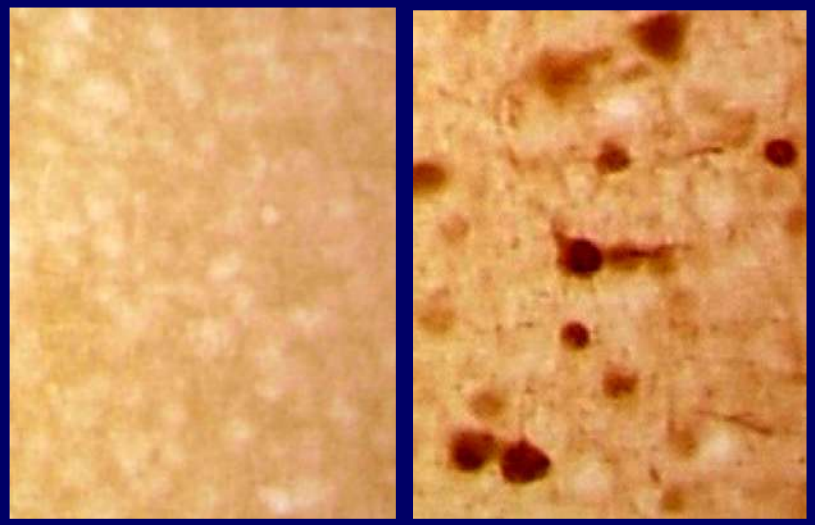


LB509 Anti-p-Ser129

Fujiwara et al NCB 4:160, 2002

Mice

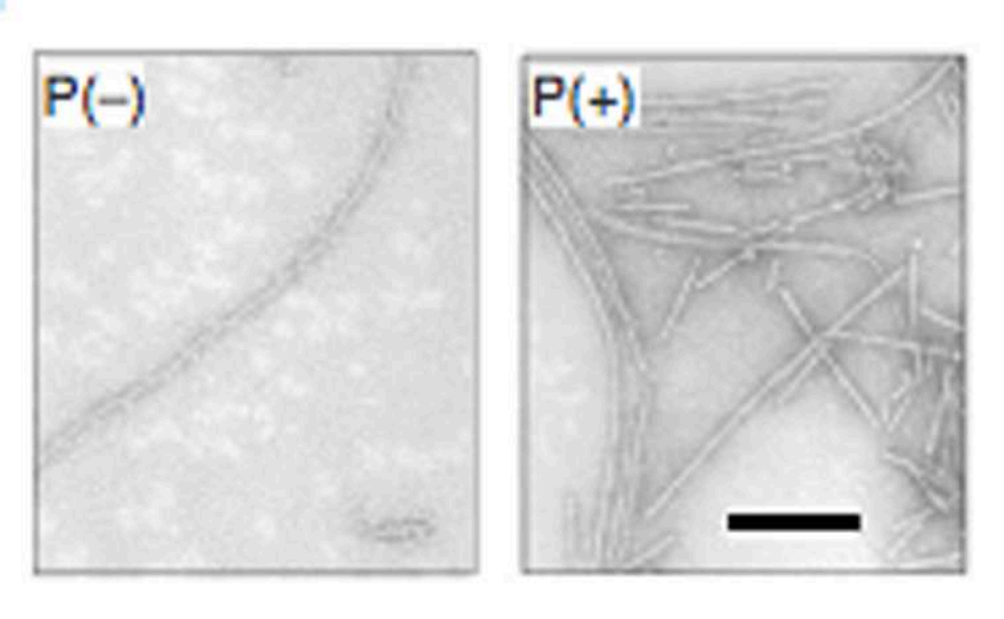
WT α-Synuclein^{Tg}



Anti-p-Ser129

Lee…Mouradian, J. Neurosci. 31: 6963, 2011

α-Synuclein Phosphorylation Promotes its Fibrillization in vitro



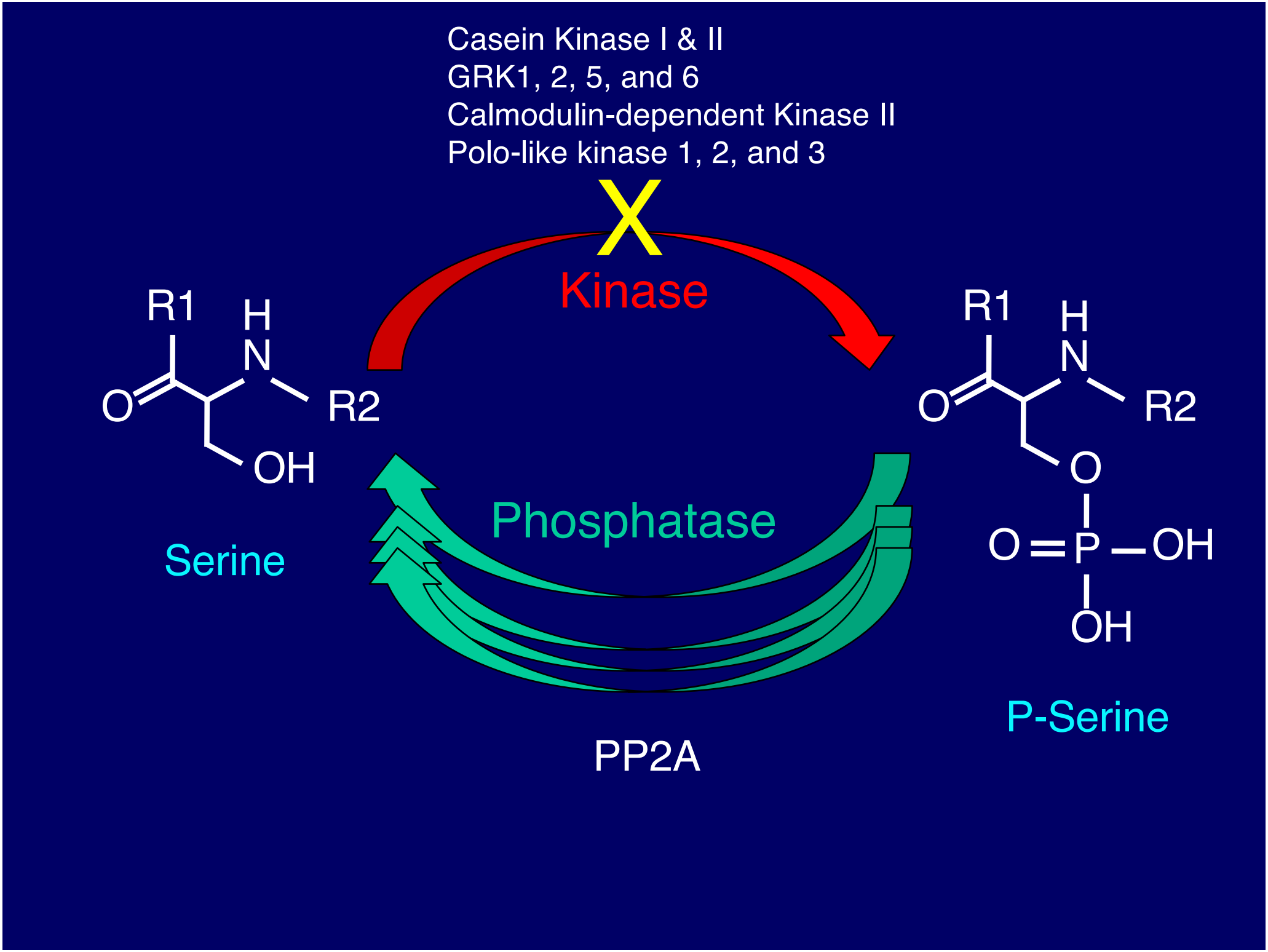
Fujiwara et al NCB 4:160, 2002

Therefore,

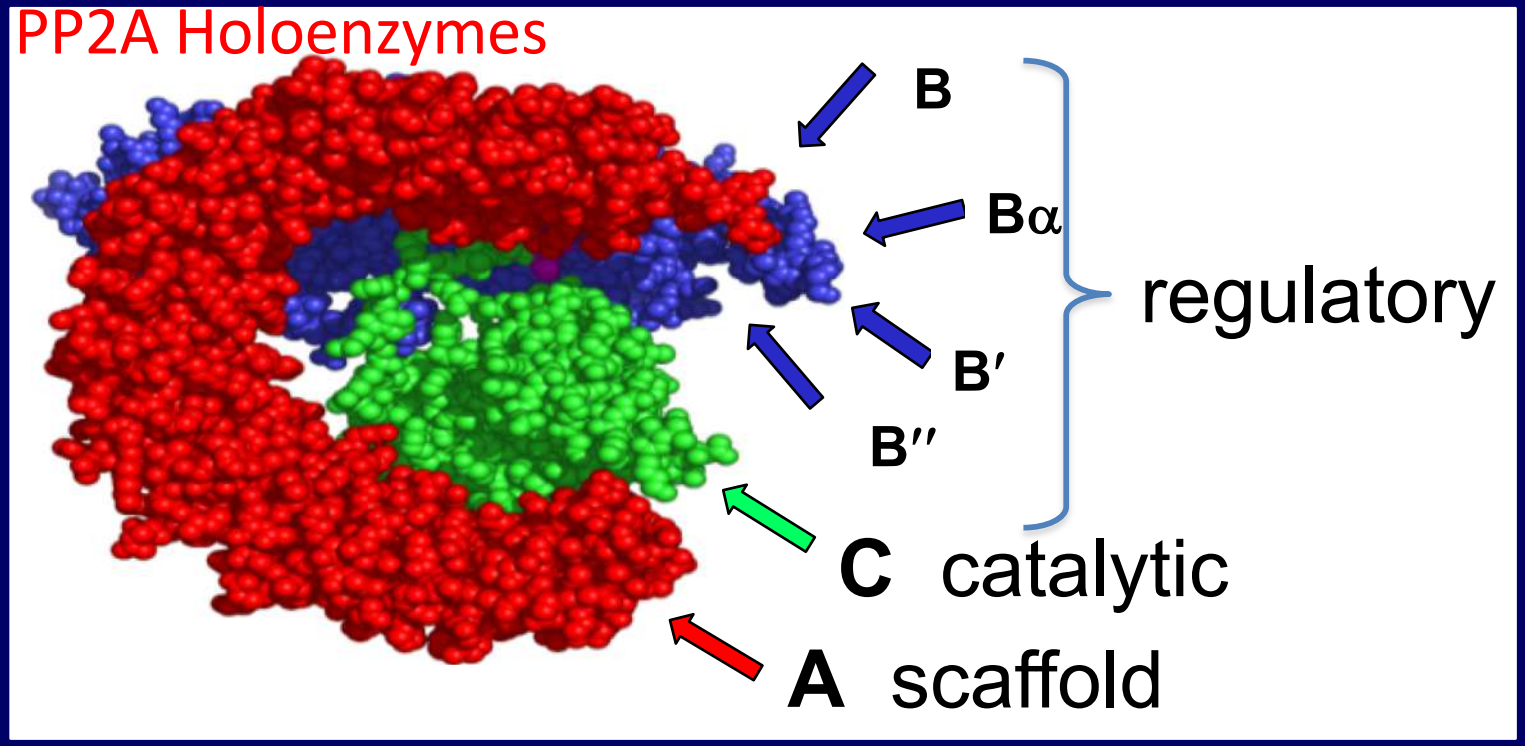
Decreasing the Phosphorylation State of

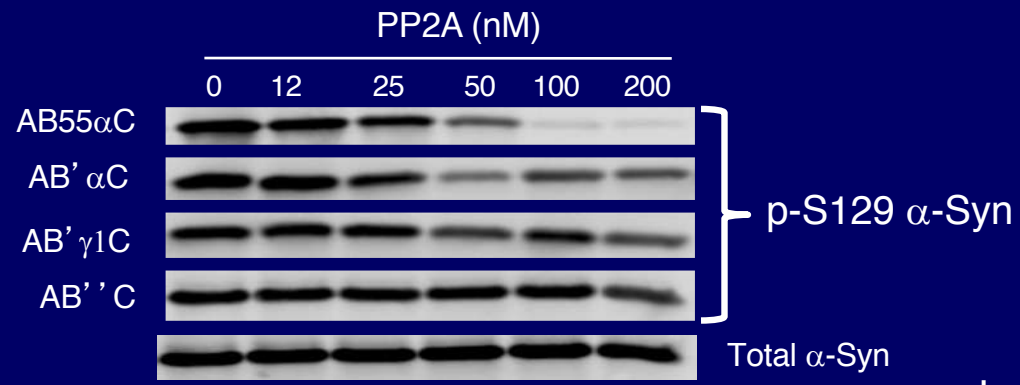
α-Synuclein is a Plausible

Therapeutic Strategy


Casein Kinase I & II
GRK1, 2, 5, and 6
Calmodulin-dependent Kinase II
Polo-like kinase 1, 2, and 3
X
Kinase
R1
H
N
O
R2
OH
Serine
Phosphatase
R1
H
N
O
R2
O
O
P
OH
OH
P-Serine
PP2A

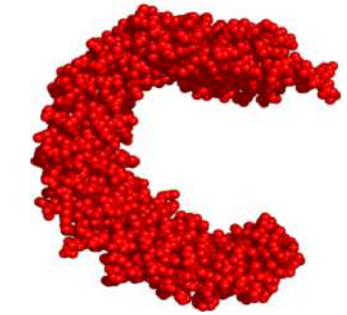
PP2A B55α is the Major Ser/Thr Phosphatase for α-Synuclein



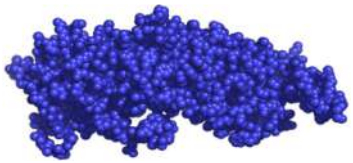


Lee et al, J. Neurosci. 31(19): 6963, 2011

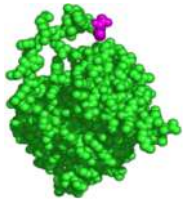
Methylation Affects PP2A-B55α Holoenzyme Assembly



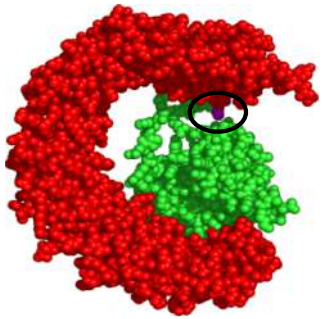
scaffold (A) subunit



regulatory (B) subunit

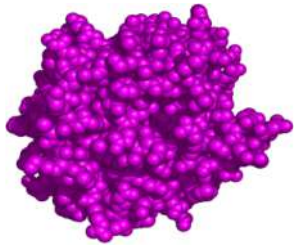


Catalytic (C) subunit



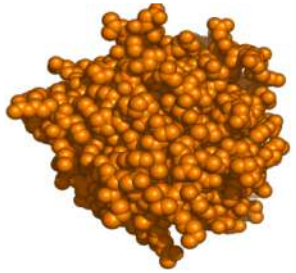
AC core dimer

LCMT-1

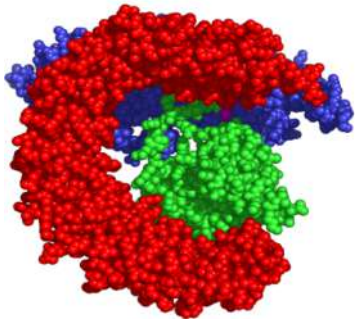


(+) CH_3

(–) CH_3



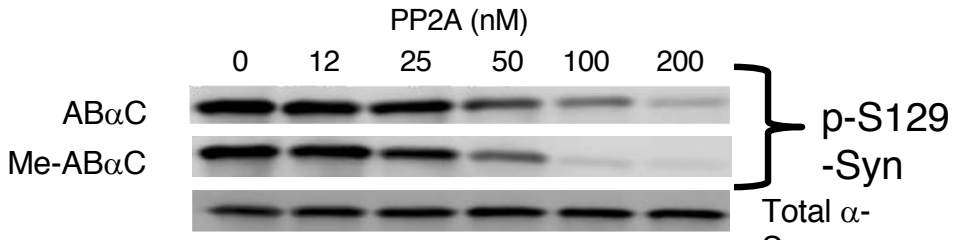
PME-1



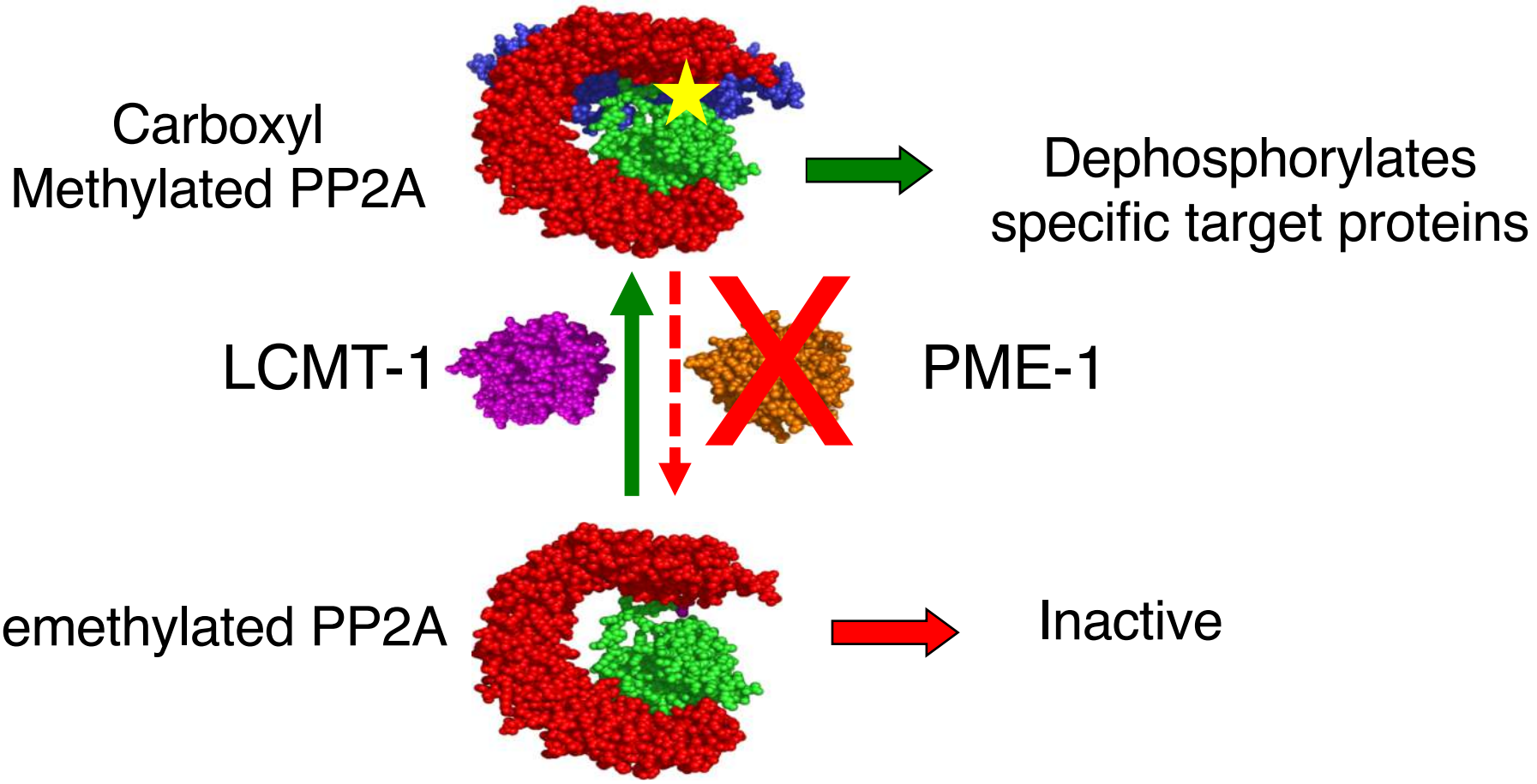
PP2A holoenzyme

Dephosphorylate specific Phospho-proteins

Methylated PP2A is more effective in de-phosphorylating α-Synuclein

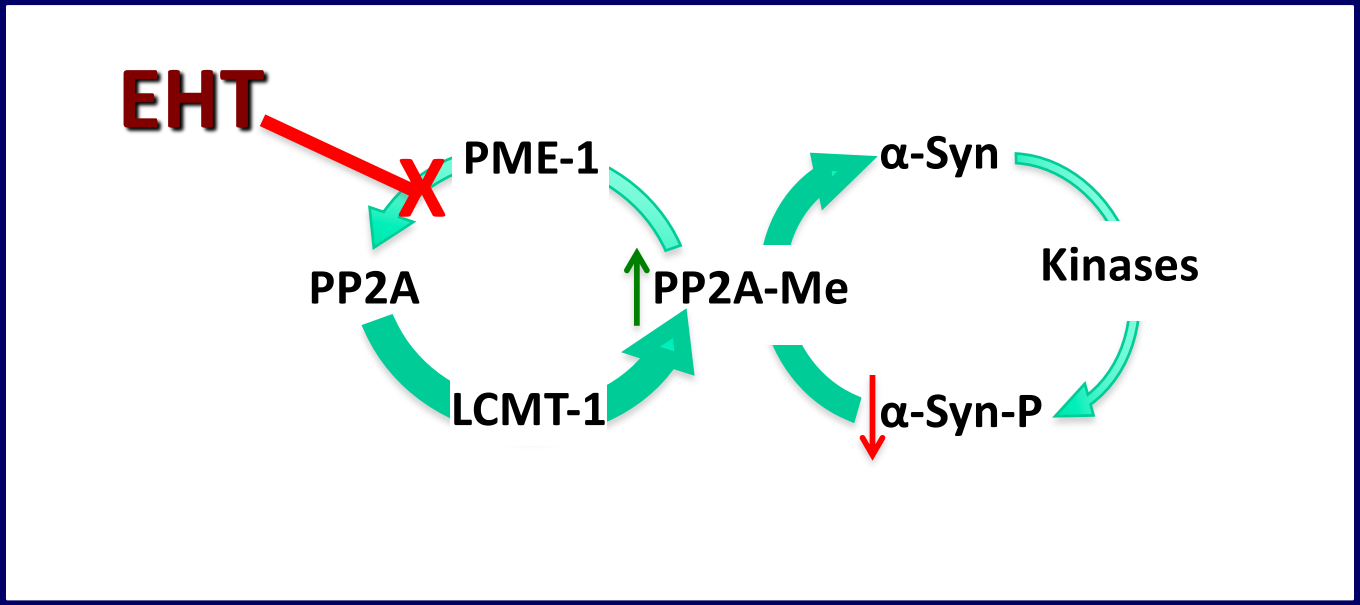


An Approach to Promote PP2A Activity



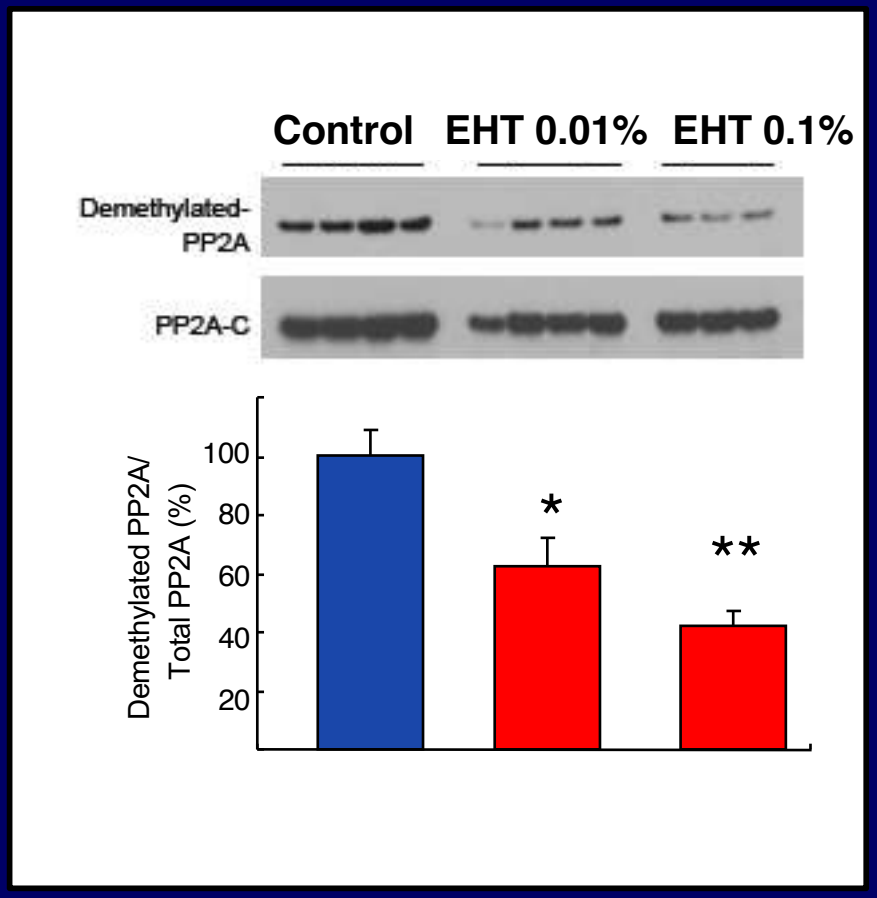
EHT Keeps PP2A Methylated leading to De-Phosphorylation of α-Synuclein

PP2A Demethylation Inhibitor

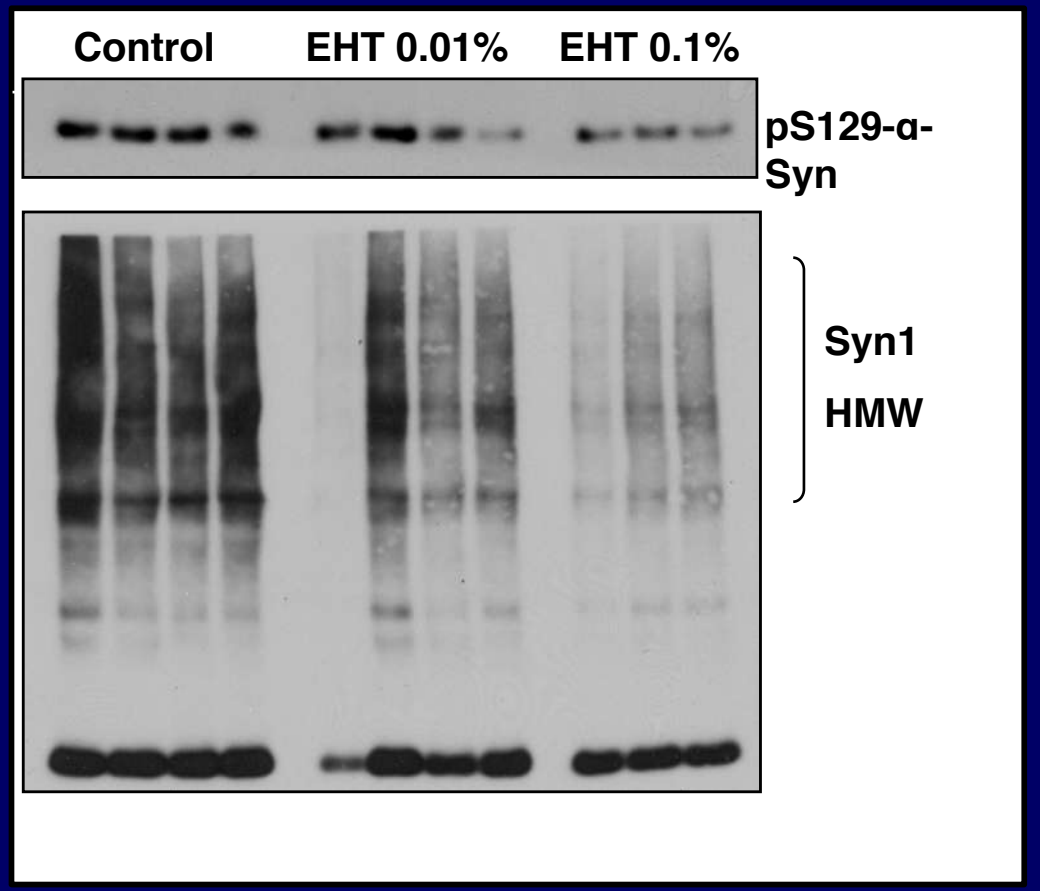


EHT Modulates PP2A Methylation and Reduces α-Synuclein Aggregation in α-Syn Transgenic Mice

- Inhibits PP2A demethylation

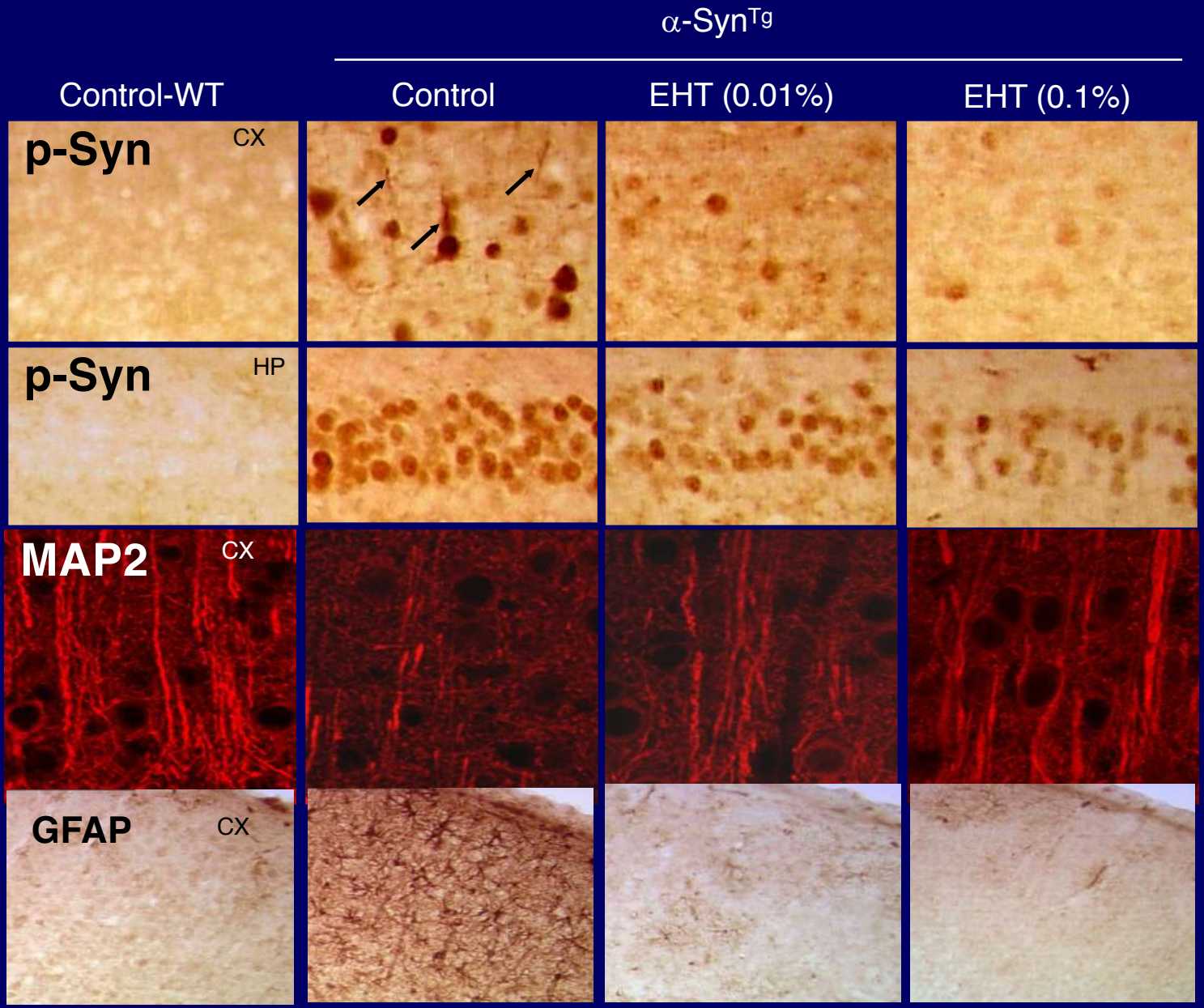


- Reduces α-synuclein S129 phosphorylation
- Reduces α-synuclein oligomers



Lee et al, J. Neurosci. 31(19): 6963, 2011

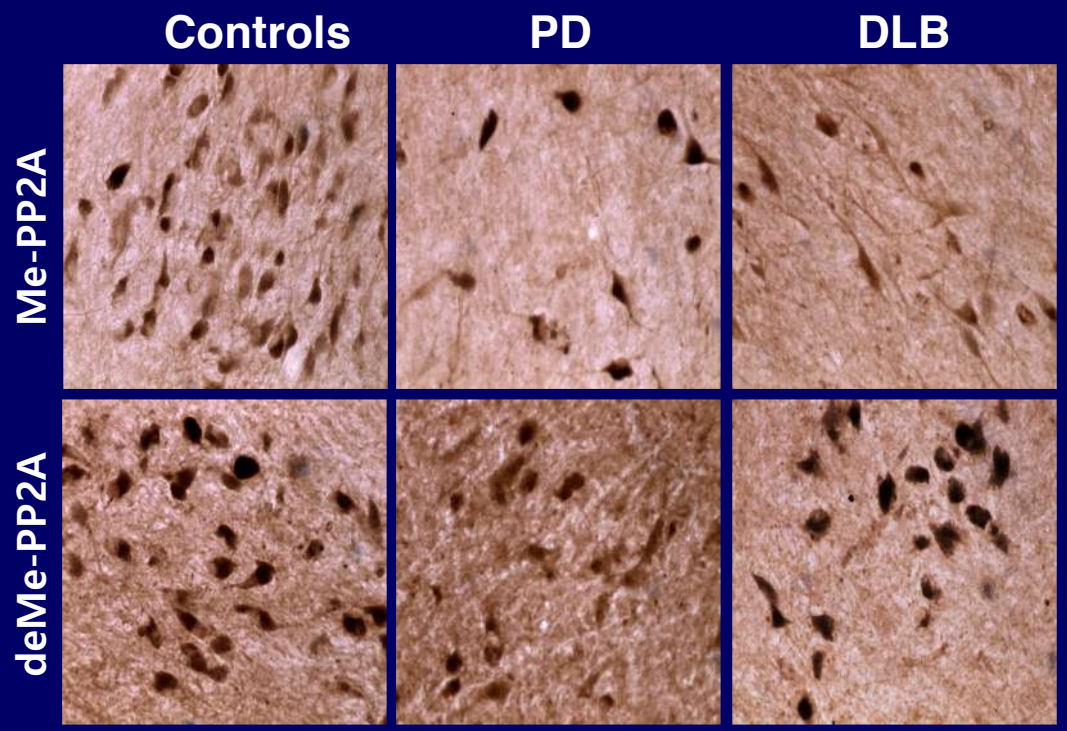
EHT Treatment Improves the Neuropathology of α-Synuclein Transgenic Mice

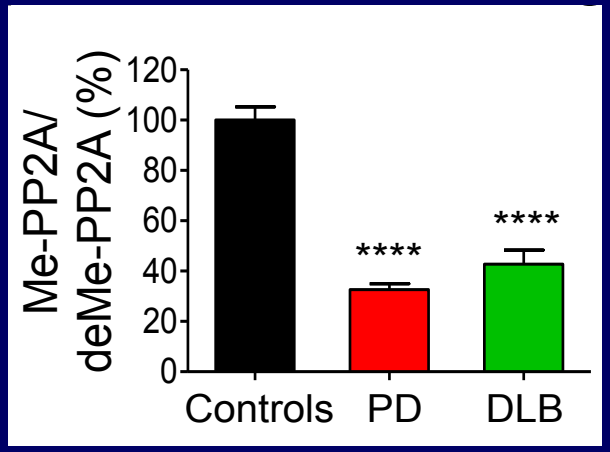


Lee et al, J. Neurosci. 31(19): 6963, 2011

What drives hyper-phosphorylation of pathogenic proteins in α-synucleinopathies and tauopathies?

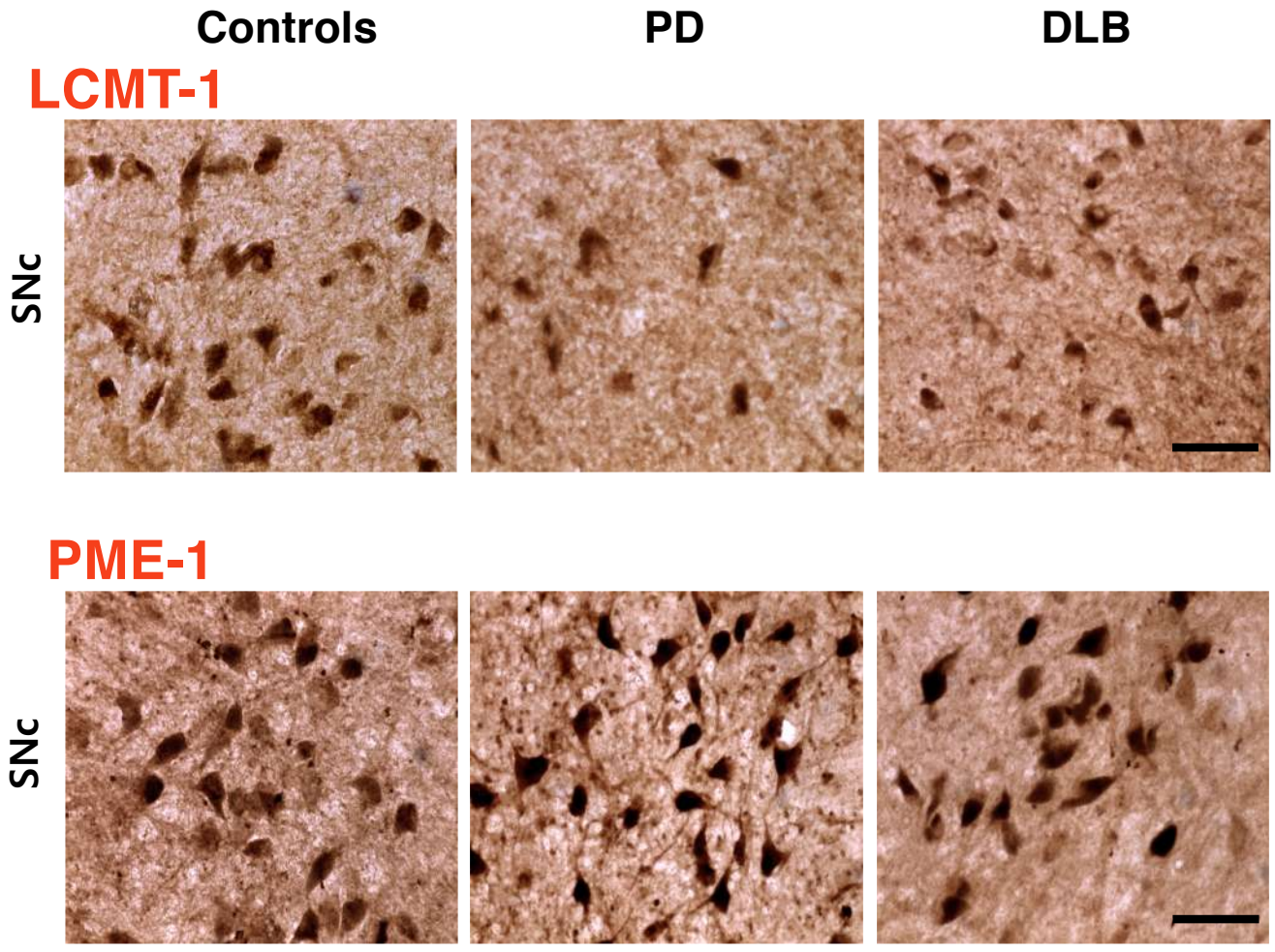
PP2A is De-Methylated in α-Synucleinopathies

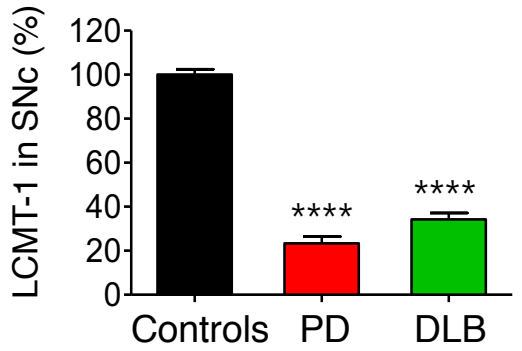


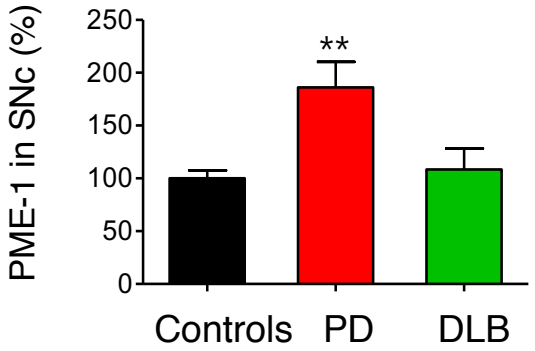


Park H.-J. et al, Ann. Clin. Transl. Neurol., 3(10):769, 2016

Dysregulation of PP2A Methylating Enzymes in α-Synucleinopathies

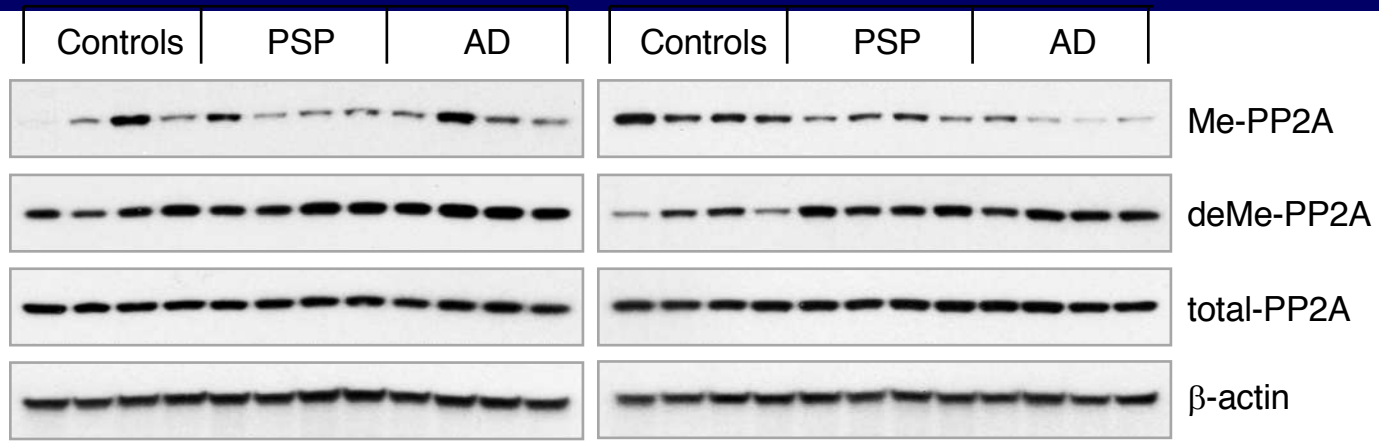


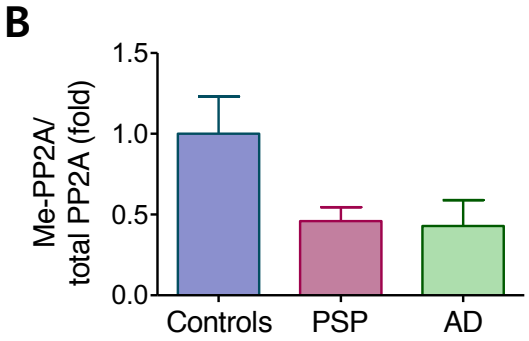


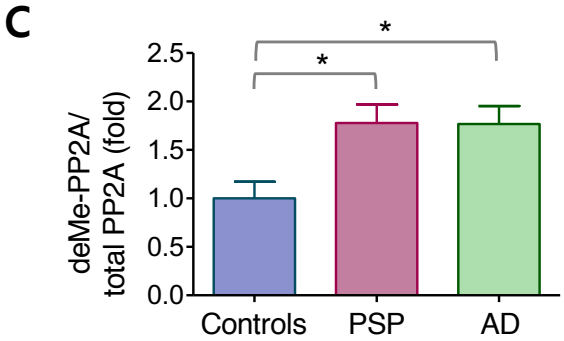


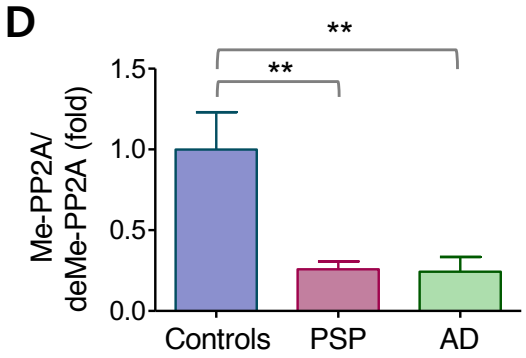
Park H.-J. et al, Ann. Clin. Transl. Neurol., 3(10):769, 2016

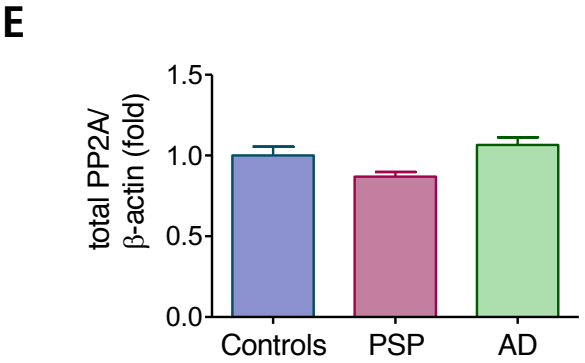
PP2A is DeMethylated in Tauopathies





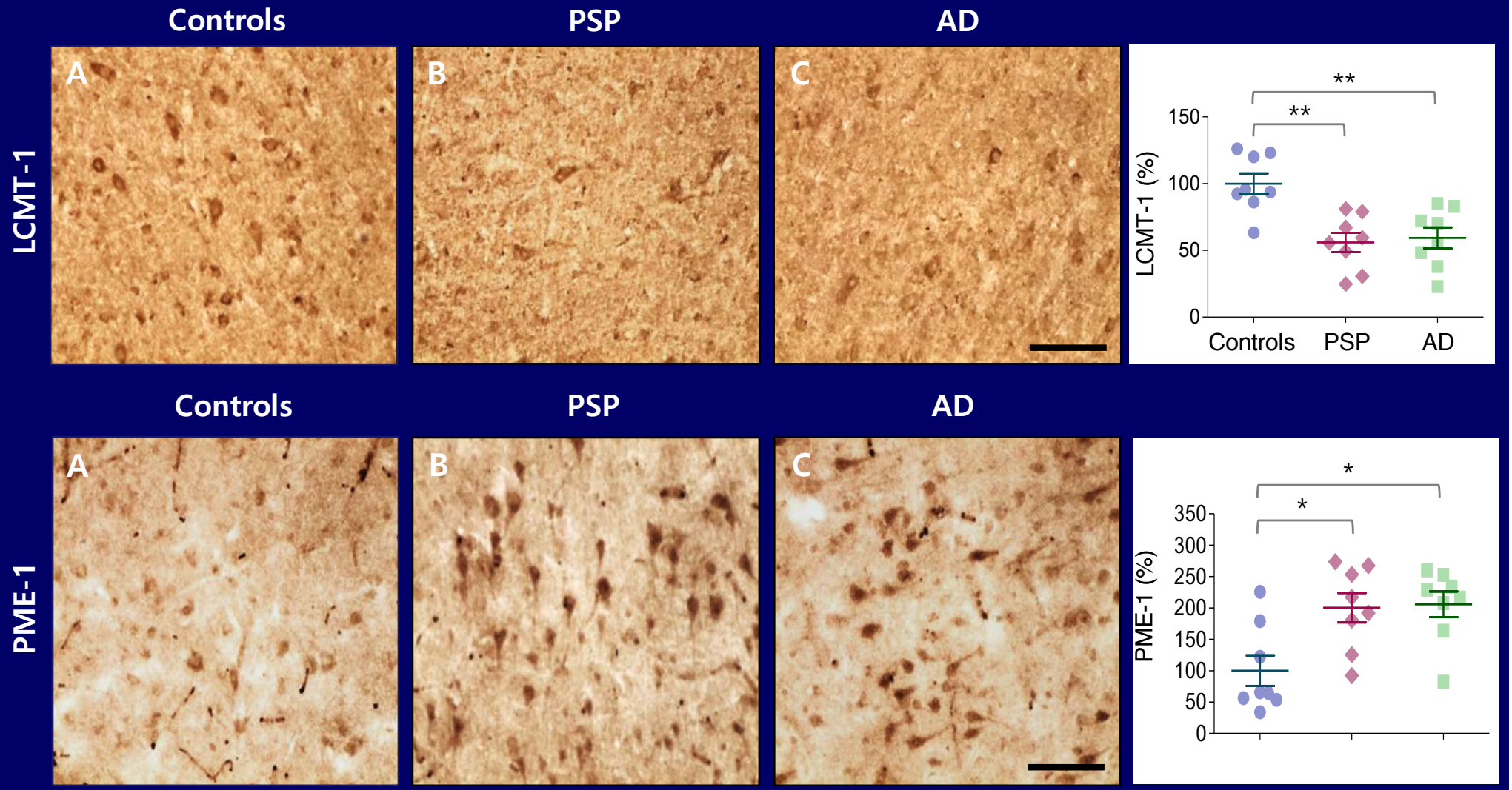






Park H.-J. et al, J. Neuropathol. Exp. Neurol, 77(2):139, 2018

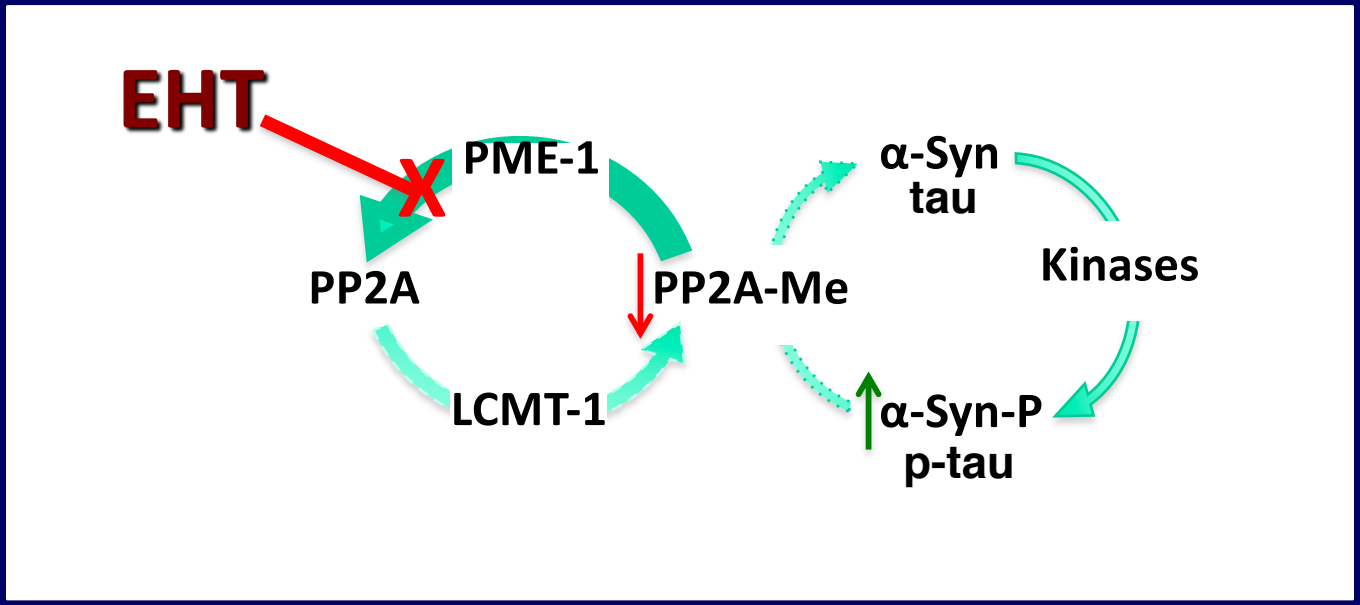
PP2A Methylating Enzymes are Dysregulated in Alzheimer and PSP



Park H.-J. et al, J. Neuropathol. Exp. Neurol, 77(2):139, 2018

Dysregulation of PP2A Methylation Leads to Hyper-Phosphorylation of α-Synuclein & tau

α-Synucleinopathy / Tauopathy



Summary

- Considerable molecular similarities exist among neurodegenerative diseases of aging
- Protein misfolding and fibrillization are considered pathogenic
- Increased levels of these proteins and their hyper-phosphorylation accelerate their misfolding
- Both these factors are tractable therapeutic targets for disease prevention and disease modification

Emotion Regulation and Cognitive Function

Mauricio R. Delgado

Department of Psychology

Rutgers University – Newark

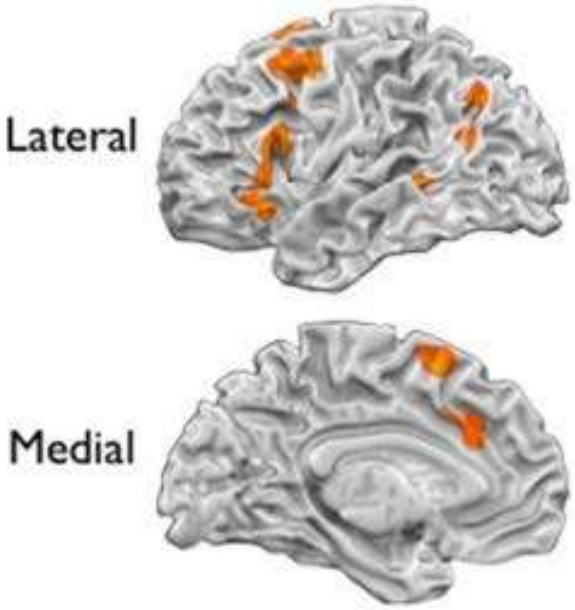
Regulation of negative emotions

- **Emotion Regulation** – Process by which we influence which emotions we have, and when and how we experience them (Gross, 1998).

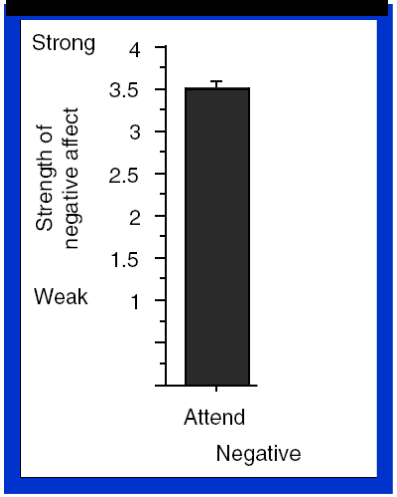
Regulation of negative emotions

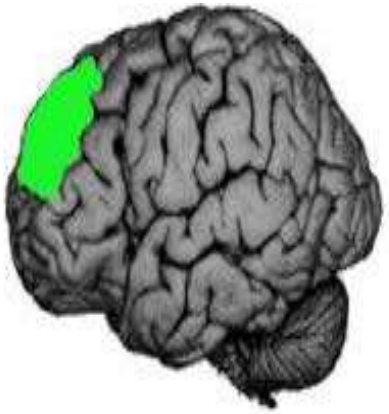
- **Reappraisal**– Reinterpret the meaning of a negative stimulus to change emotional response (Gross, 1998).

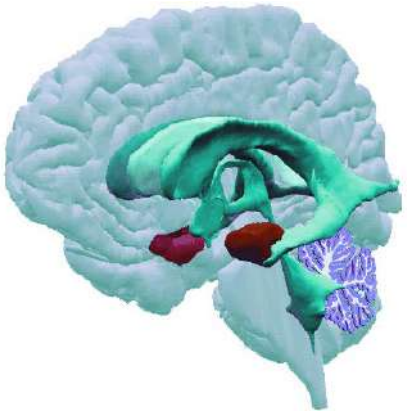
Meta-analysis of cognitive reappraisal



Buhle*, Silvers*, et al., (2014)







Ochsner & Gross, 2005

Regulation of negative emotions

- **Reappraisal**– Reinterpret the meaning of a negative stimulus to change emotional response (Gross, 1998).

e.g., Vrticka et al., 2013

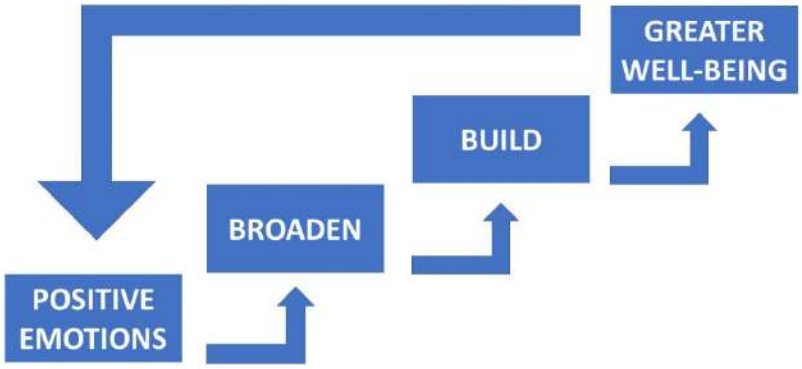
e.g., Delgado et al., 2008

e.g. Holland & Kensinger, 2013

Regulation of negative emotions

- Emotion regulation strategies such as reappraisal:
  - Not effective for everyone or in all contexts (Troy et al., 2013).
  - Recruits more effortful cognitive control processes (Strauss et al., 2016).
  - *Difficult due to age-related declines in cognitive control* (Liang et al., 2017; Shiota & Levenson, 2010)
  - Not as effective under stress (Raio et al, 2013).
  - Can lead to increases in peak cortisol reactivity in response to social or physical stressors (Denson et al., 2014).

- Broaden and build theory of positive emotion (Catalino & Fredrickson, 2011)
  - Broadens one's cognitive perspective
  - Helps build psychological resources for coping



Remember the good times…

- The retrieval of autobiographical memories can bring back emotions tied to the original experience (Westerman et al., 1996; Rubin, 2007).

- Adaptive role of autobiographical memories
  - Bolster a sense of self-identity (Bluck et al., 2005)
  - Shape future/prospective planning (Schacter & Addis, 2007)
  - Influence an individual's well-being (Young et al., 2013).

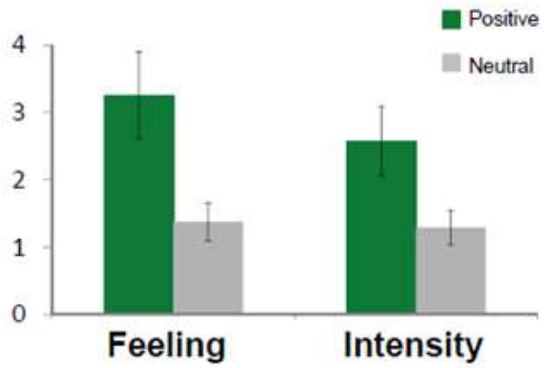
- Can the recall of positive memories recruit neural circuits involved in reward and increase subjective well-being?

Positive memory recall paradigm

First session – Autobiographical Memory Questionnaire (AMQ)

Provide brief description of memory you were personally involved in (cued recall).

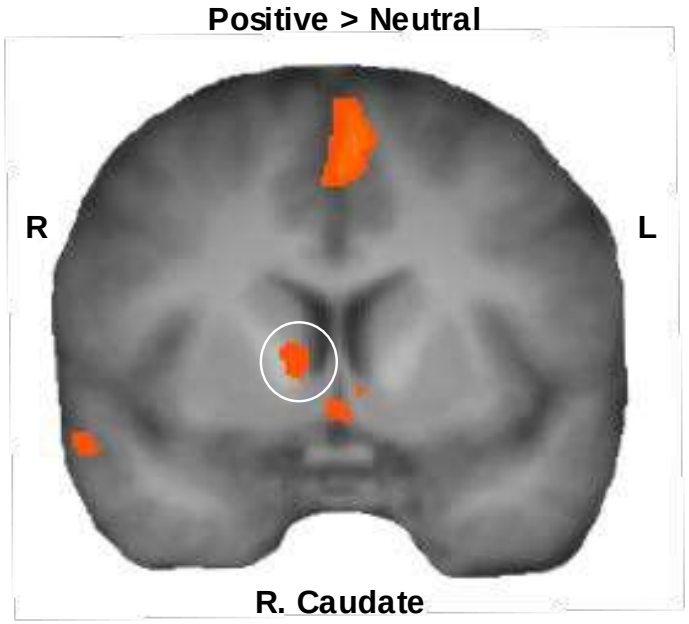
Playing in the snow

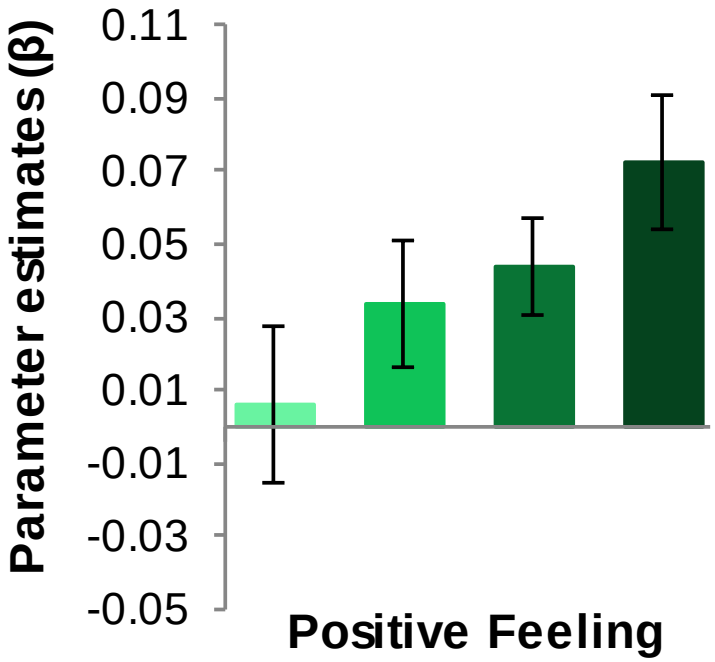


Grocery shopping

Speer, Bhanji & Delgado (2014) - *Neuron*

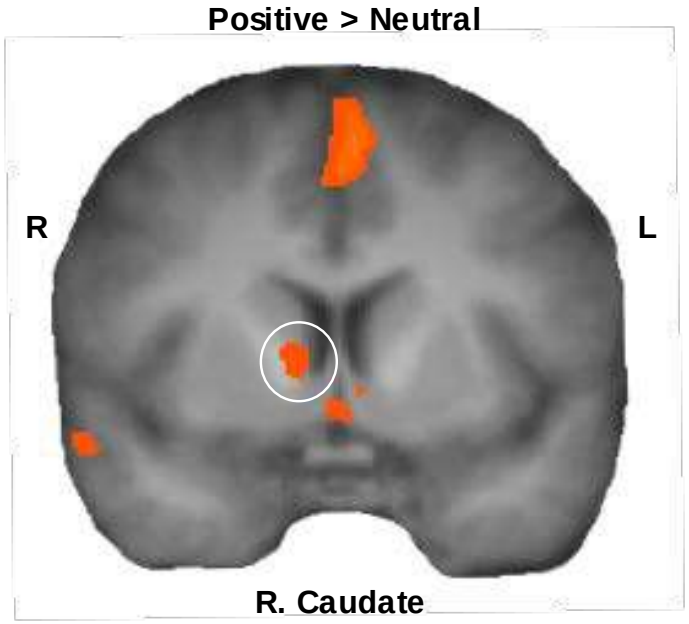
Remembering our positive past recruits reward-related regions as a function of positive feeling

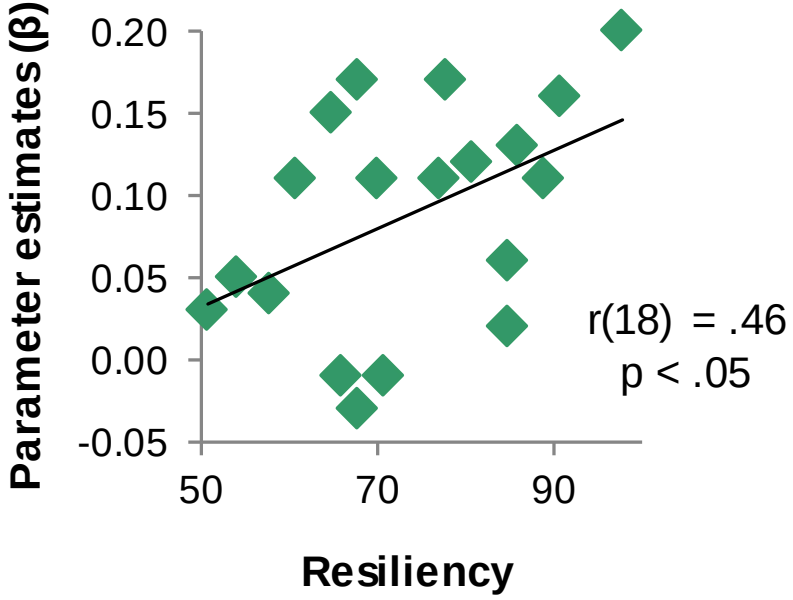




Speer, Bhanji & Delgado (2014) - *Neuron*

Remembering our positive past correlates with individual differences in resiliency

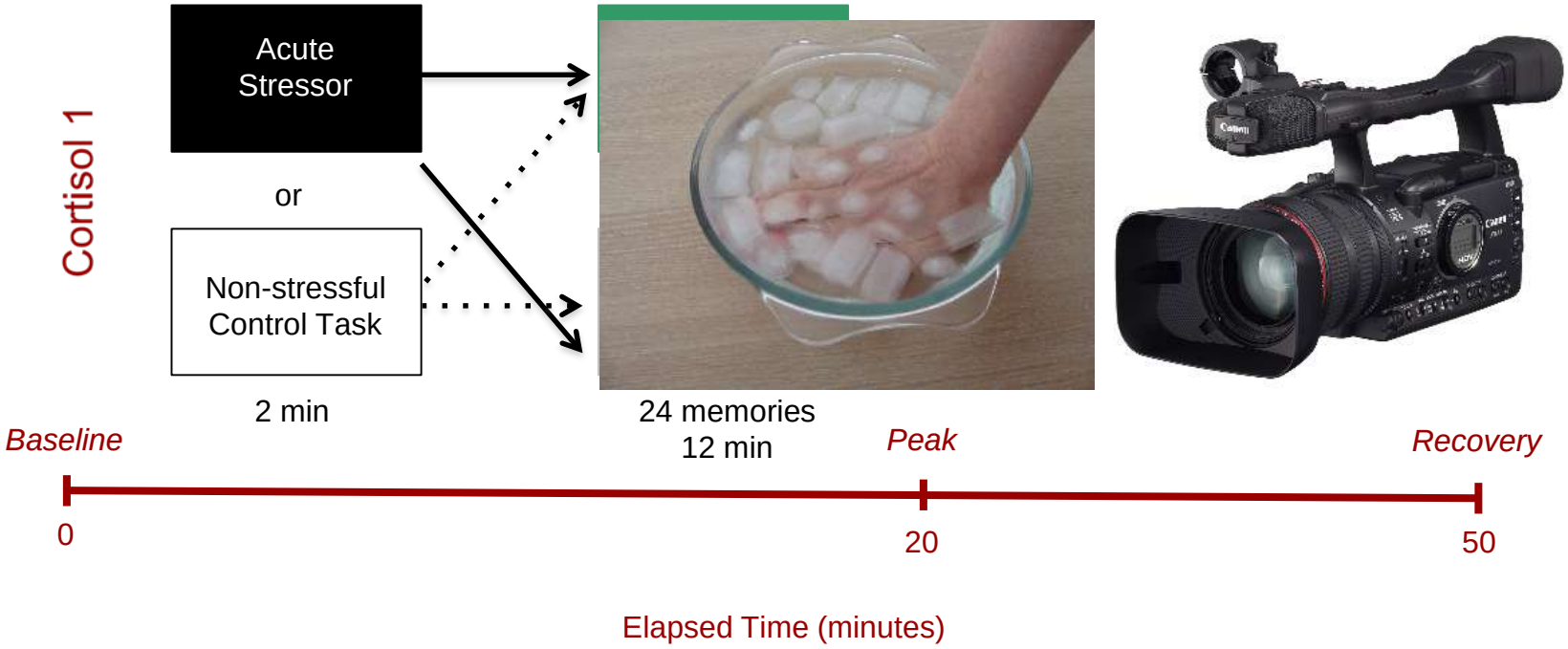




Can positive memory recall serve as an emotion regulation strategy?

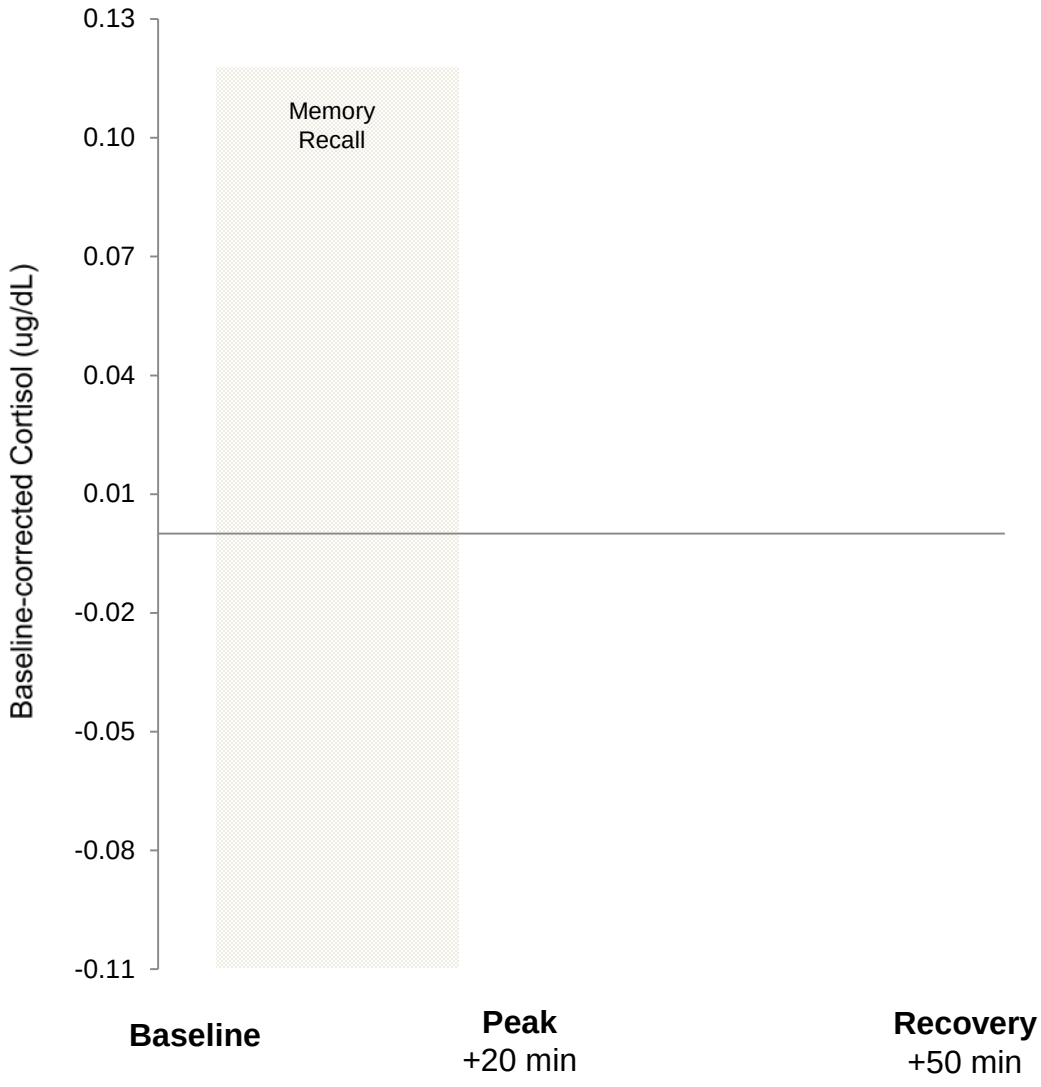
Speer, Bhanji & Delgado (2014) - *Neuron*

Reminiscing about the past while under stress



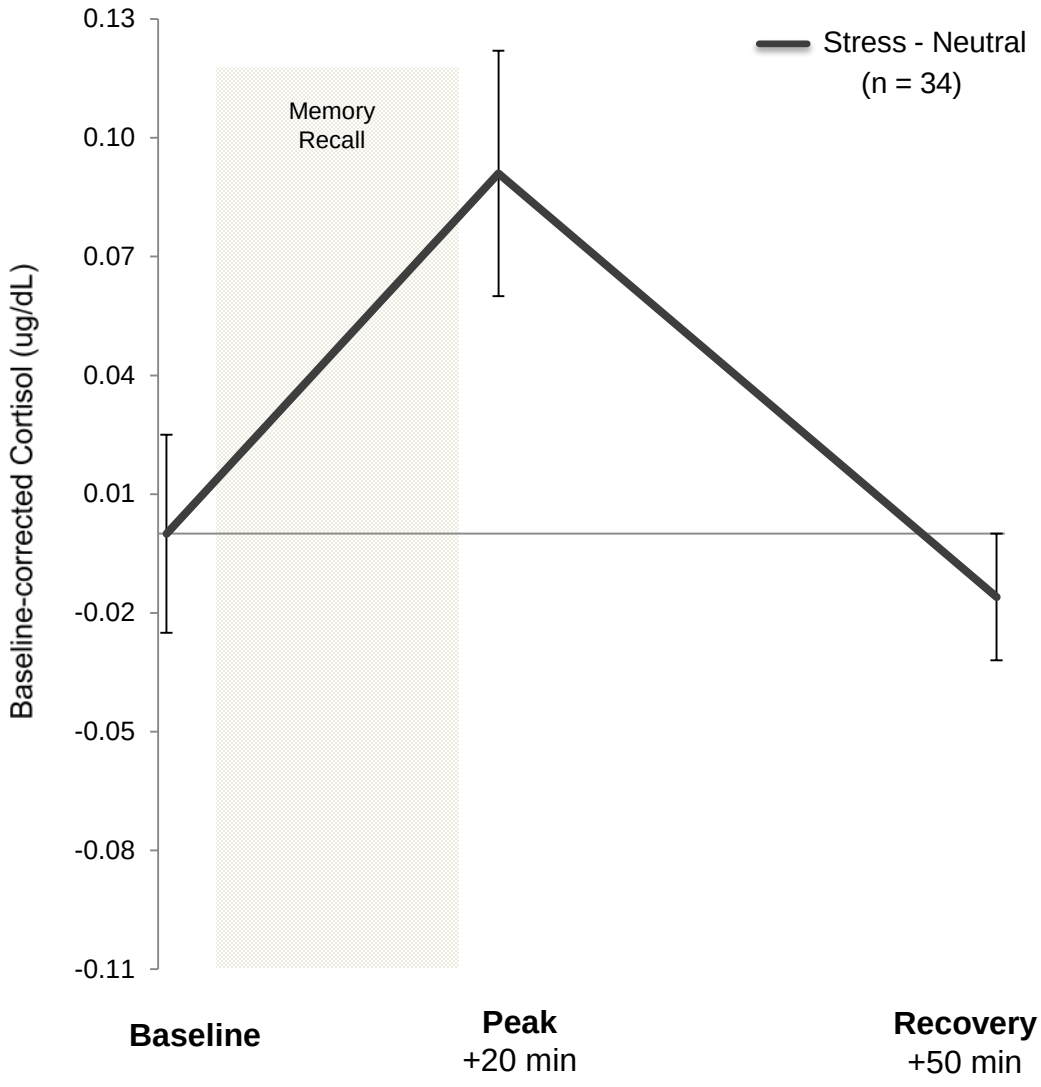
Socially evaluated cold-pressor test (Schwabe et al., 2008)

Cortisol Change by Condition and Memory Valence



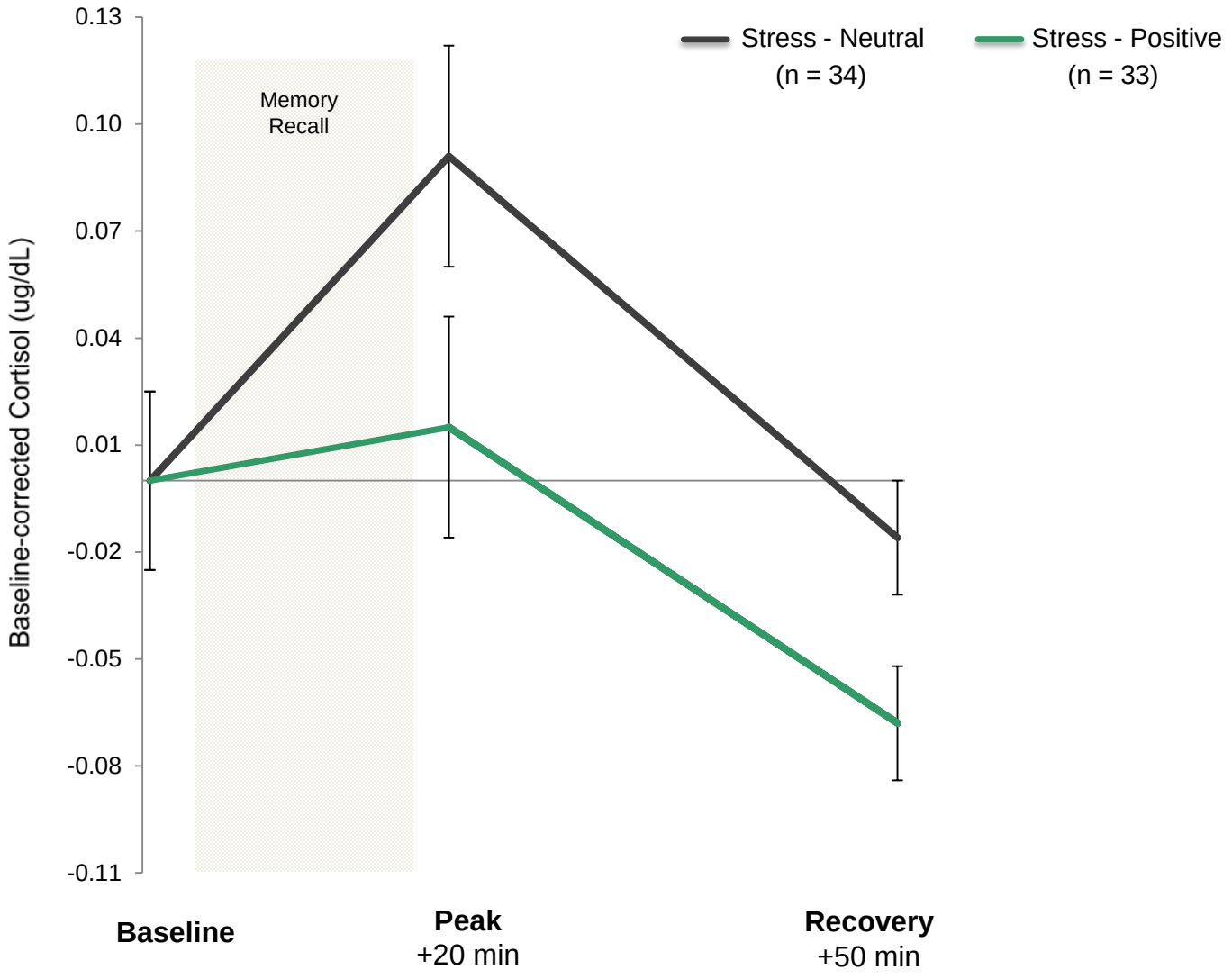
Speer & Delgado (2017) – *Nature Human Behaviour*

Cortisol Change by Condition and Memory Valence



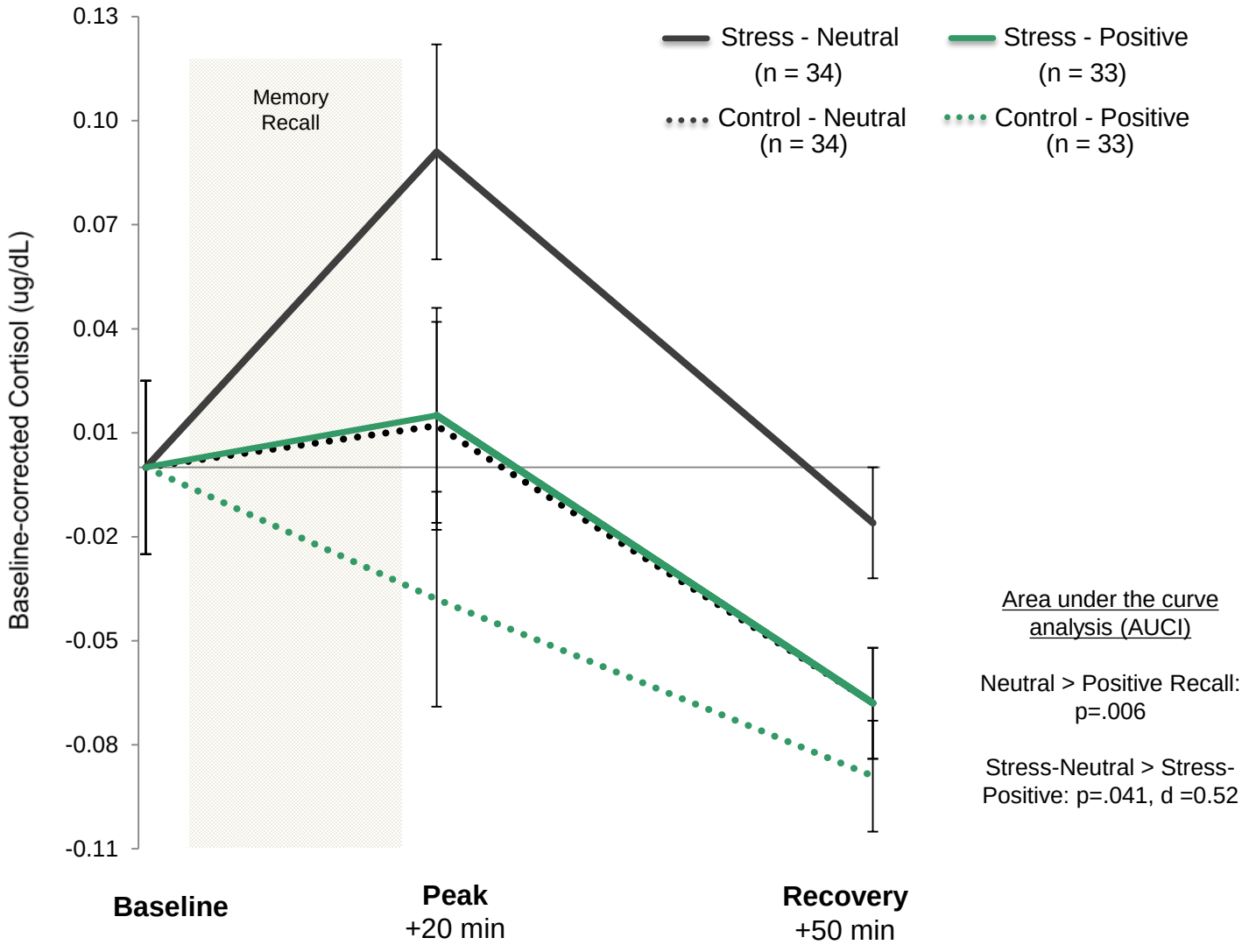
Speer & Delgado (2017) – *Nature Human Behaviour*

Cortisol Change by Condition and Memory Valence



Speer & Delgado (2017) – *Nature Human Behaviour*

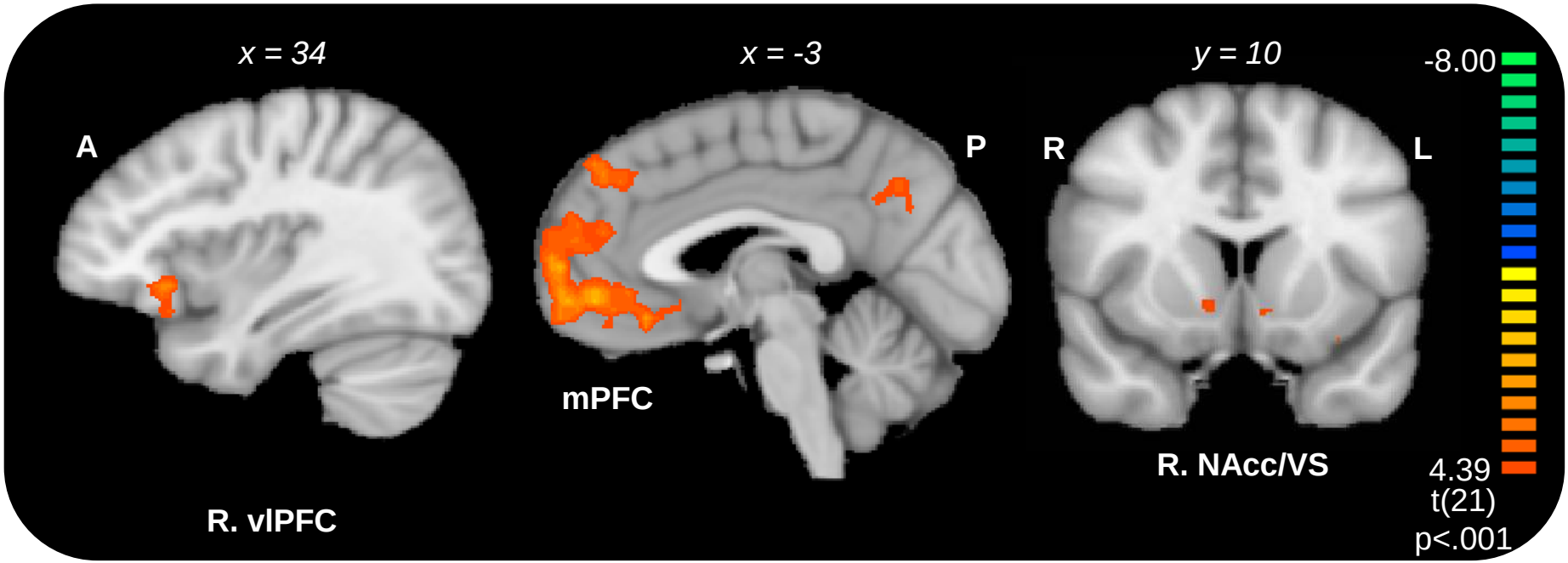
Cortisol Change by Condition and Memory Valence



Speer & Delgado (2017) – *Nature Human Behaviour*

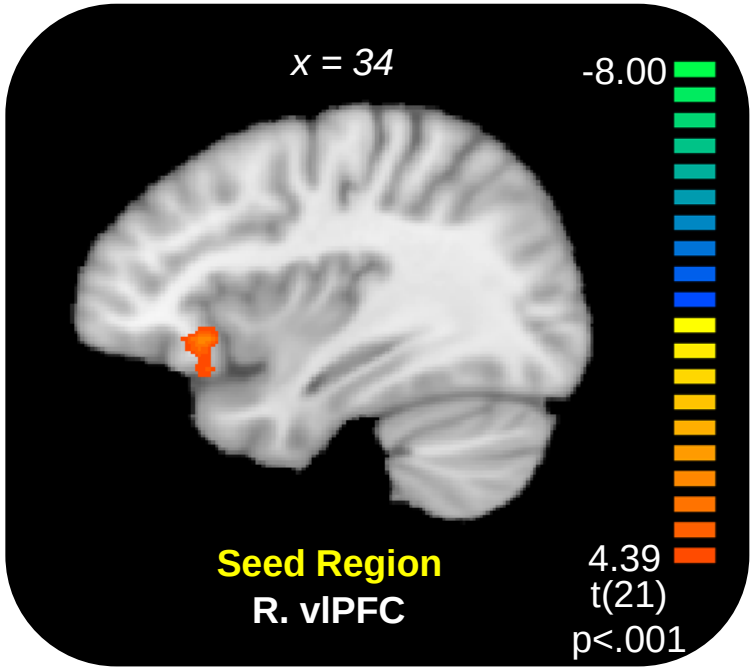
Parametric regression of feeling ratings during memory recall

Stress-Positive Group



Reminiscing about positive memories recruits regions associated with emotion regulation and reward-processing.

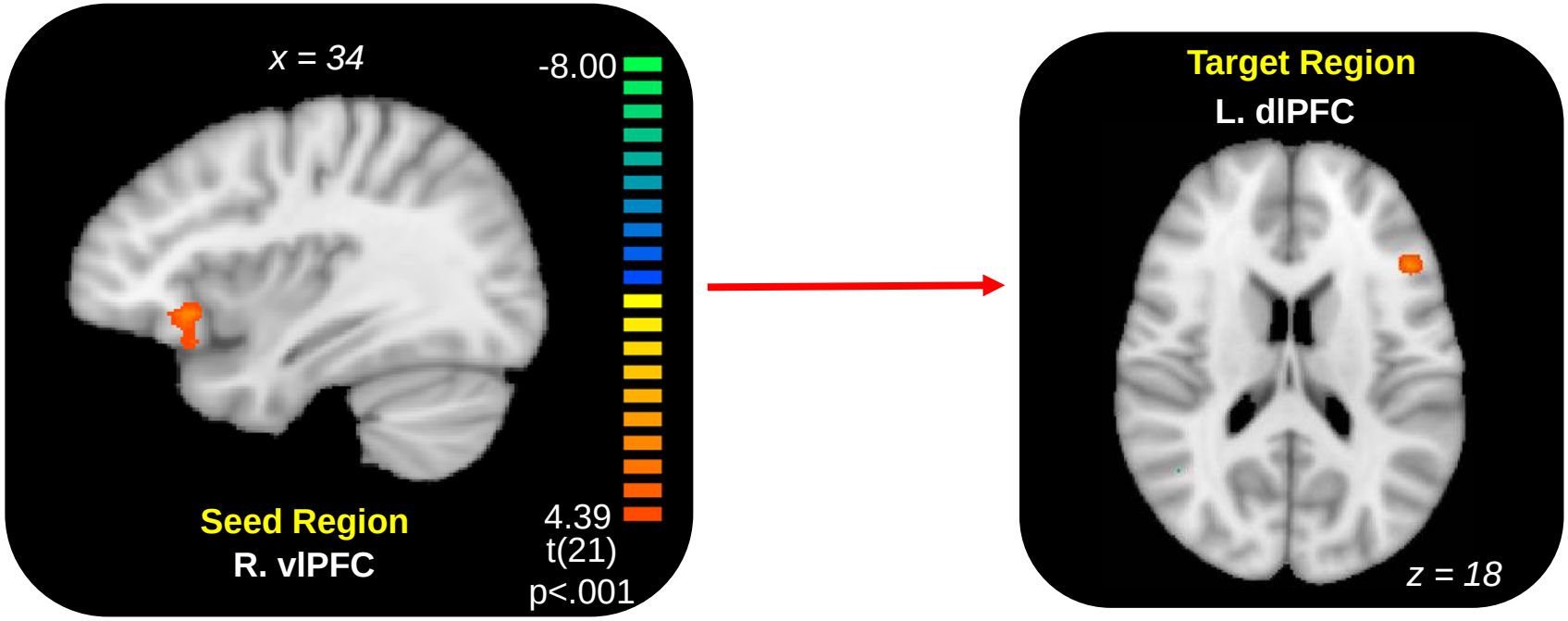
Parametric regression of feeling ratings during memory recall



- Emotion regulation
  (e.g., Ochsner et al., 2004, Lieberman et al., 2007)
- Reappraisal success
  (Wager et al., 2008)
- Response selection and inhibitory function
  (e.g., Robbins, 2007)

Psychophysiological Interaction (PPI) Analysis:
Psychological context: Feeling ratings during Memory Recall
Stress-Positive Group

Stronger vlPFC-dlPFC connectivity (emotion regulation circuitry) as a function of increased positive feelings



<u>Psychophysiological Interaction (PPI) Analysis:</u>
Psychological context: Feeling ratings during Memory Recall
Stress-Positive Group

Emotion regulation via positive emotions

- Recalling positive experiences from the past:
  - Increases positive emotions & influences mood.
  - Engages reward-related neural circuitry.

- Positive memories may serve as an alternative form of emotion regulation.
  - Dampens the physiological response to acute stress.
  - Engages neural circuitry potentially involved in emotion regulatory processes.

- *Future direction*: Finding positive meaning in the negative past changes how we feel and updates memories.
  - Positive meaning finding leads to increases in positive emotion at future retrieval, which tracks greater changes in positive memory content.

Implications for Aging

- Viability of alternative forms of emotion regulation
  - Age-related declines in cognitive function may make typical regulation strategies more effortful.
  - Similarities in reward-related circuitry (e.g., Samanez-Larkin et al., 2007)

- Positivity effect: Age related changes in motivation
  - Meta-analysis supports a positivity effect increase with age (Reed et al., 2014; Carstensen and DeLiema, 2018)
  - Associated with improved health (Kalokerinos et al. 2014) and effective in terms of future interventions (e.g., positive, rather than negative messages; Notthoff & Carstensen, 2014)

- Neural circuitry of positive emotion regulation in aging?
  - Recent work suggests shift from more lateral to medial regions in aging during emotion regulation (Van Reekum et al, 2018).

Acknowledgements

Laboratory

Current

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Stephanie Kim
Vicki Lee
Heena Manglani
Mike Niznikiewicz
David Smith

Collaborators

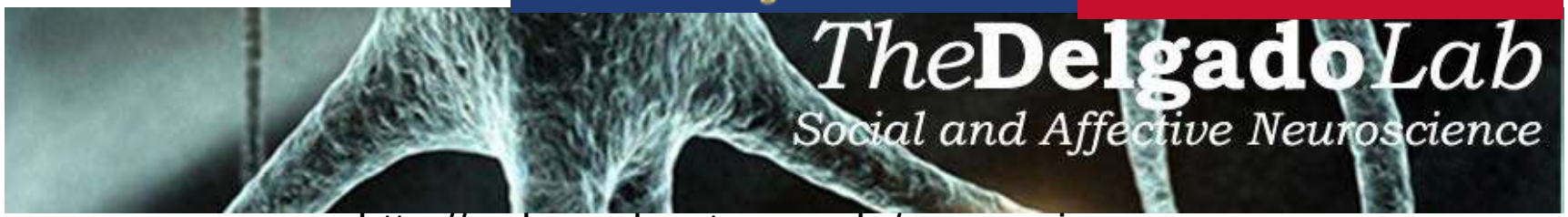
- Luke Chang
- Julie Fiez
- Liz Phelps
- Daniela Schiller

NIMH National Institute of Mental Health

NIDA NATIONAL INSTITUTE ON DRUG ABUSE The Science of Drug Abuse & Addiction

RUTGERS UNIVERSITY | NEWARK

McKNIGHT FOUNDATION

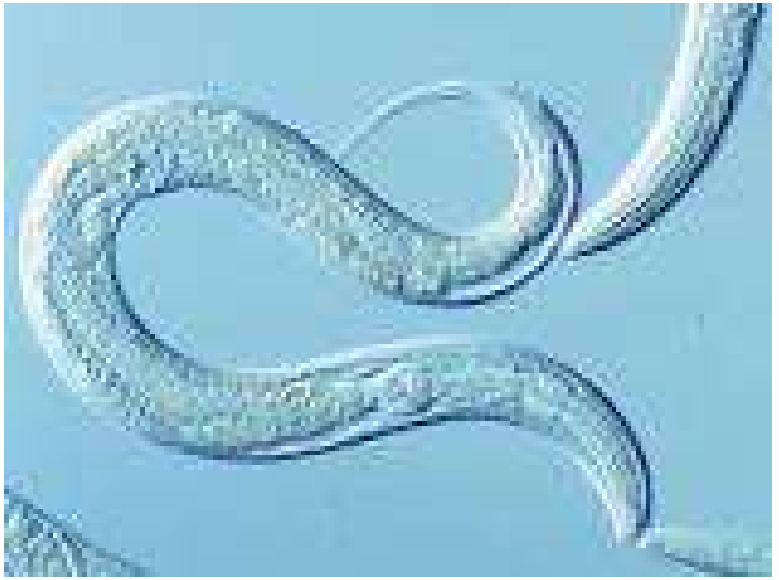


Insights into Healthspan and Neurodegeneration in C. elegans

Monica Driscoll

Professor of Molecular Biology and Biochemistry

Rutgers, The State University of New Jersey



Nelson A232 Bush **driscoll@biology.rutgers.edu**

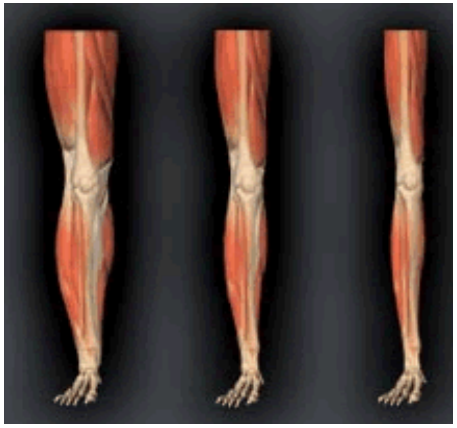
A talk in two parts:

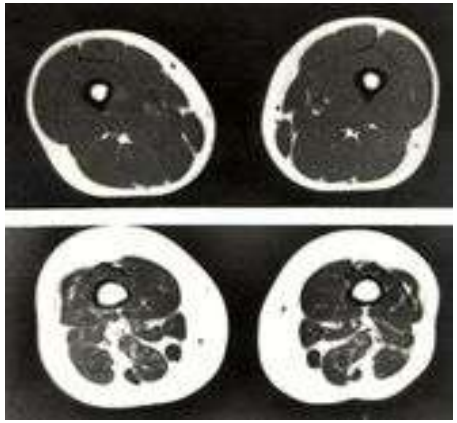
1) Basic research as the key to healthy aging

2) New biology in neuronal health

Aging involves physical decline

Sarcopenia is an inevitable component of human aging





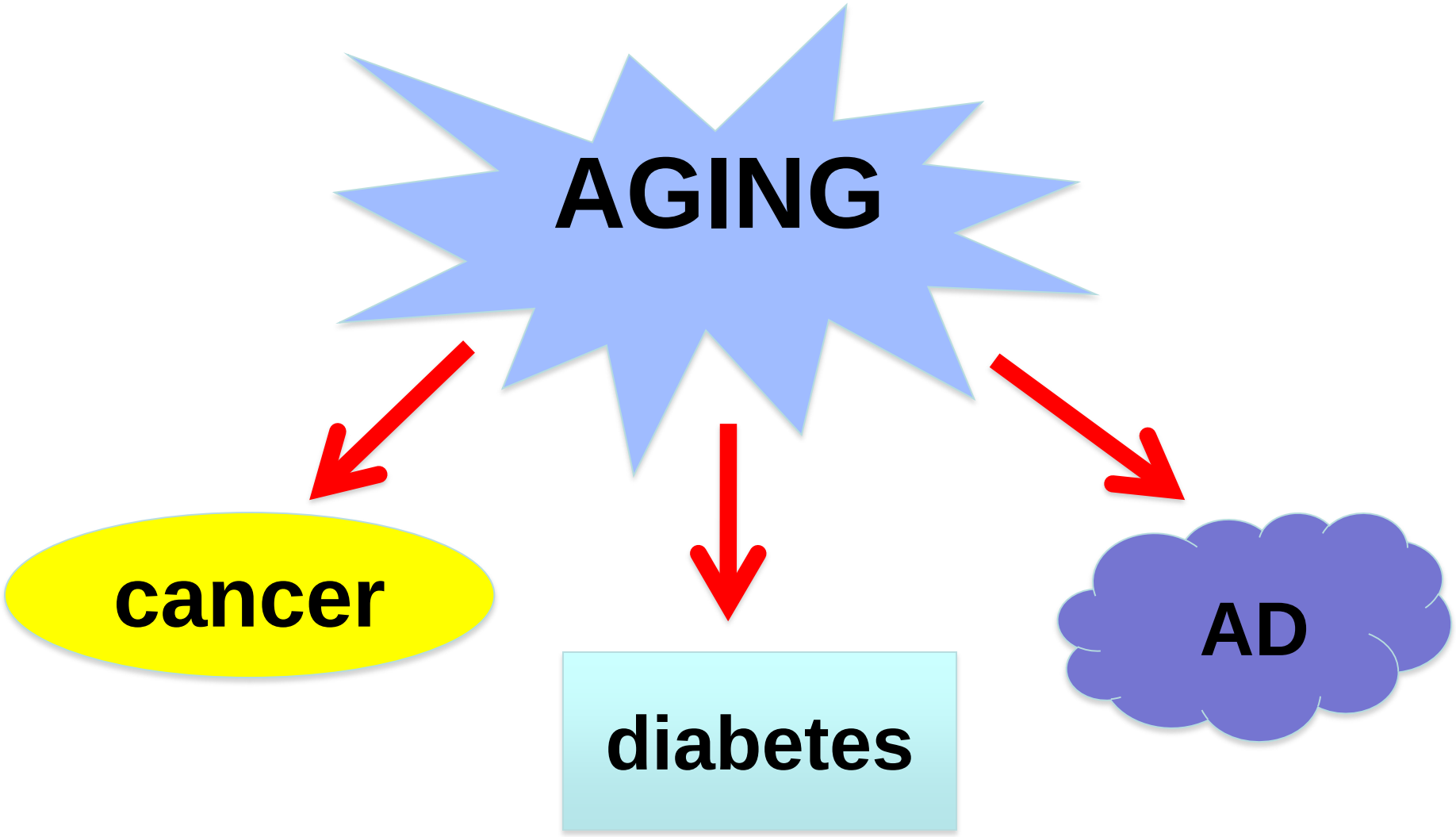
progressive loss of muscle mass and strength

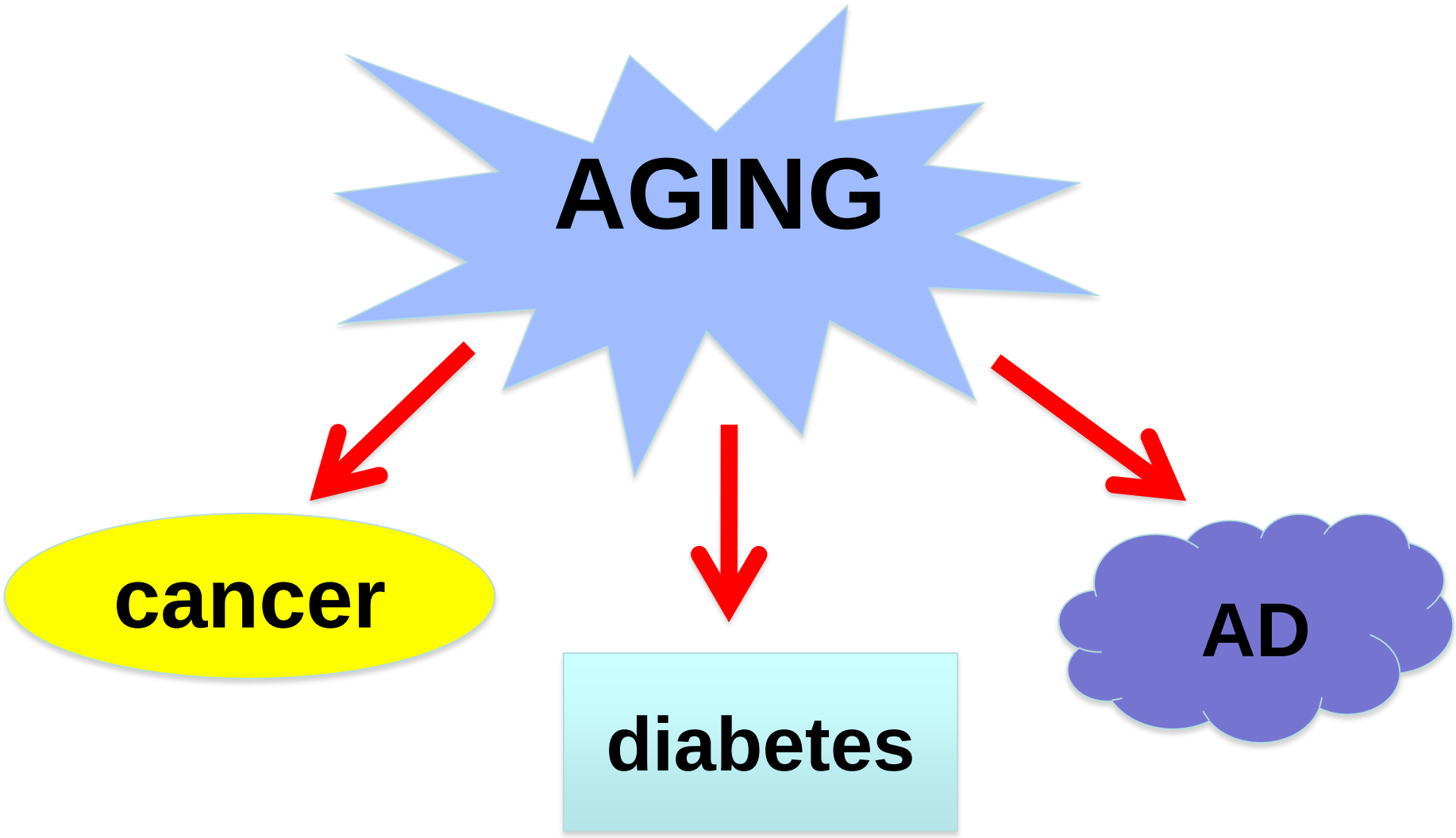
-midlife onset

need for institutional ca
falls and consequent in

Major quality of life issue; major economic issue

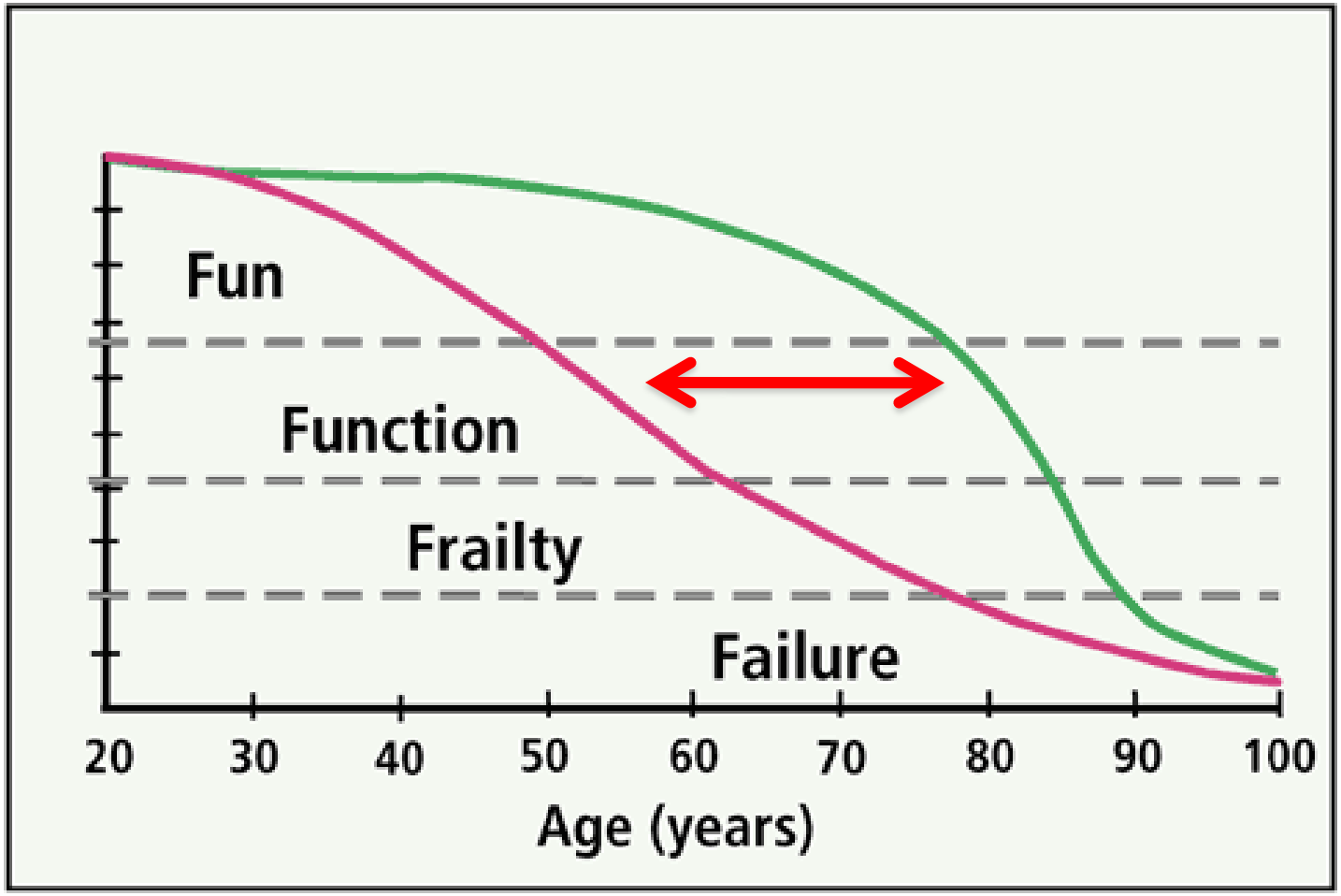
Aging is the primary risk factor for cancer, diabetes, Alzheimer's disease, and more…





decrease aging consequences
improve quality of life and delay disease

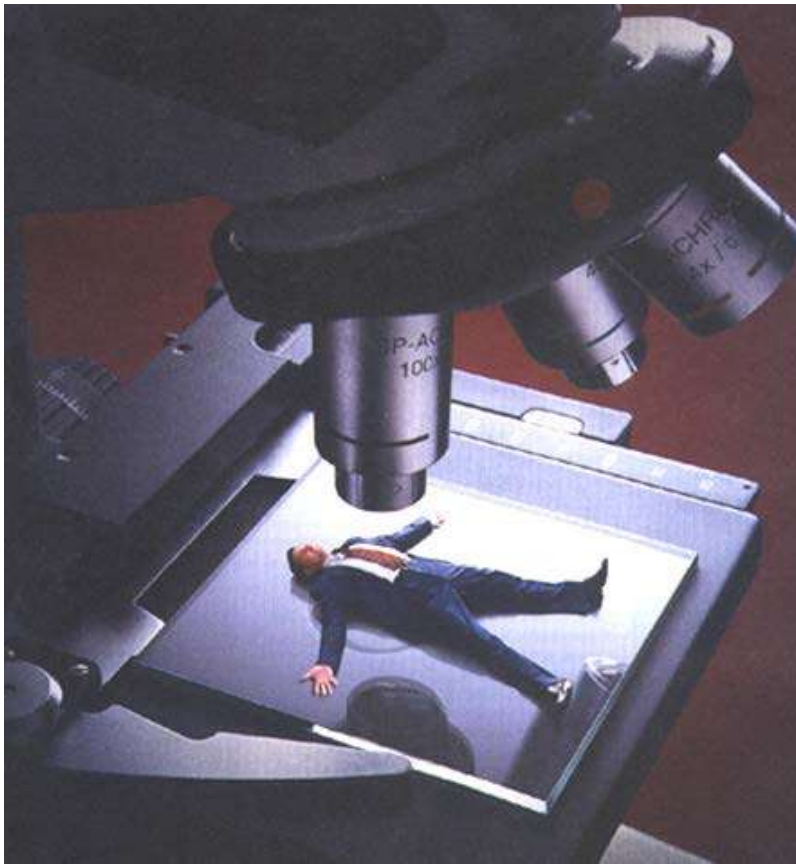
Functional ability with age



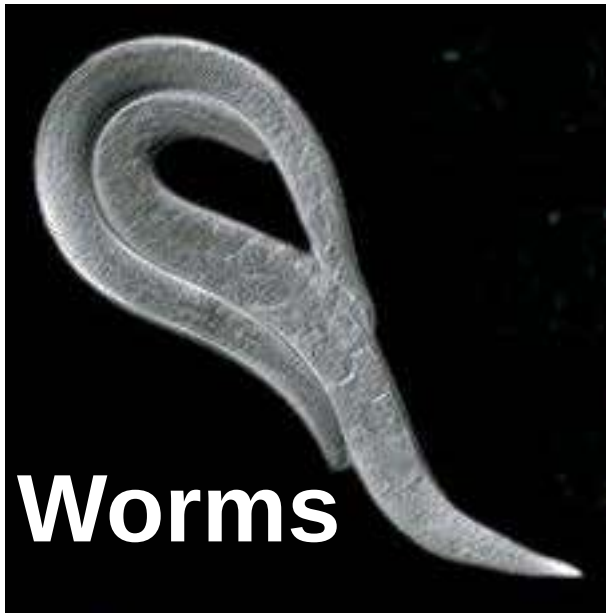
Extending healthspan is an important objective for the field

Humans make lousy experimental subjects

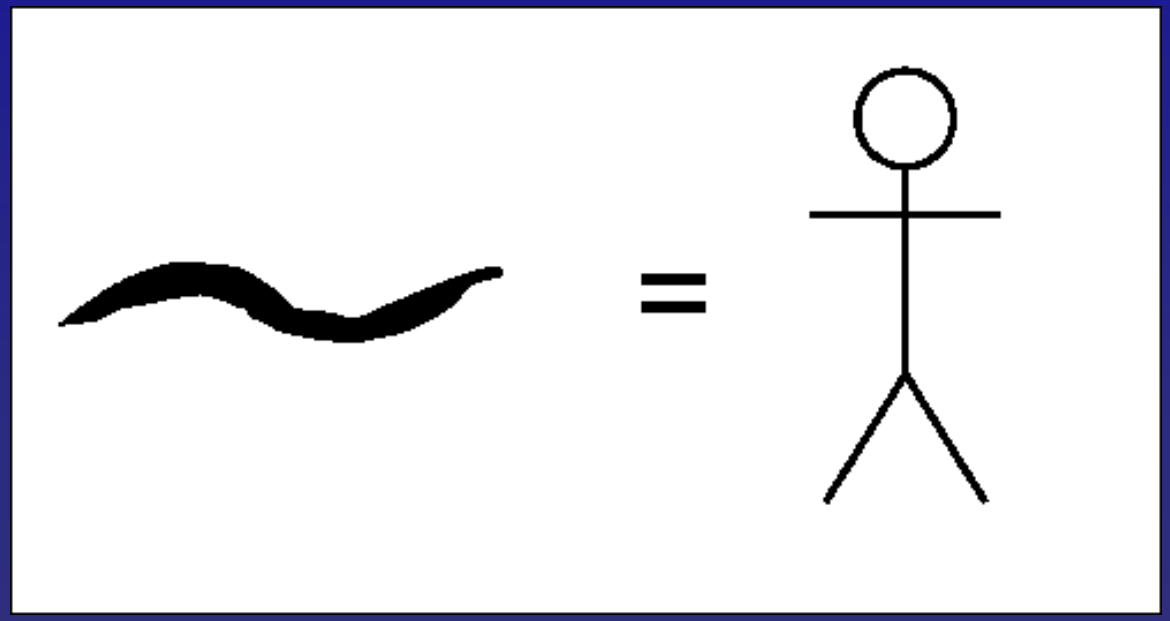
- genetically heterogeneous
- environmental differences
- slow reproduction, few offspring
- live too long
- reluctant to give up tissues



Model systems are invaluable in biology



Basic Biological Mechanisms Are Conserved



The *C. elegans* model

--959 cells

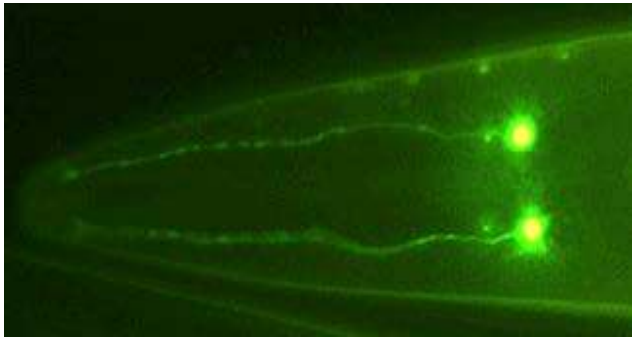
--transparent

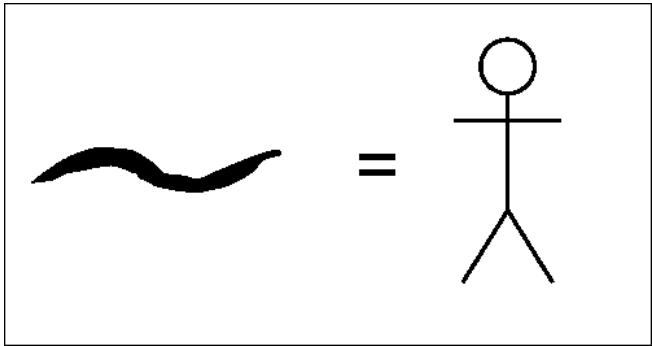
--strong genetics

--easy transgenic generation

--lives 3 weeks

Basic biological mechanisms are conserved



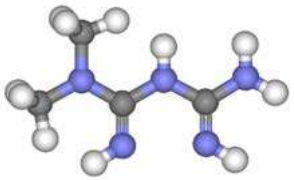


genes

diet

exercise

healthspan

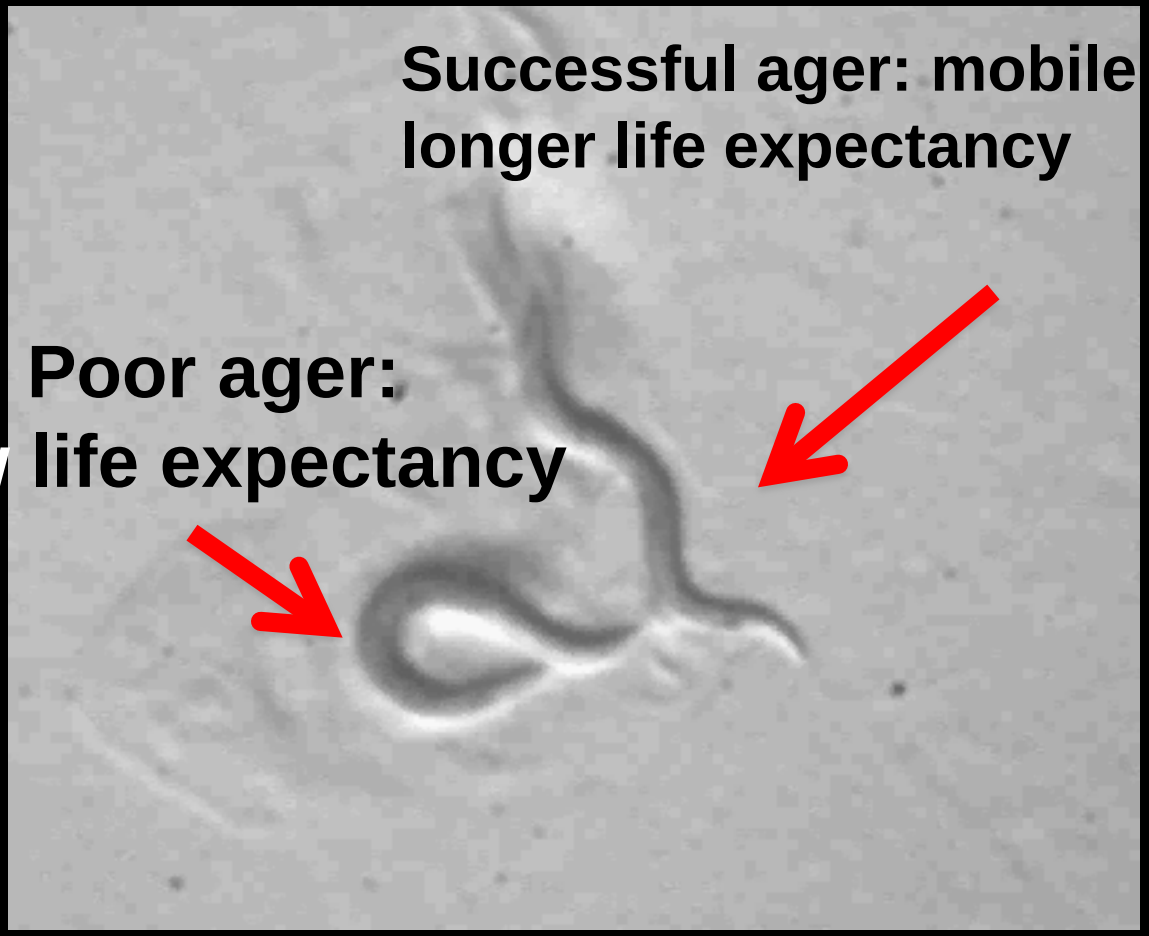


natural products

environment

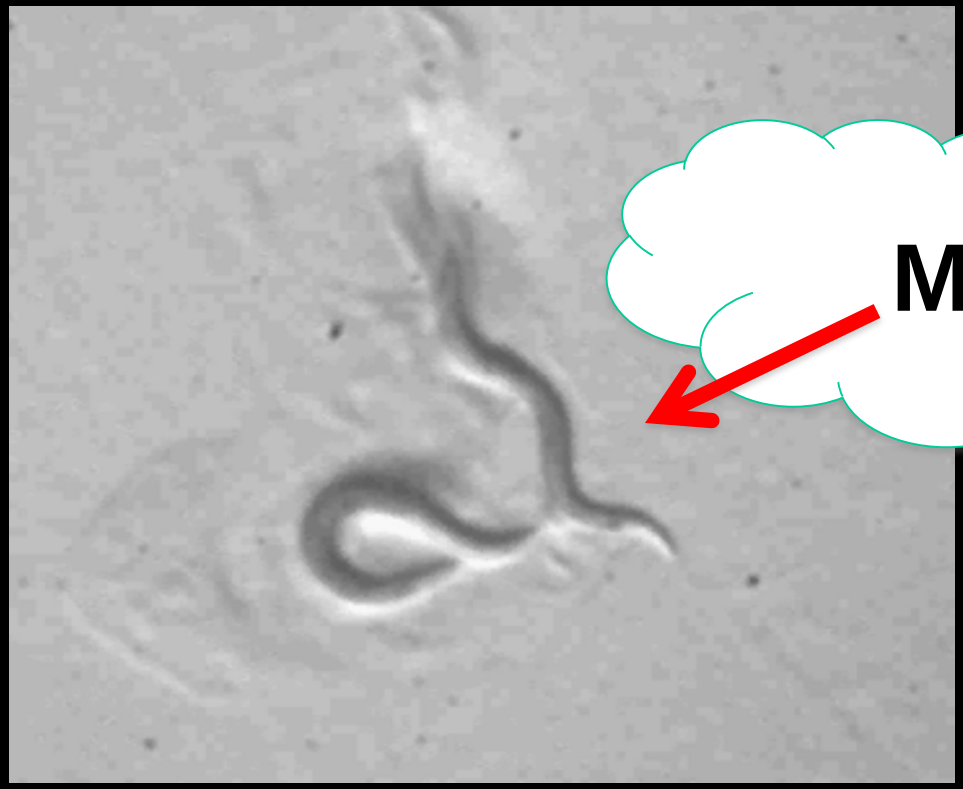
chance

Animals of the same chronological age, same genotype and same environmental experience can “age” differently



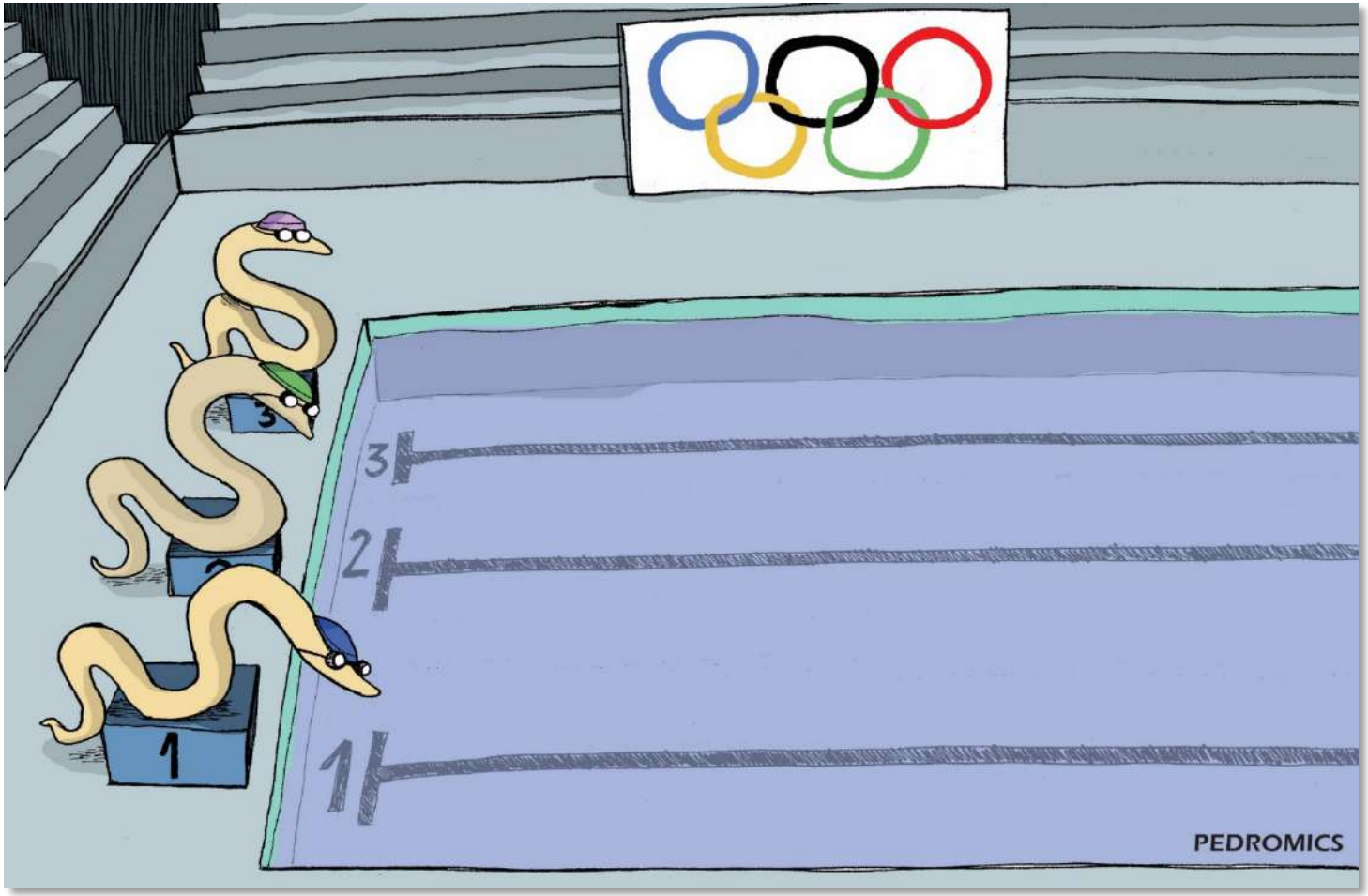
same age animals

C. elegans can age gracefully or age poorly

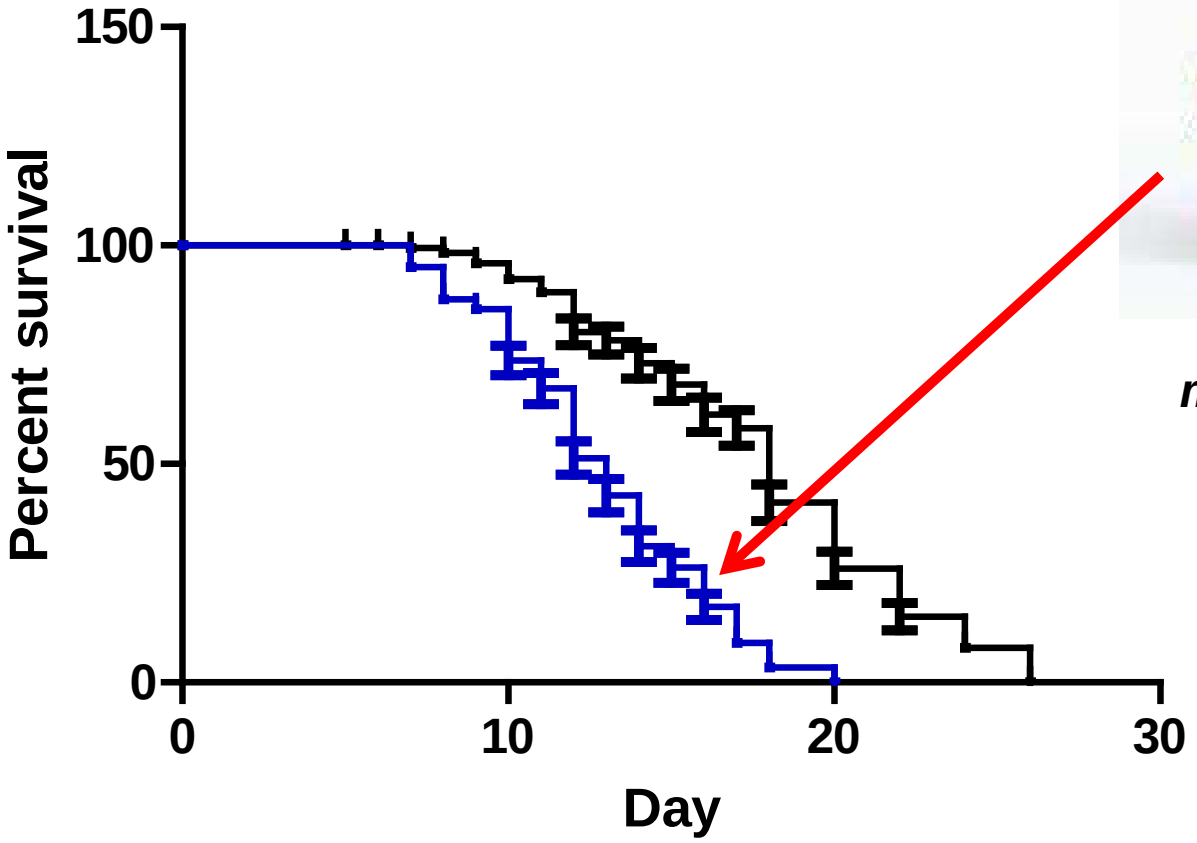


--Identifying the differences is of interest

Exercise and healthy aging

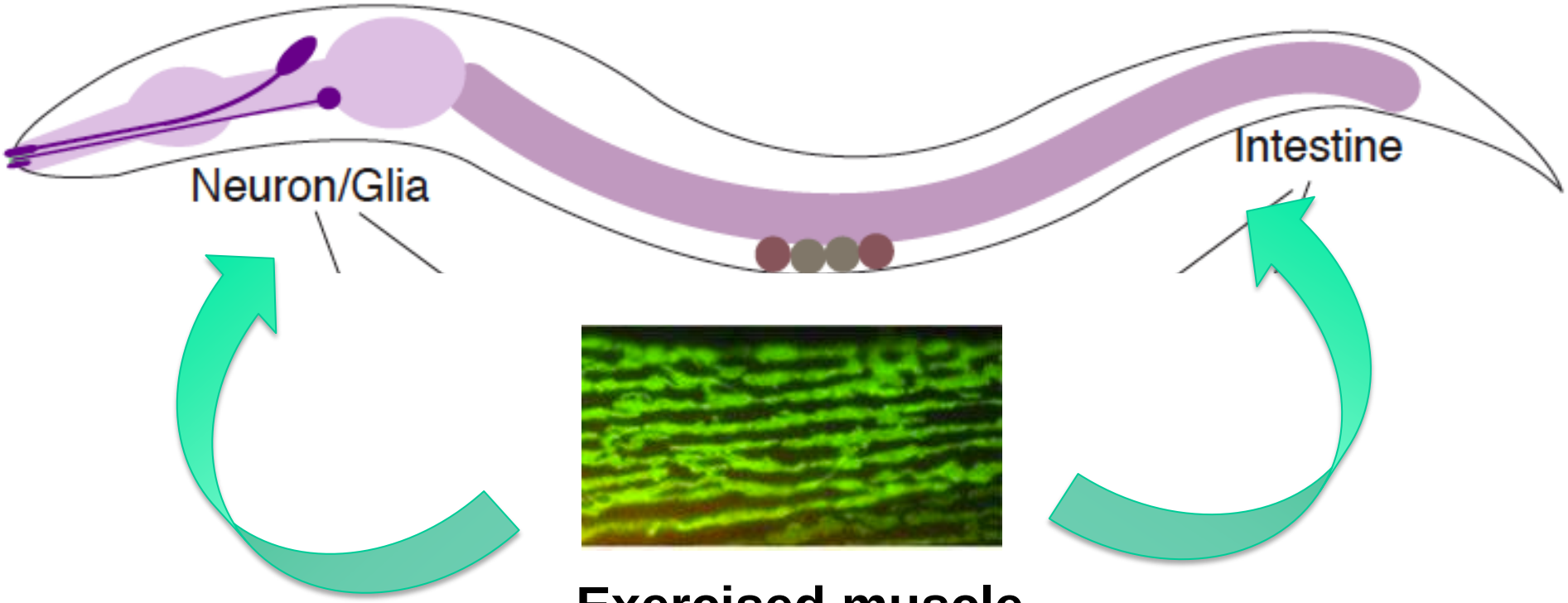

3
2
1
3
2
1
PEDROMICS

Lethargic worms that do not train have lower life expectancy



mec-10 mec-4 **mutant**

Key Question: What exercise-induced molecules dictate whole animal health?



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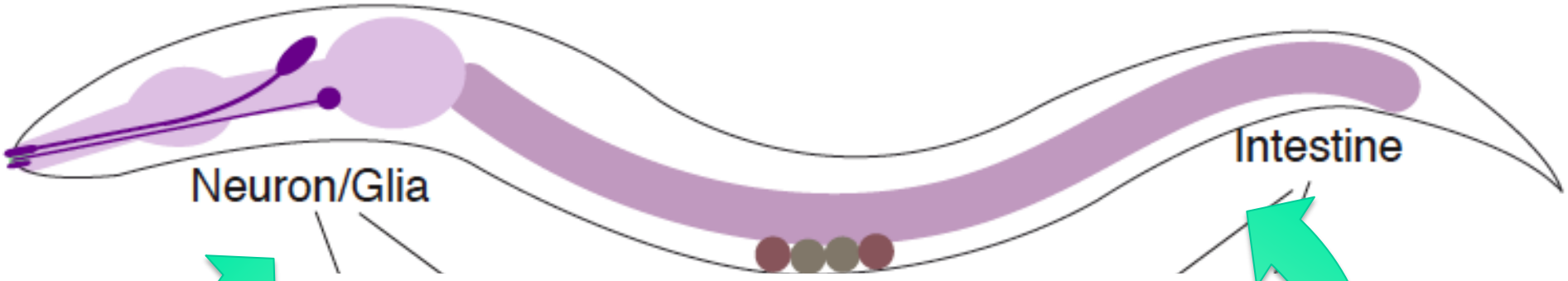
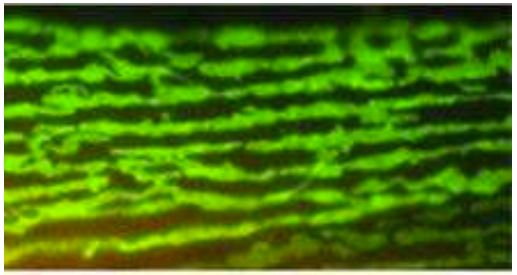
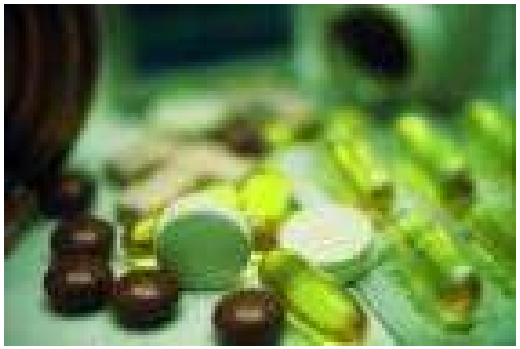


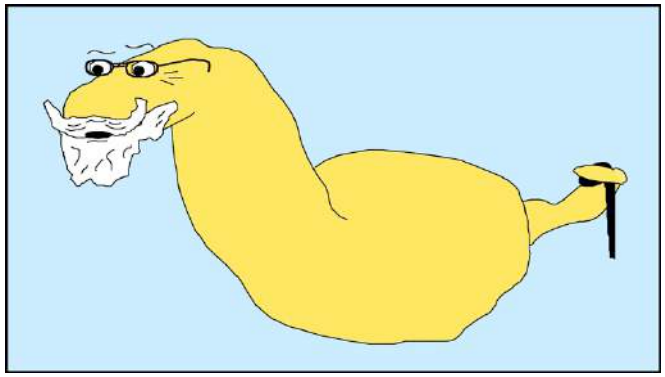


Exercised muscle

CITP

Caenorhabditis Intervention Testing Program





Our mission: **Identify pharmacological interventions that increase lifespan and/or healthspan in a robust manner using *Caenorhabditis***

The CITP Team:

- **Monica Driscoll Rutgers University, NJ**
- **Gordon Lithgow Buck Institute, CA**

- **Patrick Phillips University of Oregon**

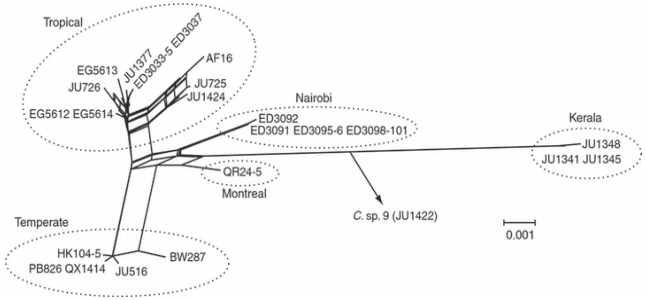
- **Max Guo NIA Project Scientist**

- **Ron Kohanski NIA Program Officer**

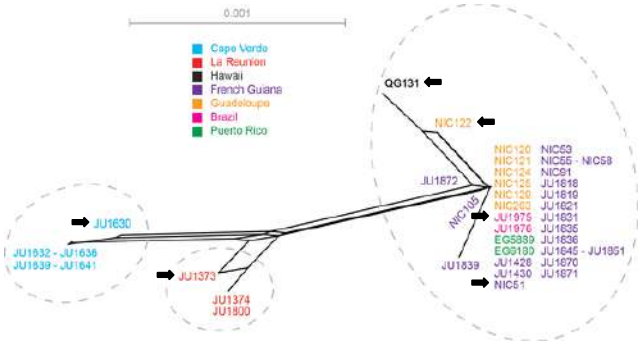
The CITP strains

maximize genetic diversity

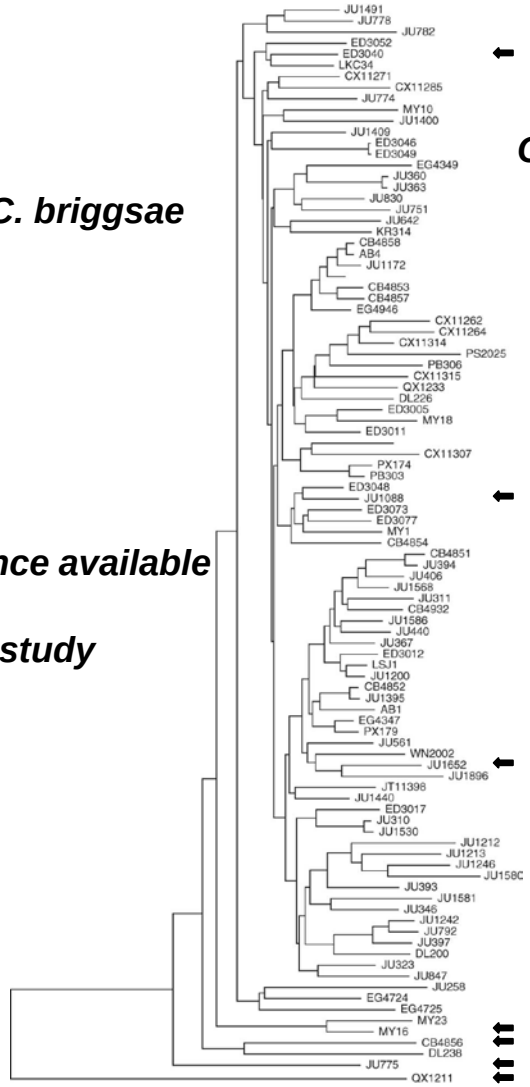
4-8 strains per species



C. tropicalis (sp. 11)



C. briggsae



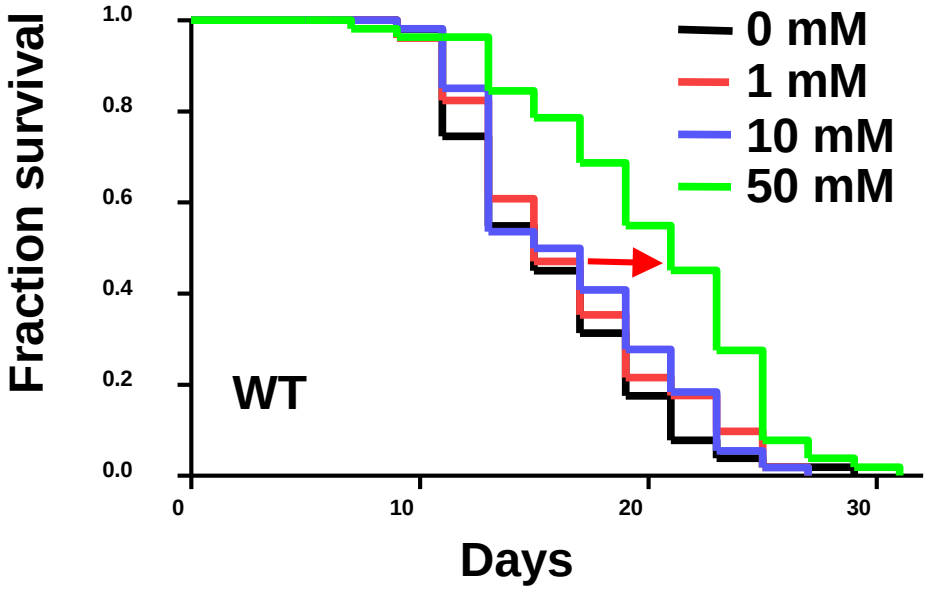
C. elegans

-genome sequence available

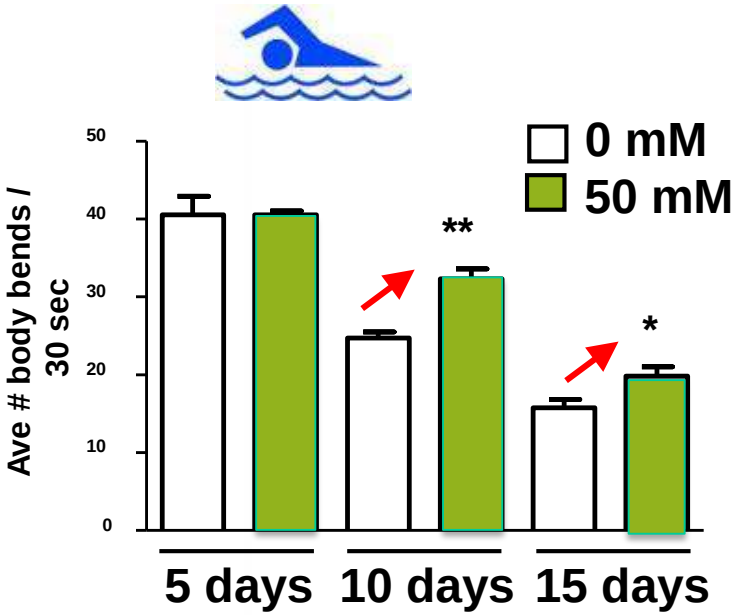
-some previous study

TAME project summary

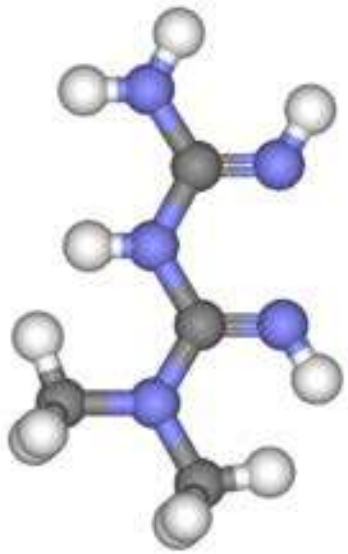
Metformin can extend *C. elegans* median lifespan..

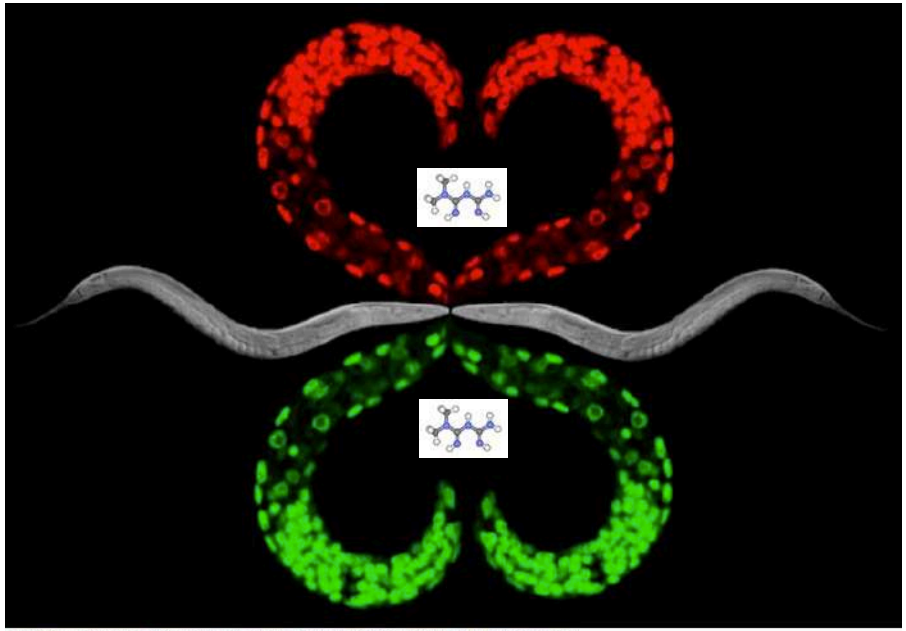


Metformin treatment improves late age swimming prowess



Metformin





C. elegans art by Ahna Skop and Tri Nguyen. Stay tuned for a #Worm17 Art Show recap.

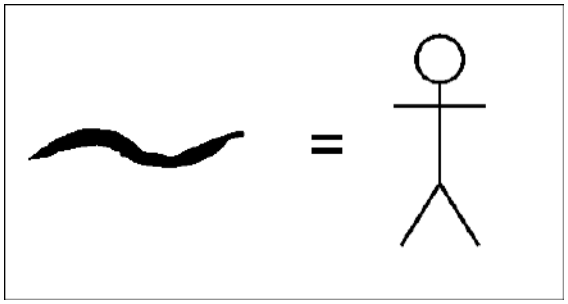
CITP

A talk in two parts:

1) Basic research as the key to healthy aging

2) New biology in neuronal health

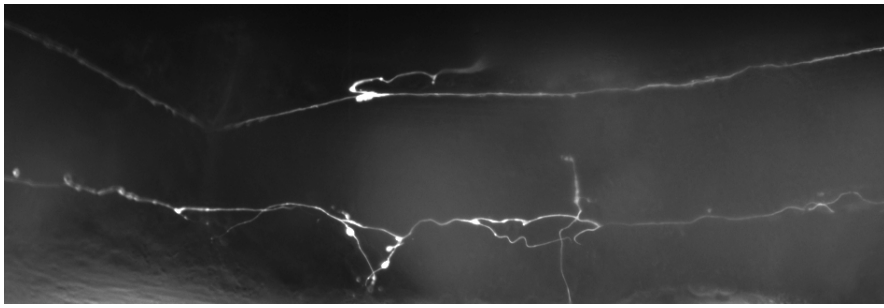
C. elegans age like humans



C. elegans **NS aging is similar to human brain aging**

--little loss of neurons by cell death

--synaptic decline



--dendrite restructuring

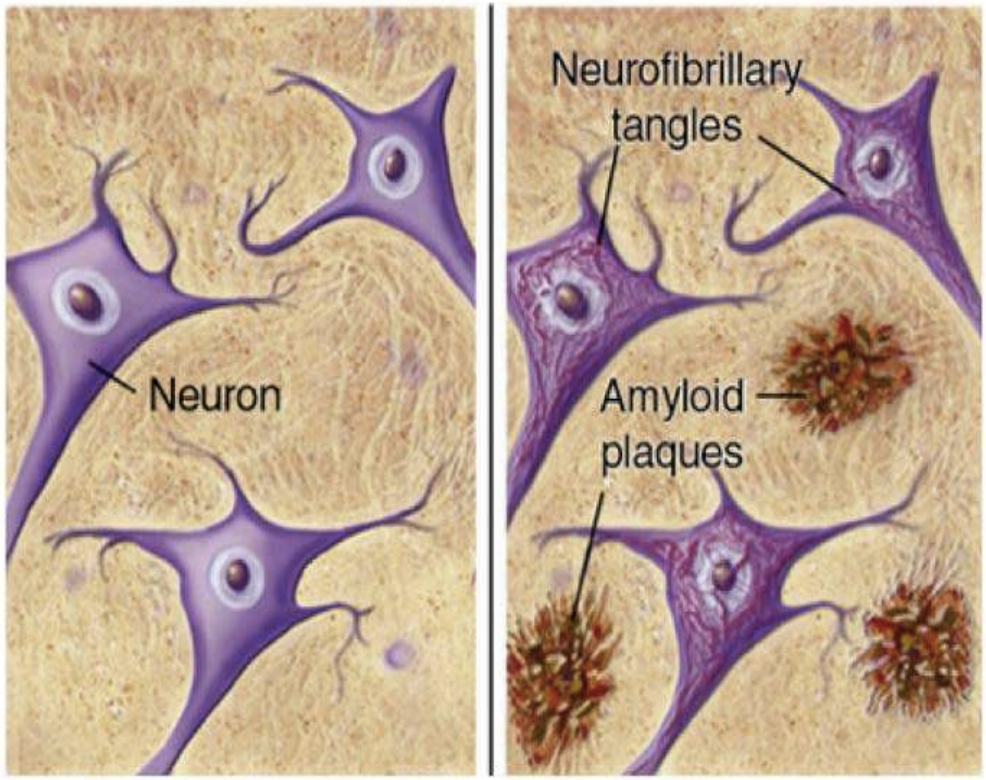
--differential susceptibility for different neurons

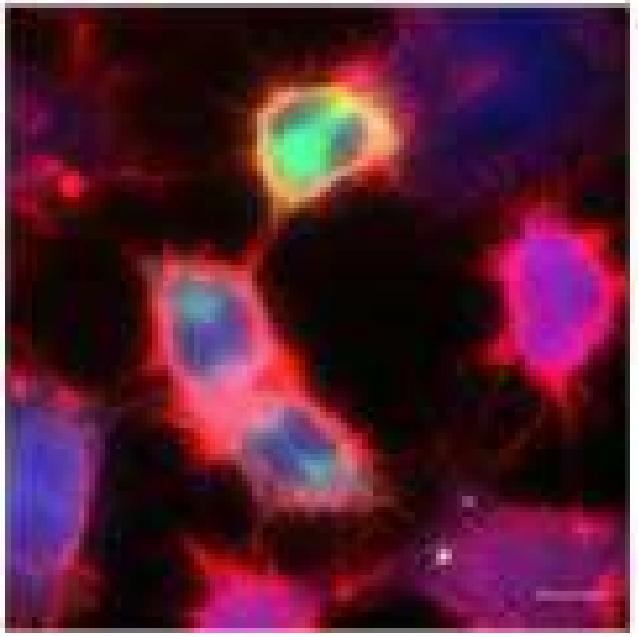
--proteostasis is important

In aging systems, trash management becomes an increasing problem

Major challenges for an aging neuron

1) Protein Aggregation





Aggregate Transfer=
worse than we thought!!

Major challenges for an aging neuron

2) Mitochondrial Dysfunction

Healthy

Age-Diminished

-Energy production

-Ca^{+2} homoeostasis

-Metabolism

--ROS production

-Cell Death

Clean up *within* the neuron:

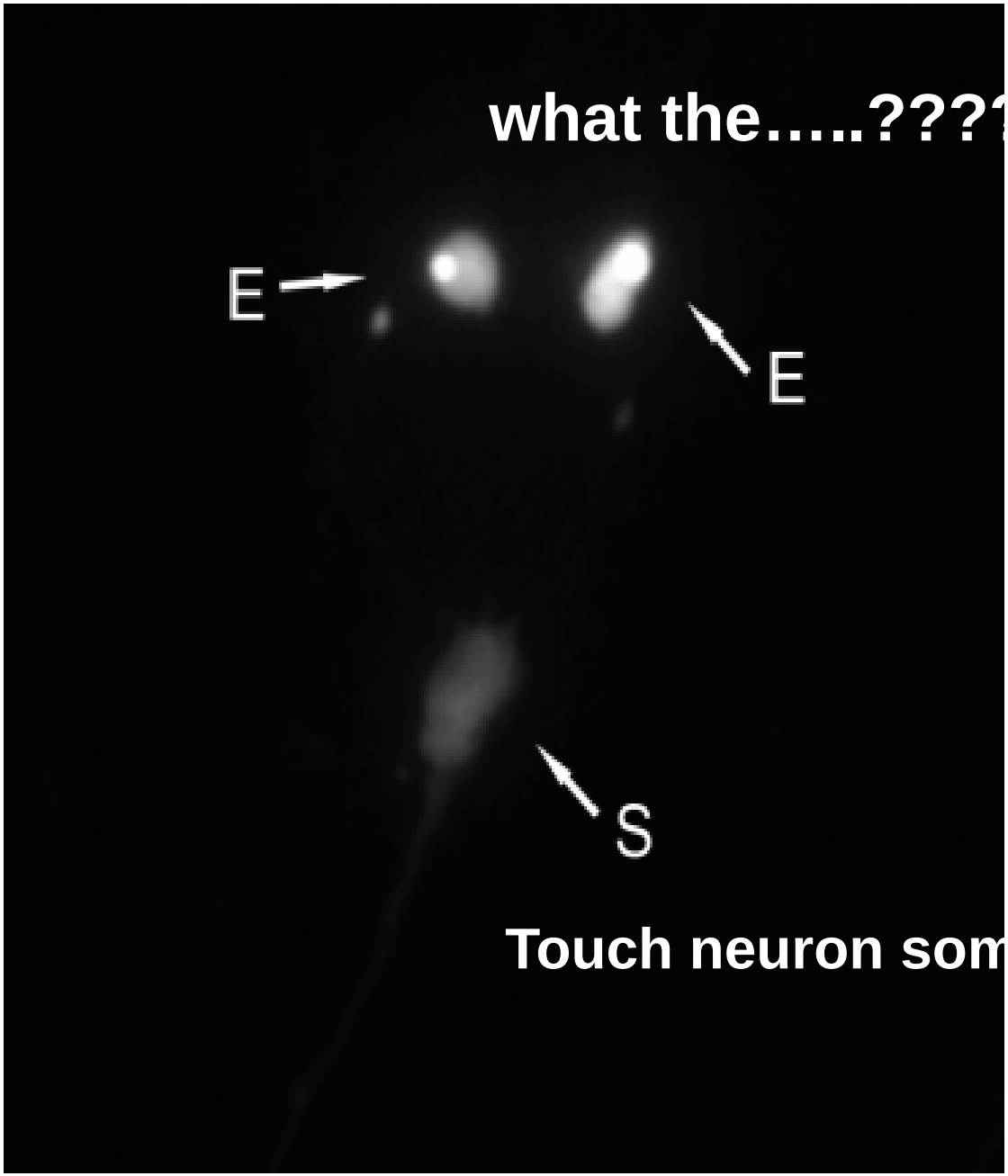
Chaperones fold

Proteasome degrades

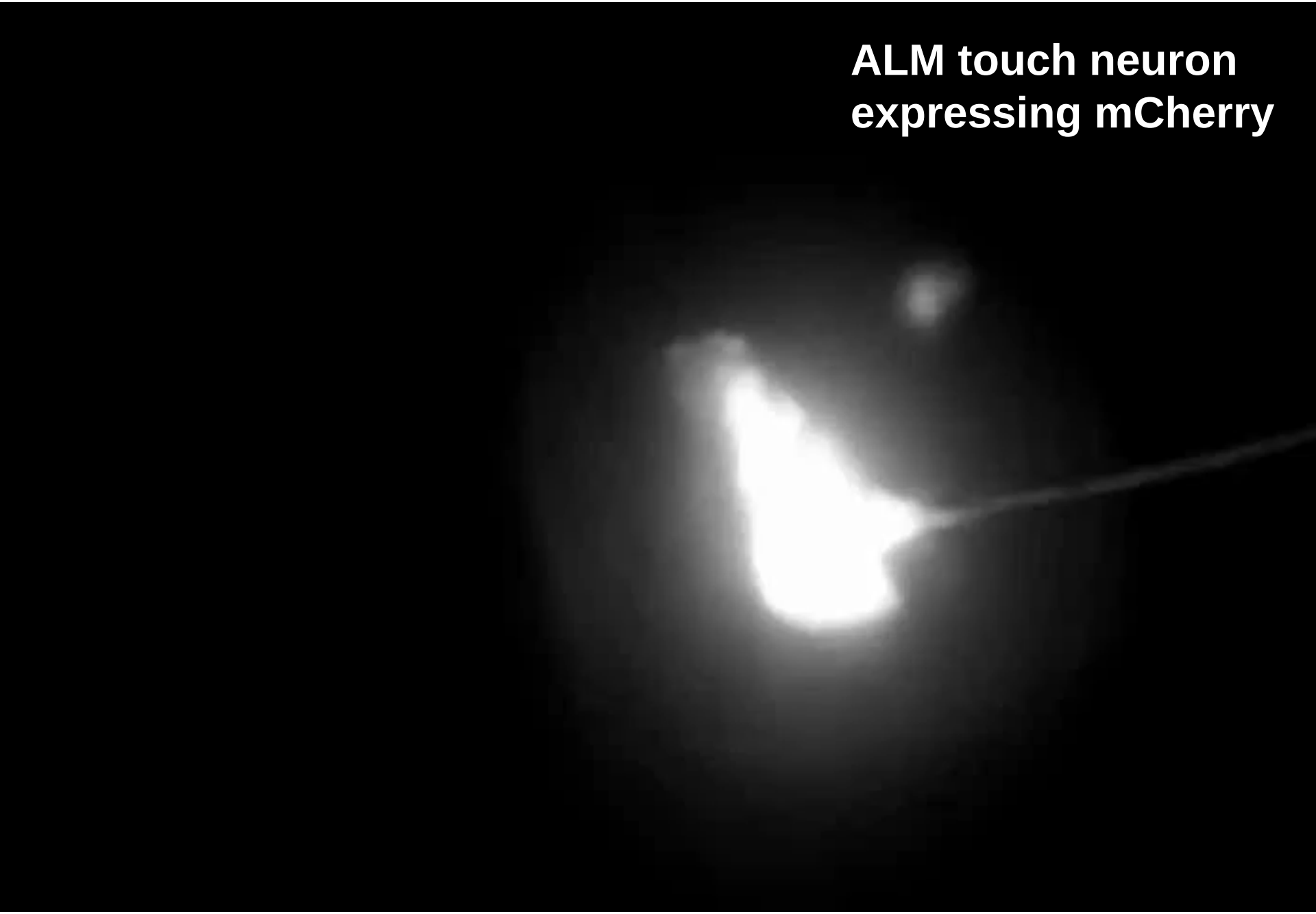
Autophagy/lysosome degrades

bizarre fluorescence appears **outside** the touch neuron

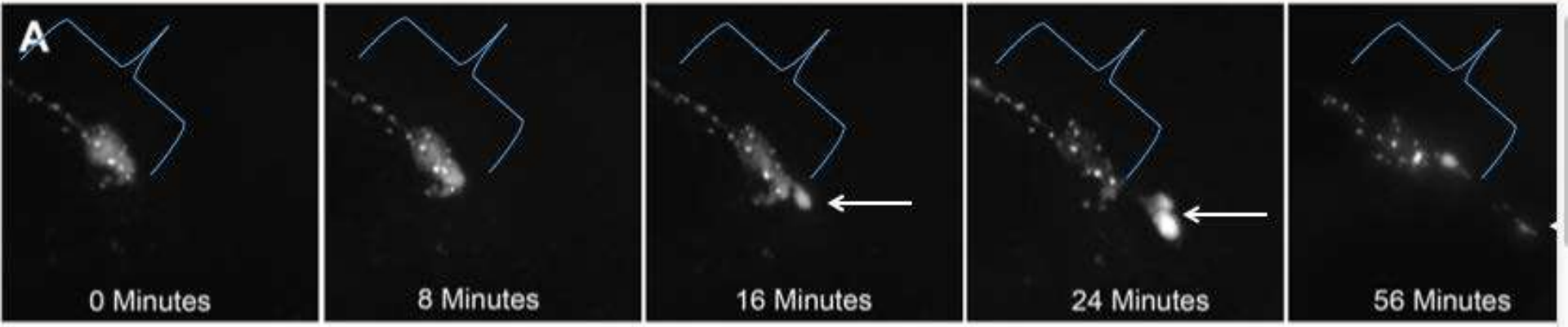
Ilija Melentijevic



$P_{mec\text{-}4}$mCherry


ALM touch neuron
expressing mCherry

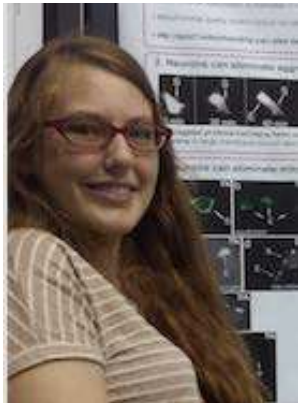
An exopher is born…..



A near-soma-sized packet is jettisoned from the cell body

Ilija Melentijevic

Meghan Arnold



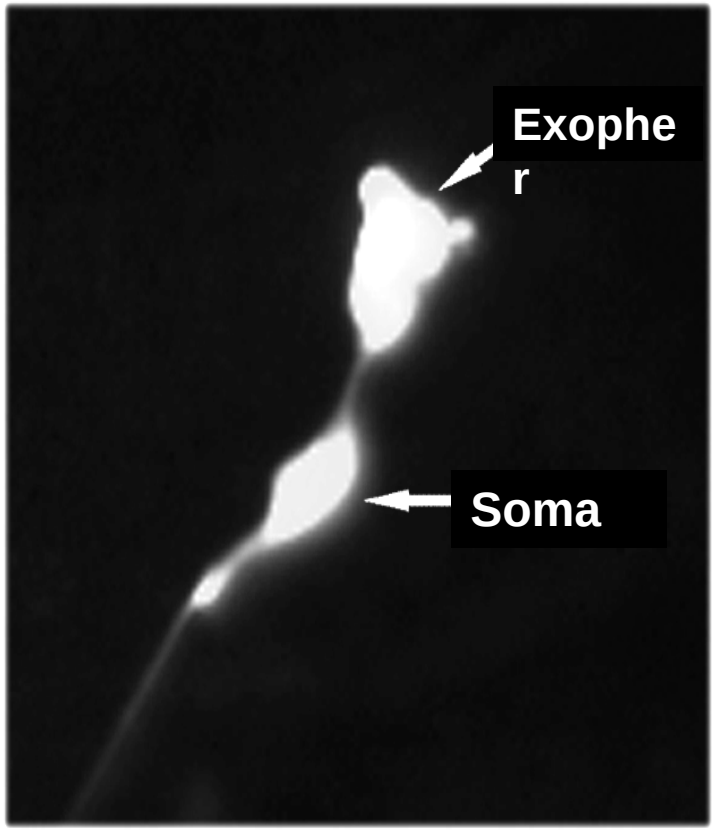
Joelle Smart

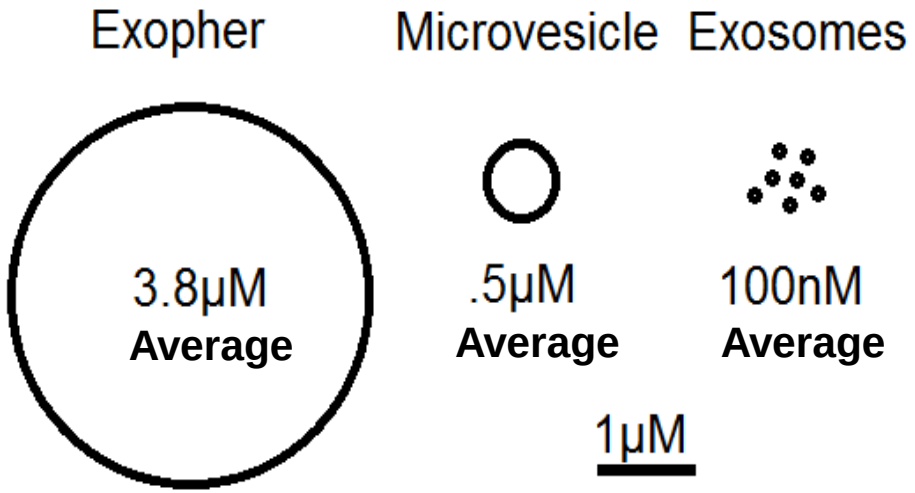
Ryan Guasp

Girish Harinath

Marton Toth

C. elegans can extrude large vesicles, or “exophers”

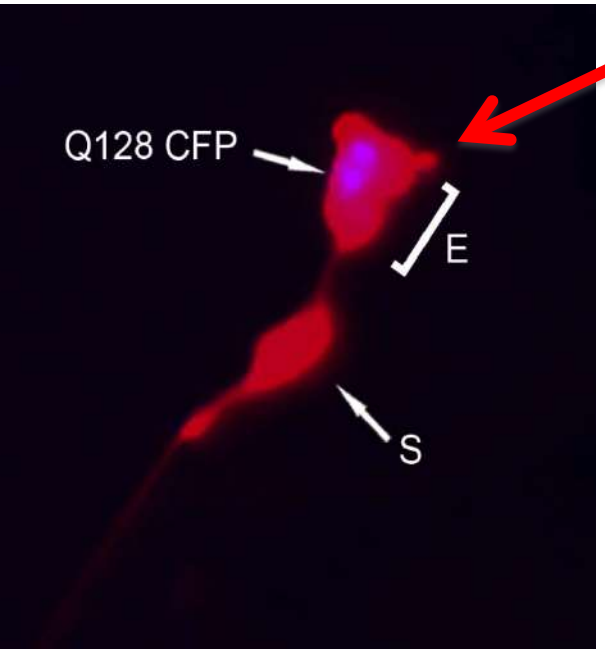


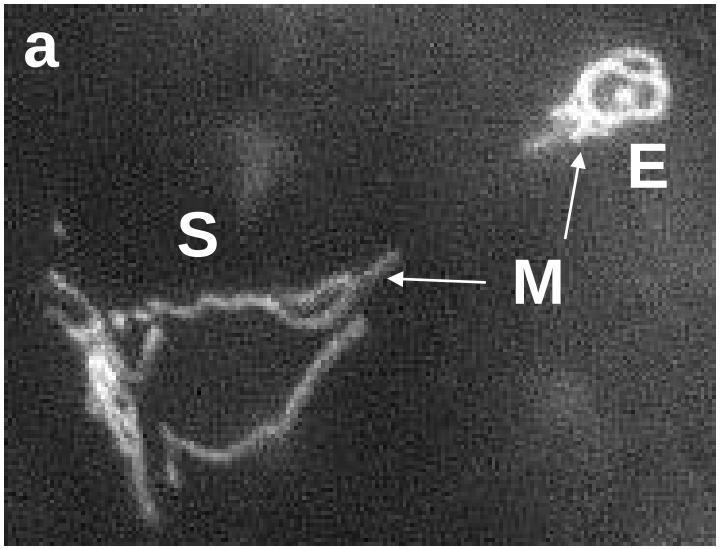


(not an exosome!!!!)

Extrusions can contain mitochondria or disease protein aggregates…

PolyQ-CFP

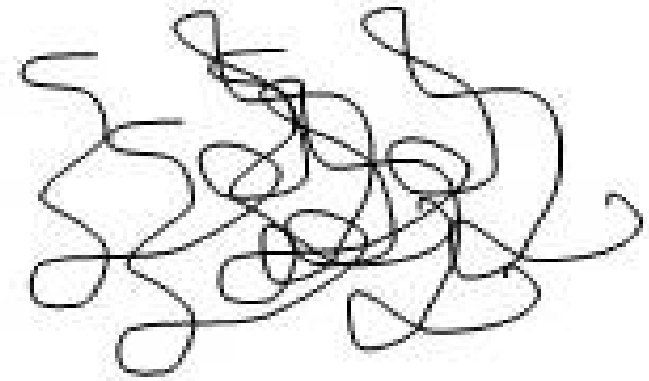




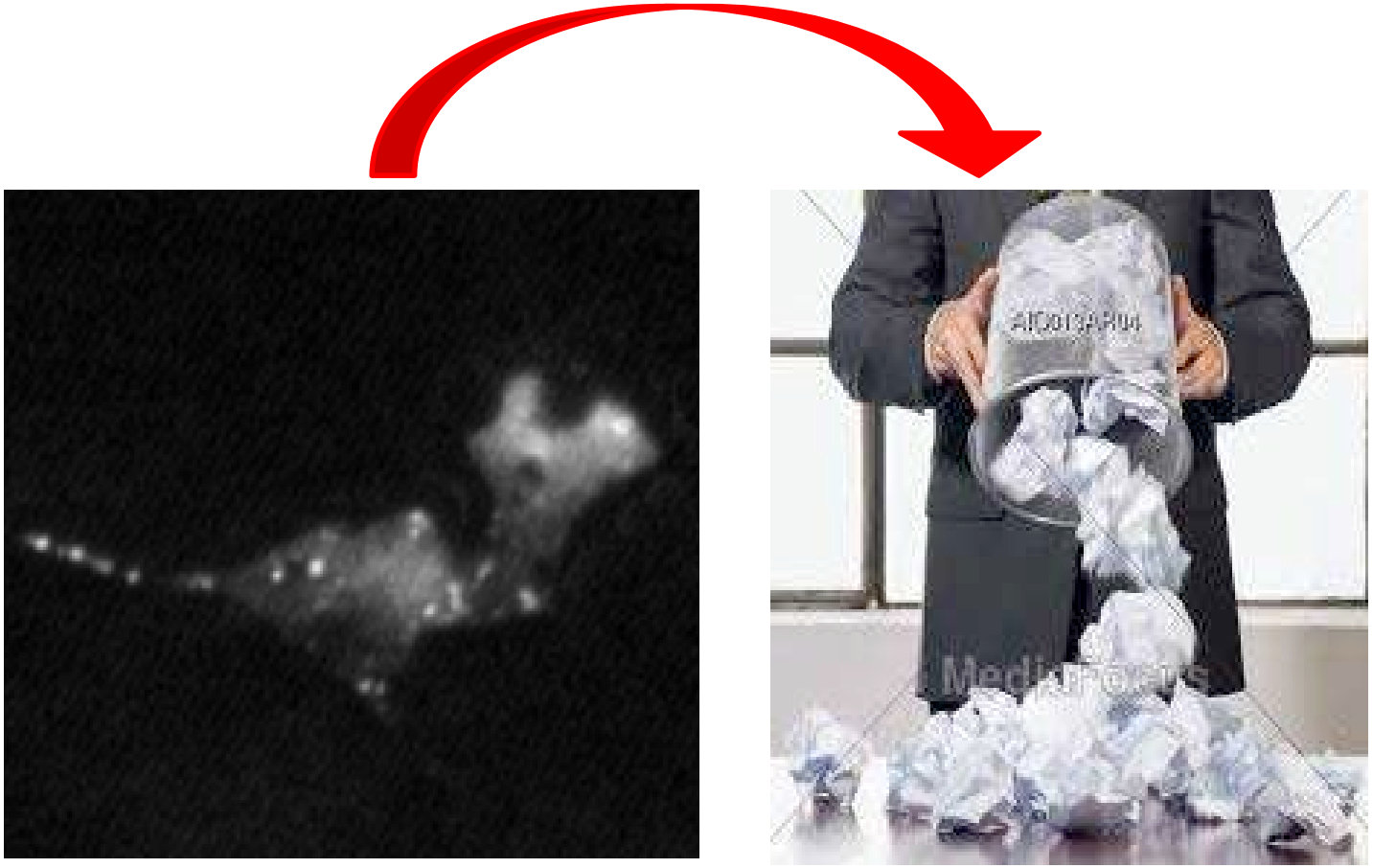
Mito-GFP

Exophers: a mechansim for dumping the trash?

Exopher production increases under Proteo-stress

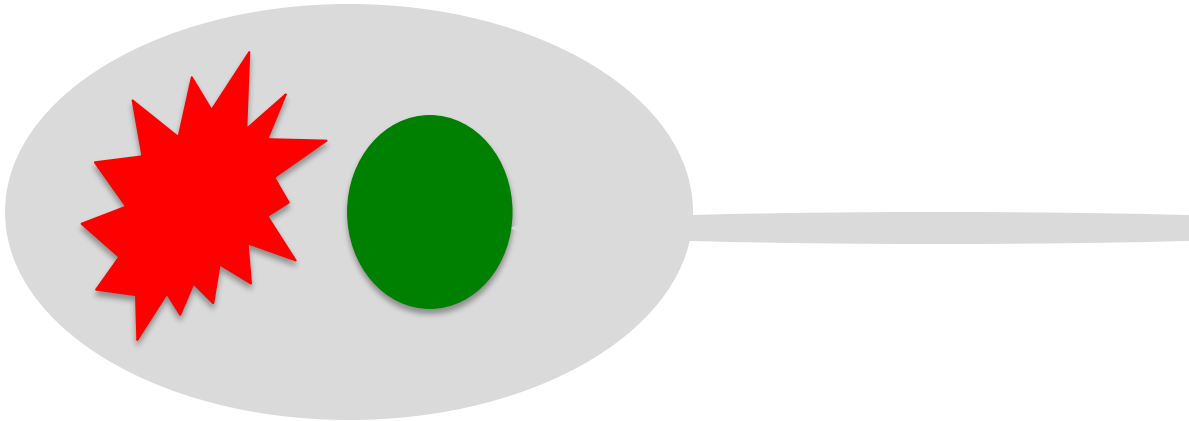


Neurons can eliminate protein aggregates and mitochondria by a dramatic extrusion mechanism



Compromising proteostasis components increases exophers

Is the mechanism selective for compromised proteins?

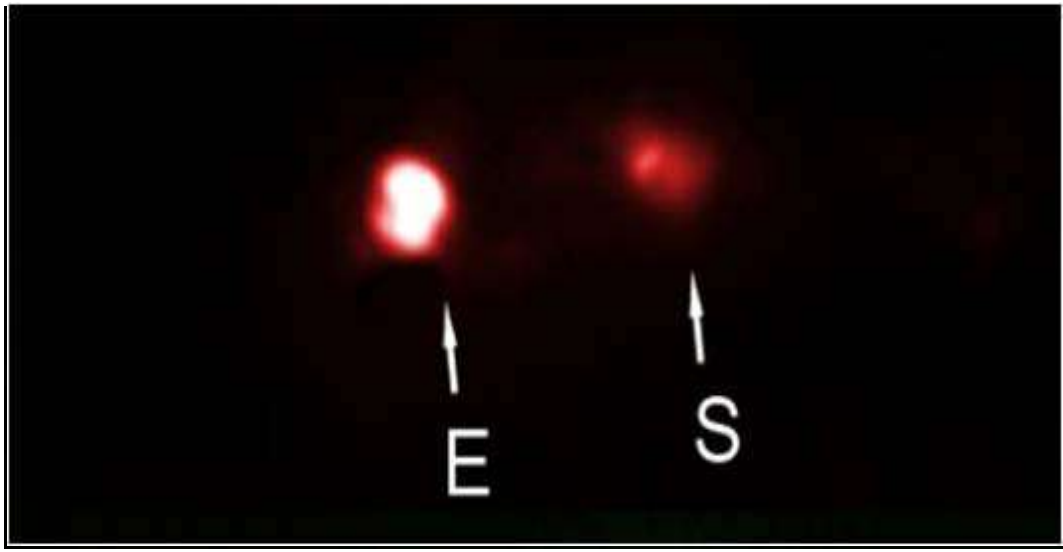


Exophers selectively include aggregates

Double label strain

mCherry (aggregating)

GFP (non-aggregating)

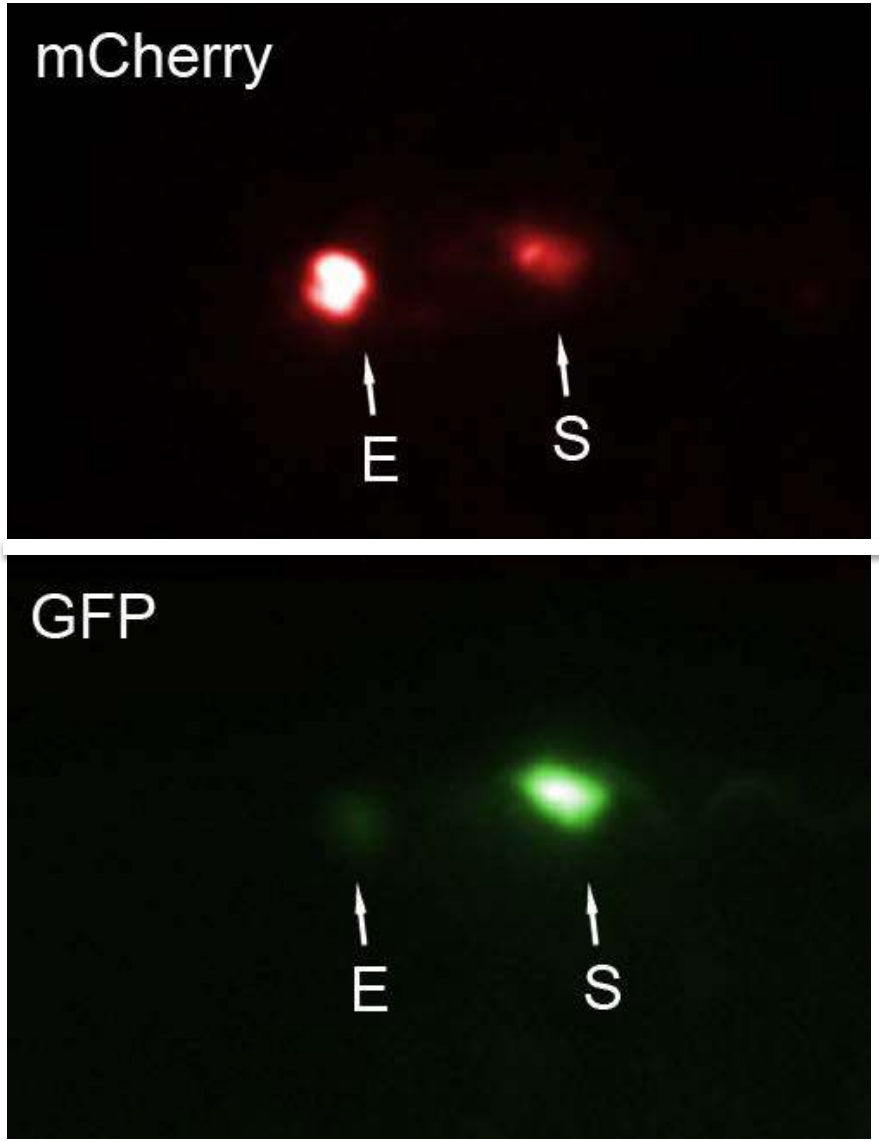


Exophers *preferentially* include aggregates

Double label strain

mCherry (aggregating)

GFP (non-aggregating)

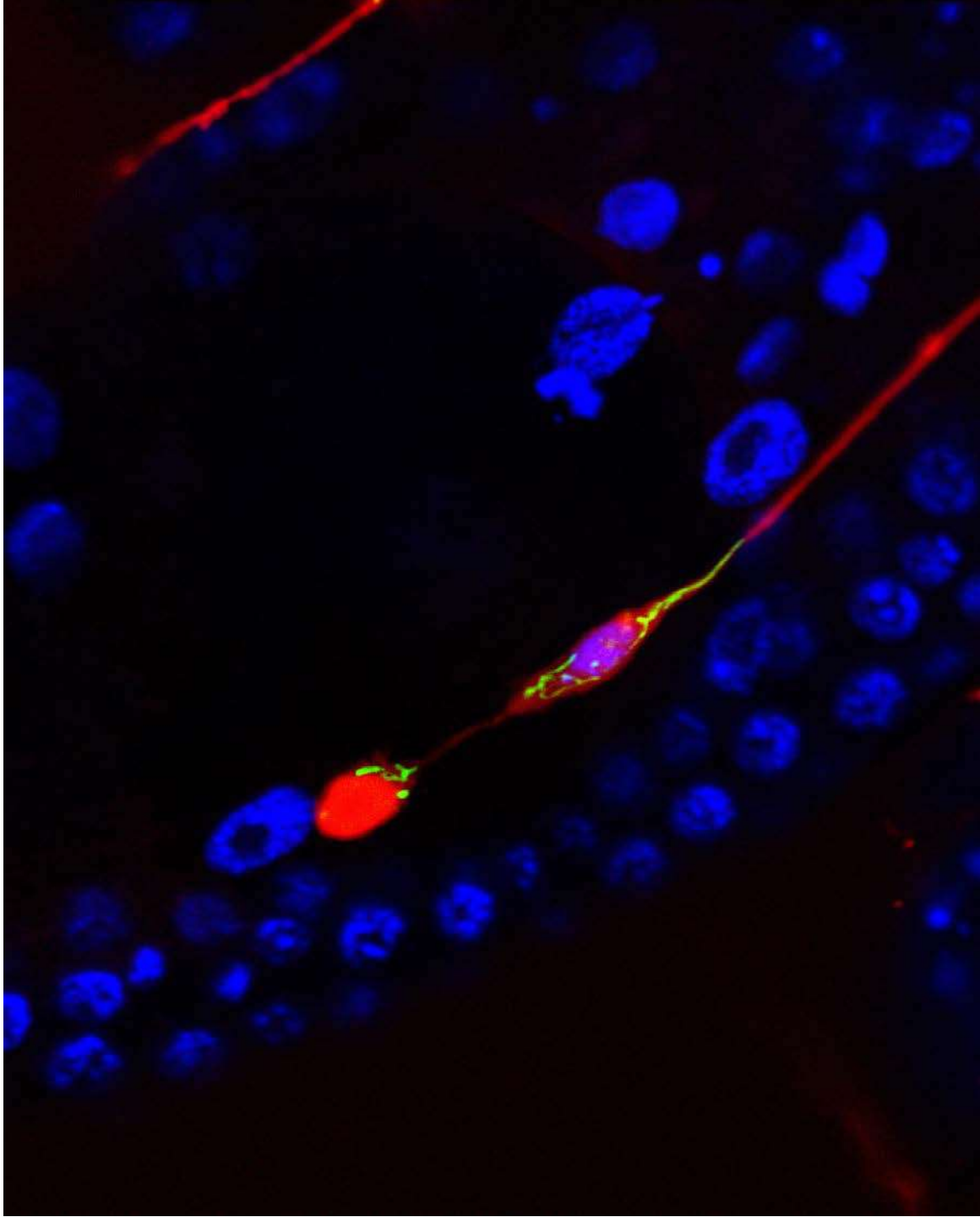


Trash is sorted away from good functional proteins and orga

Multiple types of garbage go into the same trash bag

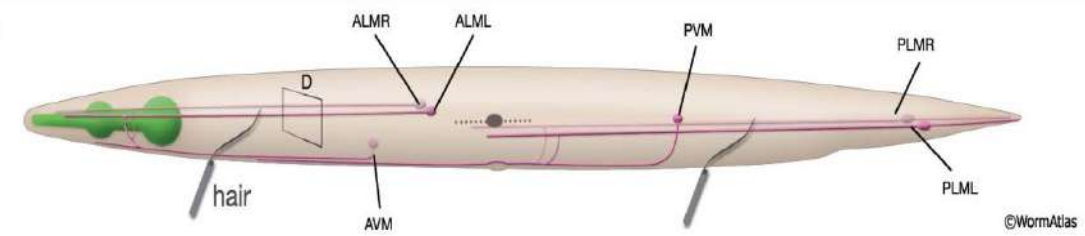
mitochondria

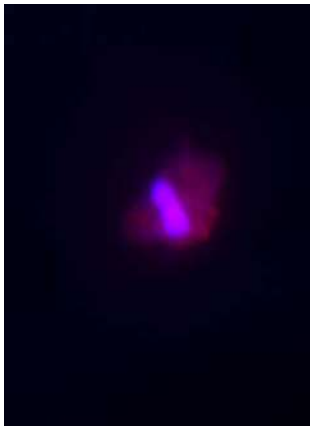
mCherry



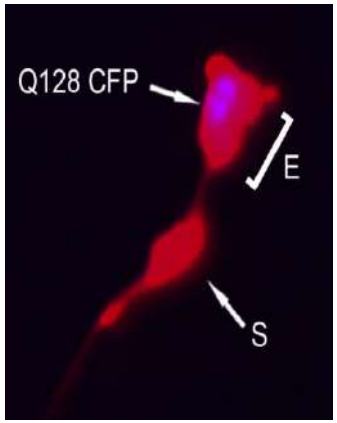
Not clearing out trash can impair functionality

Exophers appear to be neuroprotective to neurons expressing Q128

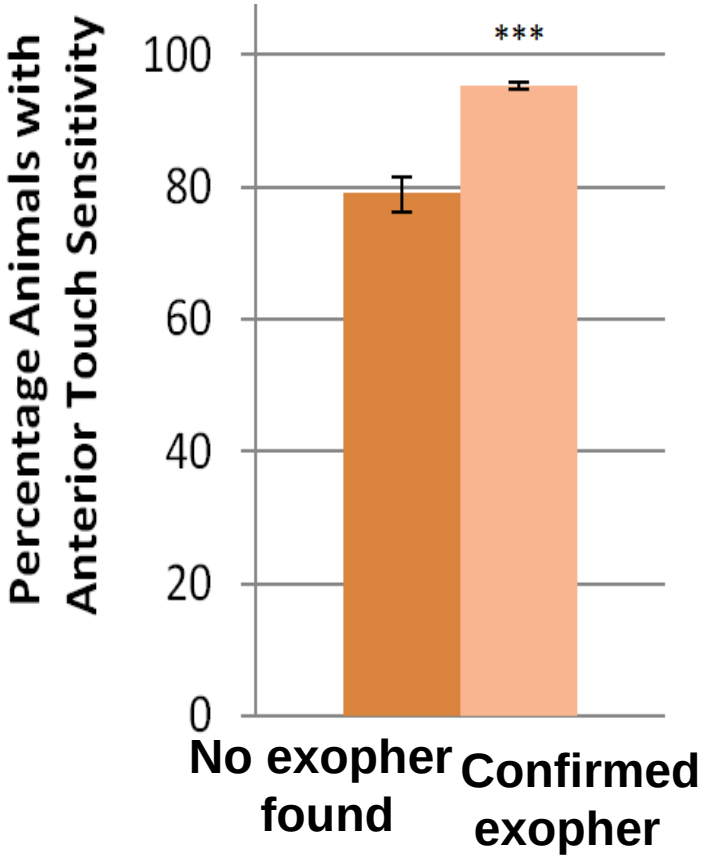




VS

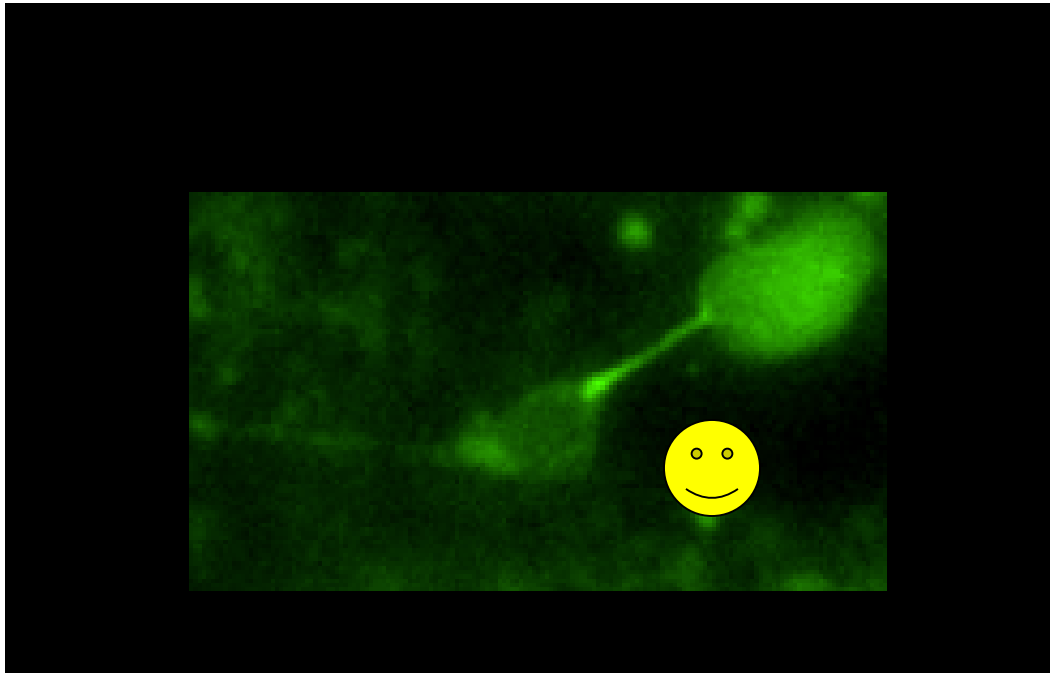


Q128 animals with an early exopher had better maintained touch sensitivity

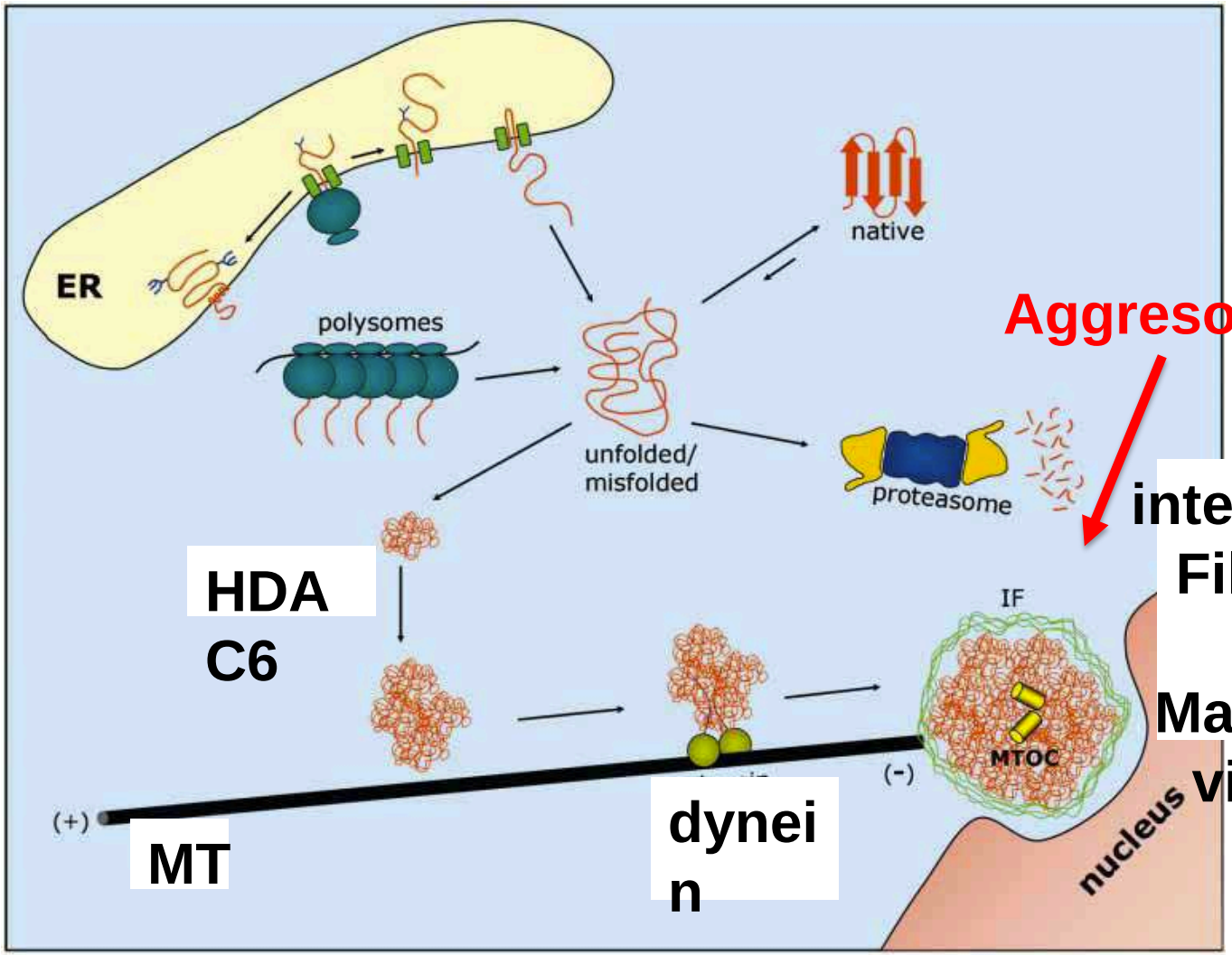


N=100

Exopher production is good for neuronal function



An aggresome-related mechanism may help organize exopher trash



Garcia-Mata, Traffic 2002 3:338

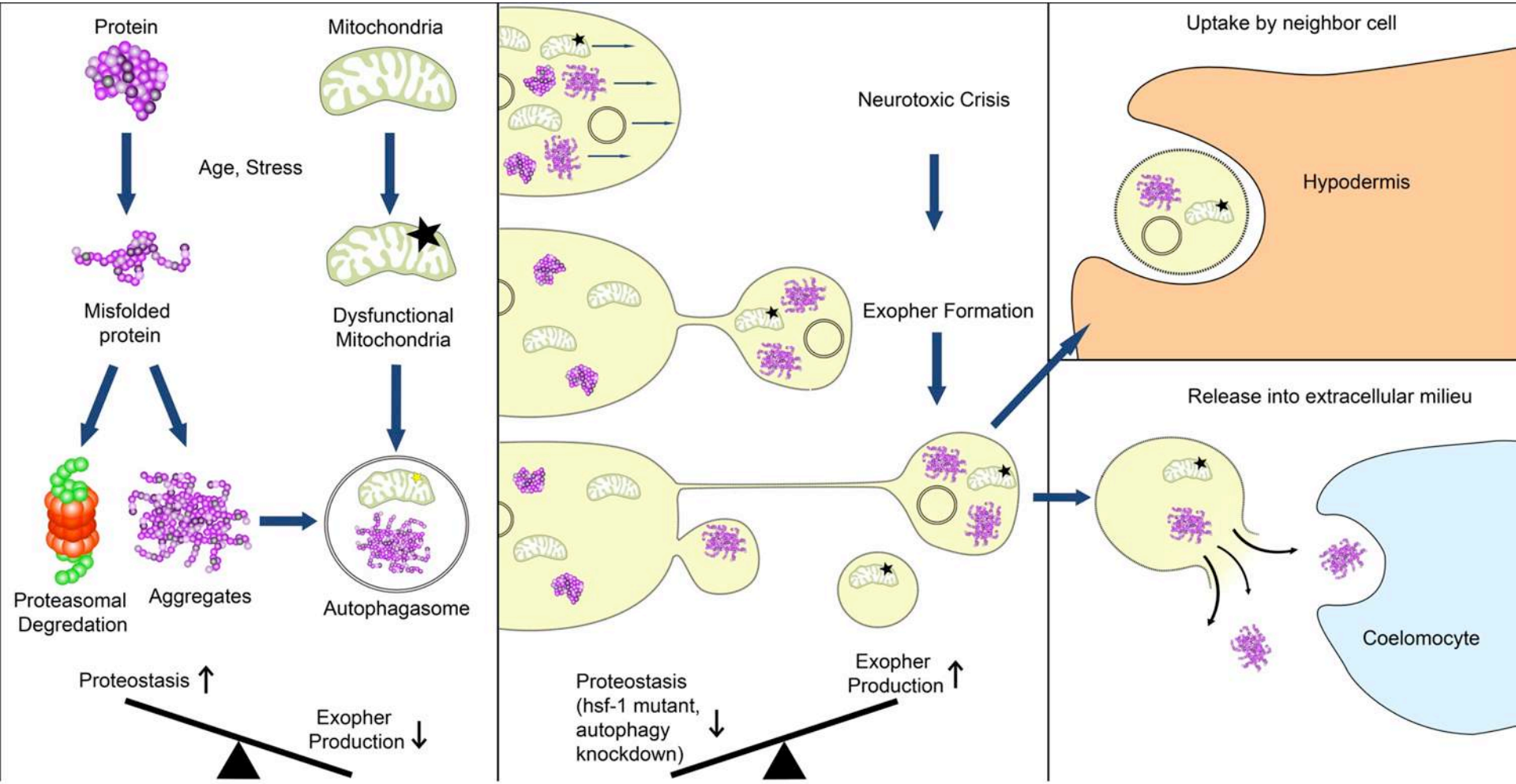
External garbage removal

Neuron

surrounding hypodermis
glia-like

coelomocytes

A C. elegans neuronal extrusion mechanism



proteostasis is critical for neuronal health

inside

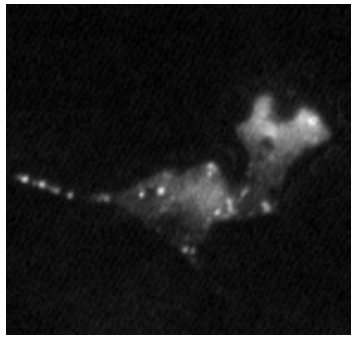
chaperones and folding quality control

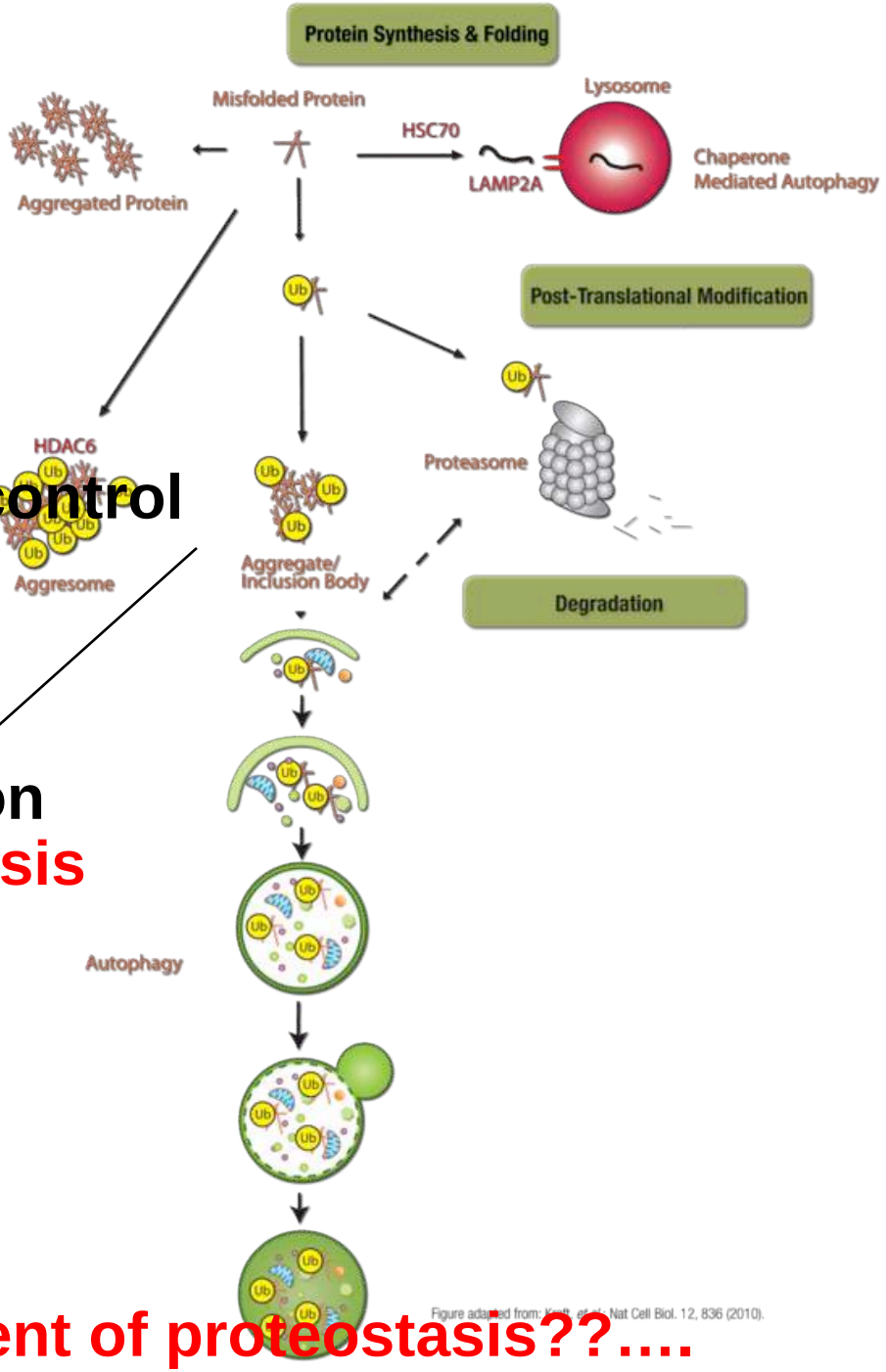
proteasome degradation

autophagy/lysosomal degradation

outside

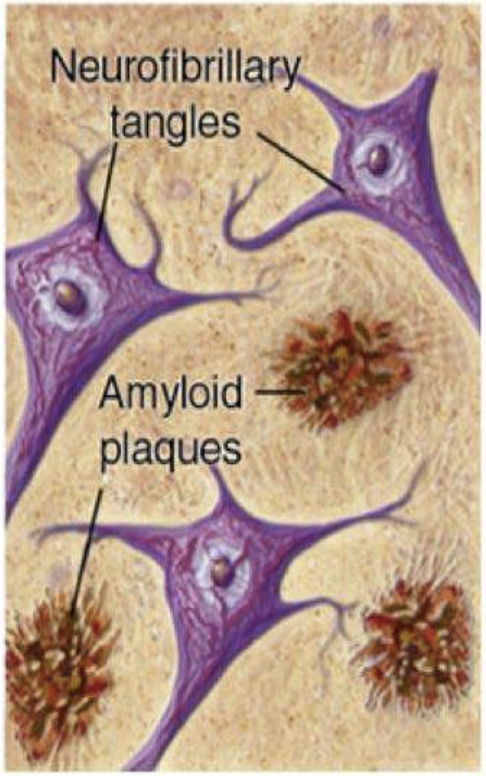
Exopher-genesis



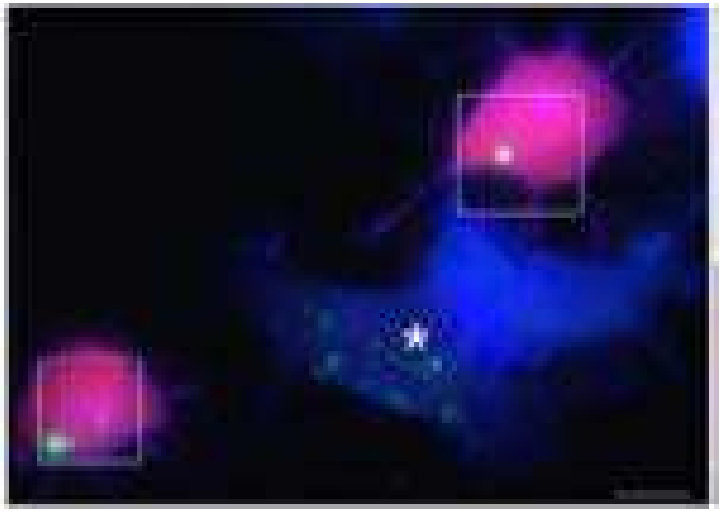


a novel but conserved component of proteostasis??….

Human neurodegenerative disease protein aggregates can be transferred between cells



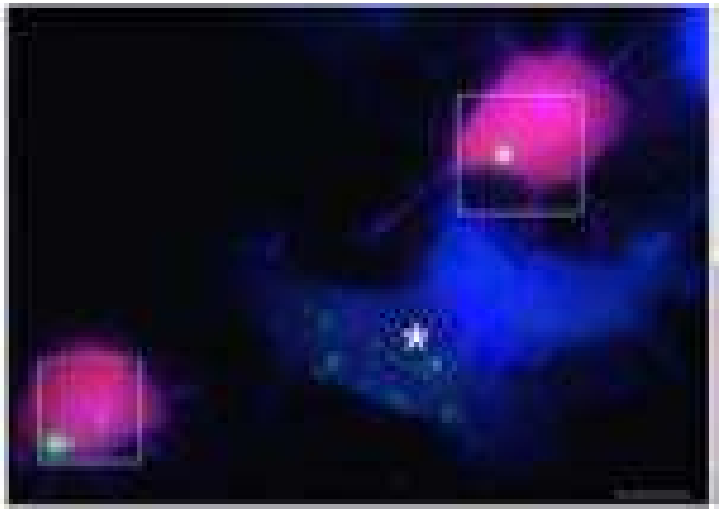
- Alzheimer's
- Parkinson's
- Huntington's
- ALS
- Prion disease

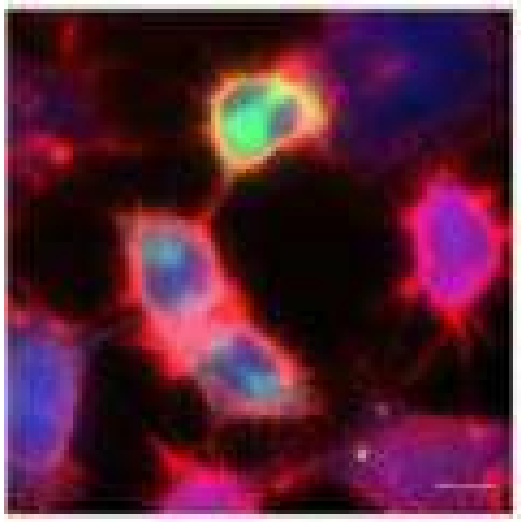


Costansa et al., J Cell Sci. 2013 126:3678-85.

Novel ideas about disease pathogenesis, new target for therapy, from the worm…

A hot topic in neurodegenerative disease is the spread of disease proteins/aggregates between neurons via some extrusion mechanism,





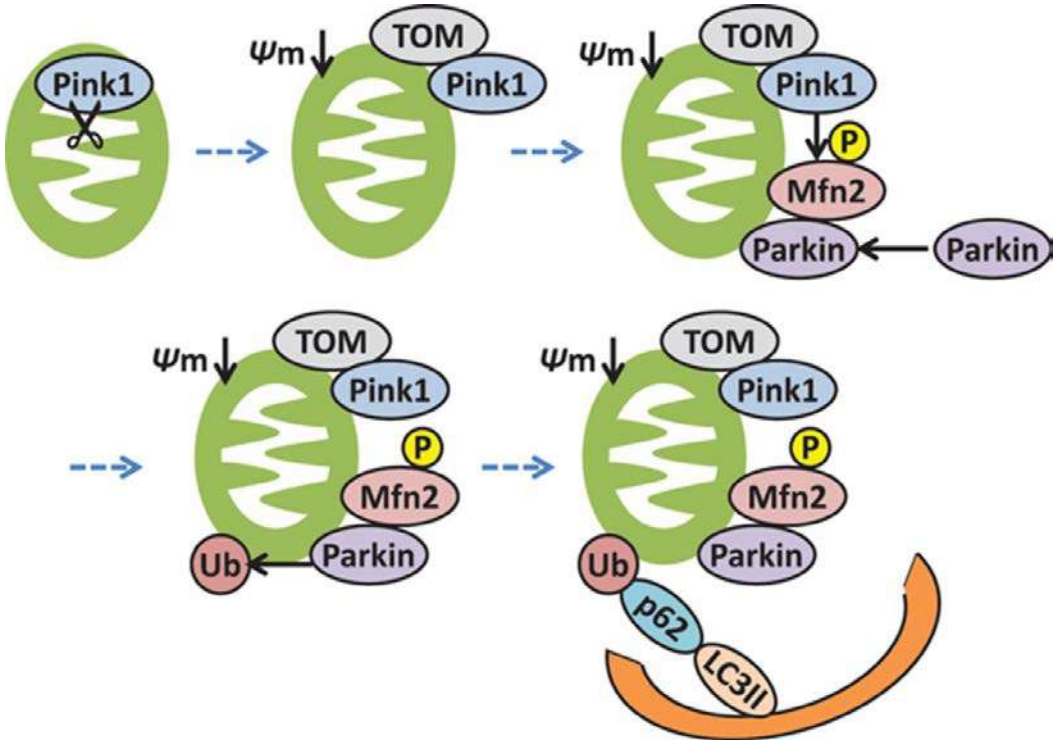
Costansa et al., J Cell Sci. 2013 126:3678-85.

postulated to contribute to disease progression and spread

Does exopher biology represent the homologous process/mechanism?

mitophagy is critical for neuronal health

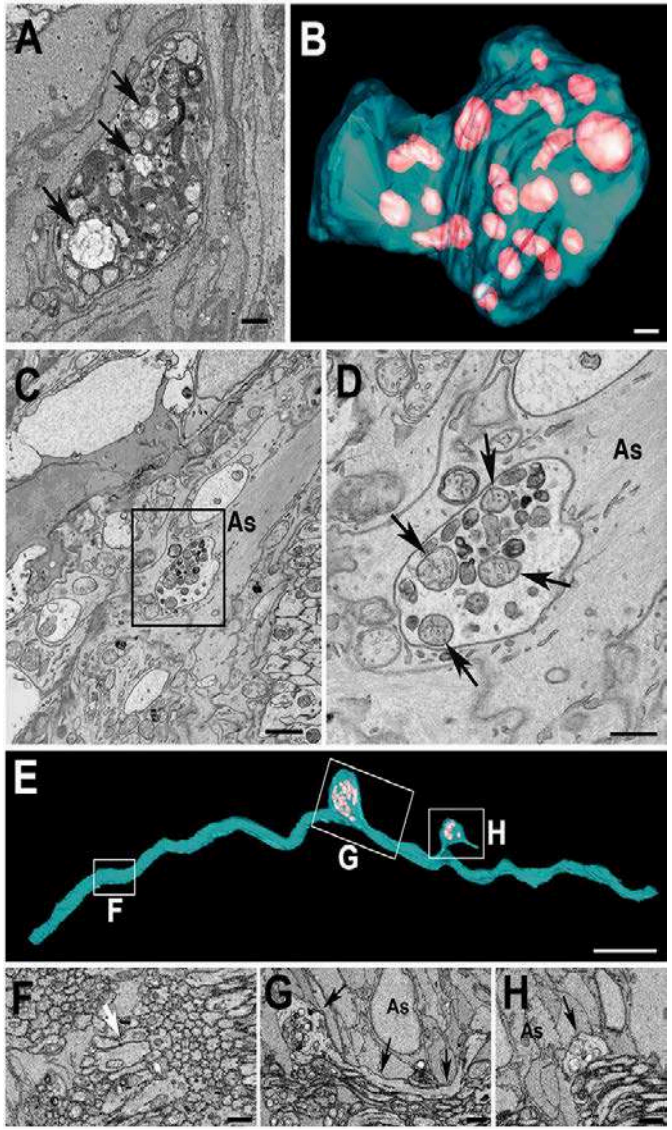
inside



outside

We postulate a novel but conserved component of mito-stasis

Mouse neurons can transfer mitochondria



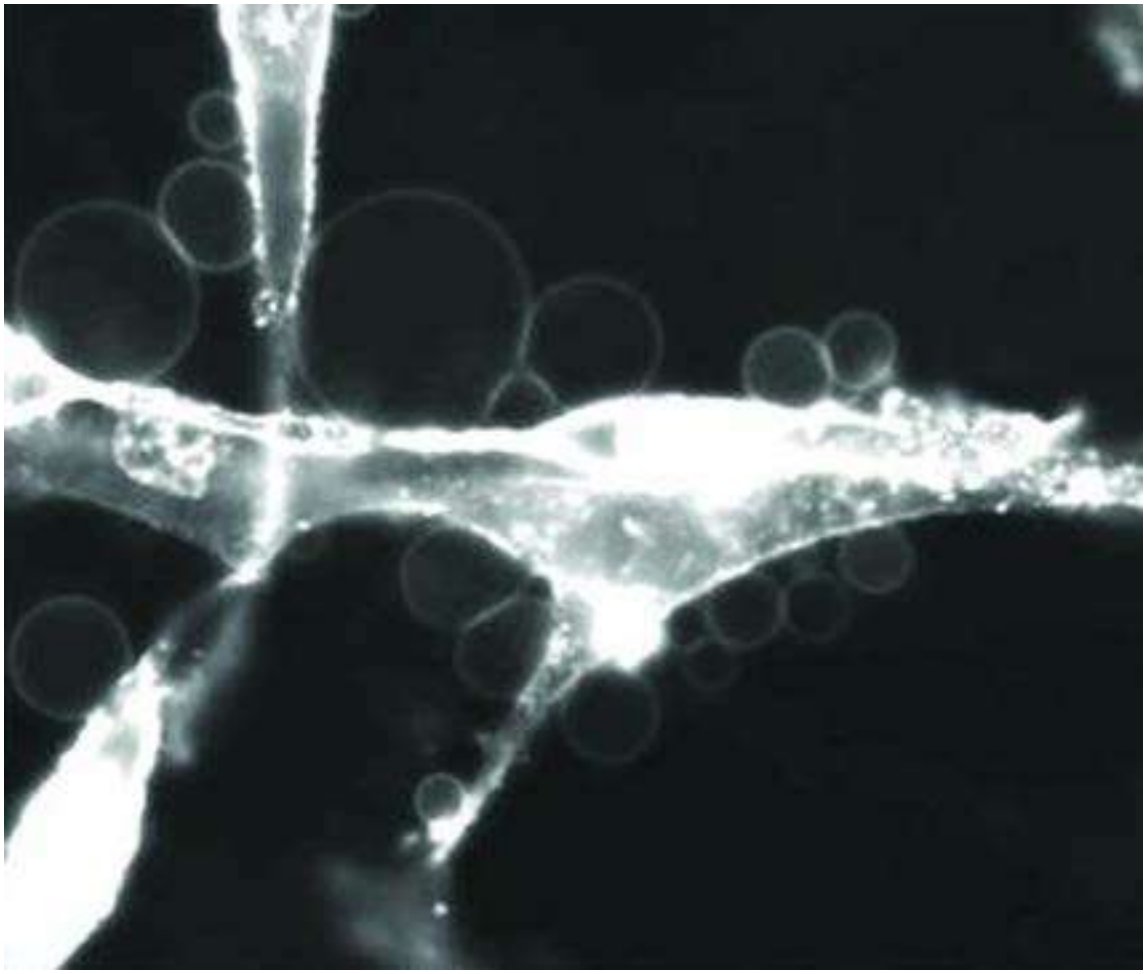
-retinal ganglion cell mitos to astrocyte neighbors

-also in superficial layers of the cerebral cortex

Davis, C.H., et al. Transcellular degra
axonal mitochondria. (Marsh-Armstr
Proc Natl Acad Sci U S A 111, 9633-9

are exopher-like processes involved?

Oncosomes: large vesicles from cultured tumor cells

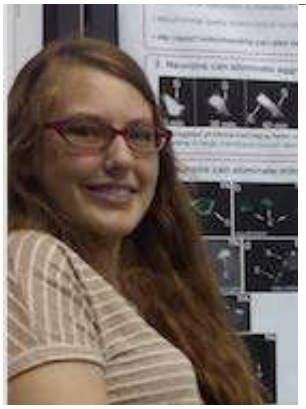


Transfer of materials….but maybe detox mechanism..

Thanks to the exopher team

Ilija Melentijevic

Meghan Arnold



Joelle Smart

Ryan Guasp

Girish Harinath

Marton Toth

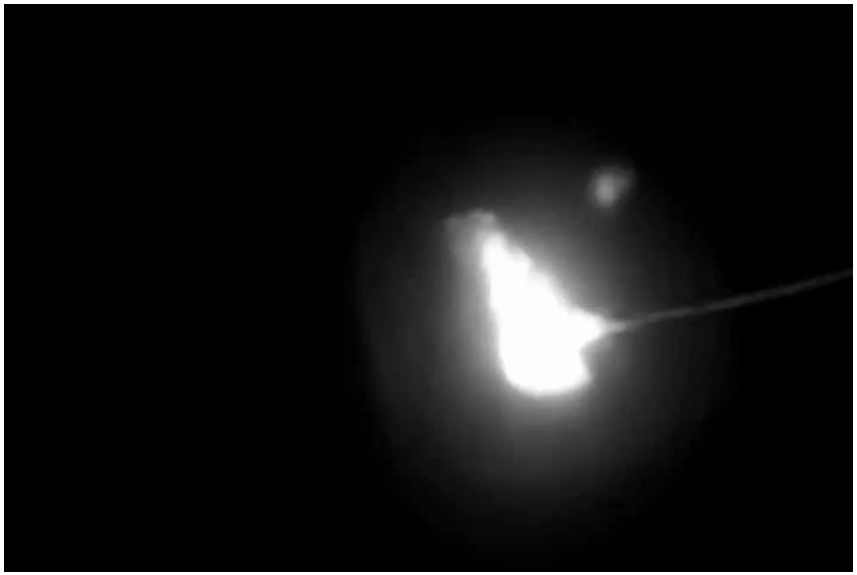
Mark Abbott

Barth Grant

Funding

National Institute of Neurological Disorders and Stroke

NIH National Institute on Aging



<u>Undergrads</u>

Wai-Kit Chia

Sanjna Patel

Helen Ushakov

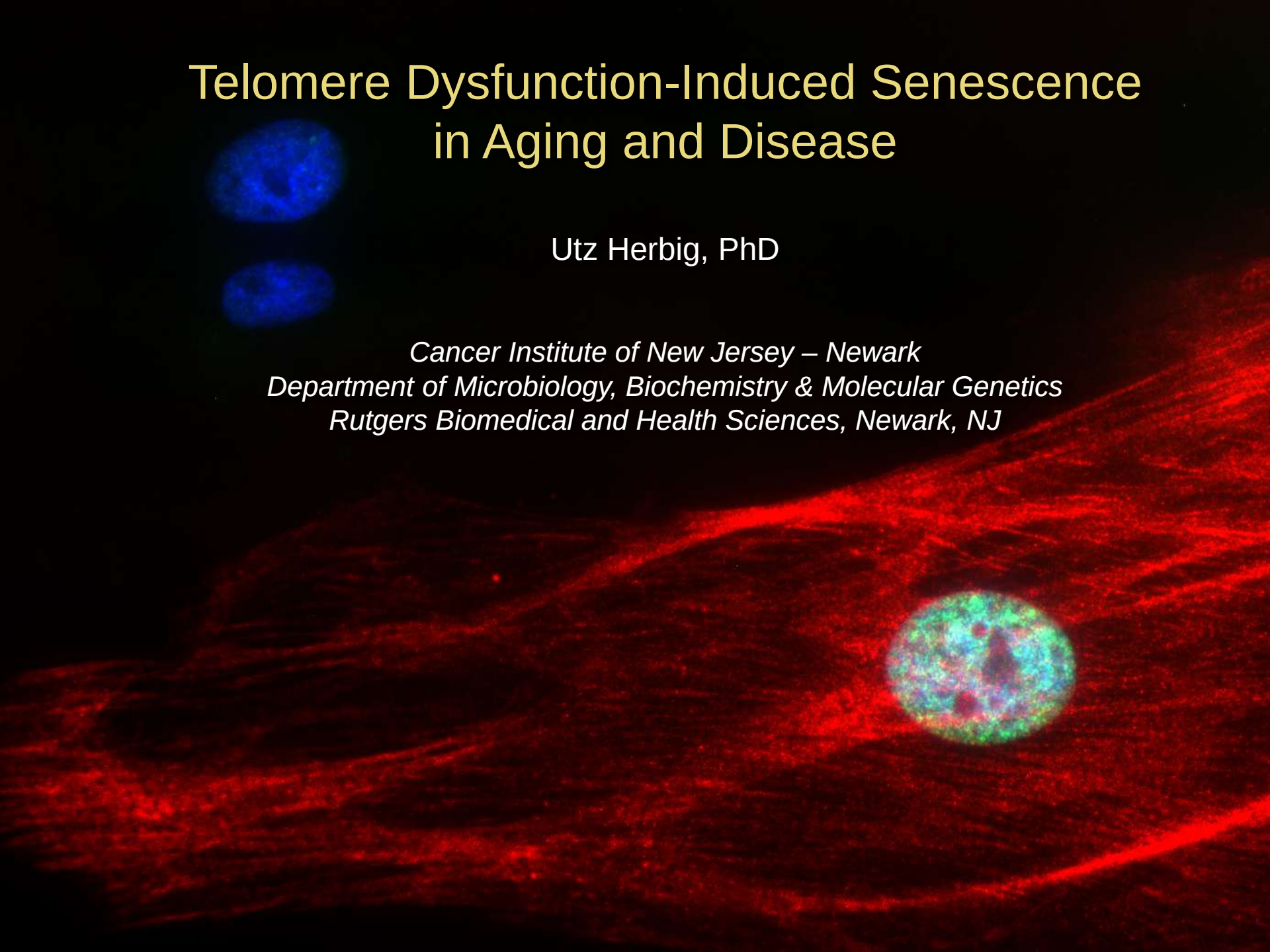
Jian Xu

Heather Theiringer

Telomere Dysfunction-Induced Senescence in Aging and Disease

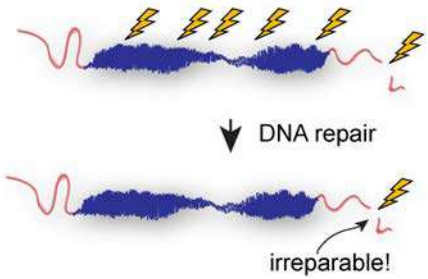
Utz Herbig, PhD

Cancer Institute of New Jersey – Newark
Department of Microbiology, Biochemistry & Molecular Genetics
Rutgers Biomedical and Health Sciences, Newark, NJ



Cellular Senescence

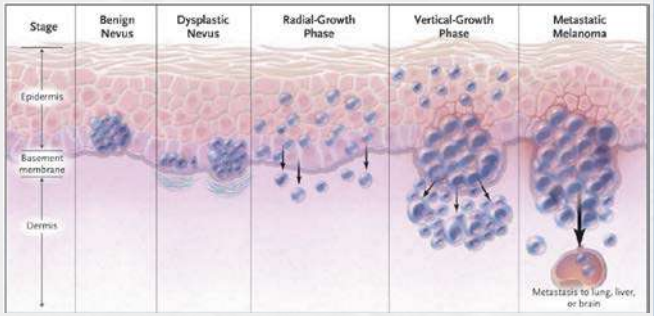
DNA Replication (Telomere Shortening)
Oncogenic Stress
DNA Damage
Oxidative Stress
Cytokines
Chromatin Changes
Developmental Cues
Mitochondrial Disturbances
Cell Reprograming
Cell-Cell Fusion



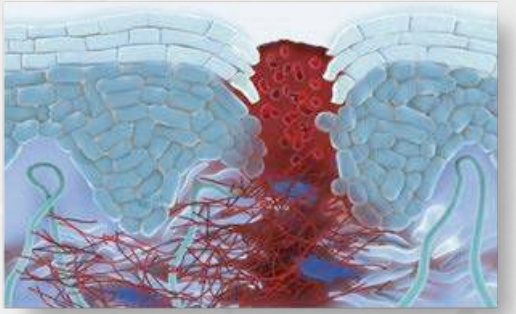
Human Diploid Fibroblasts

Biological Role of Cellular Senescence

Tumor Suppression
2005

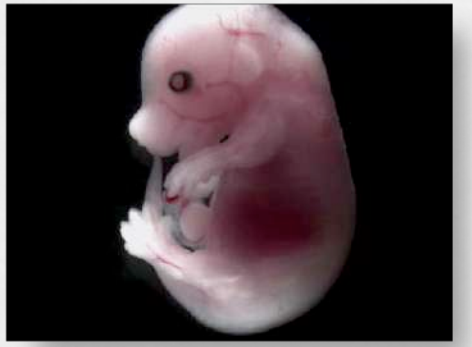


Wound Healing
2008



Aging
2011

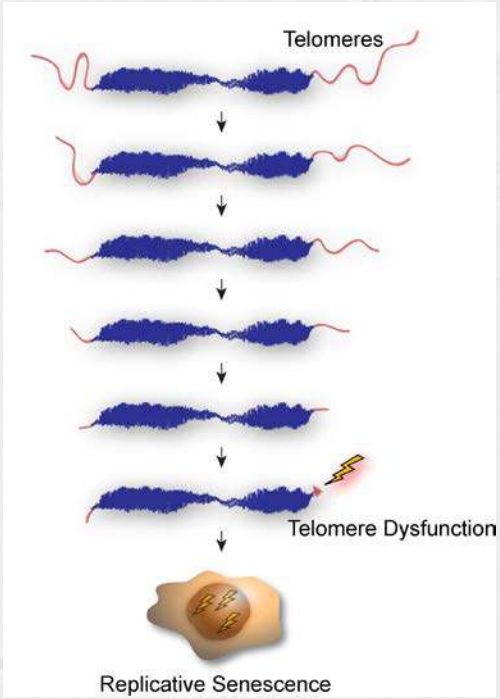
Embryonic Development
2013



Biological Role of Telomere Dysfunction-Induced Senescence - TDIS

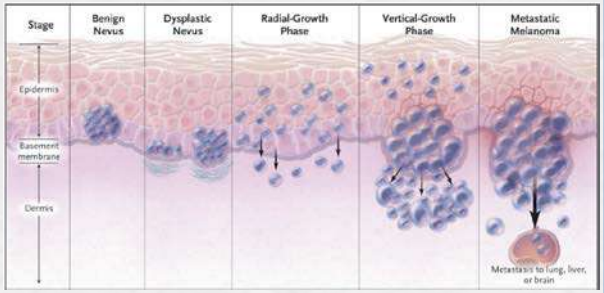
Aging

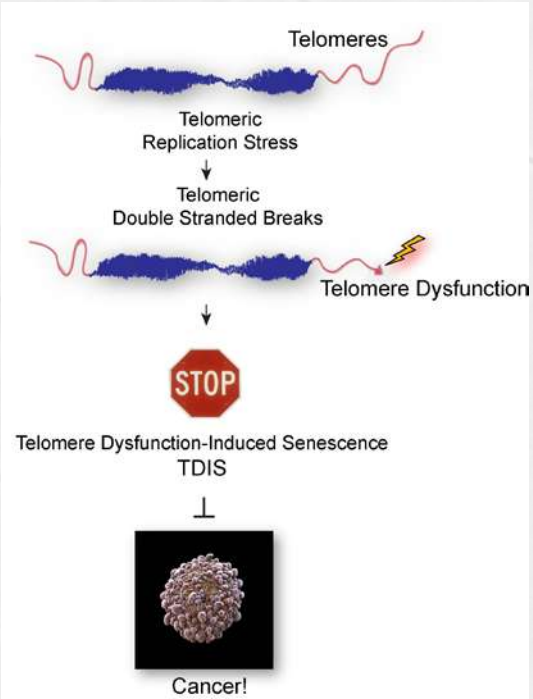
Herbig et al., 2006, Science



Tumor Suppression

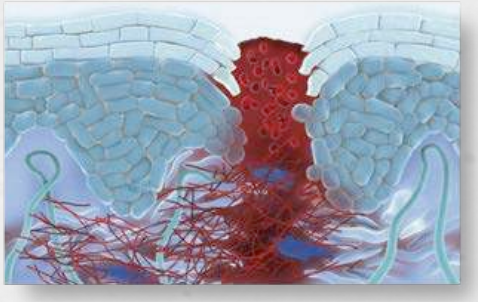
Suram et al., 2012, EMBO J

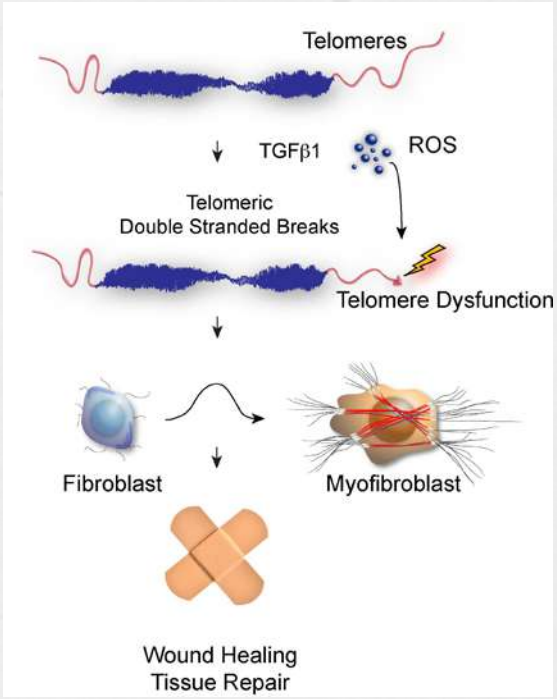




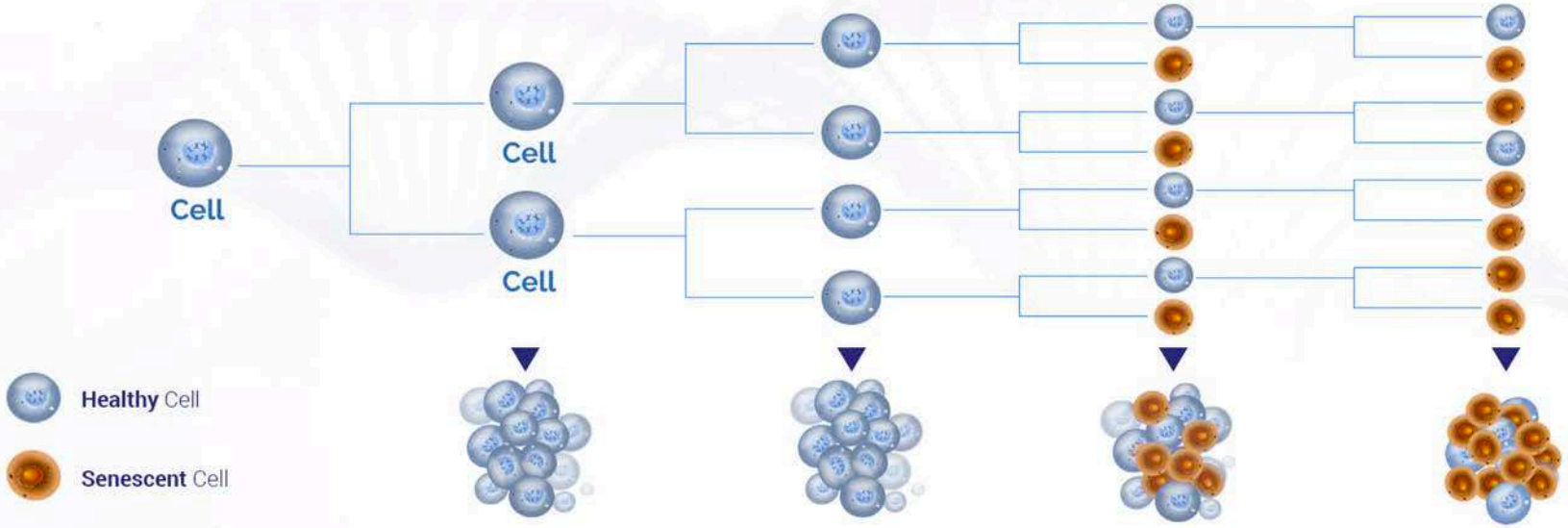
Wound Healing

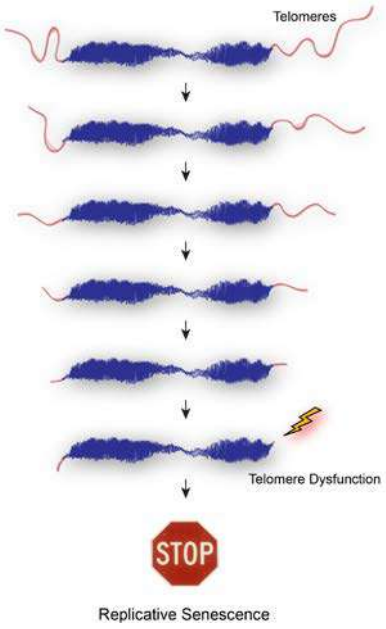
Razdan et al., 2018, Aging Cell

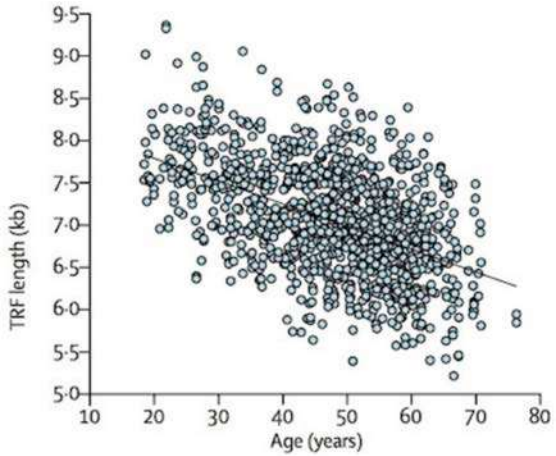




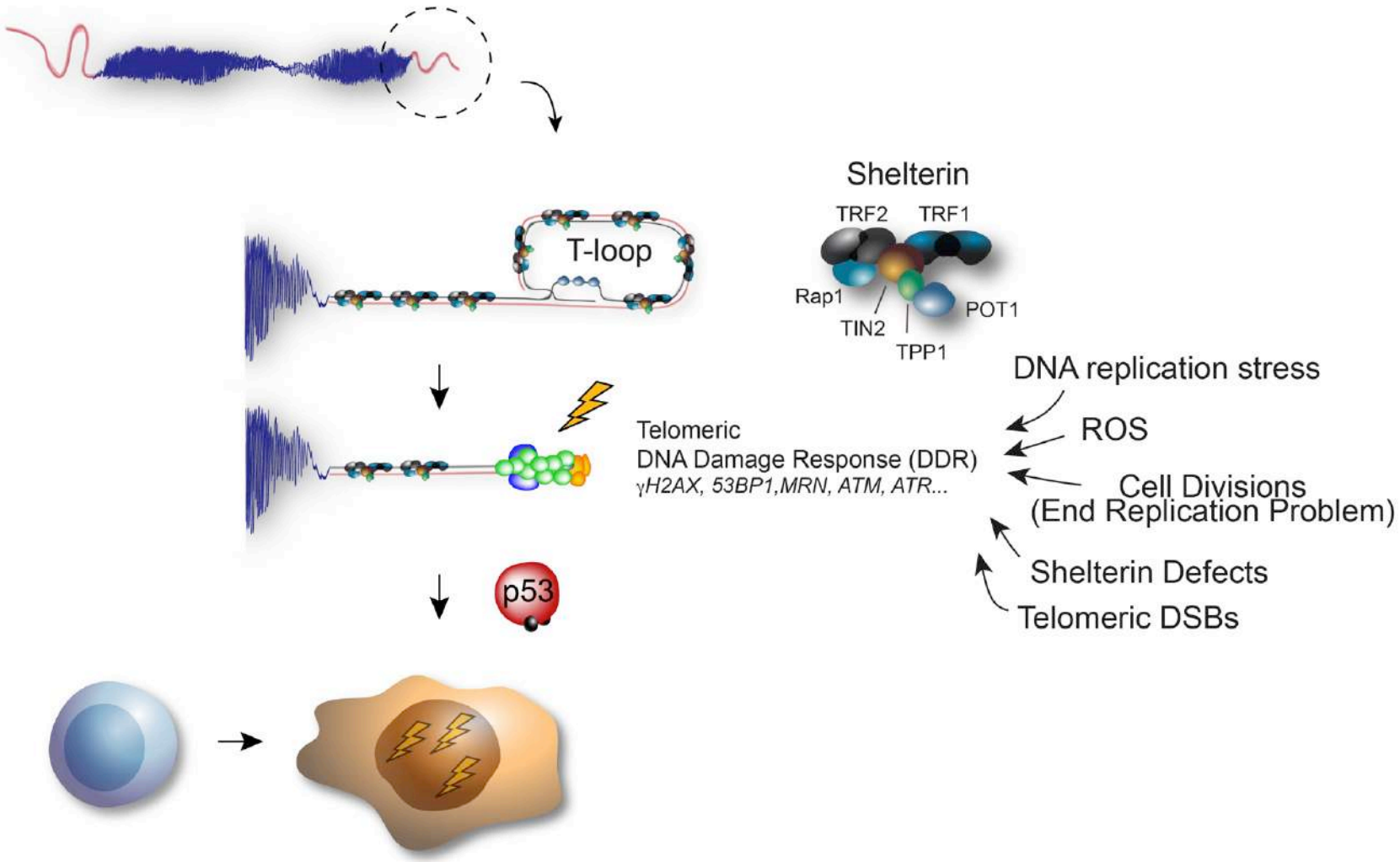
Cells Age and Undergo Replicative Senescence







Telomere Dysfunction-Induced Senescence

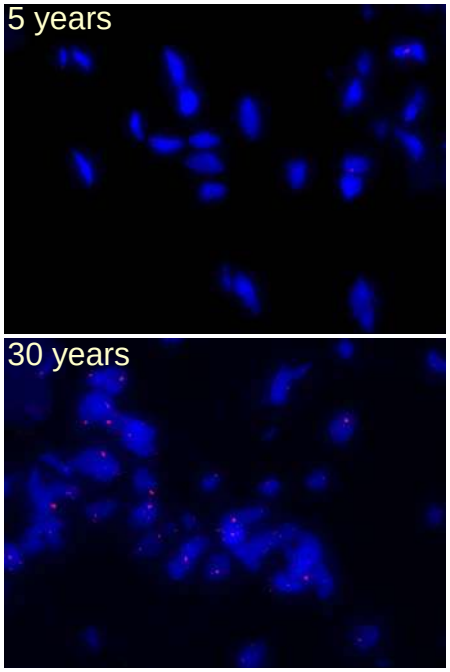


Telomere Dysfunction-Induced Senescence

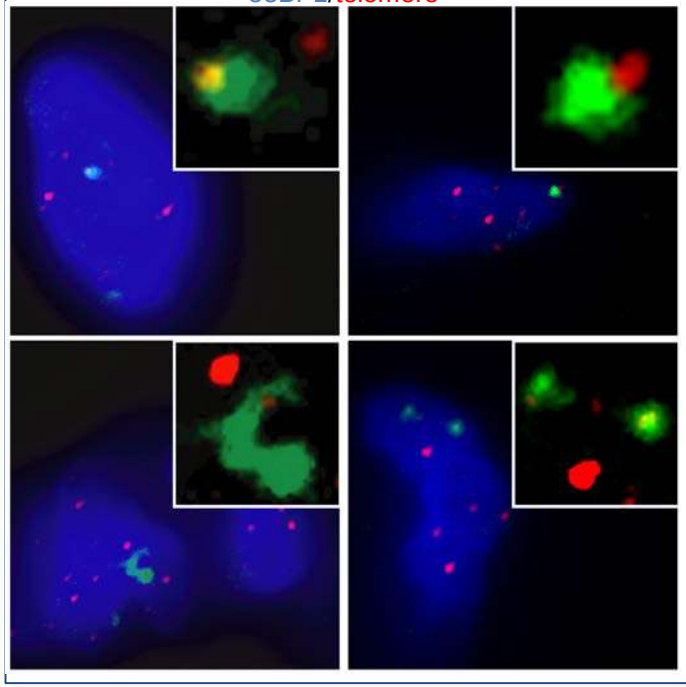
Telomere Dysfunction-Induced Senescence

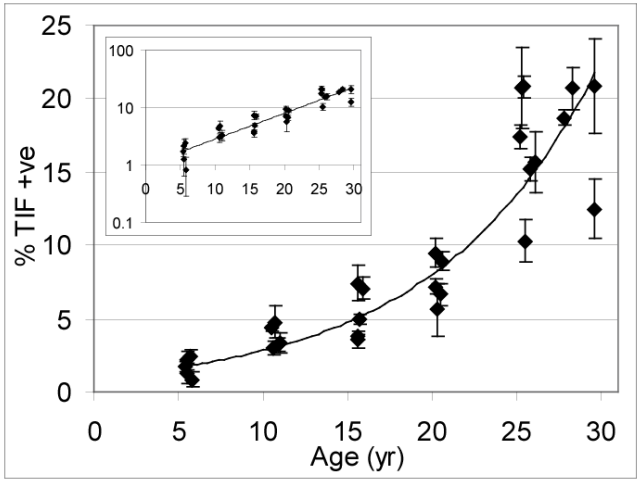
Fibroblasts
In
Dermal Tissue

53BP1/DAPI



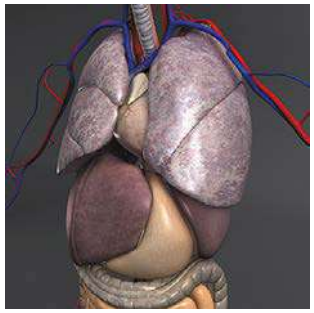
53BP1/telomere



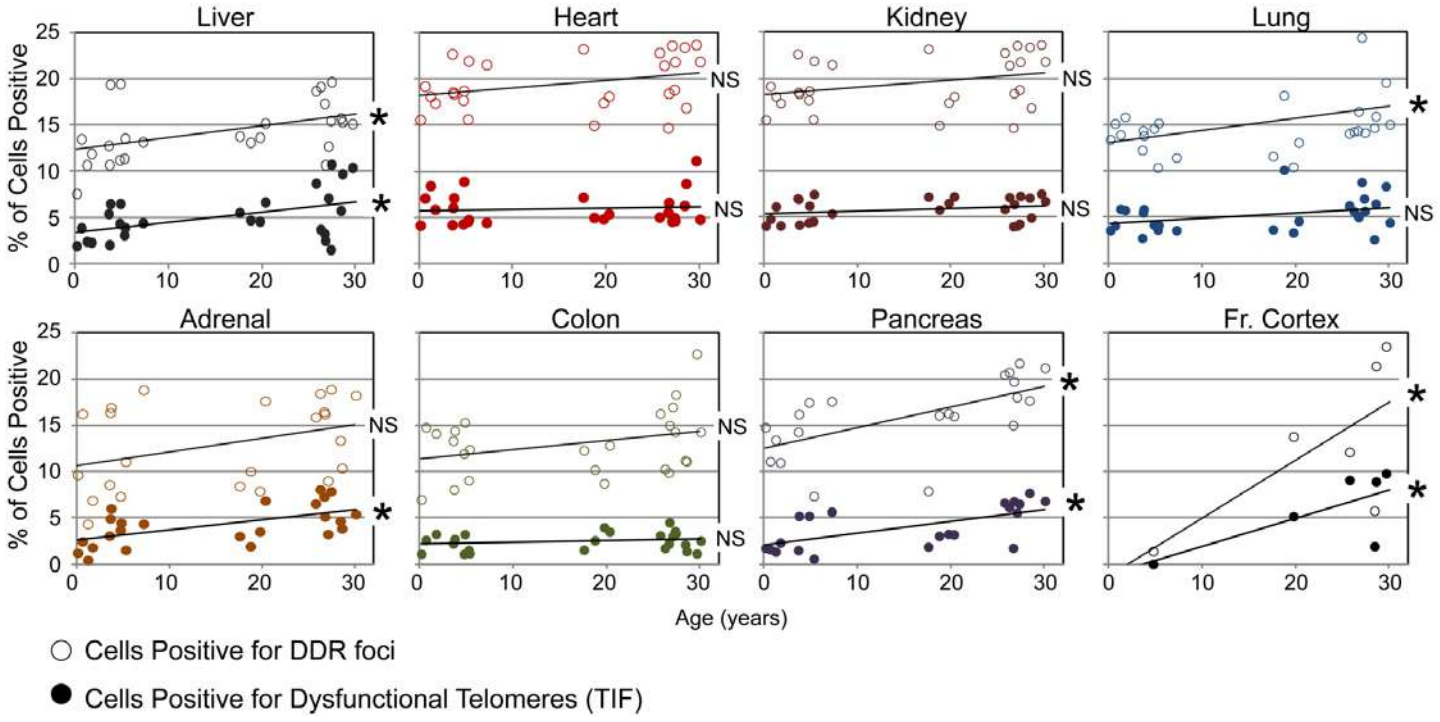


Herbig et al. Science (2006) 311:1257

Cells With Dysfunctional Telomeres Increase With Age

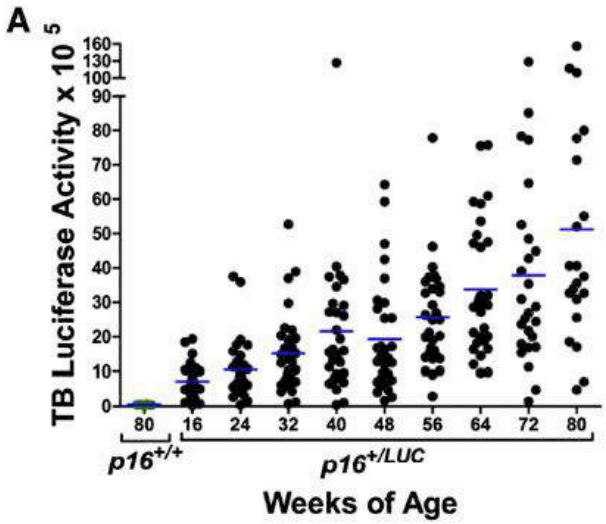


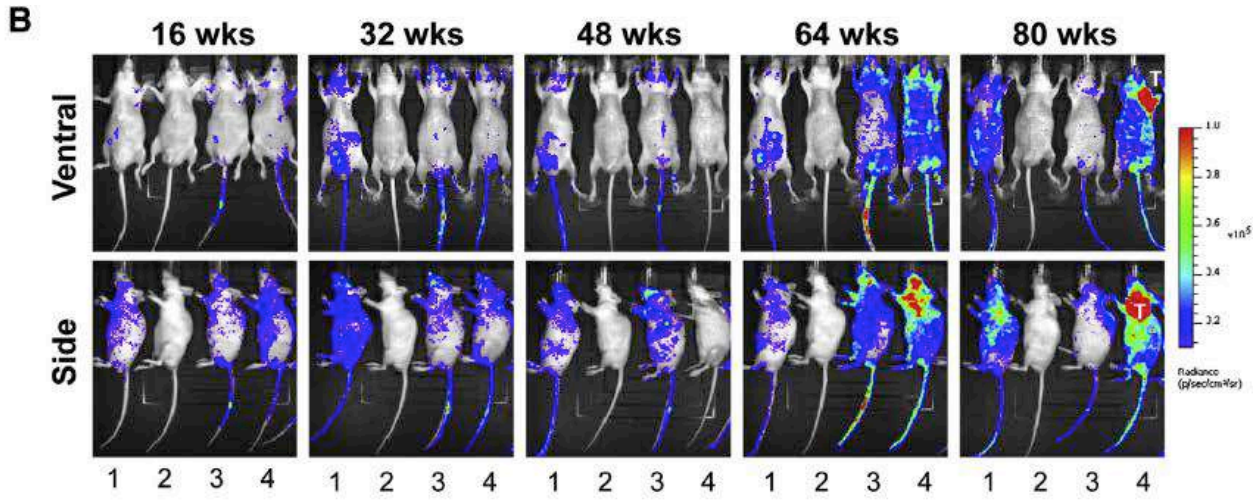
Skin (2-21%)
Liver (4-7%)
Heart
Kidney
Lung (fibroblasts,12-17%)
Adrenal Cortex (2-6%)
Colon (epithelium)
Pancreas (1-6%)
Brain (Frontal Cortex; 2-20%)



J. Kaplunov; unpublished

Mice Accumulate p16^{INK4a}-Senescent Cells With Advancing Age





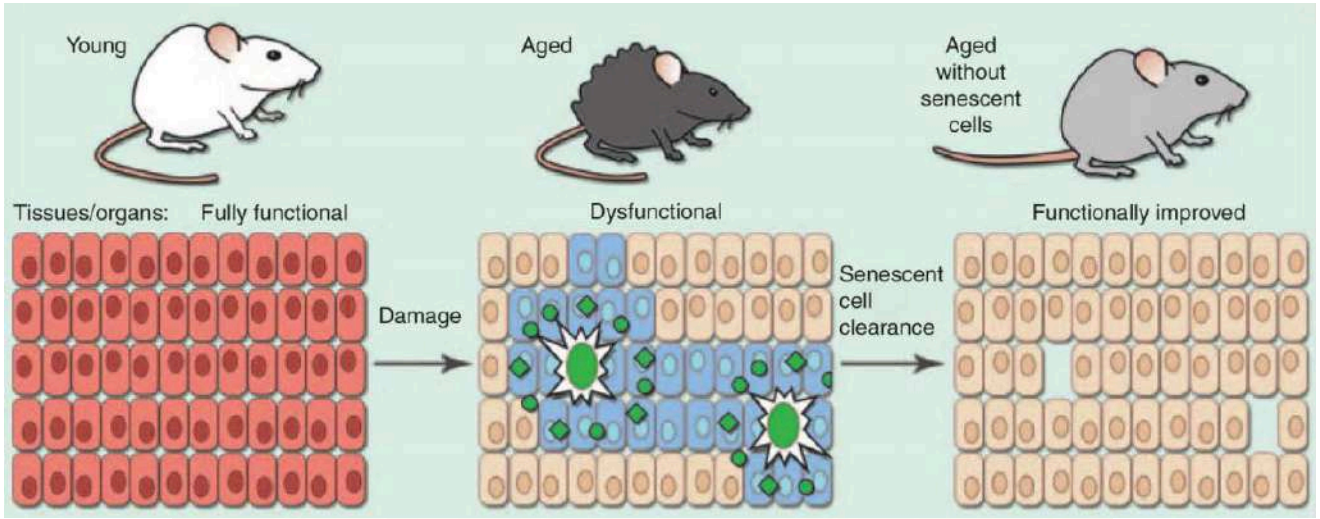
Burd et al., 2013. Cell 152: 340–351.

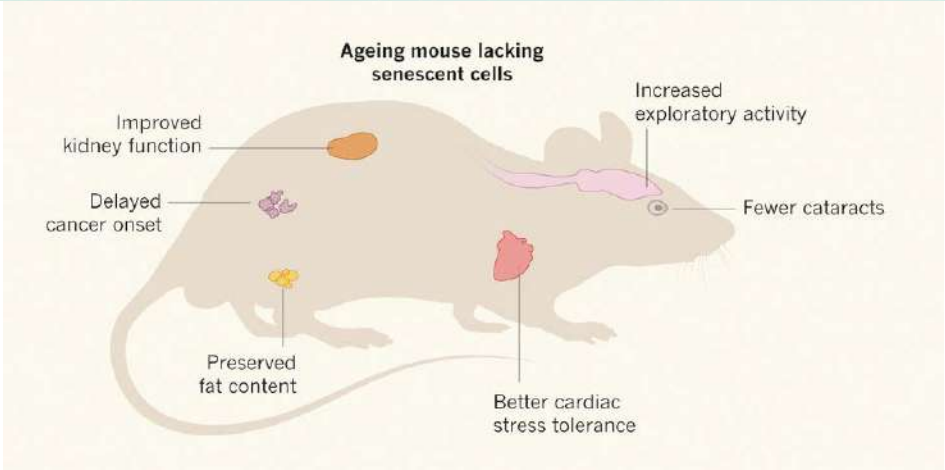
LETTER

doi:10.1038/nature10600

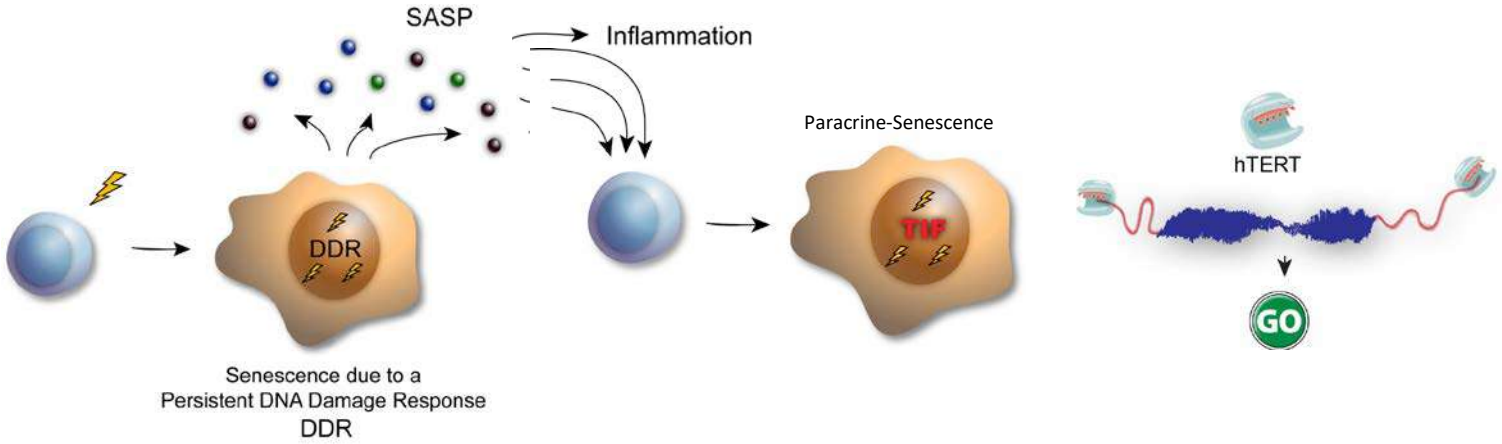
Clearance of p16^{Ink4a}–positive senescent cells delays ageing–associated disorders

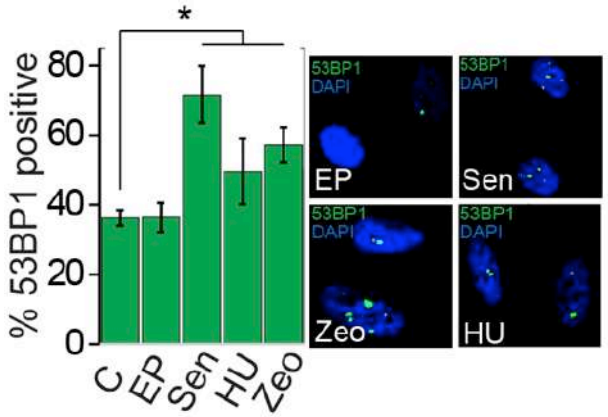
Darren J. Baker[1,2,3], Tobias Wijshake[1,4], Tamar Tchkonia[3], Nathan K. LeBrasseur[3,5], Bennett G. Childs[1], Bart van de Sluis[4], James L. Kirkland[3] & Jan M. van Deursen[1,2,3]

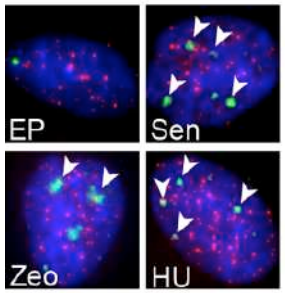


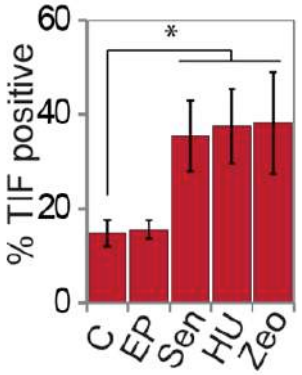


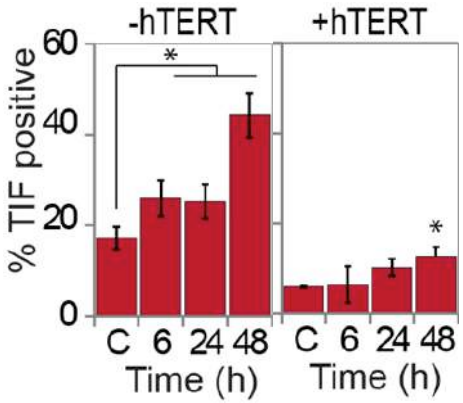
Senescence Associated Secretory Phenotype (SASP) Causes Telomere Dysfunction





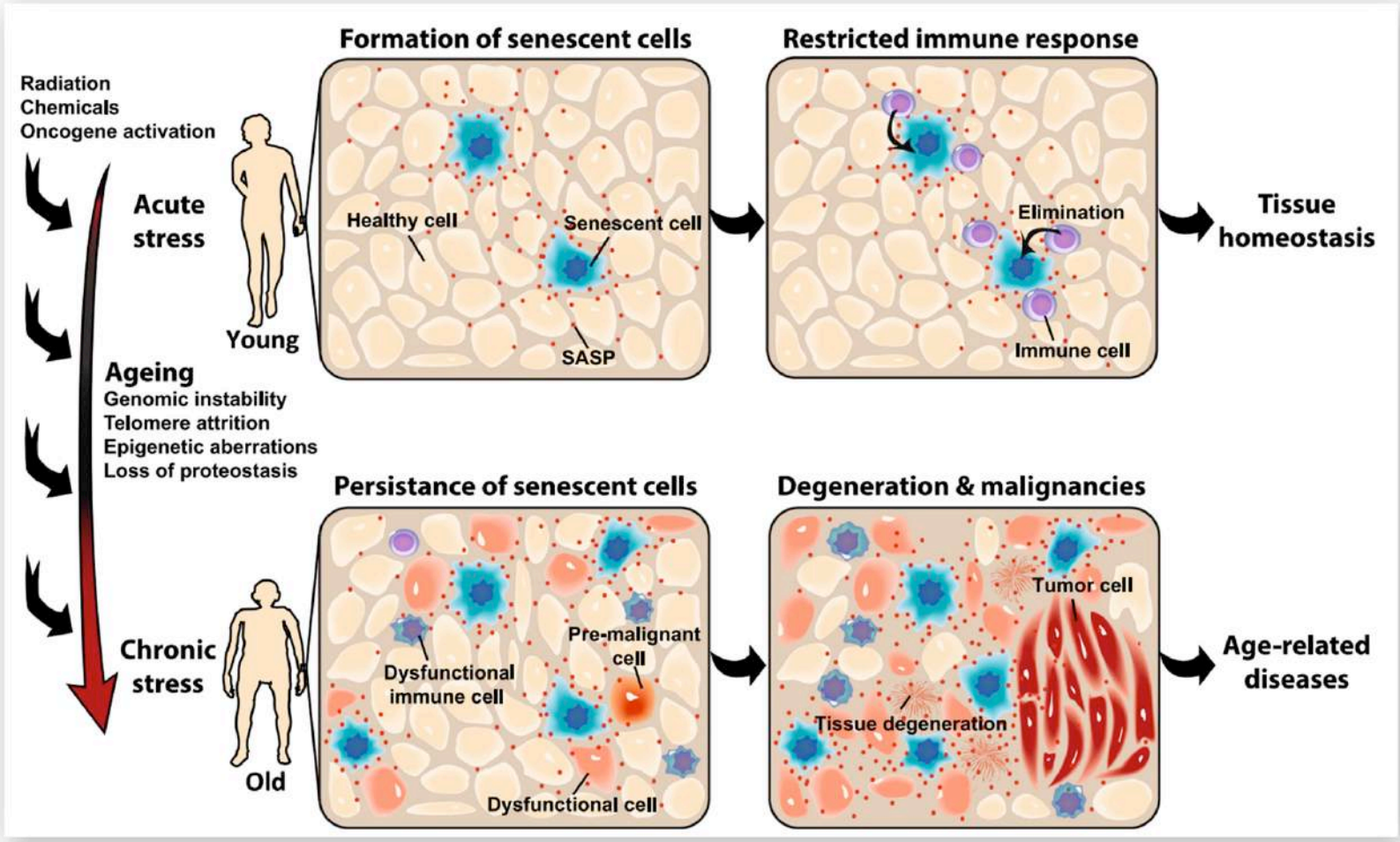






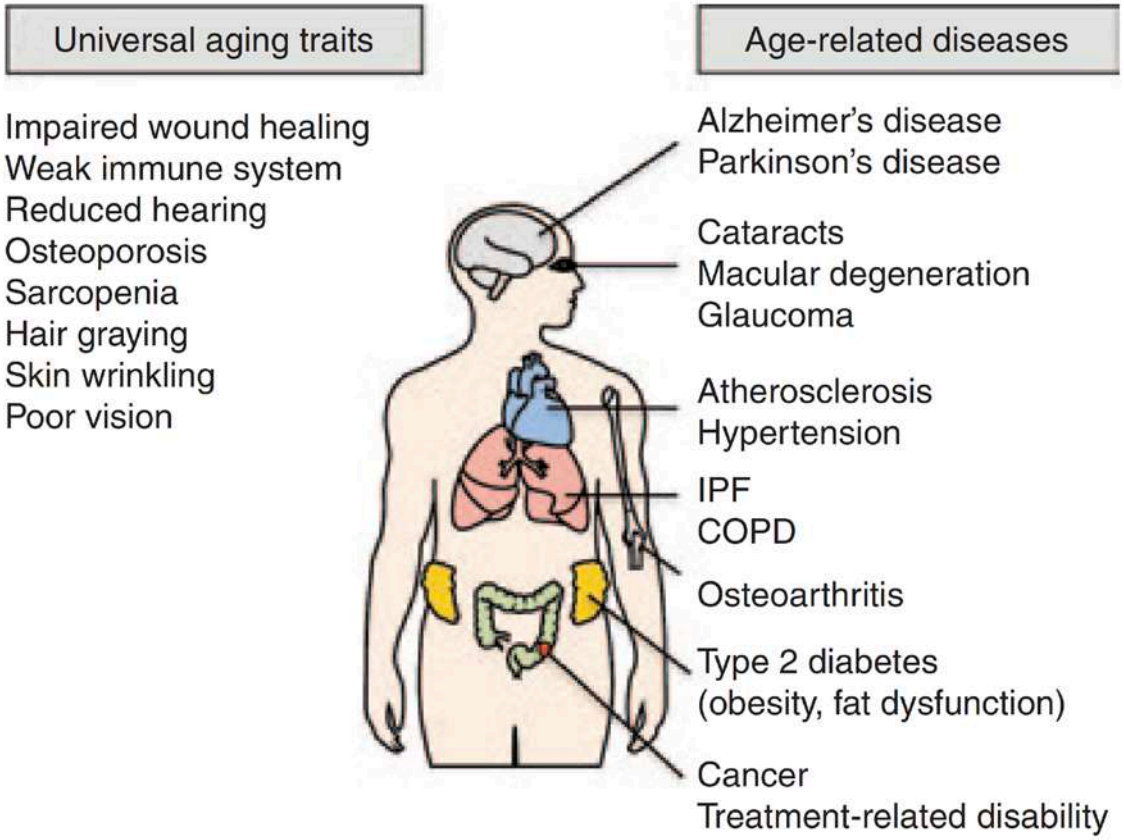
Razdan et al., 2018 Aging Cell

Senescence and Aging

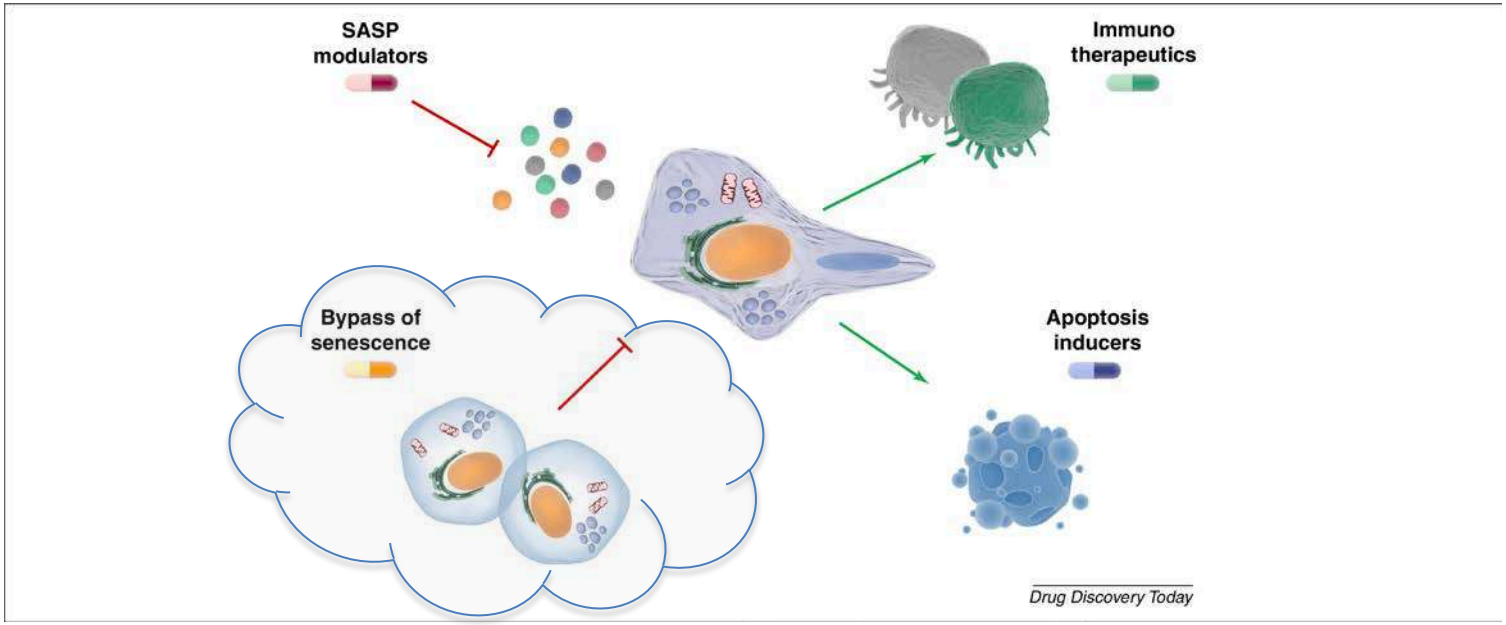


from Y. Ovadya & V. Krizhanovski; Biogerontology (2014) 15:627-642

The Accumulation of Senescent Cells Causes Aging and Age-Related Diseases



Senotherapeutic Strategies to Improve Healthy Aging



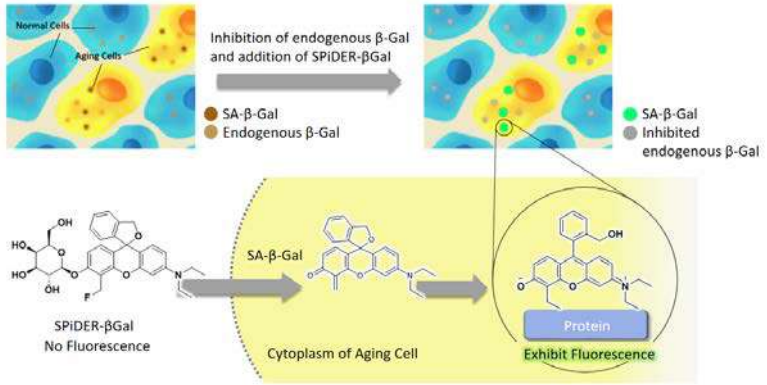
Our Current Research Efforts to Improve Healthy Aging

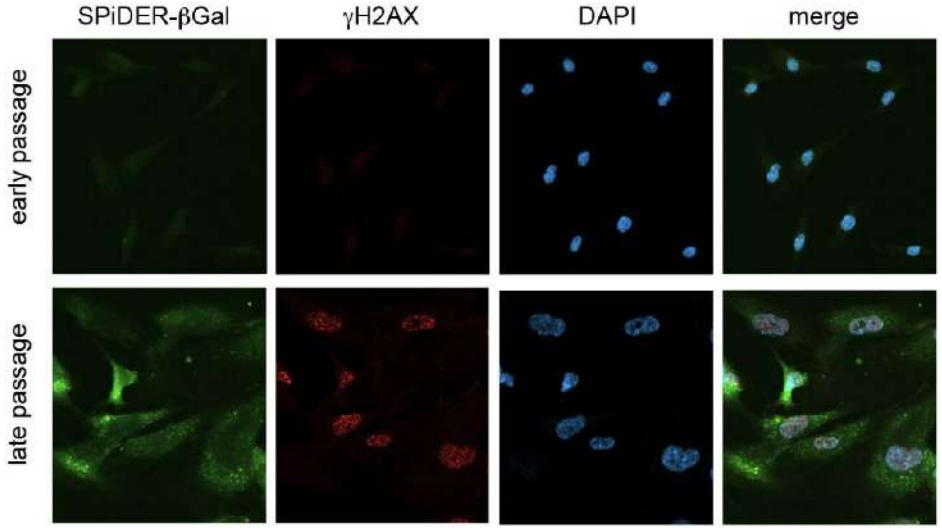
1. Improving the detection and characterization of senescent human cells *in tissue*
   Current techniques (TIF, SA-βGal, DDR-foci, SudanBlack, p16, p21, LaminB1, macroH2A…) are expensive, laborious, and time consuming. Separation of senescent cells from non-senescent cells is challenging

2. Rejuvenation of aged cells through pharmacological activation of hTERT expression
   In mice, hTERT gene therapy and TA-65 expression improves health-span and extends lifespan.

3. Inducing cellular plasticity by SASP factors
   In mice, SASP factors induce cellular plasticity and promote "stemness" of keratinocytes in a paracrine manner.

1. Improving the detection and characterization of senescent human cells in tissue

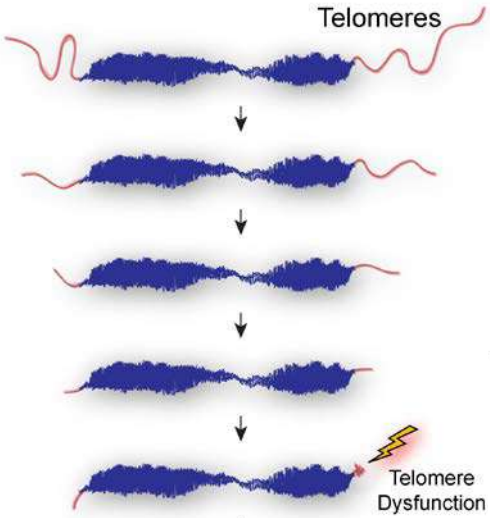




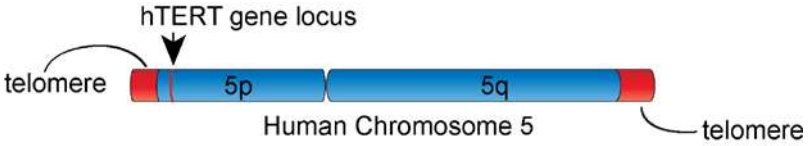
2. Rejuvenating Aging Cells

aged cell

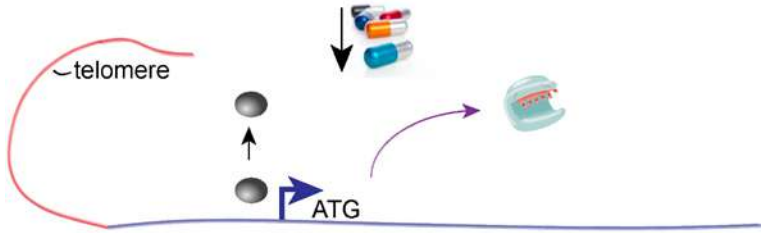
"young" cell



Aging?

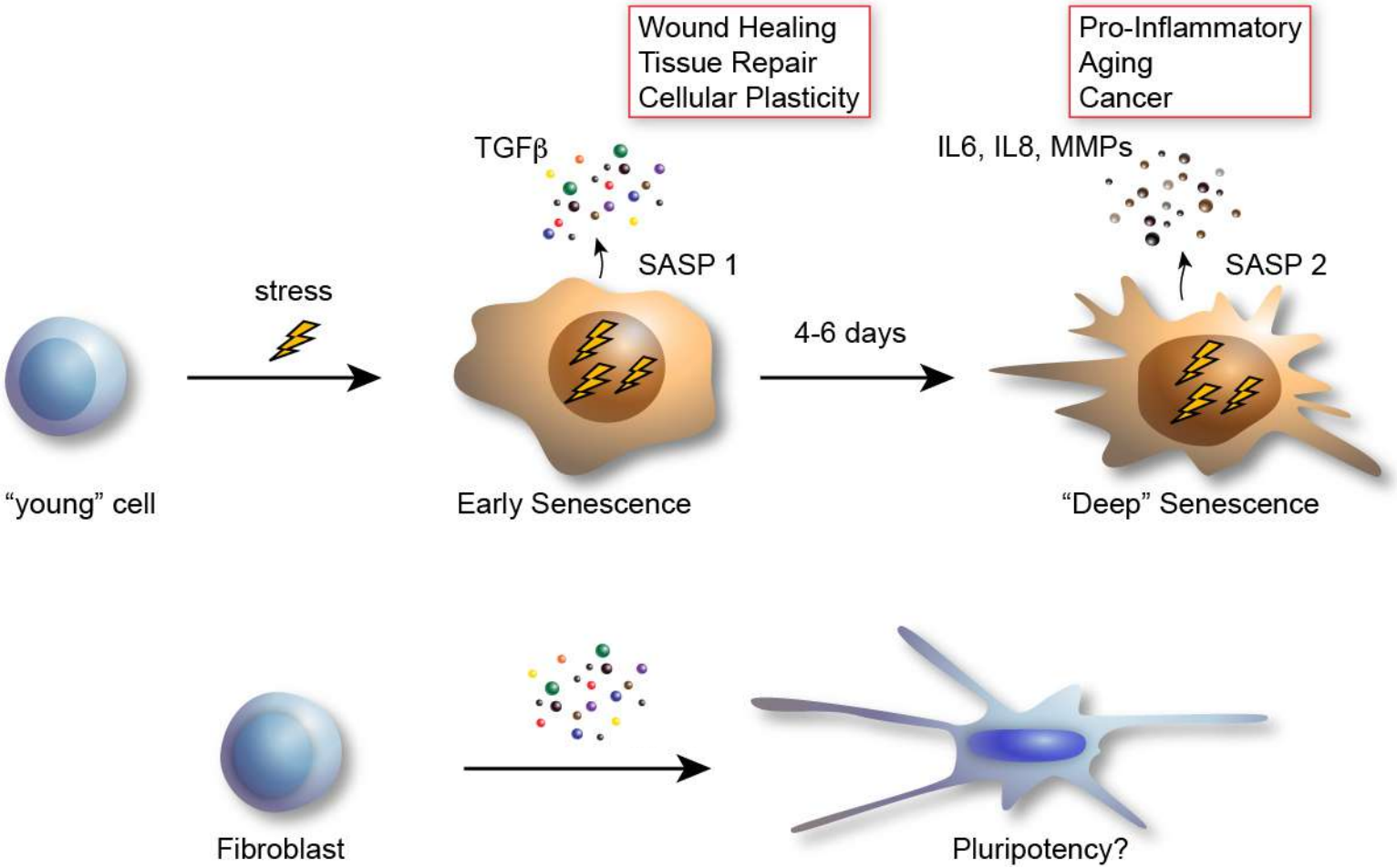


repressed hTERT promoter



active hTERT promoter

3. Inducing Cellular Plasticity



Acknowlegdements

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Clyde Phelix

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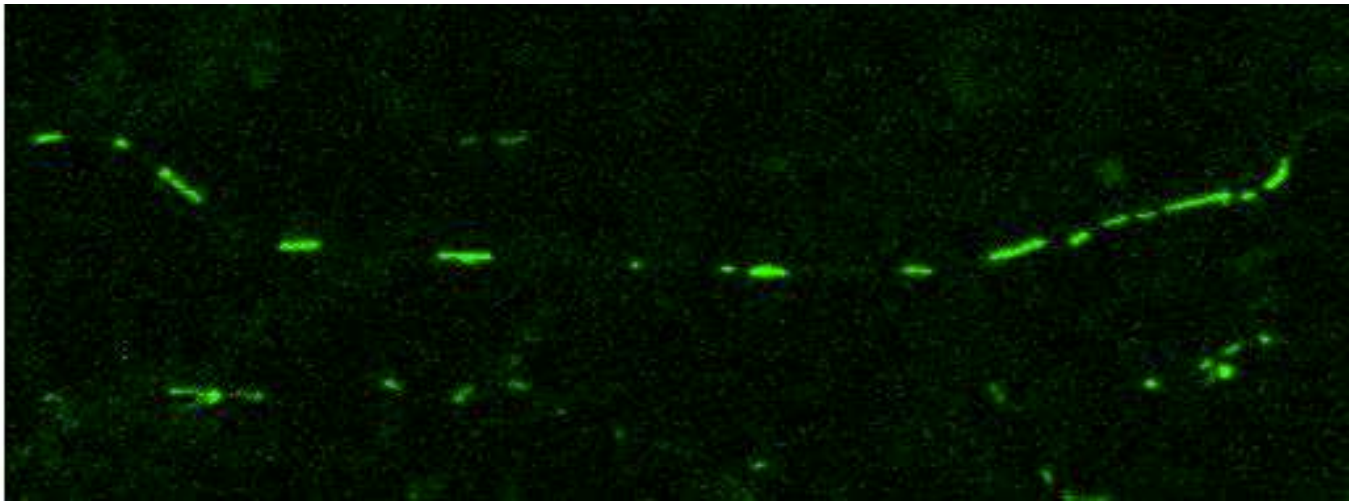
The Lawrence Ellison Foundation, A NONPROFIT CORPORATION

NIH National Cancer Institute

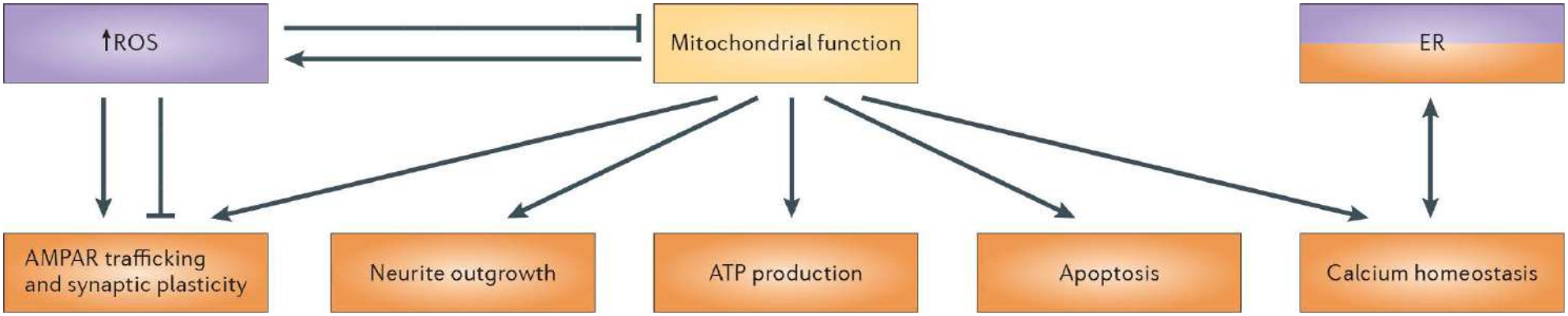
Mitophagy Regulation in Alzheimer's Disease

Qian Cai

Department of Cell Biology and Neuroscience
Rutgers University



Mitochondria are essential for neuronal survival and function



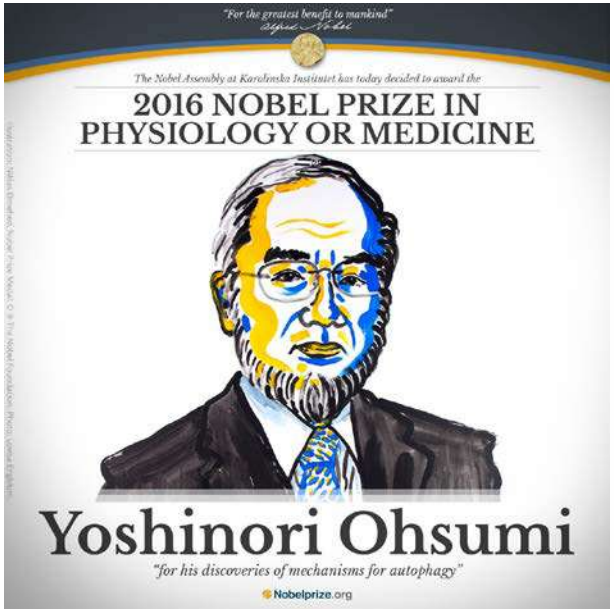
Mitochondrial dysfunction and impaired transport associate with major neurodegenerative diseases (AD, PD, ALS, HD).

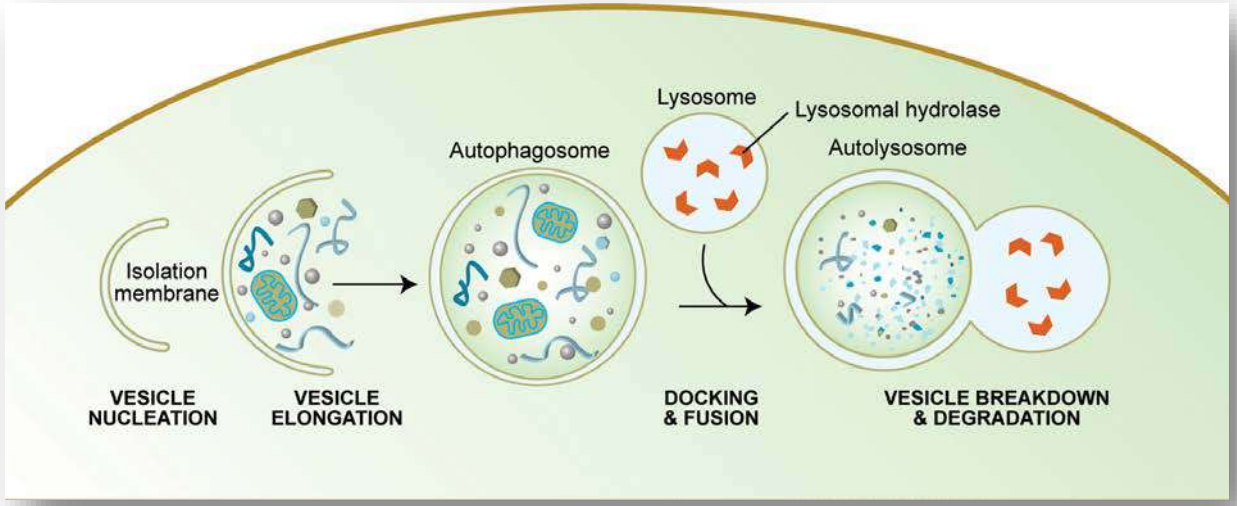
Sheng and Cai, *Nat Rev Neurosci.*, 2012

Manji et al., *Nat Rev Neurosci.*, 2012

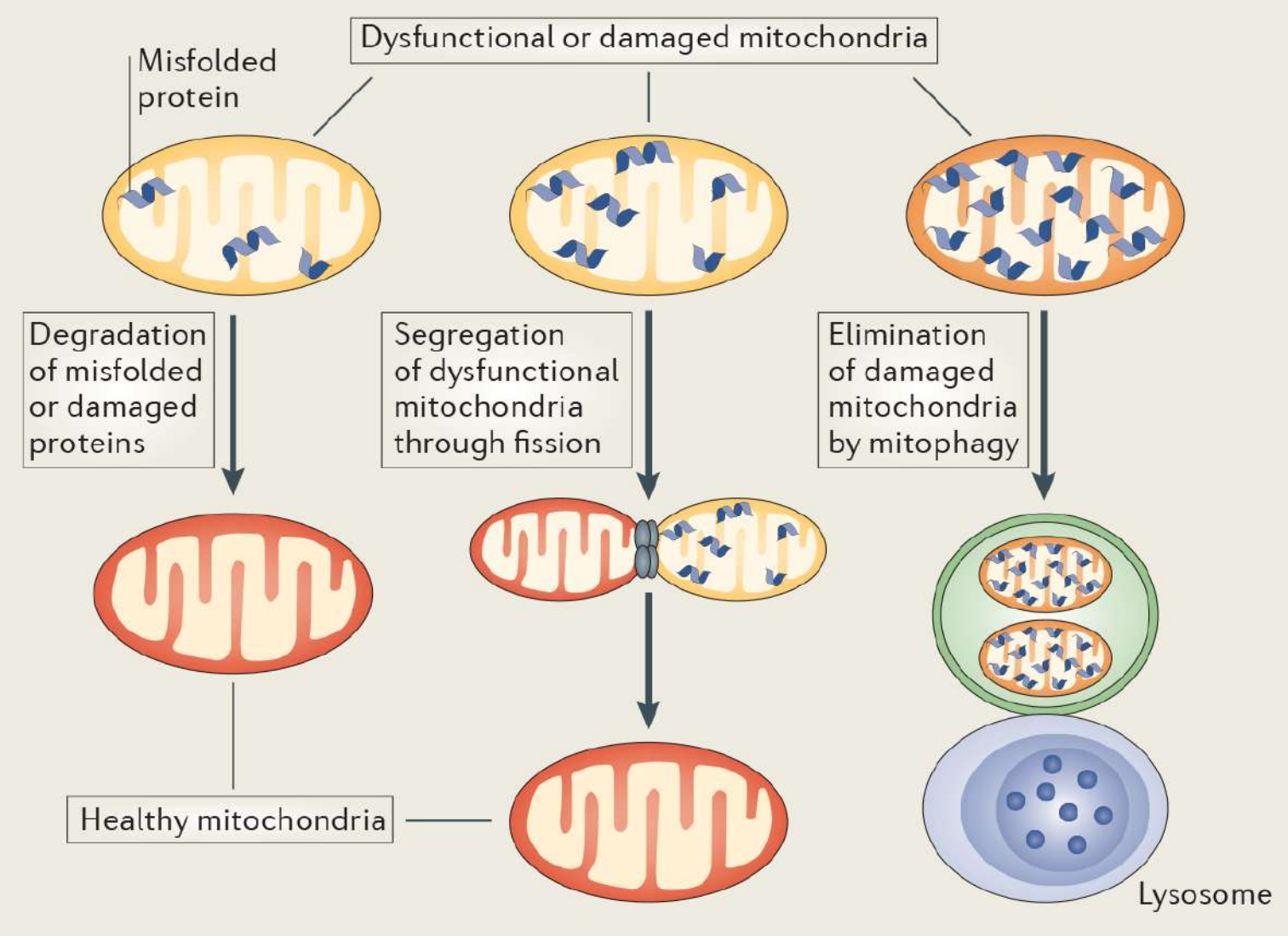
Autophagy-Lysosomal Pathway

- **Autophagy is the major cellular quality control system**
- **Deliver and degrade dysfunctional intracellular components or damaged organelles in the lysosome**
- **Defective autophagy has been indicated in major neurodegenerative diseases**





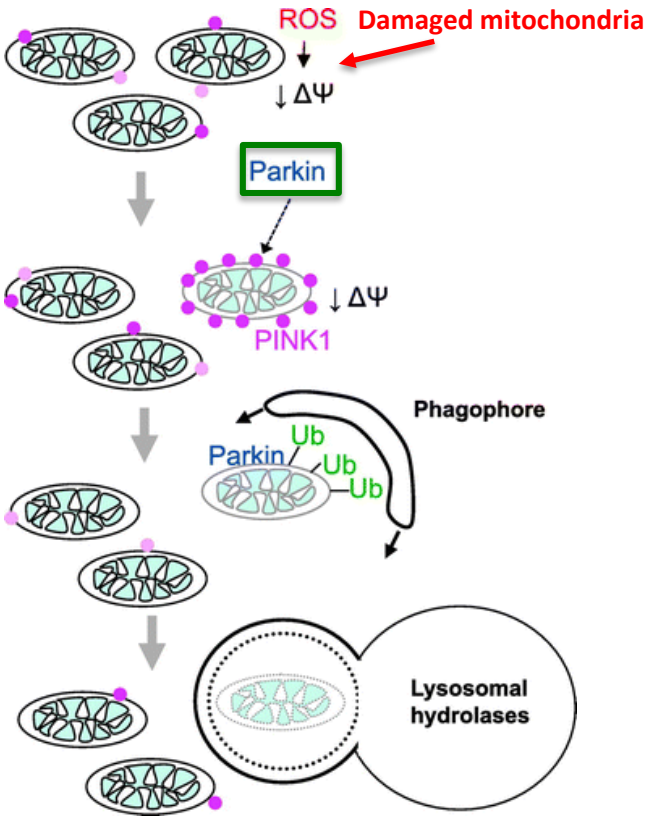
Mitochondrial quality control



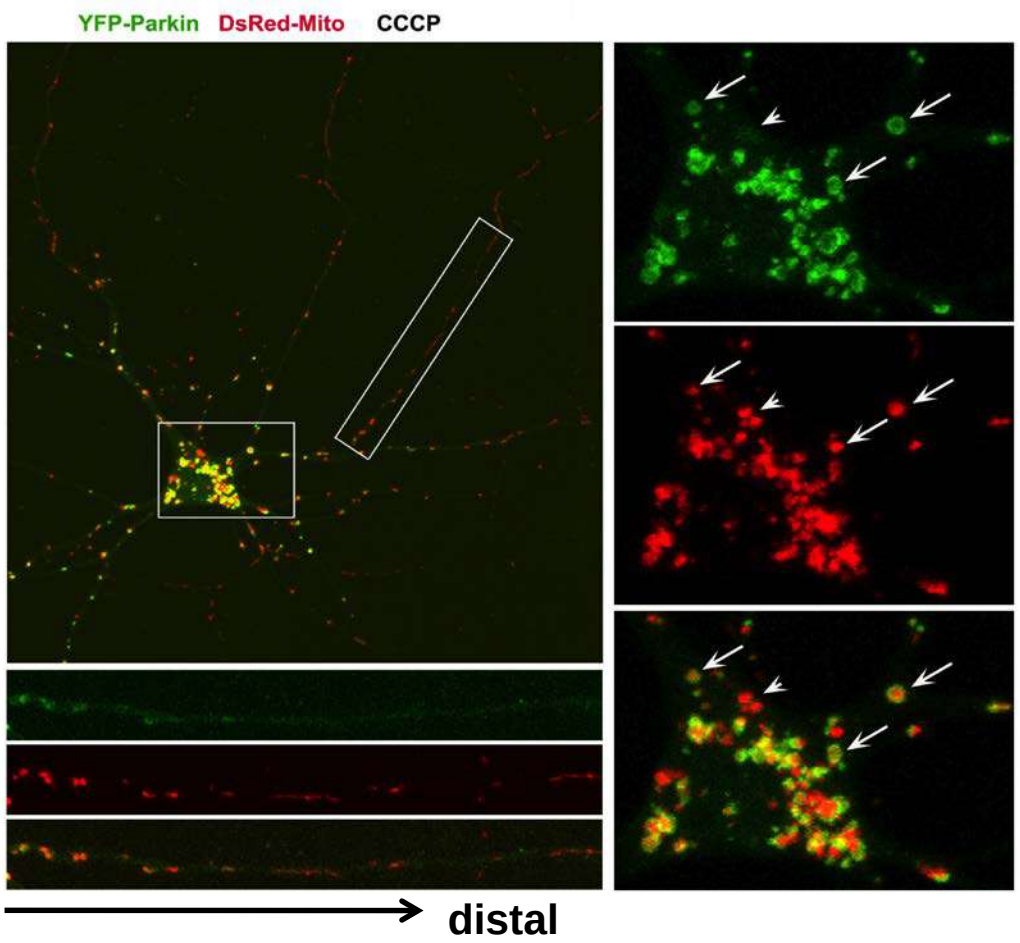
Sheng and Cai, *Nat Rev Neurosci*., 2012

Cortical Neuron Imaging Showing Dynamic and Spatial Parkin Translocation and Degradation of Depolarized Mitochondria
(Mitophagy and Impact on Mitochondrial Motility)

Parkin-Targeted Mitochondria Accumulate in the Somatodendritic Regions



The PINK1/Parkin pathway mediates mitophagy, ensuring mitochondrial integrity and function. (Narendra and Youle, 2011)

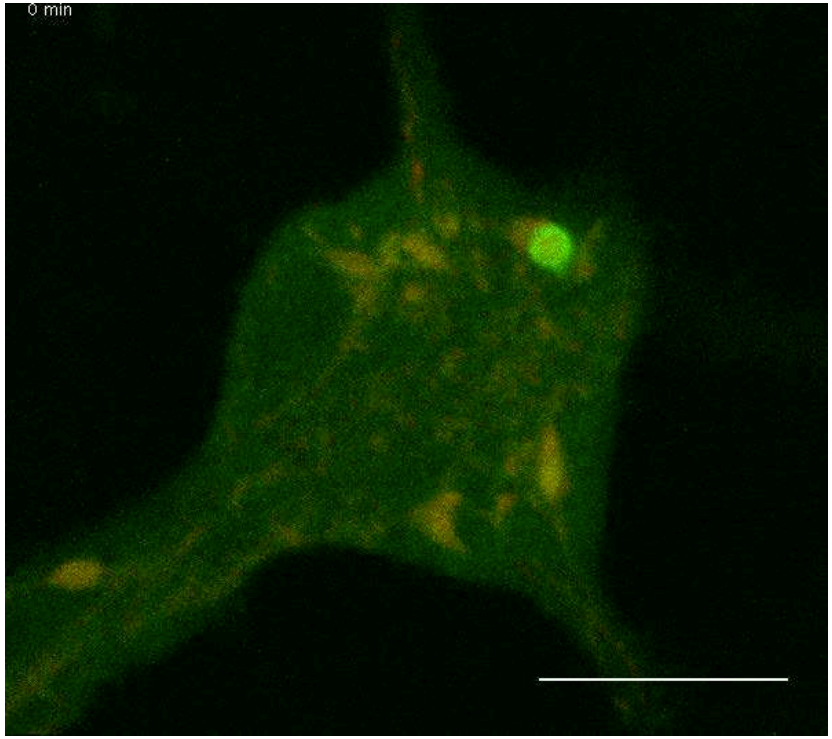


Cai et al., *Current Biology*, 2012

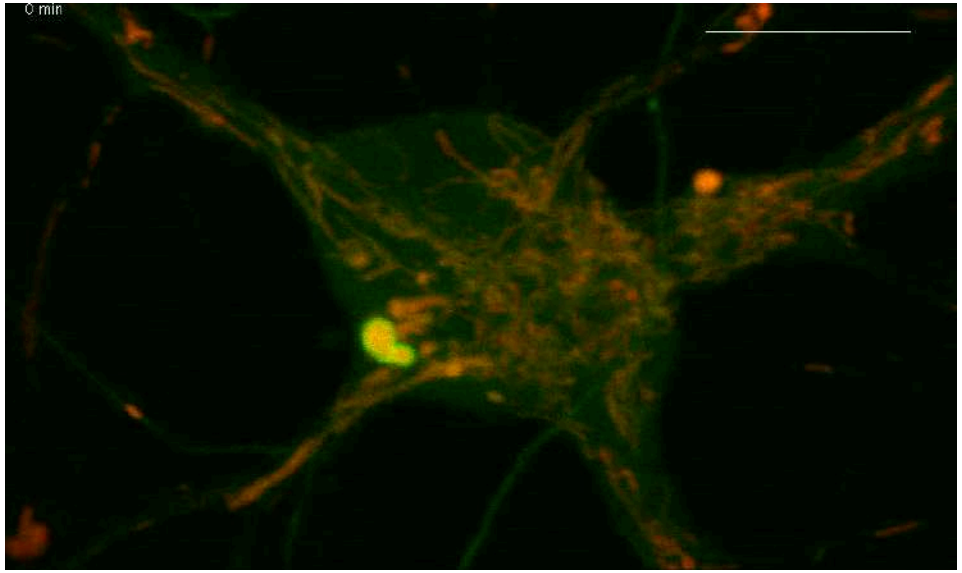
Dynamic Degradation of Parkin-Targeted Dysfunctional Mitochondria in the Soma of Live Cortical Neurons

H Zakaria
(HHMI)

YFP-Parkin **DsRed-Mito**



(Time-lapse for 170 min at 5 min-intervals)

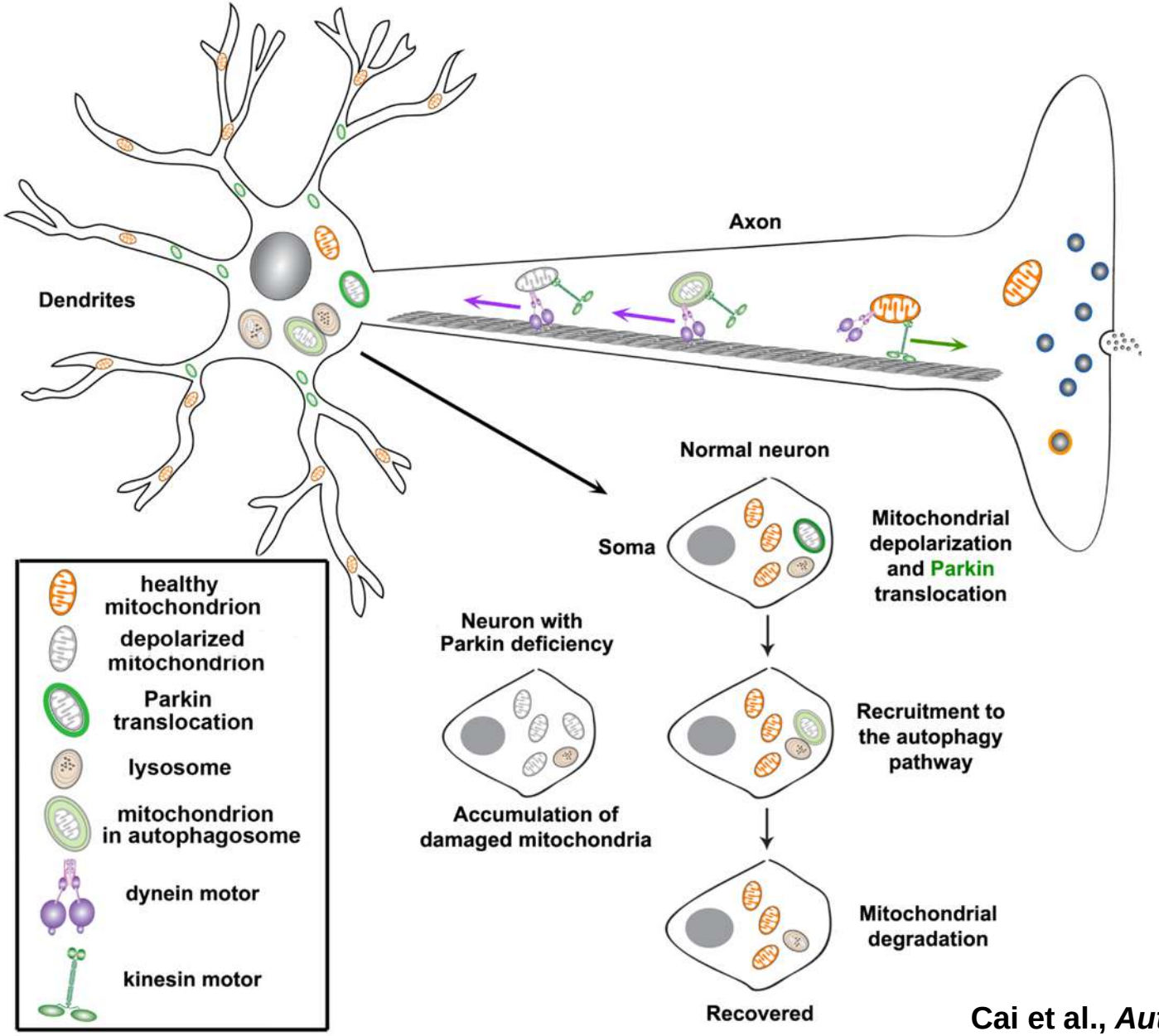


(Time-lapse for 130 min at 5 min-intervals)

The first neuronal imaging evidence showing dynamic Parkin translocation onto depolarized mitochondria for their degradation within the autophagy-lysosomal system.

Cai et al., *Current Biology*, 2012

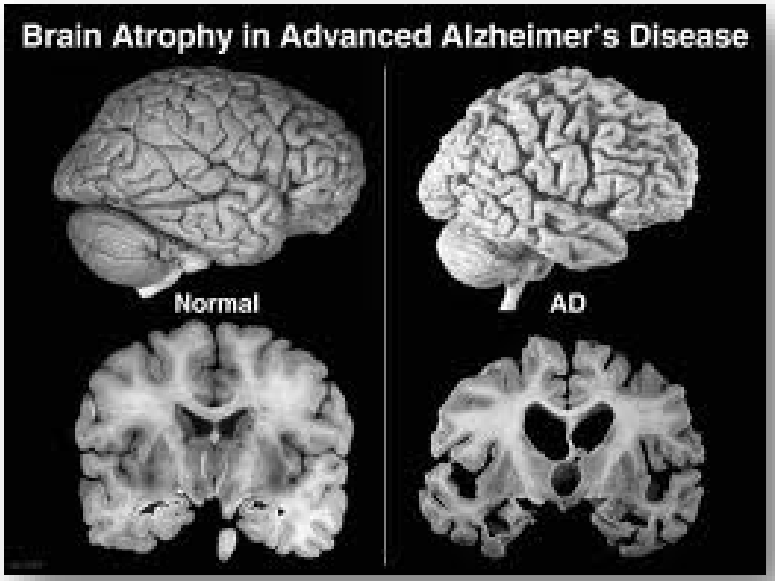
Parkin-mediated mitophagy in healthy neurons

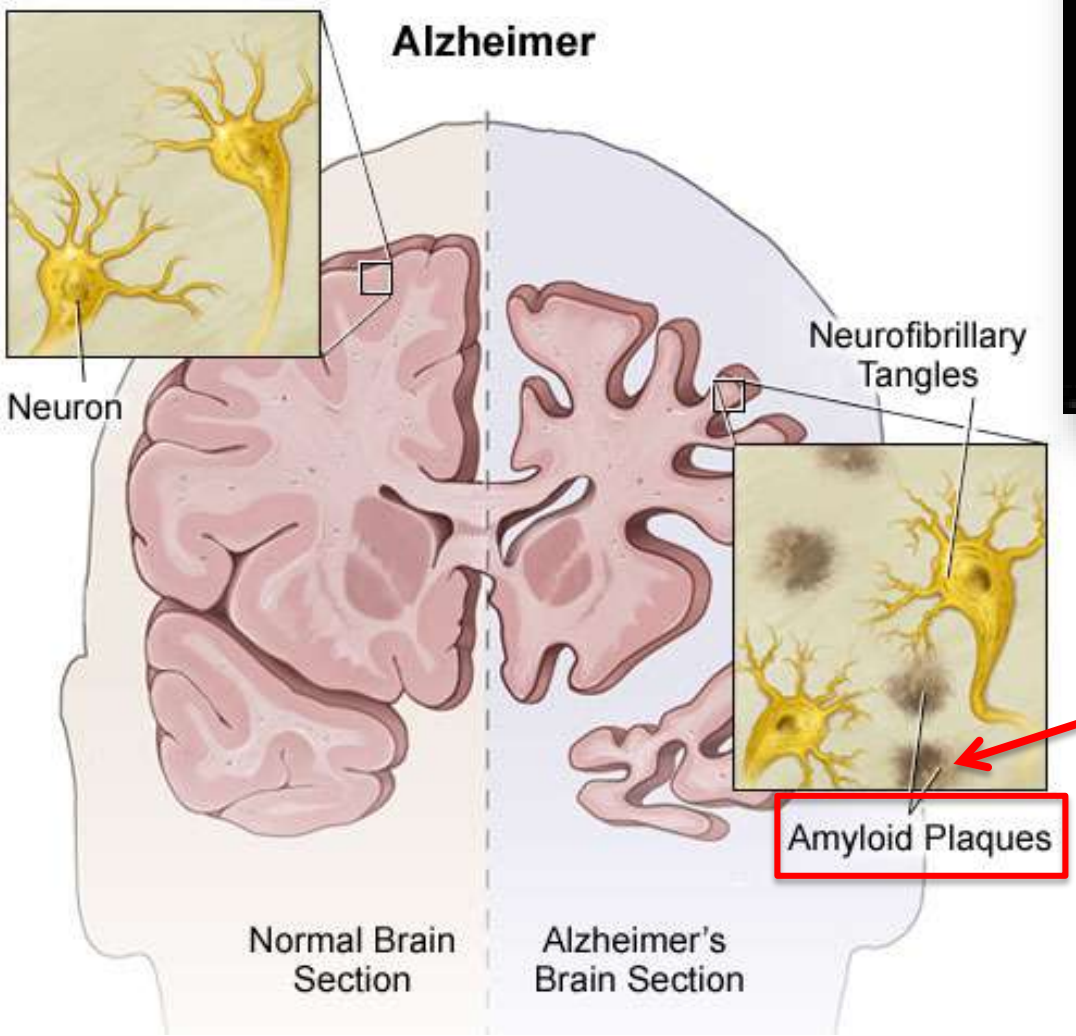


Cai et al., *Autophagy*, 2012

Cai et al., *Current Biology*, 2012

Pathogenic hallmarks of Alzheimer's disease

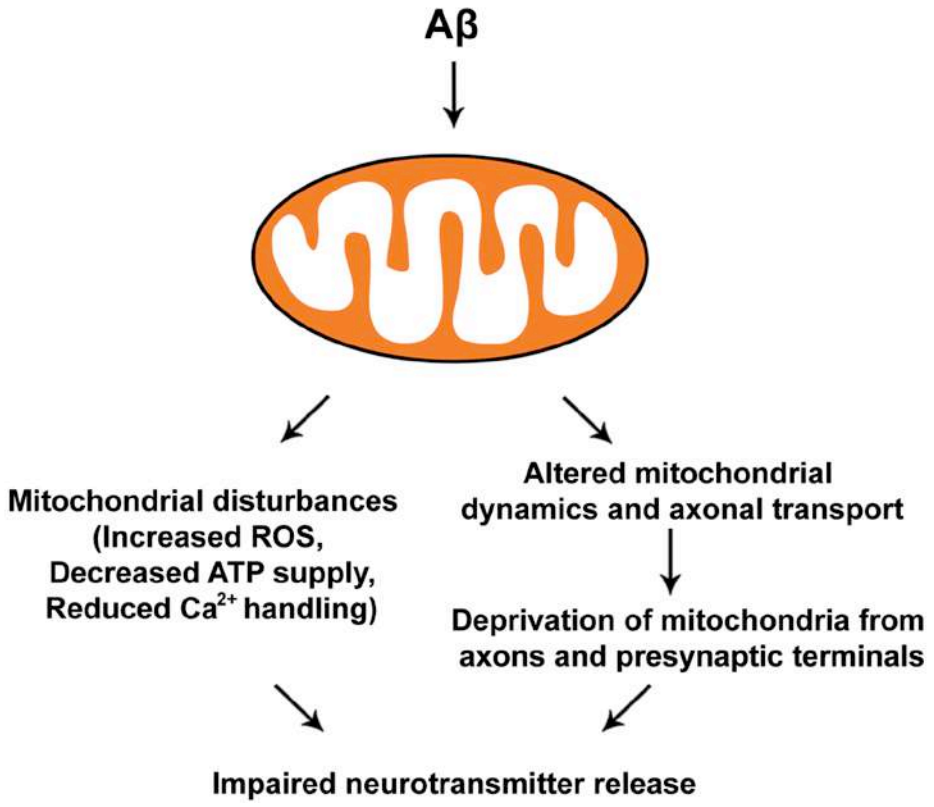




Amyloid-β (Aβ)

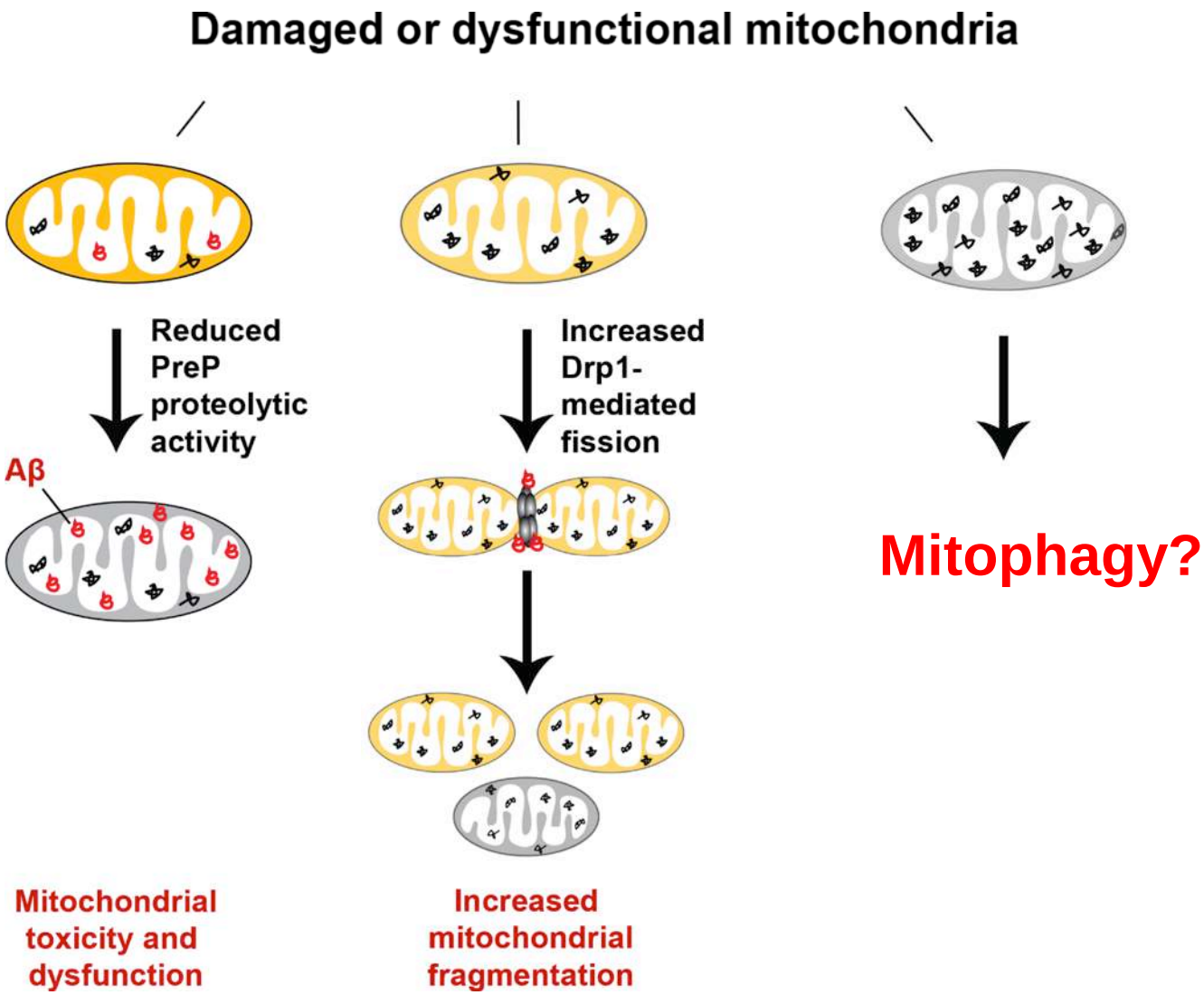
Toxic effects of Aβ on mitochondria

- **Mechanisms underlying mitochondrial defects in AD neurons**



Cai and Tammineni, *Journal of Alzheimer's disease*, 2017

Mitochondrial quality control is altered in Alzheimer's disease



Cai and Tammineni, *Frontiers in Cellular Neuroscience*, 2016

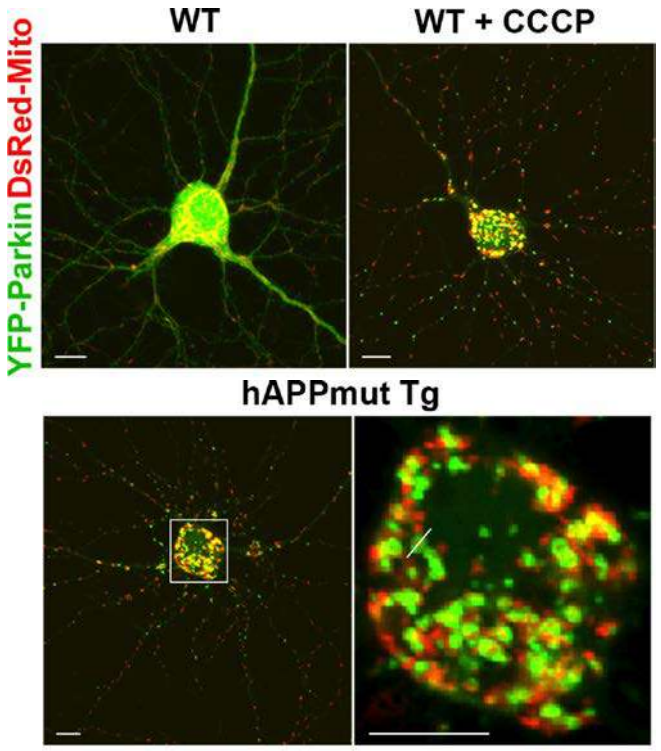
Parkin-mediated mitophagy is induced in mutant hAPP Tg neurons

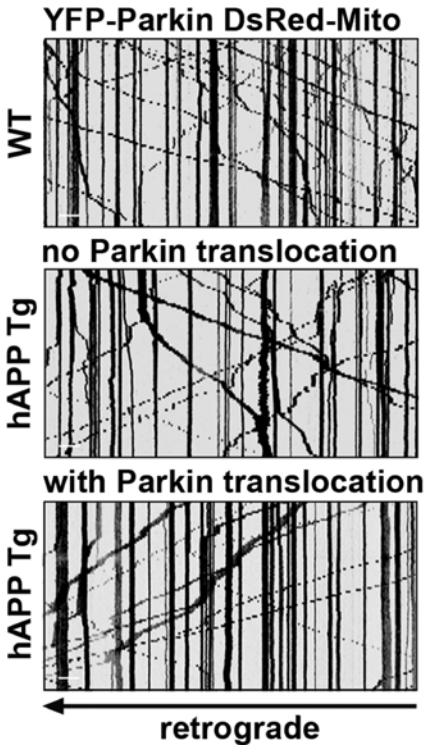
WT neuron

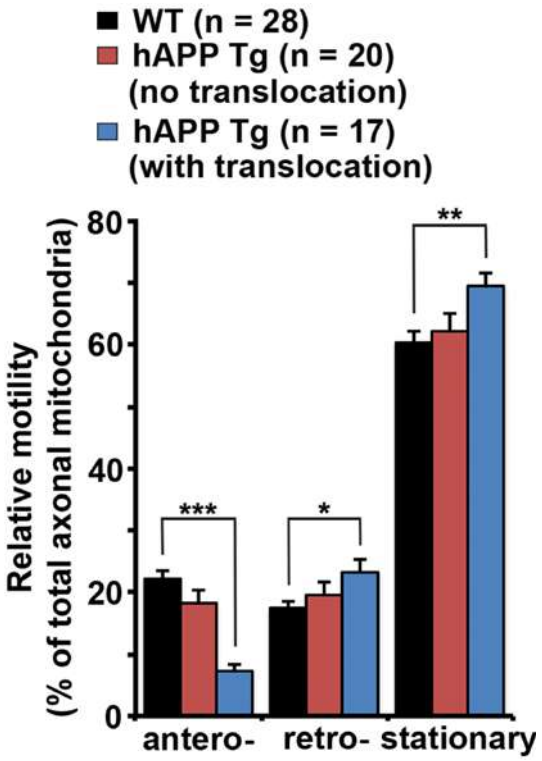
mutant hAPP Tg neuron
without Parkin translocation

with Parkin translocation

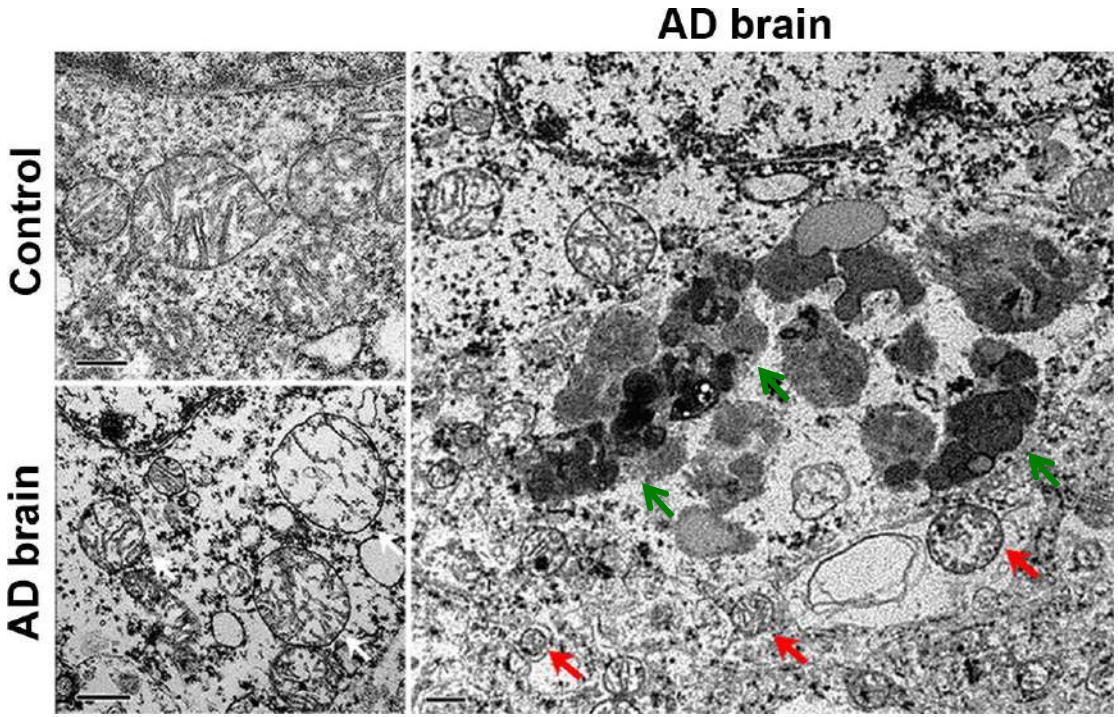
retrograde transport



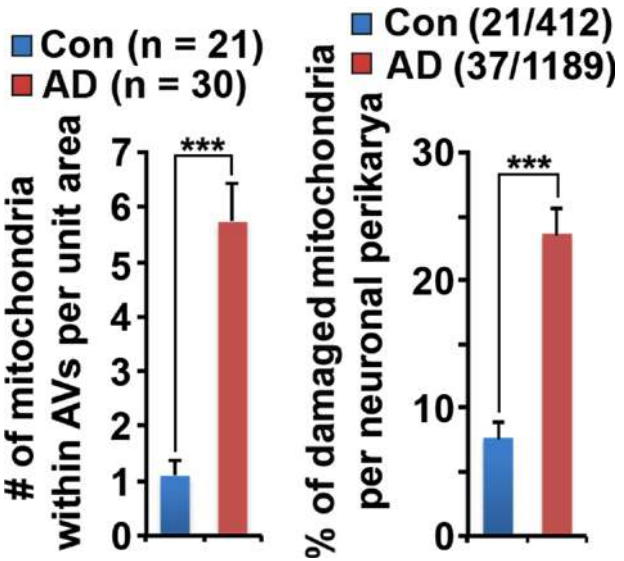




Accumulation of mitochondria within autophagic vacuoles in the hippocampus of AD patient brains



AVi (red arrows); AVd (green arrows)

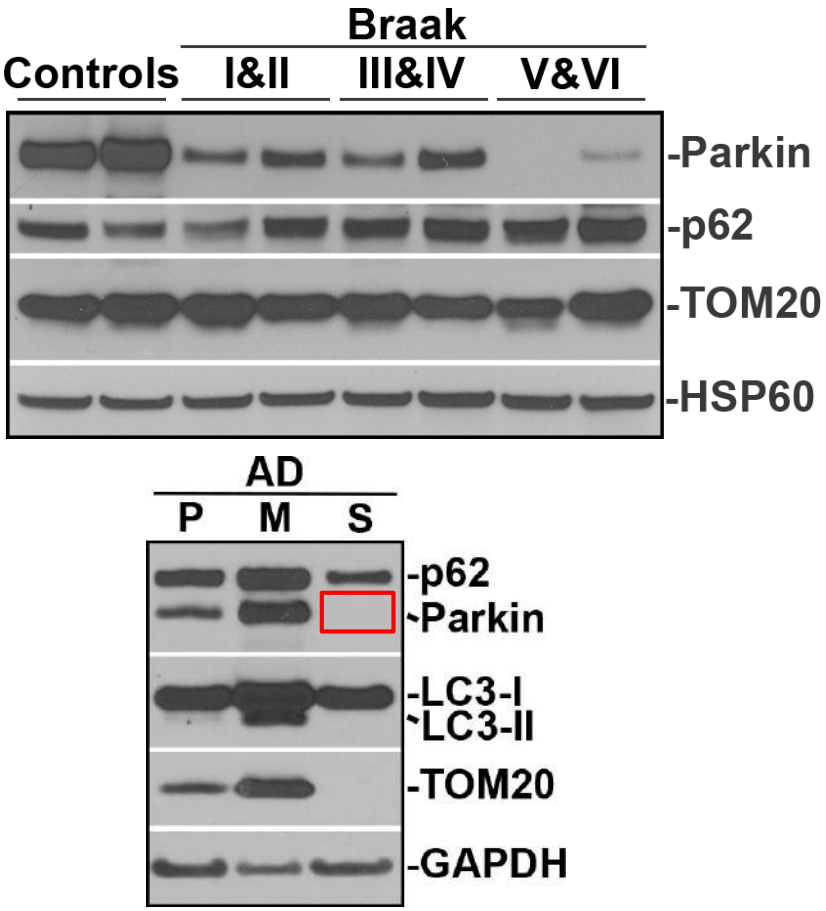


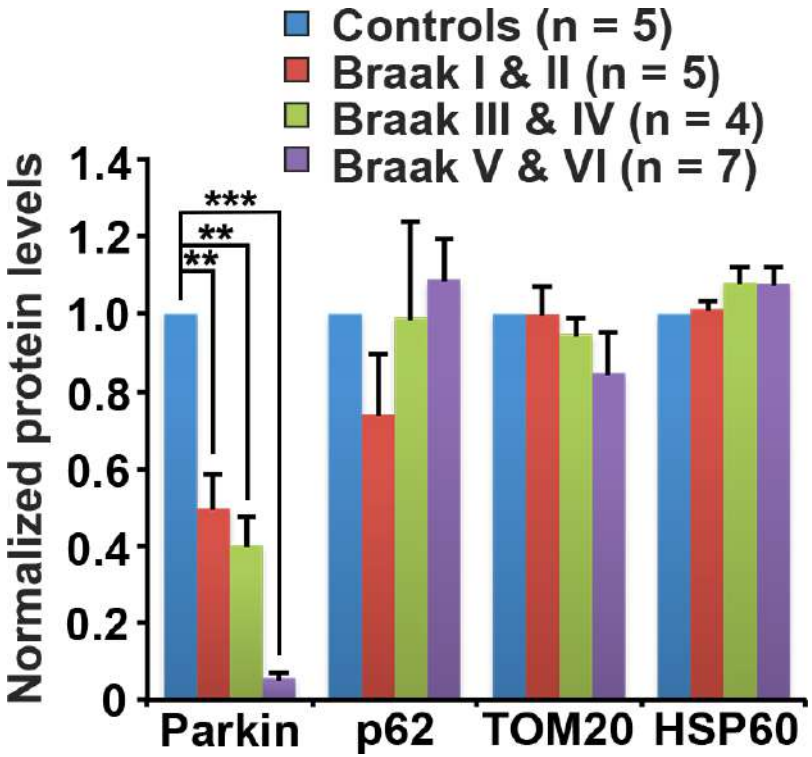
Mitophagy is induced in AD patient brains.

Aberrant accumulation of defective mitochondria in AD patient brains.

Ye et al., *Human Molecular Genetics*, 2015

Depletion of cytosolic Parkin over disease progression in AD patient brains



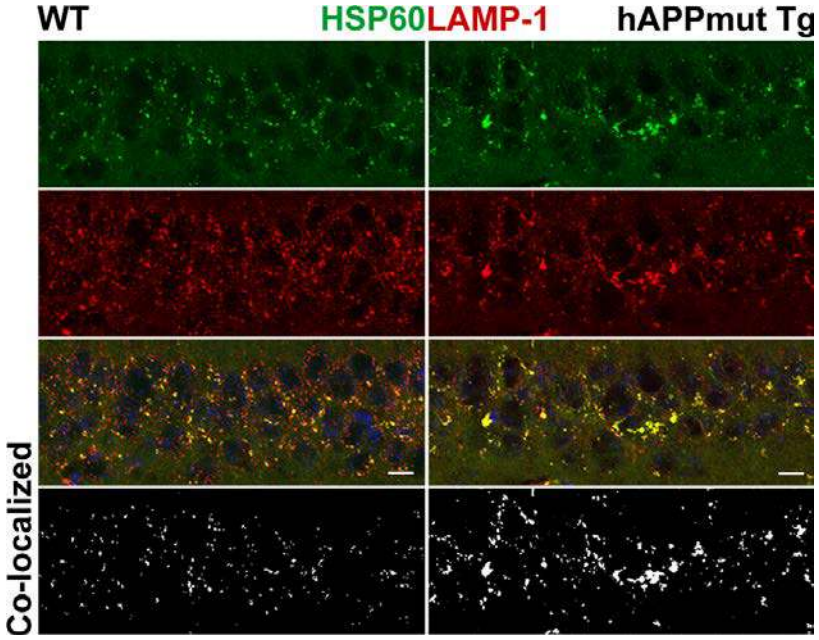


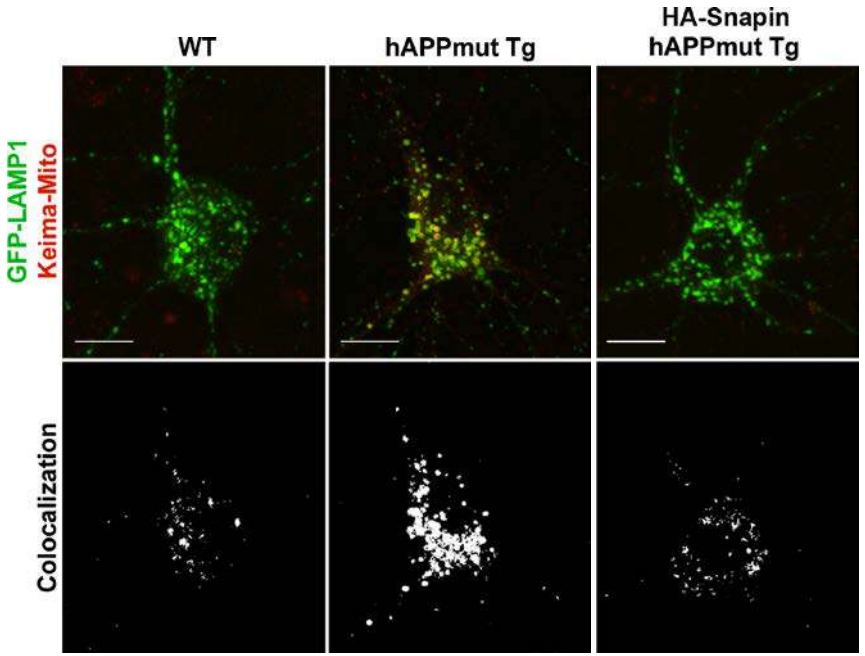
Mitophagy induction is coupled with enhanced Parkin degradation.

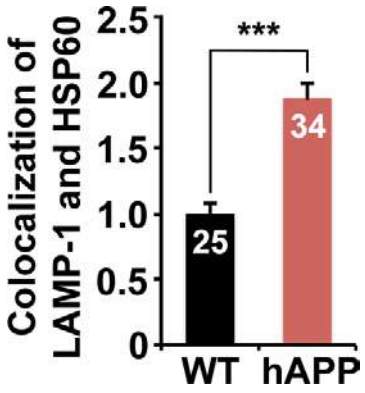
Parkin depletion leads to defects in the elimination of defective mitochondria, resulting in their aberrant accumulation in AD neurons.

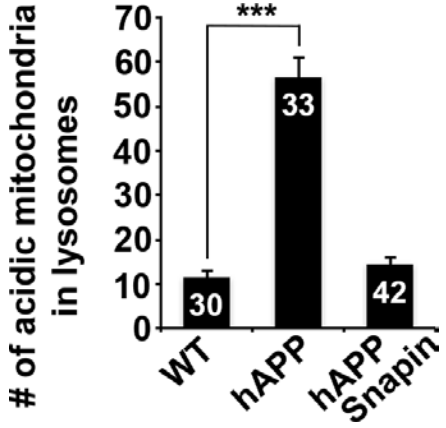
Ye et al., *Human Molecular Genetics*, 2015

Lysosomal deficits contribute to mitochondrial pathology in AD neurons



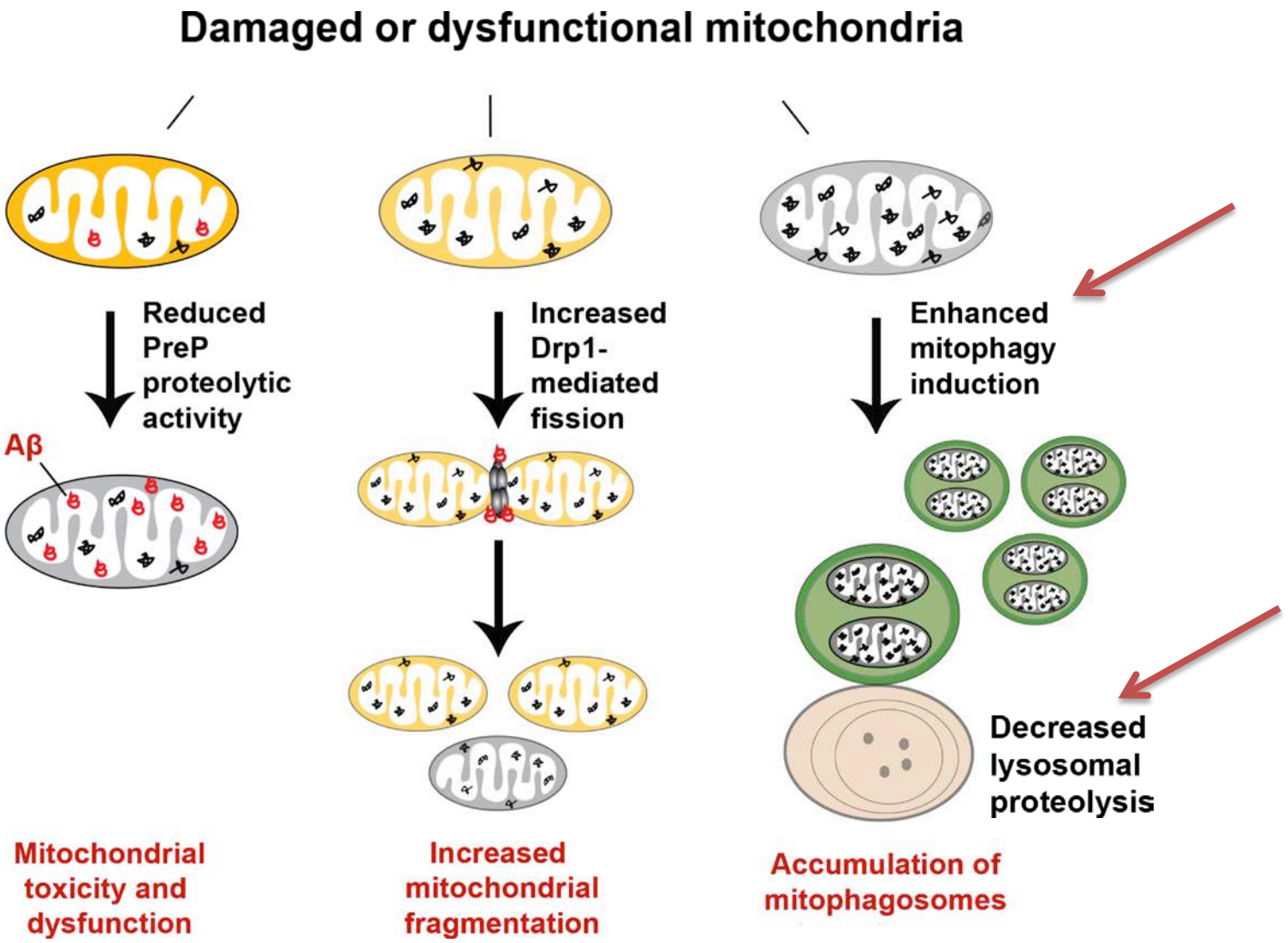






Tammineni et al., *Human Molecular Genetics*, 2017

Abnormal mitochondrial quality control in AD



Cai and Tammineni, *Frontiers in Cellular Neuroscience*, 2016

Potential fields for collaboration

- **Molecular and cellular mechanisms underlying normal aging and age-related neurodegenerative diseases**
  - **Autophagy-lysosomal regulation in aging and neurodegeneration**
  - **Axonal transport and membrane trafficking and their impacts on axonal homeostasis**
  - **Mitophagy and mitochondrial quality control in healthy, aged and diseased neurons**

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Lab Members

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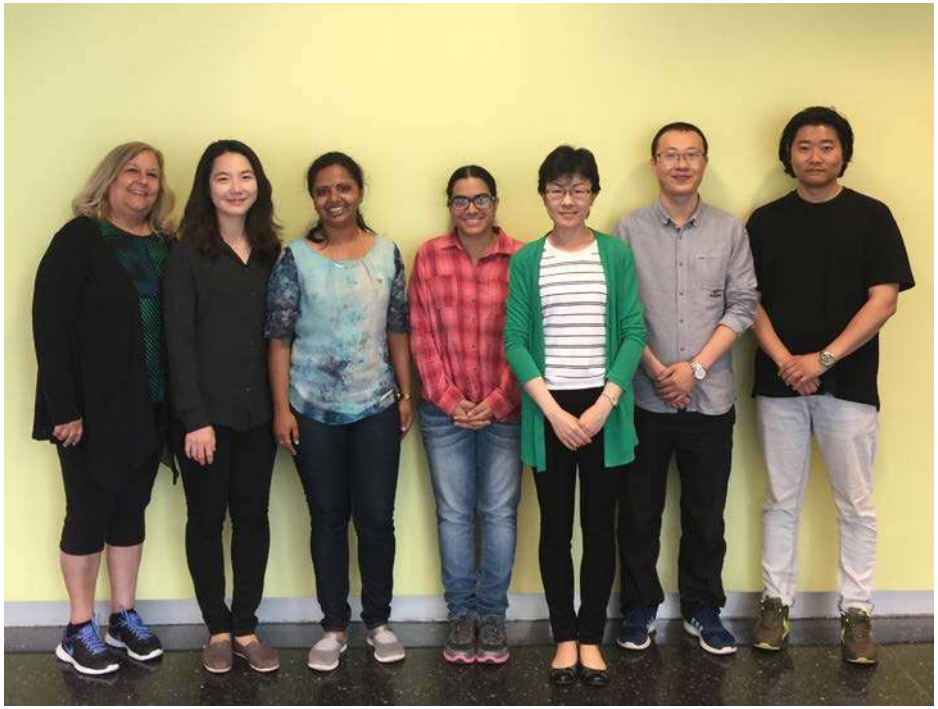

Collaborations

Zu-Hang Sheng (NINDS, NIH)
Huaibin Cai (NIA, NIH)
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Barth Grant (Rutgers)
Christopher Rongo (Rutgers)
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Rajesh Patel (Rutgers)
Valentin Starovoytov (Rutgers)

Dietary Protein and Healthy Aging: Controversies and Mechanisms

Tracy G. Anthony, Ph.D.

Professor of Nutritional Sciences

RUTGERS

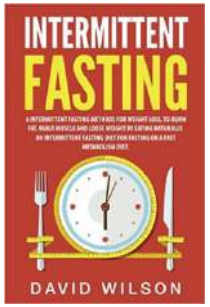
School of Environmental and Biological Sciences

October 18, 2018

States of Amino Acid Nutrition

- Toxicity
- Supplementation
- Adequacy
- Limitation
- Deprivation/ depletion
- Devoid

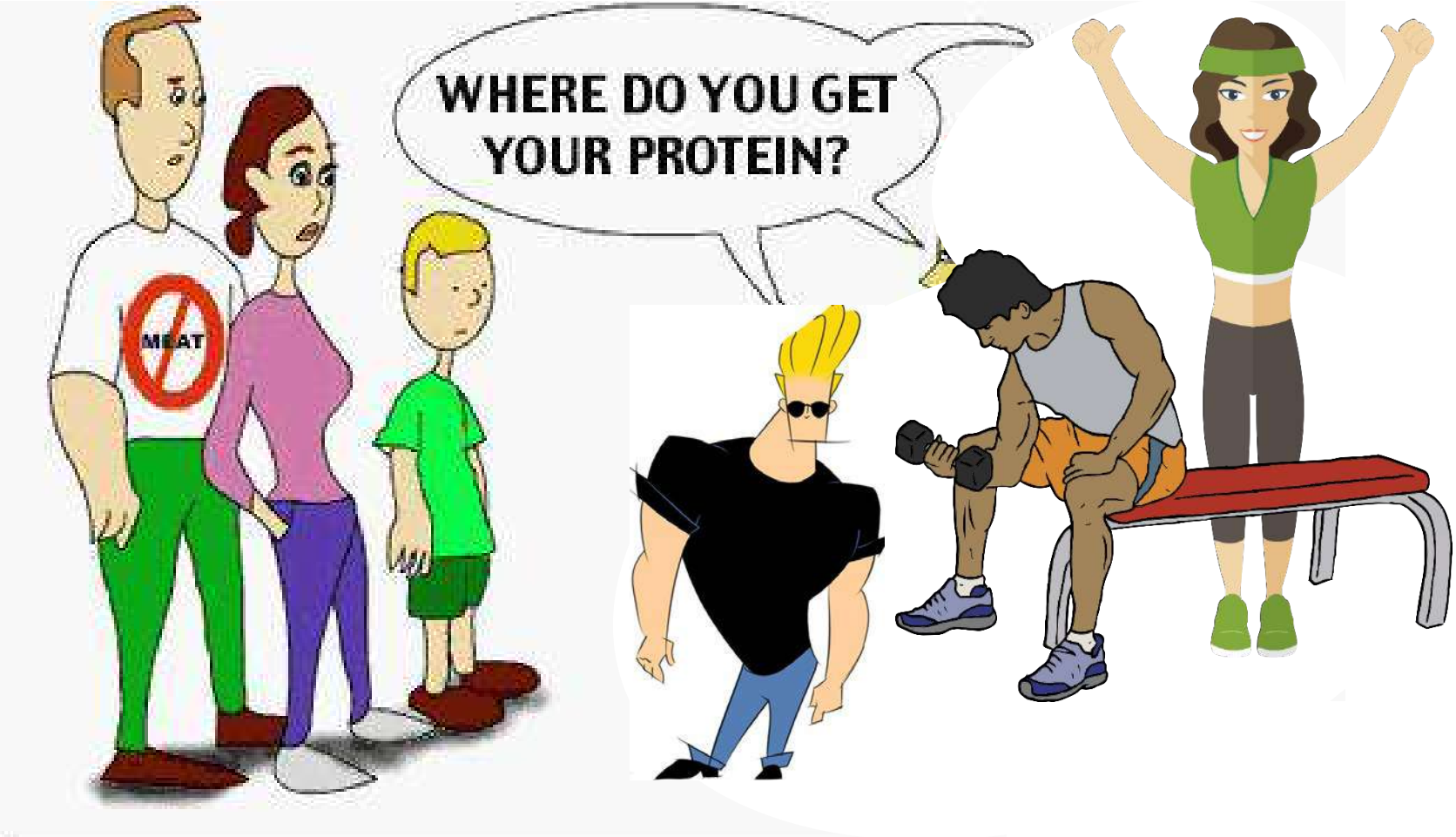
- Balanced



- Imbalanced

Insufficient for growth; *but is this unhealthy?*

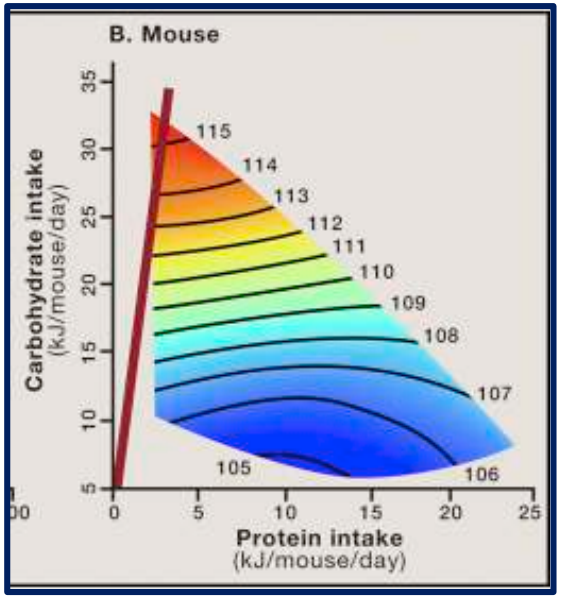
Dietary protein: obsession and controversy



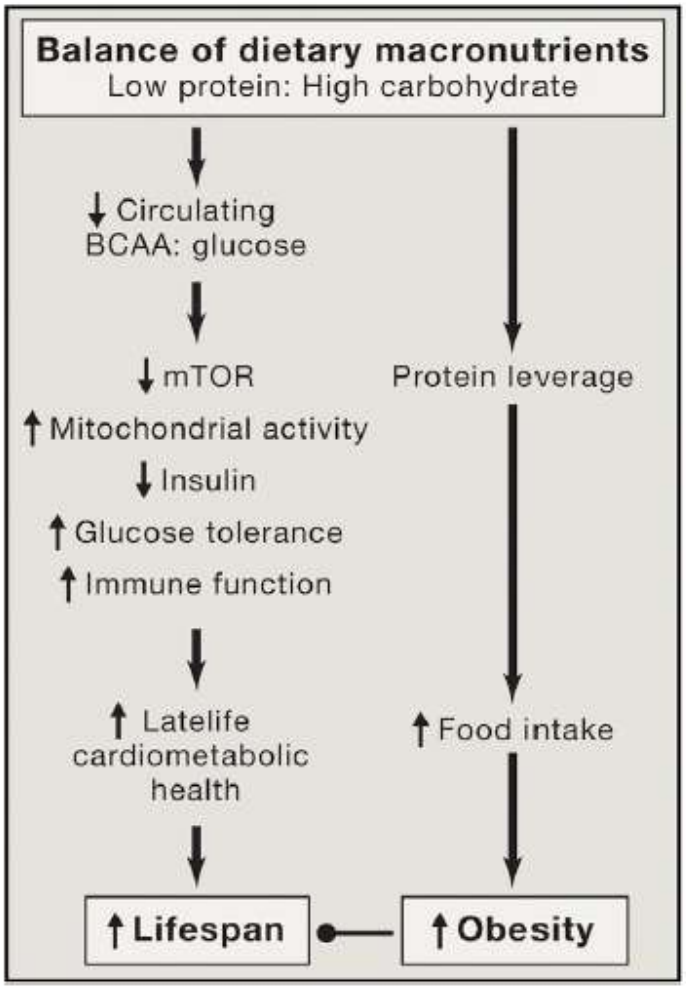
Adapted from:
http://detox-fit.com/fighting-worlds-protein-obsession/
https://hpjmh.com/2011/03/14/where-do-you-get-your-protein/
https://thevegandatabase.com/incomplete-plant-proteins-myth/

Dietary restriction: do macronutrients matter?

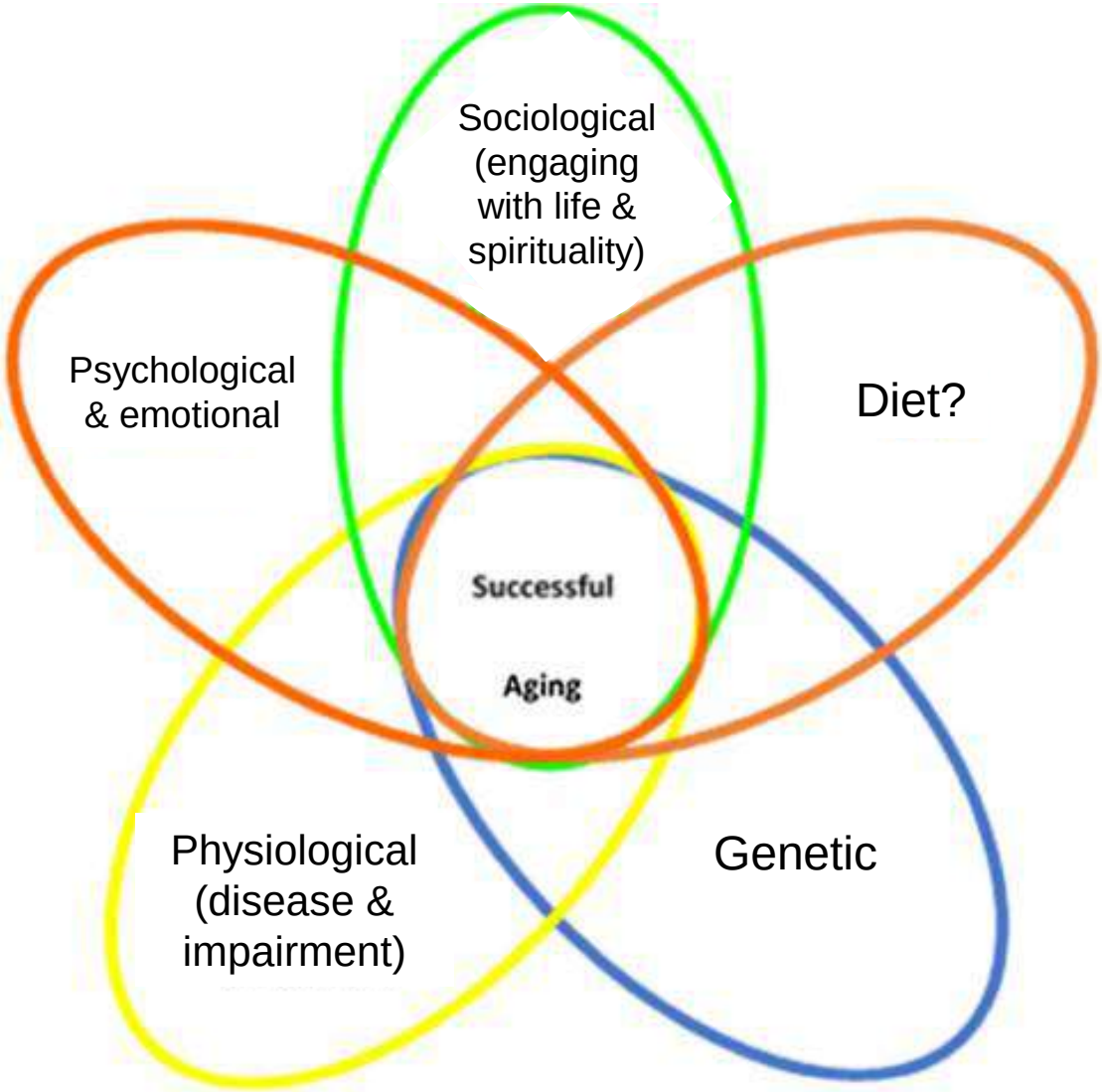
doi: 10.3390/nu8060370



Protein Leverage Hypothesis



Cell *161*, March 26, 2015



Ageing Research Reviews 39 (2017) 78–86

European Journal of Nutrition (2018) 57 (Suppl 2):S15–S34

Dietary Paradigms for Metabolic Health and Longevity

- Calorie restriction

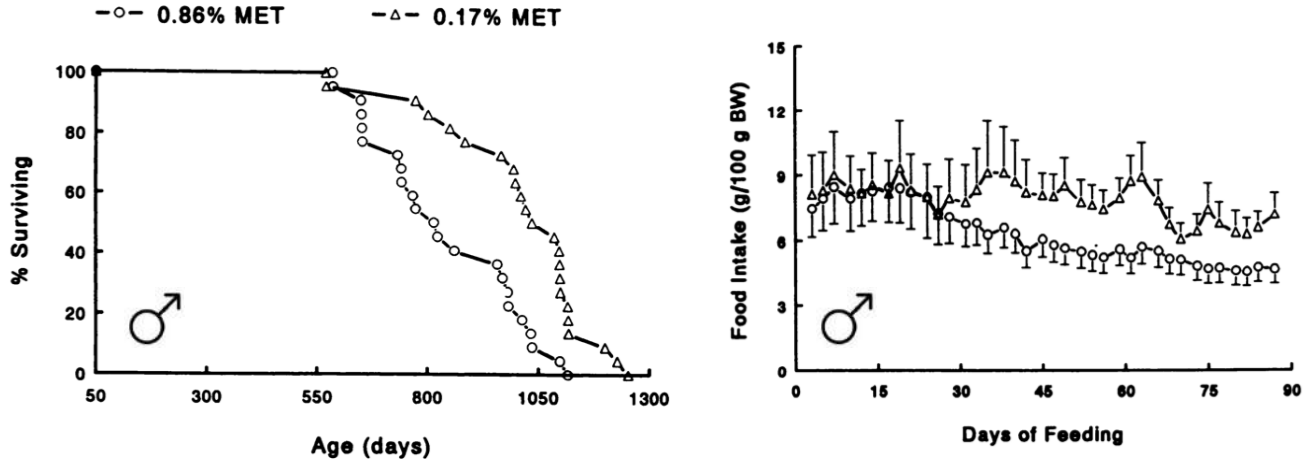
- Protein restriction

- Less animal protein, replace with plant protein

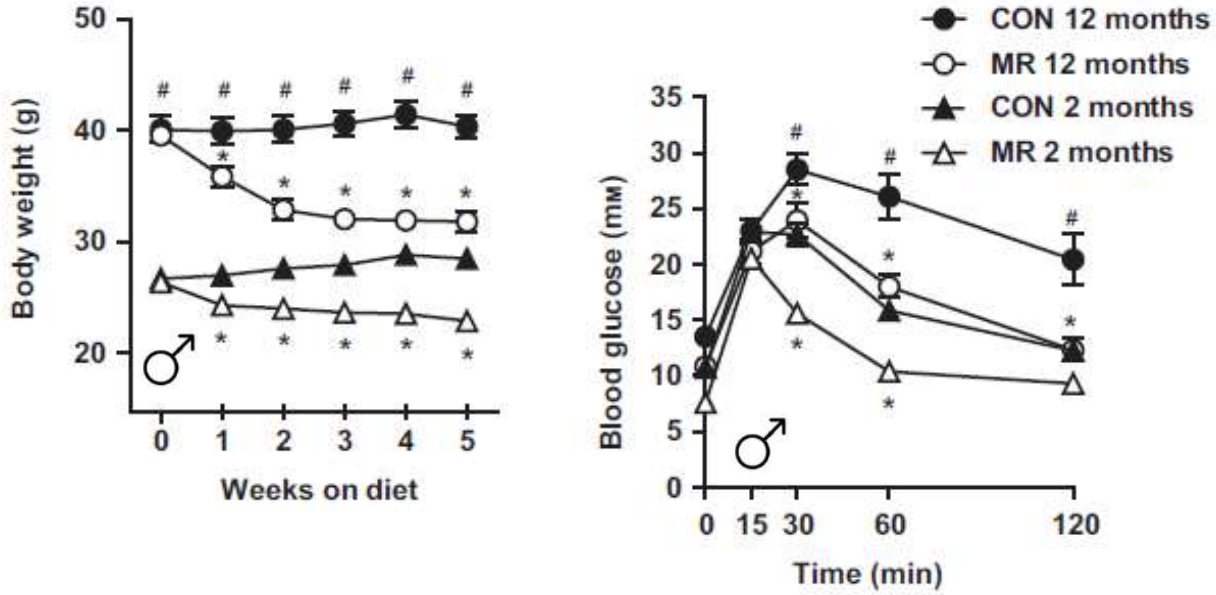
- Essential amino acid restriction

- Sulfur amino acid restriction

Sulfur Amino Acid Restriction (SAAR) extends lifespan and is associated with a lean, metabolically younger phenotype



Orentreich et al. **Low methionine ingestion by rats extends life span.** *J Nutr*. (1993) 123(2):269-74.

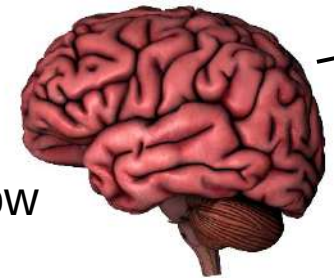


Lees et al. **Methionine restriction restores a younger metabolic phenotype in adult mice with alterations in fibroblast growth factor 21.** *Aging Cell* (2014) 13:817-827. doi: 10.1111/acel.12238

Sulfur Amino Acid Restriction: Mechanisms

♂

↑ SNS outflow

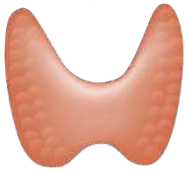


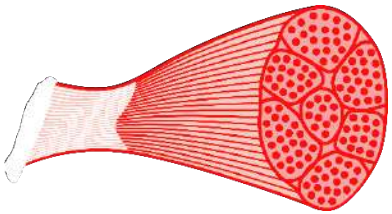
HPT Axis

↑ Thyroid function

↑ T4,T3

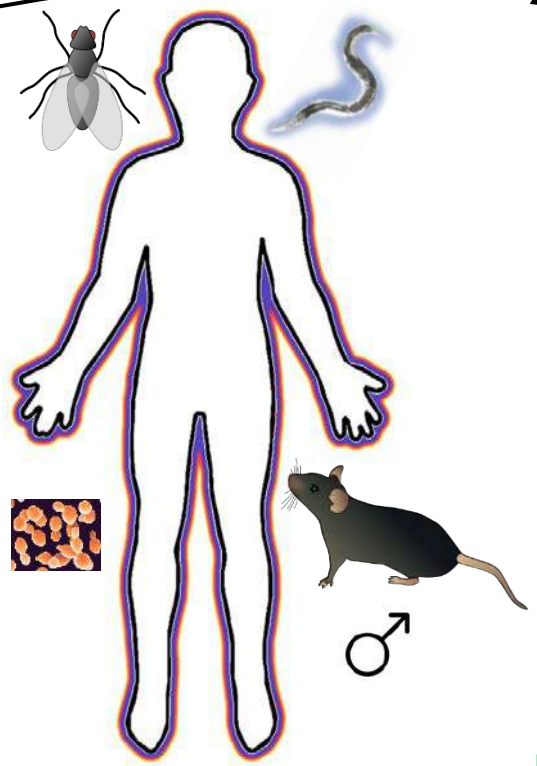
♂





↑ DIO2, TRα1

♂



↑ Food intake

↑ EE/Heat

↓ BW, % Body Fat

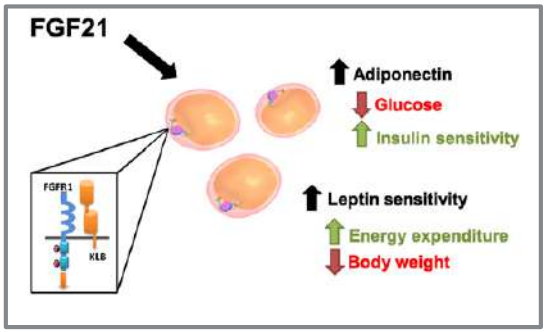
↔ % Lean Mass

↑ Glucose metabolism

↑ Lifespan 30-40%

↑ Uncoupled respiration

↑ *de novo* lipogenesis, TCA

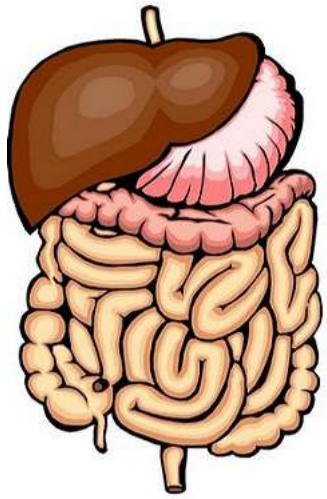


↑ FAO ♀♂

Insulin sensitivity

↓ *de novo* lipogenesis

FGF21



Gut microbiota ?

What's so special about SAAR?

- SAAR has stronger metabolic effects versus leucine restriction (LR).

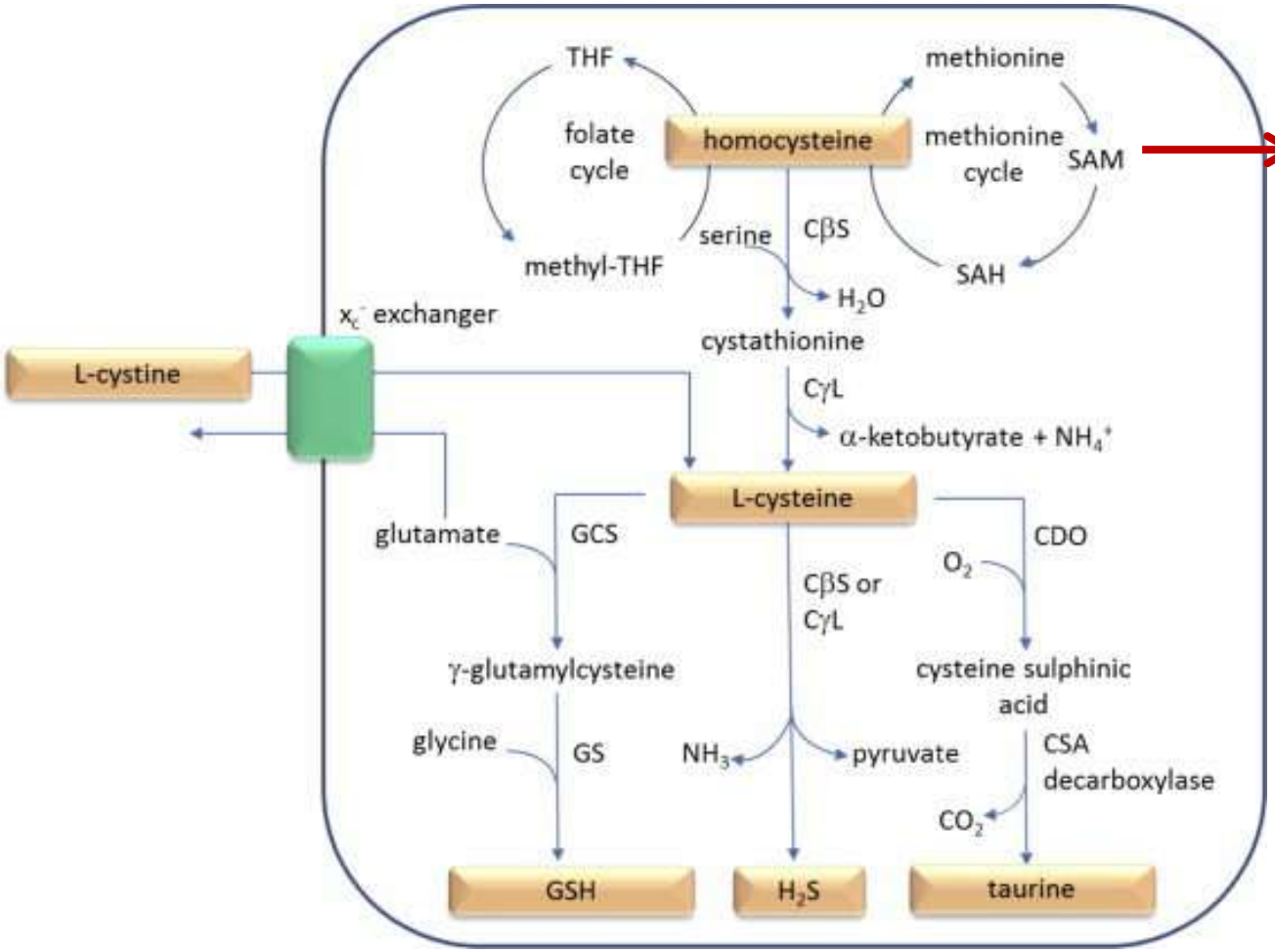
	Compared to Control diet:	
Measured after 8 wk:	**SAAR**	**LR**
Food intake	↑↑ (+38%)	↑ (+22%)
Body weight	↓↓ (-25%)	↓ (-16%)
% body fat mass	↓↓ (-30%)	↓ (-22%)
Fasting insulin	↓↓ (-81%)	↓ (-48%)
Fasting glucose	↓	↔
Glucose clearance	↑↑	↑
Circulating FGF21	↑↑↑	↔
Liver triglyceride content	↓	↔
Liver lipogenic genes	↓	↔

Biofactors. 2015 November 12; 41(6): 391–402. doi:10.1002/biof.124

SCIENTIFIC REPORTS | 7: 9977 | DOI:10.1038/s41598-017-10381

♂

Potential ways sulfur amino acid restriction improves health span

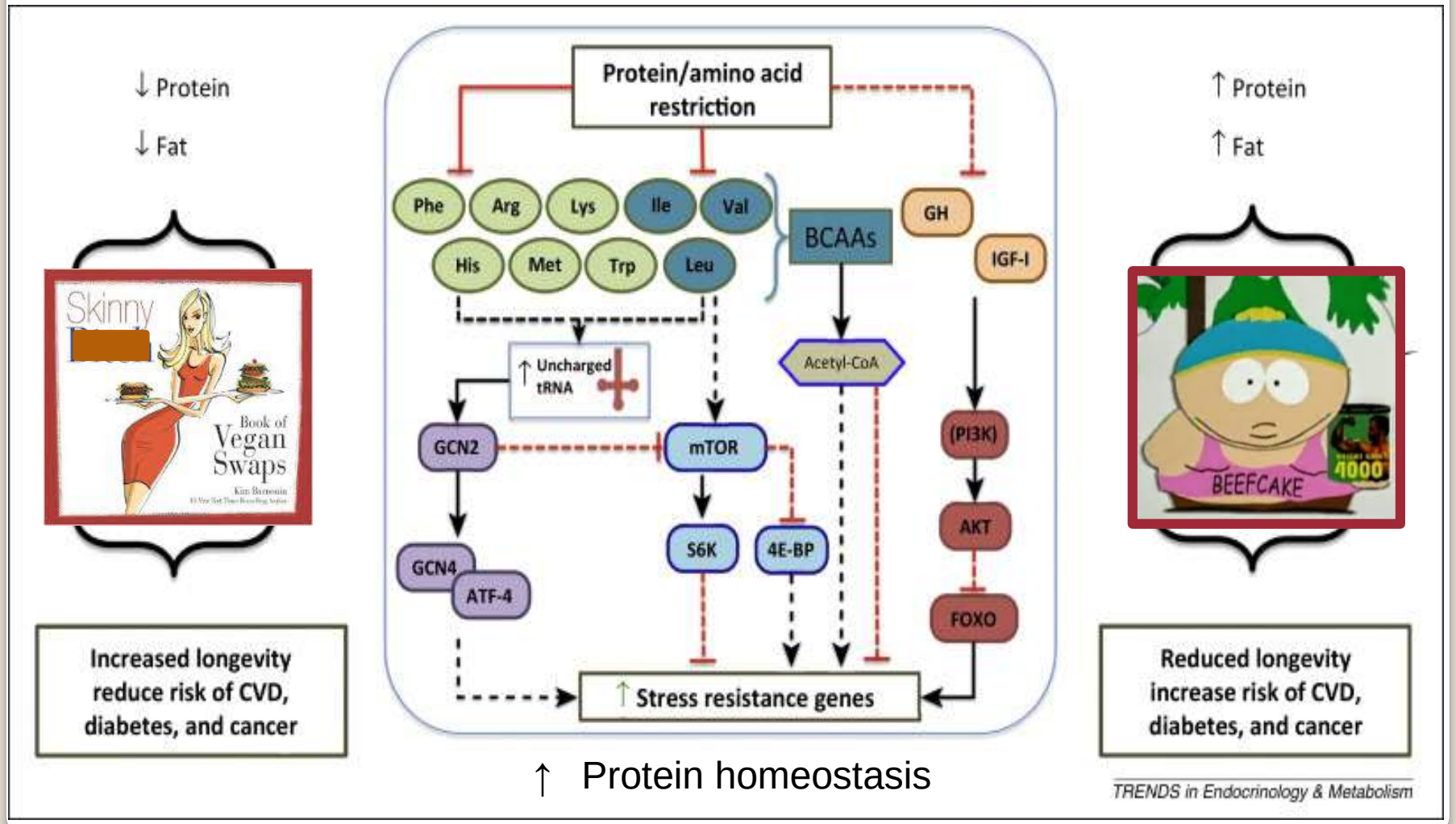


methylation
histones/DNA
phospholipids
neurotransmitters
creatine synthesis

↑ antioxidant defenses, mitochondrial function

Adapted from: https://www.researchgate.net/publication/276164612_Thiol_redox_homeostasis_in_neurodegenerative_disease/figures?lo=1

Proposed Mechanisms for how Dietary Restriction Promotes Healthspan



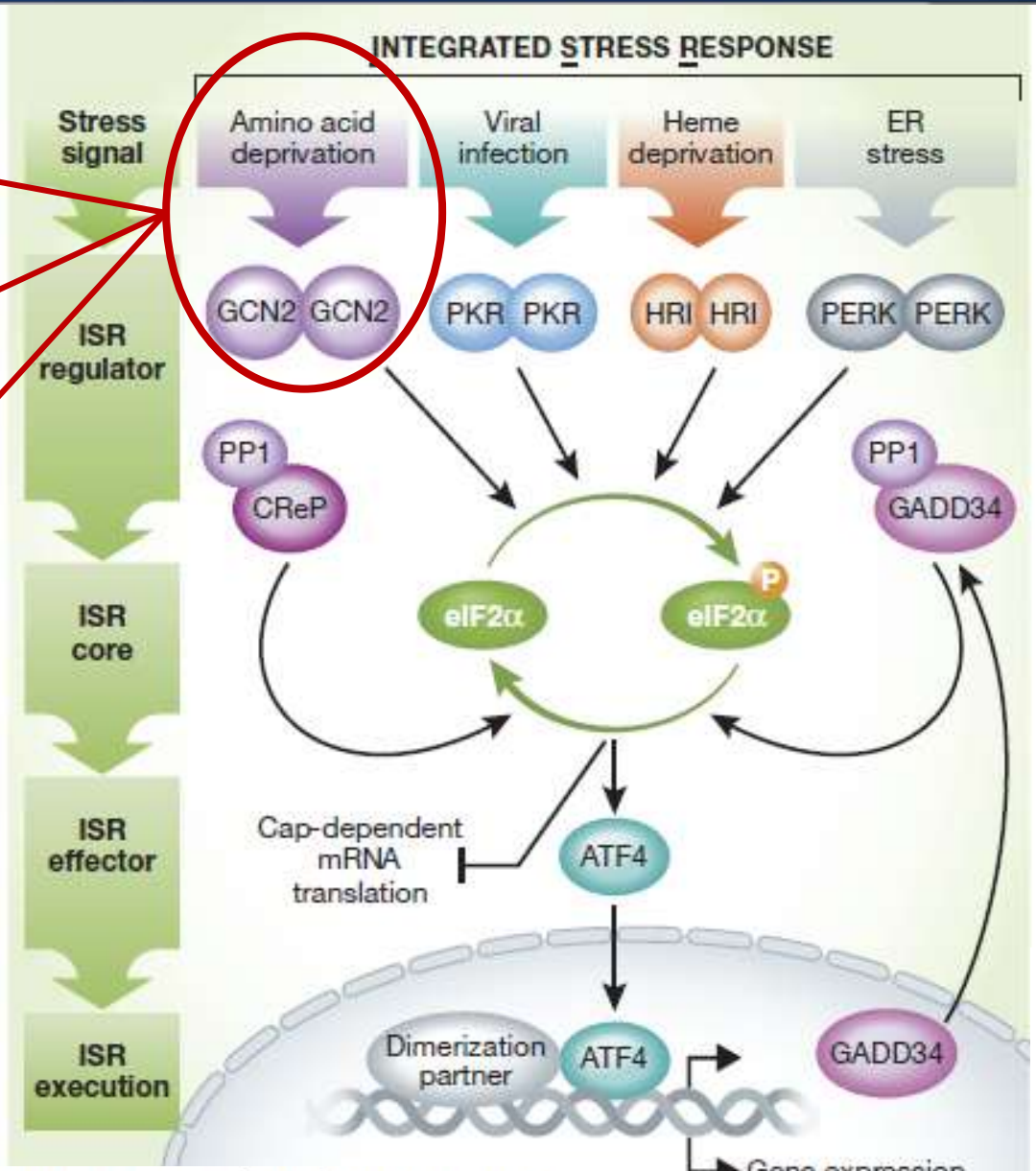
Adapted from: Mirzaei et al., 2014

Integrated Stress Response

Diet

Drugs

Genetics

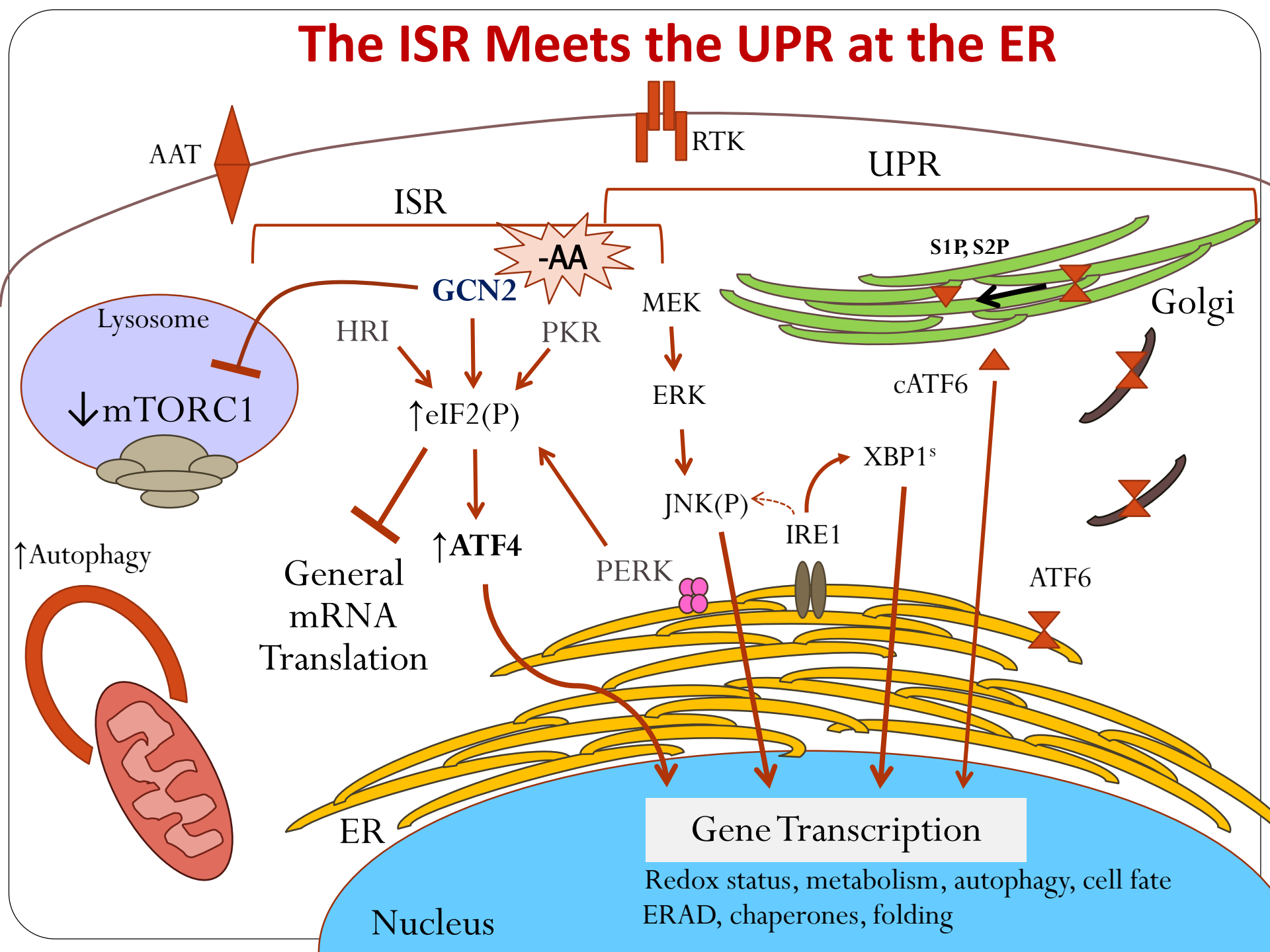


ISR Functions

Adaptation

Hormesis

Preconditioning


The ISR Meets the UPR at the ER
AAT
RTK
UPR
ISR
-AA
GCN2
S1P, S2P
Golgi
Lysosome
↓mTORC1
HRI
PKR
MEK
ERK
cATF6
↑eIF2(P)
XBP1s
JNK(P)
IRE1
↑Autophagy
↑ATF4
General
mRNA
Translation
PERK
ATF6
ER
Gene Transcription
Redox status, metabolism, autophagy, cell fate
ERAD, chaperones, folding
Nucleus

Potential Areas for Collaboration:

Mechanisms linking dietary restriction with aging biology.

- Nutrient sensing pathways (ISR, mTOR)
- Proteostasis control (UPR, autophagy)
- Environmental factors (temperature, light, physical activity/exercise as medicine)

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Thank you! Questions?

Developing Sustainable Models of Dementia Behavioral Interventions

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Ernest Mario School of Pharmacy & Rutgers School of Public Health

Rutgers Healthy Aging Symposium | October 18, 2018

DISCLOSURE: This work was previously presented at the International Association for Geriatrics and Gerontology (IAGG) San Francisco, 2017

CO-AUTHORS:
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Laura N. Gitlin, Drexel University
Eric Jutkowitz, Brown University
Richard H. Fortinsky, University of Connecticut

FUNDING STATEMENT: Supported by National Institute on Aging Grant #3R01AG044504 (Principal Investigator: R. Fortinsky)

What is COPE-CT?

- Care of Patients with Dementia in Connecticut (COPE-CT) is a 12-month in-home supportive behavioral intervention aimed at delaying nursing home admission through a set of services available as an add-on to the existing Connecticut Medicaid program
- Consists of occupational therapists and nurses working with the PwD and CG in the PwD's home over 4 months to increase the PwD's physical ability as well as teach the CG skills to manage the PwD's dementia symptoms
- COPE-CT RCT aims to determine whether adding these services improves the QOL of the PwD and the CG, and to evaluate their confidence in using these strategies
  - RCT includes a cost-benefit analysis from the Connecticut Medicaid (payer) perspective to determine if COPE-CT yields a net financial benefit to the Connecticut Medicaid program

COPE –CT Cost Study: Part of a Larger Body of Rutgers HOPE Collaborative Work

Dementia Behavioral Intervention	Study Type	Cost Analysis Type	Location(s)	Lead Behavioral Scientist(s)
Tailored Activity Program (TAP)	Pilot	Post Hoc Intervention Costs	Philadelphia	Gitlin
Customized Activity Program (CAP)	Efficacy	Prospective Cost Effectiveness	Baltimore Sydney	Gitlin Clemson
Caring for Older Persons in their Environment (COPE)	Transla-tional	Prospective Cost Benefit	Connecticut (statewide)	Fortinsky
Maximizing Independence (MInd) at Home	Efficacy	Prospective Cost Benefit	Baltimore	Samus
Adult Day Services Plus (ADS+)	Effective-ness	Prospective Cost Effectiveness	US (nationwide)	Gaugler and Gitlin (Co-PIs)

What is "net financial benefit"?

- A measure in cost benefit analysis
- Net benefit = (b – c)
  - b is the total financial benefits of the treatment, in $ vs. comparison group (incremental)
  - c is the total cost of the treatment, in $, vs. comparison group (incremental)
  - Implement the treatment if net benefit > 0$ AND purchaser is willing to pay (WTP) for it

$$\text{Net Benefit}_i = \sum_{t=1}^{n} \frac{b_i(t) - c_i(t)}{(1+r)^{t-1}}$$

Where $b_i(t)$ = benefits (in $US) derived in COPE study year t
$c_i(t)$ = costs (in $US) during COPE study year t
$1/(1+r)$ = discount factor at annual interest rate r
n = lifetime of the study

- Calculating b and c typically involves summation of many cost variables in both the treatment and control groups
- WTP is measured separately using contingent valuation method

OBJECTIVES OF PROJECT EXAMPLE

1. Share COPE intervention costs for occupational therapist (OT) and nurse (RN) components

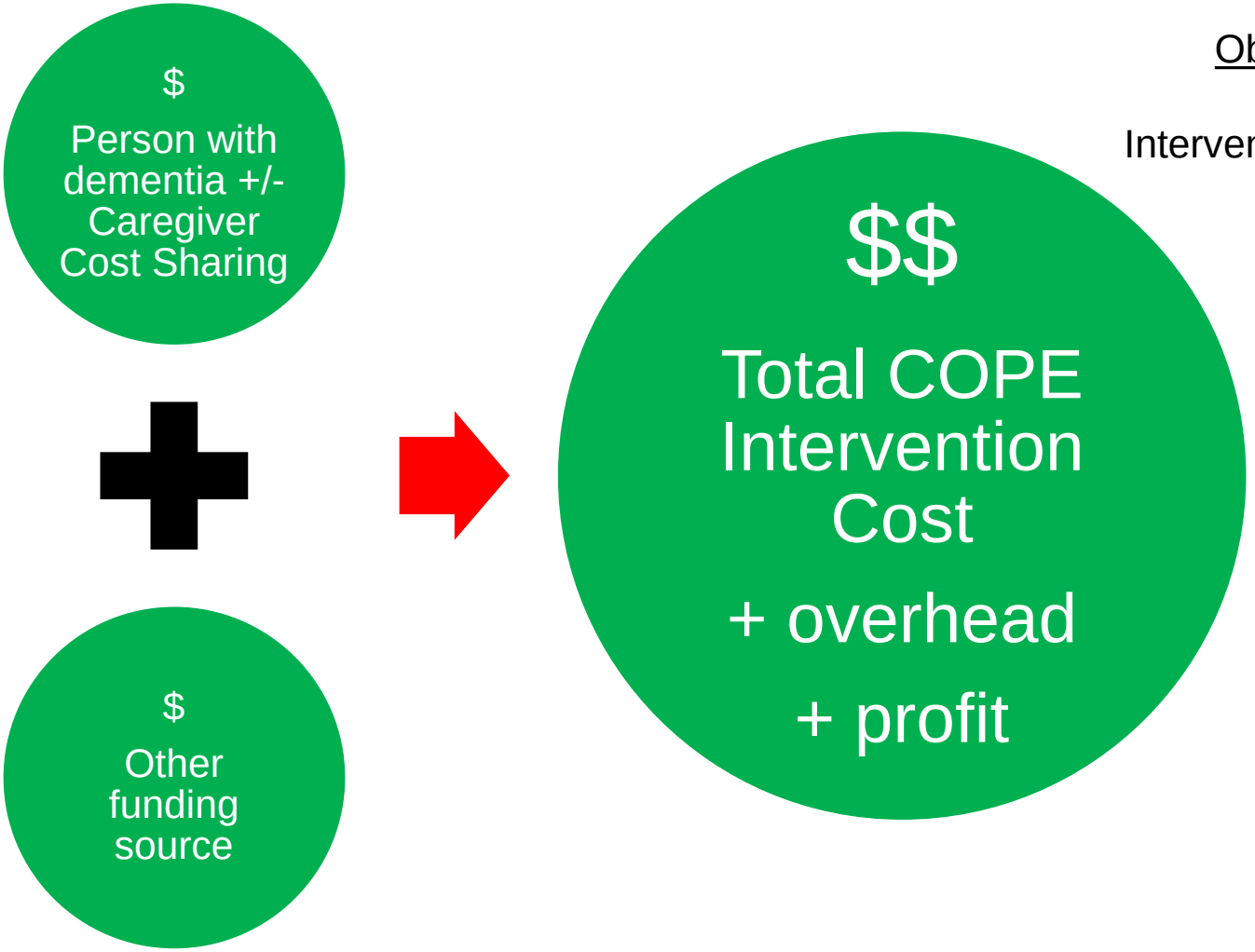
2. Report willingness to pay (WTP) for a dementia support program at baseline

3. Explain linkage between intervention costs and WTP as components of a sustainable financing strategy

FINANACING COPE: A CONCEPTUAL ILLUSTRATION

Objective 2:
WTP

Objective 1:
COPE
Intervention Cost



Payers

Provider

METHODS

1. COPE INTERVENTION COSTS

- Costs considered include:
  - One RN initial in-home assessment and follow-up telephone call
  - Up to 10 in-home OT visits per participant in the intervention arm
- Data sources:
  - RN and OT time records
  - Mileage reimbursement records
- Assumptions:
  - RN wage rate $37.18/hr[1]
  - OT wage rate $41.66/hr[1]
  - Fringe benefits rate 30.2%[2]
  - Travel speed assumed to be 50 miles per hour
  - Mileage reimbursement $0.575/mile[3]
  - Costs are $US 2015

[1] May 2015 State Occupational Employment and Wage Estimates, Connecticut. Bureau of Labor Statistics website. US Department of Labor website https://www.bls.gov/oes/2015/may/oes_ct.htm#29-0000. Accessed June 05, 2017.
[2] Employer Costs for Employee Compensation – December 2015. Bureau of Labor Statistics. US Department of Labor website. https://www.bls.gov/news.release/archives/ecec_03102016.pdf. Accessed June 08, 2017.
[3] Revenue Procedure Notice 2014-79. Administrative, Procedural, and Miscellaneous. Internal Revenue Service website. https://www.irs.gov/pub/irs-drop/n-14-79.pdf. Updated December 29, 2014. Accessed June 08, 2017.

2. WILLINGNESS TO PAY

- WTP was asked of caregiver using a contingent valuation method
- WTP scenario was developed with investigator input
- Baseline sample
  - Date of data cut: 06/22/2017
  - Available sample: 220 caregivers at baseline
- Data analyzed for the full sample as well as by Connecticut Home Care Program for the Elderly (CHCPE) category

BASELINE WTP SCENARIO

- ❑ $0/session
- ❑ $25/session
- ❑ $50/session
- ❑ $75/session
- ❑ $100/session
- ❑ $125/session
- ❑ $150/session
- ❑ $175/session
- ❑ $200/session
- ❑ Other price/session: _____

RESULTS

1. COPE INTERVENTION COSTS

- Available sample = 85 participants
- 12 interventionists (3 RN, 9 OT)
- Overall results (comprising RN and OT visits):

	Mean	SD	Min	Max	Total
Total visit time (hours)	11.02	5.81	0.58	24.92	936.93
Total visit cost	$590.27	$314.58	$28.24	$1,338.87	$50,173.14
Total round-trip mileage	241.97	180.26	14.00	1157.60	20567.20
Total mileage cost	$139.13	$103.65	$8.05	$665.62	$11,826.14
Total travel time (hours)	4.84	3.61	0.28	23.15	411.34
Total travel time cost	$257.39	$194.98	$13.55	$1,253.74	$21,878.23
Total intervention cost	**$986.79**	**$538.77**	**$55.71**	**$2,530.29**	**$83,877.51**

2. WILLINGNESS TO PAY

- Baseline WTP per session, comprising all CHCPE categories:

	n	Mean[a]	SD	Min	Max
Baseline	220	$56.05	$55.13	$0	$200

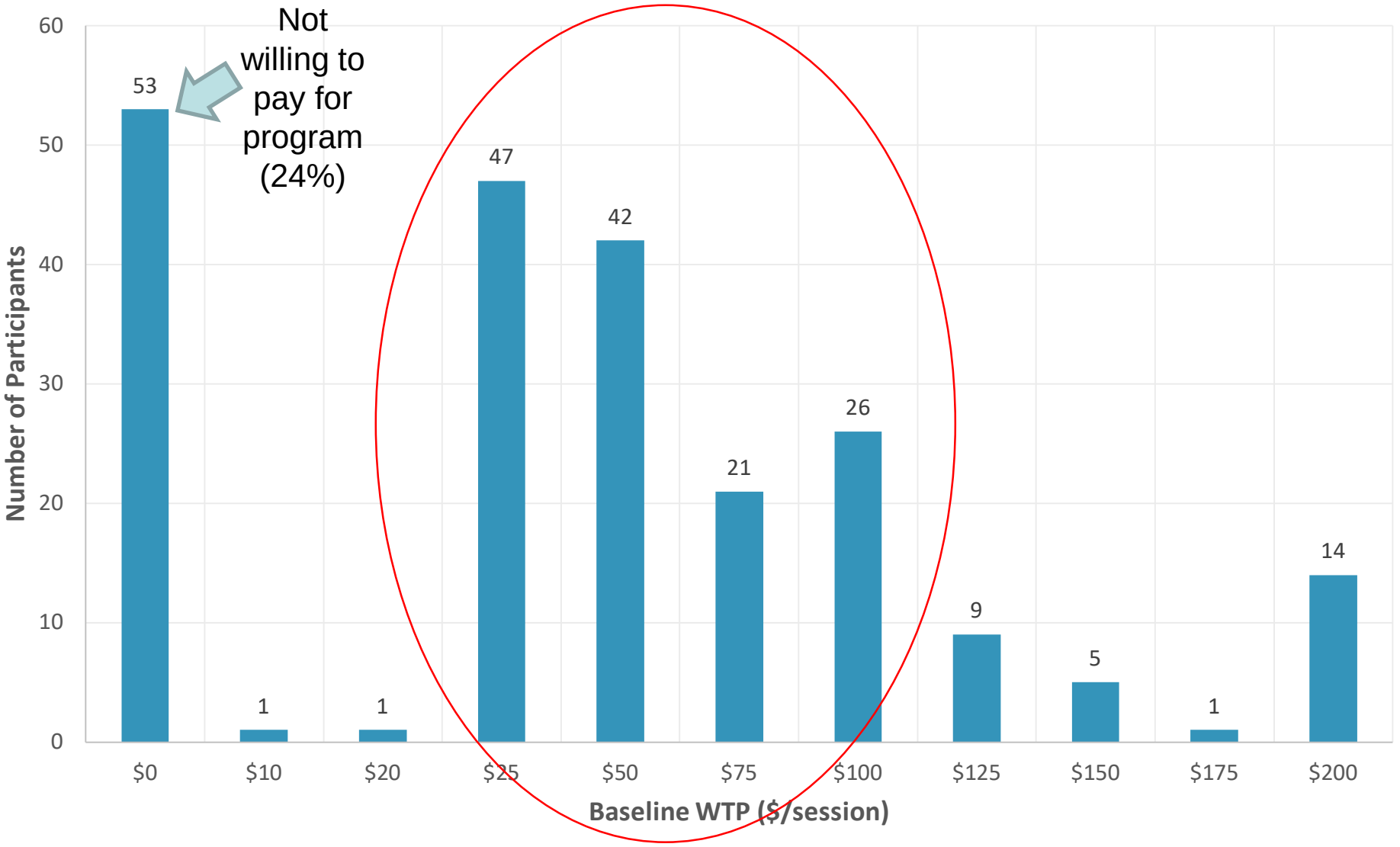
- Baseline WTP per session, by CHCPE category:

CHCPE Category	n	Mean[b]	SD	Min	Max
1	4	$87.50	$25.00	$50	$100
2	66	$57.58	$56.50	$0	$200
3	150	$54.53	$55.07	$0	$200

Pairwise differences in means not statistically significant at BL ($p > 0.05$ for all three pairs)

2. WILLINGNESS TO PAY, continued

Distribution of Baseline WTP (n=220)



KEY LEARNINGS SO FAR

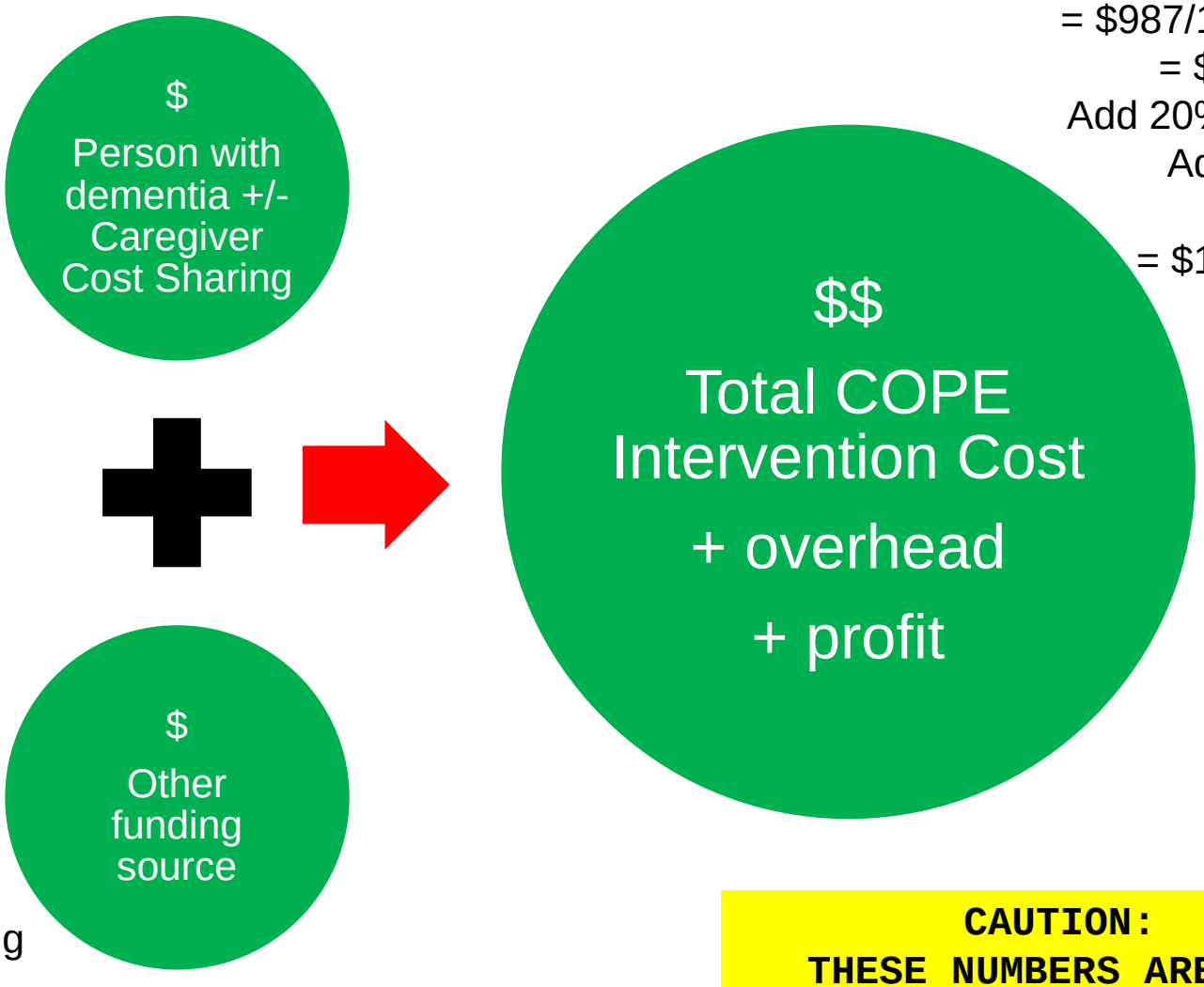
1. Intervention costs:
   - Intervention delivery accounts for 60% of total costs
   - Travel (mileage reimbursement + travel time) accounts for 40% of total costs
     - There is an opportunity to increase efficiency
2. WTP:
   - 24% not WTP but 76% are WTP
   - Mean WTP/session = $56
   - No detectable difference in WTP by CHCPE category

LIMITATIONS

1. Intervention costs do not yet include:
   - Time cost of OT telephone calls
   - Telephone charges
   - Supply costs (e.g., activity supplies, documentation forms)
   - Program supervision / fidelity monitoring
2. WTP:
   - May change after receiving COPE
   - “Willingness” to pay does not necessarily equate to ability to pay or affordability
   - Group assignment was not considered in this analysis

WE ARE STARTING TO PAINT A PICTURE…

IF WTP =
$56/session



IF Total COPE Intervention Cost
= $987/10 sessions
= $98/session
Add 20% overhead
Add 5% profit
TOTAL
= $123/session

THEN other funding would need to be
= $67/session

CAUTION:
THESE NUMBERS ARE FOR ILLUSTRATION PURPOSES ONLY

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laurapizzihope

Email:

laura.pizzi@rutgers.edu

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Examining How Healthy Brain Aging Begins in Childhood

IMAGE
(not included for mass distribution)

Emily A. Greenfield, PhD

School of Social Work

Institute for Health, Health Care Policy, and Aging Research

Rutgers, The State University of New Jersey

egreenf@ssw.rutgers.edu

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RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY

Paradigm Shift in Social Gerontology

IMAGE
(not included for mass distribution)

Settersten, R.A. (2017). Some things I have learned about aging by studying the life course. *Innovation in Aging, 1*(2). doi: 10.1093/geroni/igx014

Image © Tom Hussey
https://www.tomhussey.com/PROJECTS/REFLECTIONS/thumbs

"Old age as a life phase is inherently different from earlier phases because there is a long past that must be taken into account. That long past reflects the fact that aging is a lifelong process."

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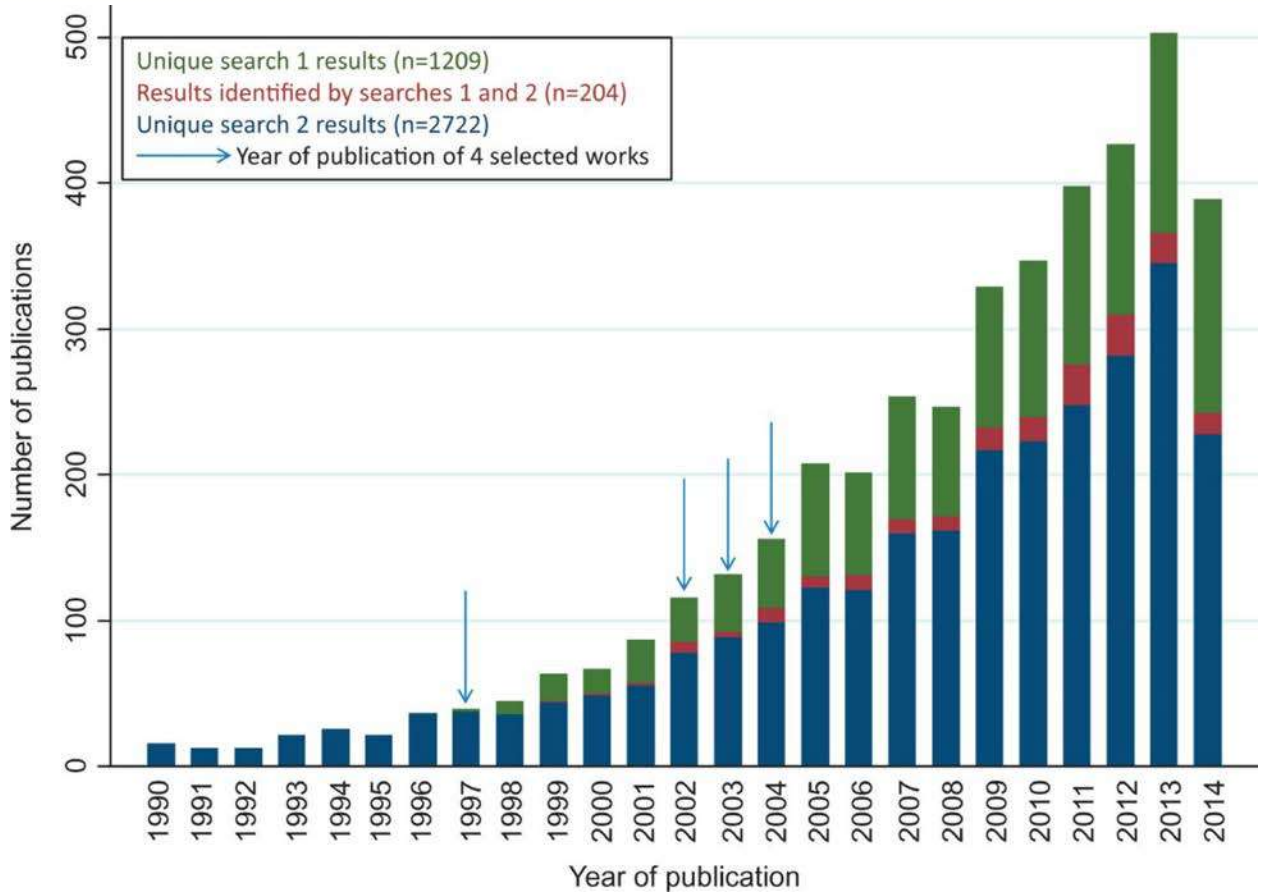
Paradigm Shift within Epidemiology



Ben-Shlomo, Y., Cooper, R., & Kuh, D. The last two decades of life course epidemiology and its relevance for research on ageing. *International Journal of Epidemiology, 45*(4), 973-988. doi: 10.1093/ije/dyw096

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Do Inequalities from Childhood Matter for Later Life Cognitive Health?

IMAGE
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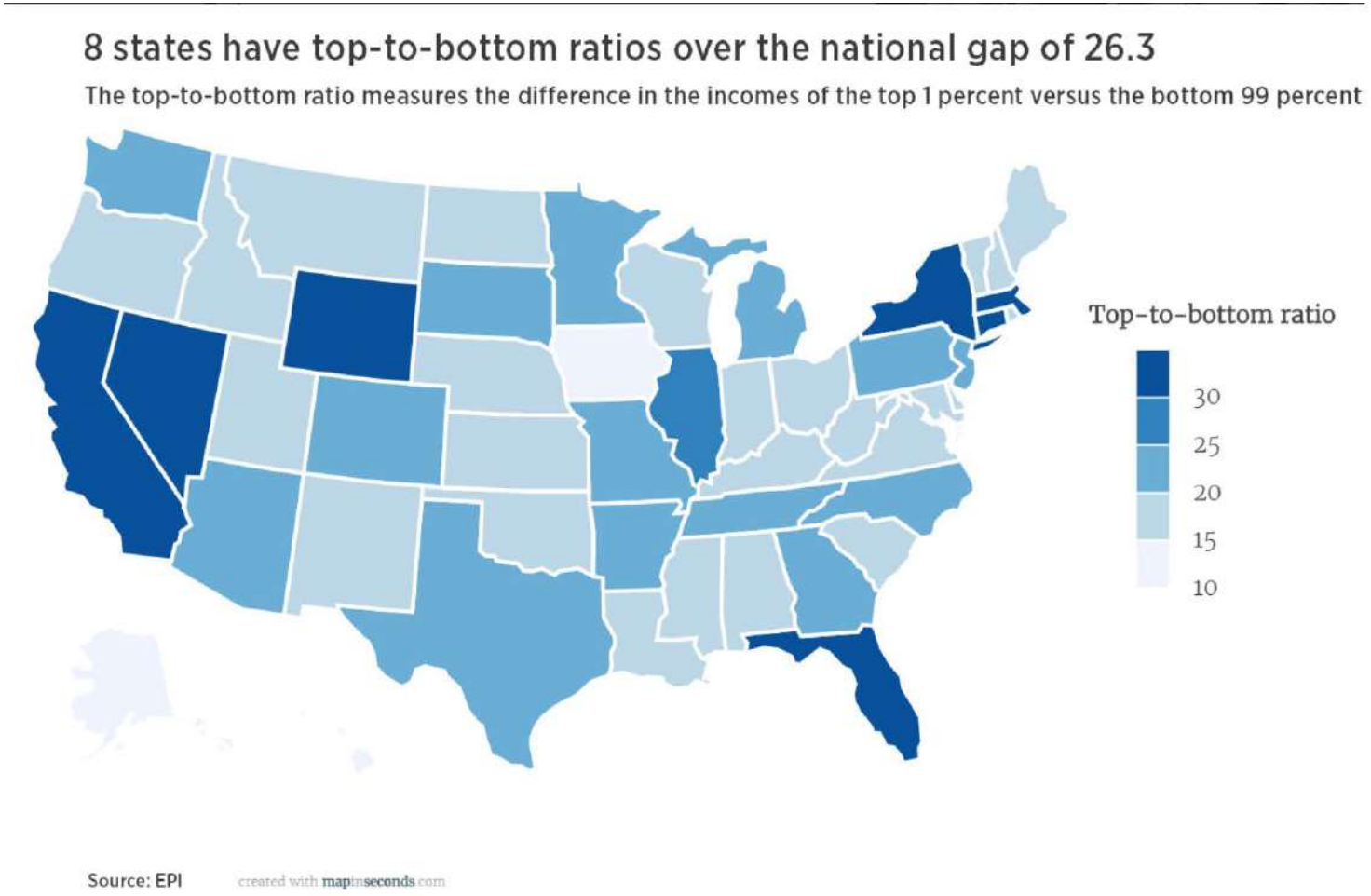
Inequality among Families Today



https://www.cnbc.com/2018/07/19/income-inequality-continues-to-grow-in-the-united-states.html

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U.S. National Plan to Address Alzheimer's Disease: 2017 Update

Goal 1: Prevent and Effectively Treat Alzheimer's Disease and Related Dementias by 2025

Research continues to expand our understanding of the causes of, treatments for, and prevention of AD/ADRD. Goal 1 seeks to develop effective prevention and treatment modalities by 2025. Ongoing research and clinical inquiry can inform our ability to delay onset of AD/ADRD, minimize its symptoms, and delay its progression. Under this goal, HHS will prioritize and accelerate the pace of scientific research and ensure that as evidence-based solutions are identified and quickly translated, put into practice, and brought to scale so that individuals with AD/ADRD can benefit from increases in scientific knowledge. HHS will identify interim milestones and set ambitious deadlines for achieving these milestones in order to meet this goal.

In 2016/2017, Goal 1 showed substantial progress across a spectrum of research areas, thanks to the continued support from our national leadership and the American public, the dedication of study volunteers and their families and caregivers, and the valued work of clinicians and scientists.

Federal funding devoted to AD/ADRD research has expanded over the past several years, reflecting intensified national interest in finding ways to treat these devastating diseases. The National Institutes of Health (NIH) played a lead role by redirecting $50 million in funding in fiscal year (FY) 2012 and allocating $40 million in FY 2013 to promising avenues of AD/ADRD research. Federal appropriations increases to the NIH budget by $100 million in FY 2014 and $25 million in FY 2015, primarily directed toward AD/ADRD research, were also approved. However, the biggest increases in funding came in FY 2016 and FY 2017, following Congressional passage of the Consolidated Appropriations Act 2016 (P.L. 114-113) and the Consolidated Appropriations Act, 2017 (P.L. 115-31). The FY 2016 appropriations directed an unprecedented additional $350 million toward AD/ADRD research, with an additional $400 million provided for this research in FY 2017; increasing overall NIH funding from Congress for AD/ADRD research by $912 million from FY 2012 to FY 2017. In FY 2017 alone, NIH estimates spending $1.4 billion on AD/ADRD research. This enormous infusion of resources enabled the launch and expansion of research programs and invigorated investigator-initiated research, further accelerating progress towards the Plan's ultimate research goal: finding effective interventions to treat or prevent AD/ADRD by 2025. [See https://www.congress.gov/115/bills/hr244/BILLS-115hr244enr.pdf.]

NIH was already poised to integrate the extraordinary new funds into its research portfolio. In July 2015, NIH released the first of what is now an annual professional judgment budget for Congress -- and the American people -- estimating the costs of accomplishing the research goals of the National Plan to Address Alzheimer's Disease. This report is known as a "bypass budget" because of its direct transmission to the President and subsequently to Congress without modification through the normal federal budget process. The most recent estimate, submitted in July 2017, outlines funding needs for the most promising research approaches for FY 2019. [See https://www.nia.nih.gov/about/sustaining-momentum-nih-takes-aim-alzheimers-disease-related-dementias.]

Advancing the Empirical Evidence, while Contributing to Theory

National Institute on Aging

WISCONSIN LONGITUDINAL STUDY

RUTGERS School of Social Work

Childhood Socioeconomic Status and Later L… Evidence Fr… Wisconsin L… Study

Emily A. Green… and Sara M. Mo…

Abstract

Objectives: This stud… predictor of later life … for associations. **Me**… Wisconsin Longitudin… educational attainmen… Memory and language… years. **Results:** Glob… levels of language/ex… involving parents' edu… when accounting for p… parental income and … We found no associa… **Discussion:** Findings … differences in childho…

[1]Rutgers, The State Univer…
[2]Boston College, Chestnut…

Journal of Aging and Health
1–27

DOI: 10.1177/0898264318783489

Social Science & Medicine
Volume 212, September 2018, Pages 219-226

Childhood socioeconomic status and genetic risk for poorer cognition in later life

Sara M. Moorman [a], Kyle Carr [a], Emily A. Greenfield [b]

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Highlights

- Higher childhood SES predicted better language/executive function in older adulthood.
- APOE ε4 carrier status was unrelated to language/executive function.
- For memory, APOE ε4 carriers had differential susceptibility to childhood SES.
- Differential susceptibility dissipated with age.

Abstract

The ε4 allele of the APOE gene is associated with poorer cognition in later life. This study aimed to advance understanding of how environments potentially moderate this genetic risk by focusing on childhood socioeconomic status (SES). Previous research across diverse national contexts has found that older adults from higher-SES families in childhood demonstrate better cognitive functioning than their lower-SES counterparts. Nevertheless,

GE

WLS Sample

IMAGE
(not included for mass distribution)

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A Unique Data Source

- The Measures
  - Neurocognitive assessments
    - Age 65 and 72
    - Memory and language/executive functioning
  - Prospective measures from adolescence
  - Careful attention to status attainment of parents and the participant
  - Genetic data

- The Sample
  - White, high school graduates from Wisconsin
  - Yet still diverse in important ways (e.g., rural versus urban)

Summary of Findings (So Far)

- SES associated with baseline levels of cognition at age 65, not so much with change
- Larger associations for language/executive functioning than memory
- Associations involving parental education larger and more robust than parents' occupational status and income
- Post-secondary educational attainment and adolescent IQ account for much of the association between parental SES and later life cognition

Summary of Findings (So Far)

- Evidence for differential susceptibility to APOE-4, specifically:
  - For memory
  - At age 65

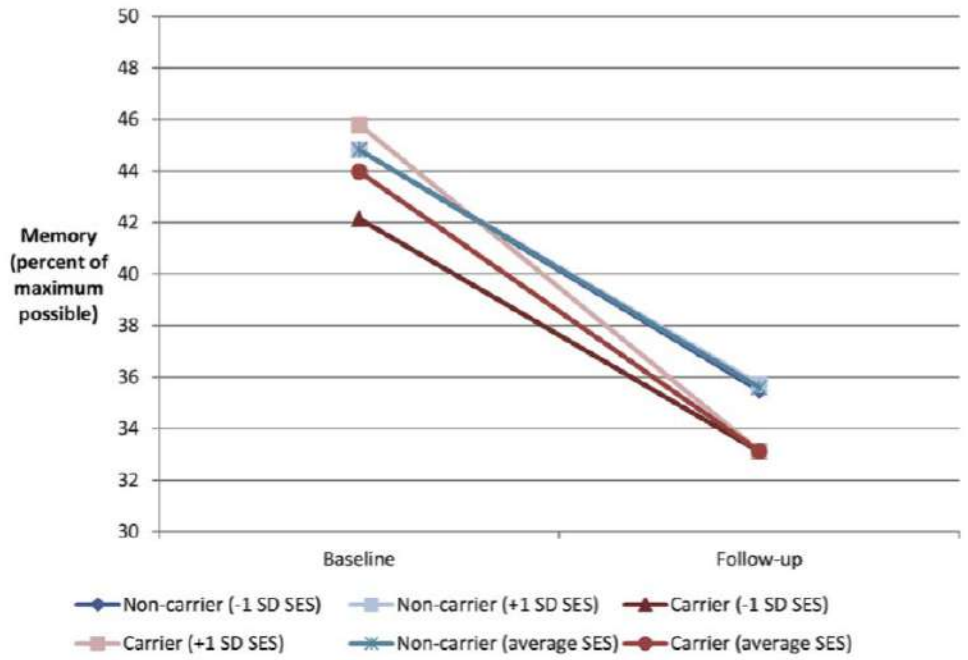

Fig. 2. Gene-by-environment interaction of APOE ε4 carrier status and childhood socioeconomic status over a seven-year period.

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Implications

- *For research*: Consistent evidence that childhood matters.
- *For theory*: Constellations of risk and protective factors stemming from childhood.
- *For society*: Forging greater connections across policy on children's health and healthy aging.

Next Steps

- Latent transition analyses to model more subtle changes between ages 65 to 72
- School quality as another aspect of childhood inequality
- Propensity score analysis concerning long-term implications of post-secondary education

Childhood Inequality and Brain Aging among African American Adults

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Thank You!

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IMAGE
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Grant funding: NIA-R01AG057491-02S1

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Age, Cohort, and Gender Variations in Problem Sleep

Jen-Hao Chen, Ph.D.
Department of Sociology &
Health Sciences Center
Rutgers University (Camden)

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Age and Sleep

- Sleeping well is essential for health and well-being
- Poor sleep in old age is associated with
  - Chronic diseases
  - Cognitive decline
  - Mortality
- Estimates from cross-sectional studies show that approximately one-fifth to 40% of older adults report at least one symptom of insomnia (Foley, Monjan, & Brown et al., 1995; Lauderdale, Schumm, & Kurina et al., 2014)

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Age-Related Changes in Sleep

- Along with the physical changes that occur as we get older, changes to our sleep physiology are a part of the normal aging process (Klerman & Dijk, 2008; Skeldon, Derks, & Dijk, 2016)
- As people age they tend to report having a harder time falling asleep and more trouble staying asleep than when they were younger
- It appears to be self-evident that problem sleep increases with age

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Age-Related Changes in Sleep

- However, the general hypothesis of increasing problem sleep with age may overlook the role of many factors in shaping age growth trajectory of problem sleep
  - Health changes
  - Experience and transitions over the life course
- Not considering these factors may overlook potential disparities in trajectories of problem sleep among the general population of older adults

A Life Course Perspective

- Changes in problem sleep may mirror change in an individual's social life
- Individuals from the same birth cohort experience and expose to common social conditions and events at the same time point
  - It is expected age growth trajectory of problem sleep differs by cohort

Gendered Life Course

- Life course is gendered
  - Men and women expose to different social roles and life transitions
  - Previous studies show that women usually play the role of caregiver in their families, and this role is considered a unique social risk factors for problem sleep that disproportionally affects women (Burgard, 2011; Venn, Arber, Meadows, & Hislop, 2008)
  - It is expected the gendered life course lead to differences in age growth trajectory of problem sleep between men and women

Health and Retirement Study (HRS)

- A nationally representative, longitudinal survey of US older adults (50 years old or older) starting from 1992
  - Follow every two years
  - A new cohort of elderly 50 years every six years
- Measures of problem sleep available in 2002, 2004, 2006, 2010, 2014
- A total of 91,302 person-year observations (38,464 for men and 52,838 for women)

Measures of Problem Sleep

- Four questions concerning sleep
  - “How often do you have trouble falling asleep?”
  - ”How often do you have trouble with waking up during the night?”
  - ”How often do you have trouble with waking up too early and not being able to fall asleep again?”
  - “How often do you feel really rested when you wake up in the morning?”
- Answers range from “most of the time”, “sometimes”, “rarely or never”
  - A scale is created (ranging from 0-8)

Analytical Strategy

- Organizing life histories of sample members into six cohorts
  - Born 1929 and earlier
  - Born 1930-1935
  - Born 1936-1941
  - Born 1942-1947
  - Born 1948-1953
  - Born 1954-1959
- Using 2-level multilevel model
  - First level: survey wave
  - Second level: individuals

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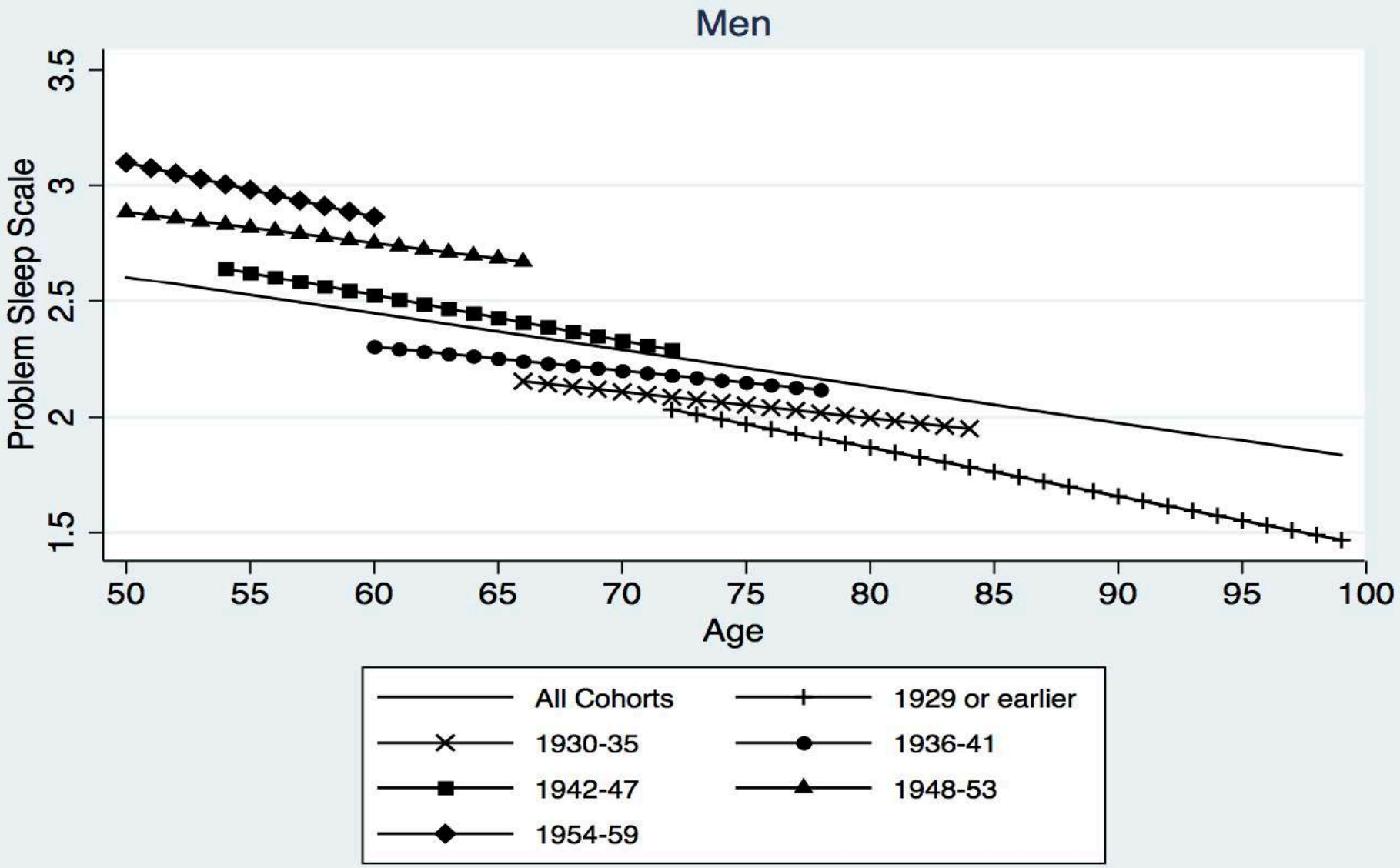
Men
Problem Sleep Scale
1.5
2
2.5
3
3.5
50
55
60
65
70
75
80
85
90
95
100
Age
All Cohorts
1929 or earlier
1930-35
1936-41
1942-47
1948-53
1954-59

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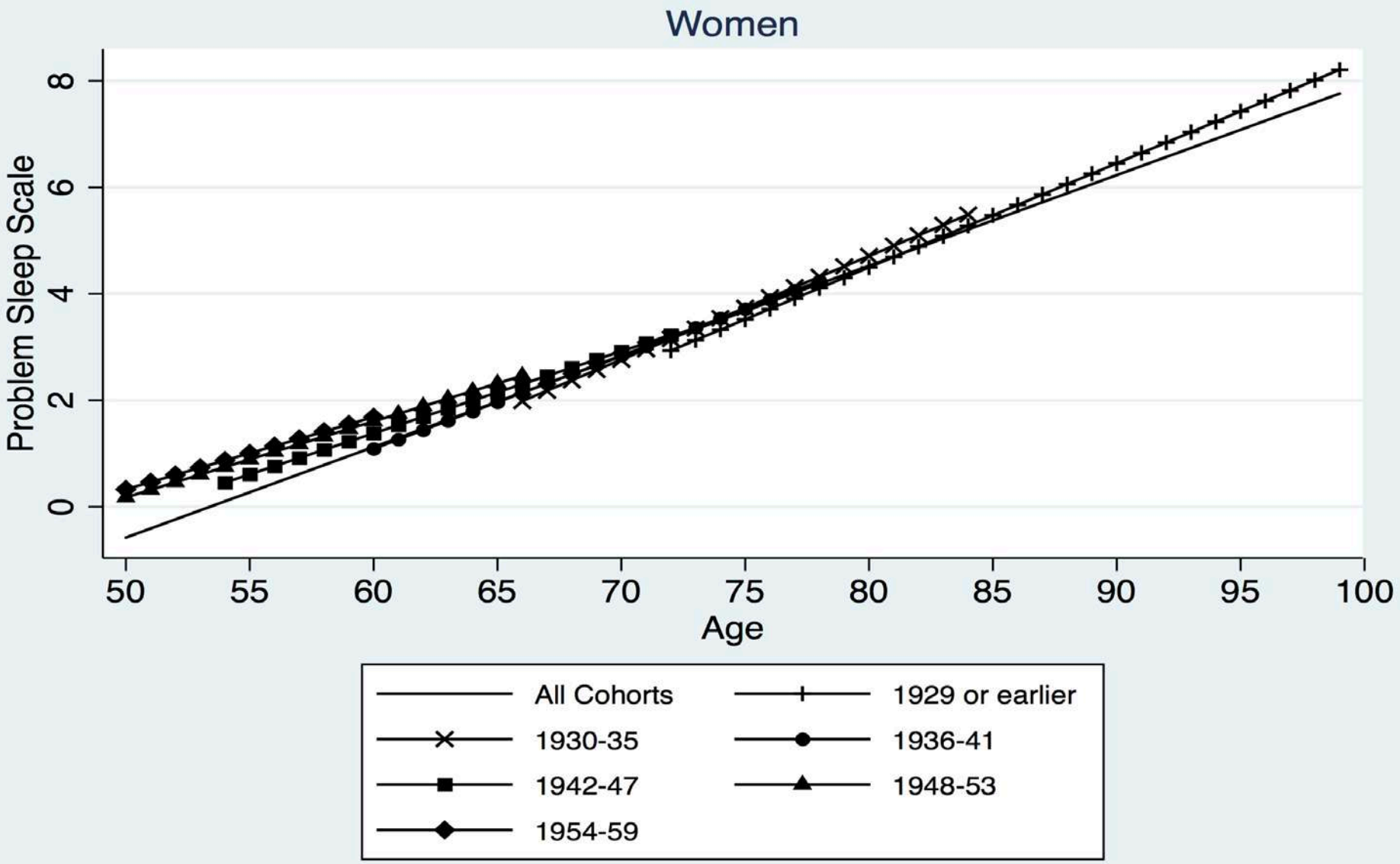
Women
Problem Sleep Scale
0
2
4
6
8
50
55
60
65
70
75
80
85
90
95
100
Age
All Cohorts
1929 or earlier
1930-35
1936-41
1942-47
1948-53
1954-59

Conclusion

- My study reveals gender differences in age growth trajectory of problem sleep
- For men
  - Problem sleep does not increase with age
  - There is no cohort difference in problem sleep
- For women
  - Problem sleep increase with age
  - Younger cohorts increase at a faster pace
  - Younger cohorts also begin with higher level of problem sleep than older cohorts

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Implications

- The results contradict the general hypothesis that age is an independent risk factor for problem sleep for the general population of older adults
- Problem sleep is not destiny for individuals in old age, efforts can be made to improve sleep health and reduce health disparities
- Gender difference in survival may partly explain the gendered patterns

Next Steps

- Research & Collaboration
  - Identifying mechanisms that produce gender and cohort differences
  - Examining consequences of cohort and gender disparities in sleep
  - Collecting new data with more sleep measures and pooling data for further analysis
- Funding
  - NIH “Mechanisms and Consequences of Sleep Disparities in the US” (R01, R21)

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Supporting Health in Older Adults Living with Psychiatric Conditions

Michelle Zechner, PhD, LSW, CPRP
Assistant Professor

Rutgers, The State University of New Jersey
Rutgers Biomedical and Health Sciences
School of Health Professions
Department of Psychiatric Rehabilitation and Counseling Professions

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Challenges to Healthy Aging

- Premature morbidity & mortality
- Complex inter-connected psychiatric and health needs
- Likelihood of accelerated aging in cognitive, functioning and physiological domains(Jeste et al., 2011)
- Poorly trained workforce

How can we support health for people living with psychiatric conditions and co-morbid health conditions?

Identify/test integrated models of practice

- Integrate mental health and physical health care policies & services
- Identify and test holistic models of clinical programming in mental health and aging settings (8 Dimensions of Wellness)

Zechner, M., & Kirchner, M. P. (2013). Balanced Life: A pilot wellness program for older adults in psychiatric hospitals. *Psychiatric Rehabilitation Journal*, *36*(1), 42-57.

Zechner, M., Pratt, C., Barrett, N., Dreker, M. & Santos, S. (2018). *Multi-Dimensional Wellness Interventions for Older Adults with Serious Mental Illness: A Systematic Literature Review.* Manuscript under review.

Increase Motivation for Physical Activity

- Older persons with psychiatric conditions are sedentary
- PA improves psych sxs, health, cognition & well-being
- Need to increase motivation & adherence

Zechner, M., McDonald, M, King, T., Jahnke, R., & Monroy-Miller, C. Engaging older adults using Tai Chi at a psychiatric hospital. *American Journal of Psychiatric Rehabilitation.* In press.

Zechner, M. & Gill, K. (2016). Predictors of Physical Activity in Persons with Mental Illness: A Social Cognitive Model. *Psychiatric Rehabilitation Journal*. *39*(4), 321-335.

Gill, K., **Zechner, M.,** Anderson, E., Swarbrick, M. & Murphy, A. (2016). Wellness for Life: A Pilot Inter-Professional Intervention to Address MetS, *Psychiatric Rehabilitation Journal*, *39*, 147-153.

Prepare the Workforce

- Mental health providers have limited understanding of aging
- Providers in the aging system are challenged by people living with psychiatric conditions
- Need for specialized training

Zechner, M. R., Birkmann, J. C., Sperduto, J., & Pratt, C. (2018). Sensitizing Inpatient Mental Health Staff to the Challenges of Aging. *Journal of Psychosocial Nursing and Mental Health Services*, 56(4), 12-16.

Next Steps

- Identification and testing of effective psychosocial interventions to improve quality of life and improve health outcomes for older adults with co-morbid psychiatric & physical health chronic conditions
- Explore motivation for physical activity
- Refine educational strategies to build workforce competencies in aging and mental health across settings