A Basic Scientist's Perspective on Aging Organisms







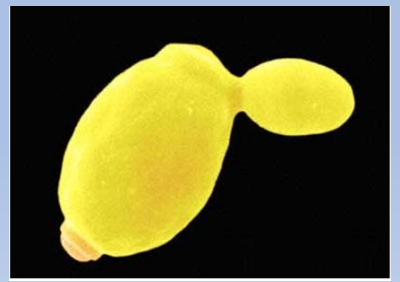
Steven N. Austad, PhD

Scientific Director, American Federation for Aging Research

&

Distinguished Professor, Department of Biology

University of Alabama at Birmingham



"MICE LIE"

"We are very well placed to move away from animal-based models."

"How often animal models mislead us"

"While humans and animals may share genes, some studies have shown there could be functional differences between organ and body systems that may result in some translational limitations."

"NIH will no longer seek proposals exclusively for animal models"

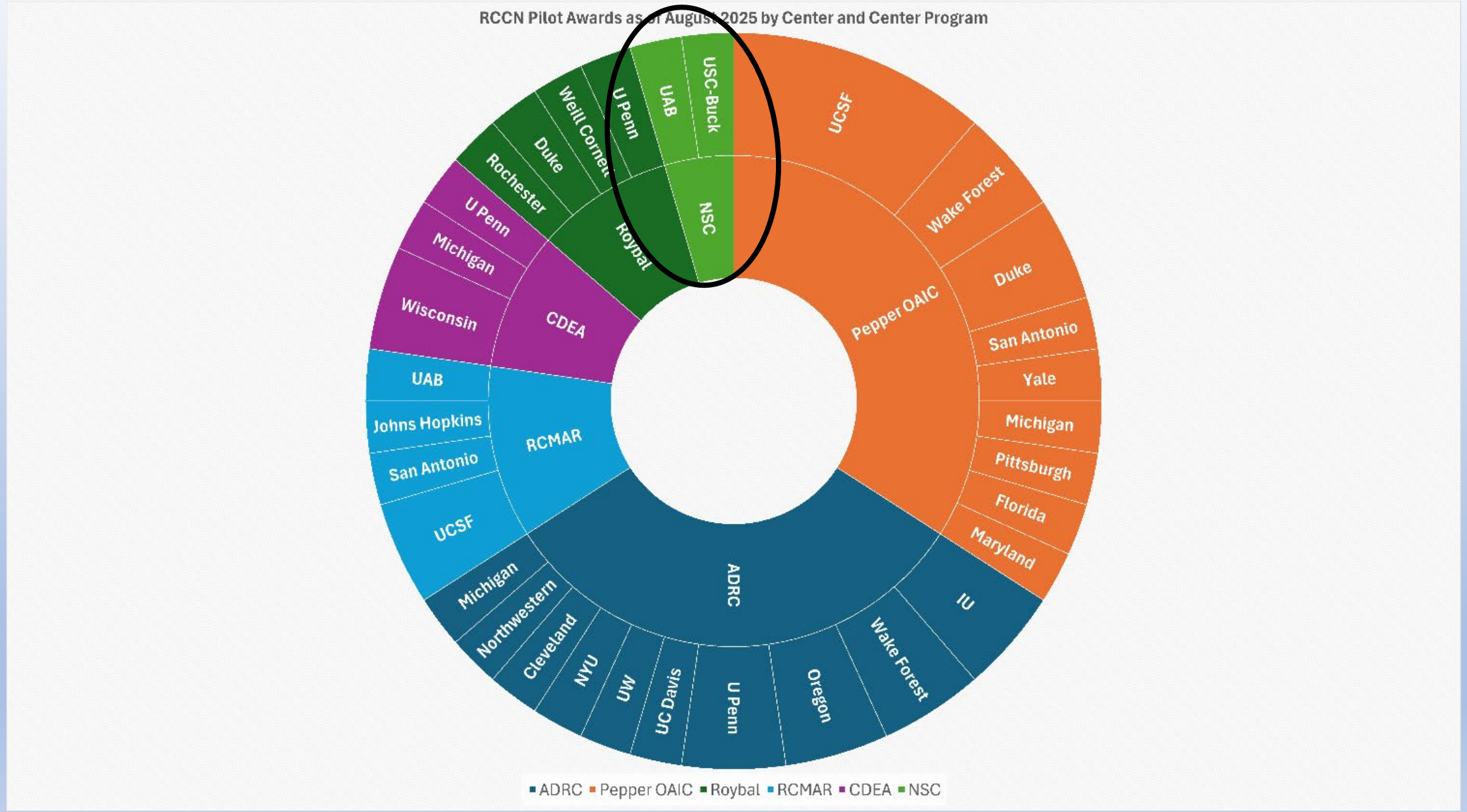
NIH grant review staff will "participate in mitigation training to address any possible bias towards animal studies."

The Seven RCCN Centers Programs

1. Alzheimer's Disease Research Centers (ADRCs)
2. Artificial Intelligence and Technology Collaboratories (AITCs)
3. Centers on the Demography and Economics of Aging (CDEAs)
4. Claude D. Pepper Older Americans Independence Centers (OAICs)
5. Nathan Shock Centers of Excellence in the Basic Biology of Aging (NSCs)
6. Resource Centers for Minority Aging Research (RCMARs)
7. Roybal Centers for Translational Research in the Behavioral and Social Science of Aging



RESEARCH
CENTERS
COLLABORATIVE
NETWORK


RCCN Pilot Awards as of August 2025 by Center and Center Program
USC-Buck
UAB
U Penn
Weill Cornell
Duke
Rochester
Roybal
NSC
UCSF
Wake Forest
Duke
San Antonio
Yale
Michigan
Pittsburgh
Florida
Maryland
Pepper OAIC
U Penn
Michigan
Wisconsin
CDEA
UAB
Johns Hopkins
San Antonio
UCSF
RCMAR
Michigan
Northwestern
Cleveland
NYU
UW
UC Davis
U Penn
Oregon
Wake Forest
IU
ADRC
ADRC
Pepper OAIC
Roybal
RCMAR
CDEA
NSC

What use are animal models for aging research?

The three T's of animal aging research

1. Translation
2. Targets
3. Tools







Are animal models useful for translation?

- ~1/3rd of highly-cited animal trials make it to human trials (Hackam, et al, 2006 JAMA)
  - Of that 1/3rd , only 8% make it through Phase 1 (FDA, 2004)
- Of 5,820 drugs entering phase I trials, 10.4% FDA approval (Hay, et al. 2014)
- Cancer trials
  - 16 IGF-1R inhibitors, 183 trials, 12,000 trial participants, cost ~$2 billion
  - 0 approved for use (Jentsch, et al, 2023 Ophthamol Sci)
- Alzheimer's trials
  - Over 300 successful mouse trials (Shineman, 2011)
  - 2 FDA approved drugs

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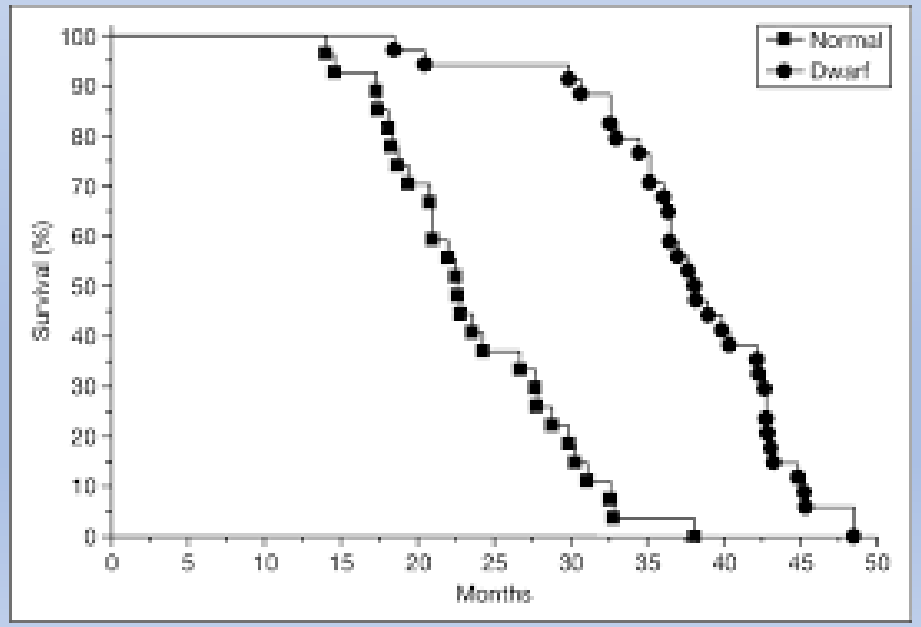


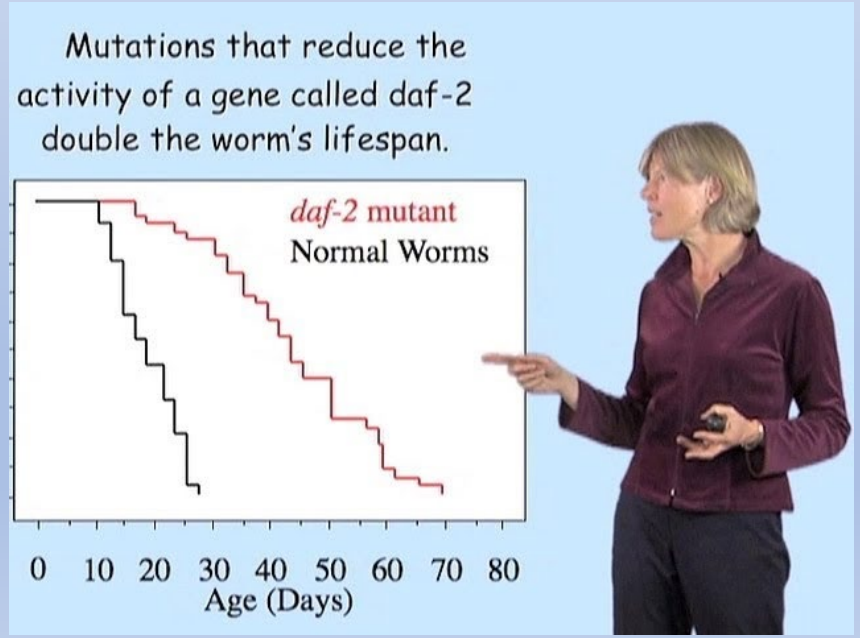
Reduced Insulin/IGF activity



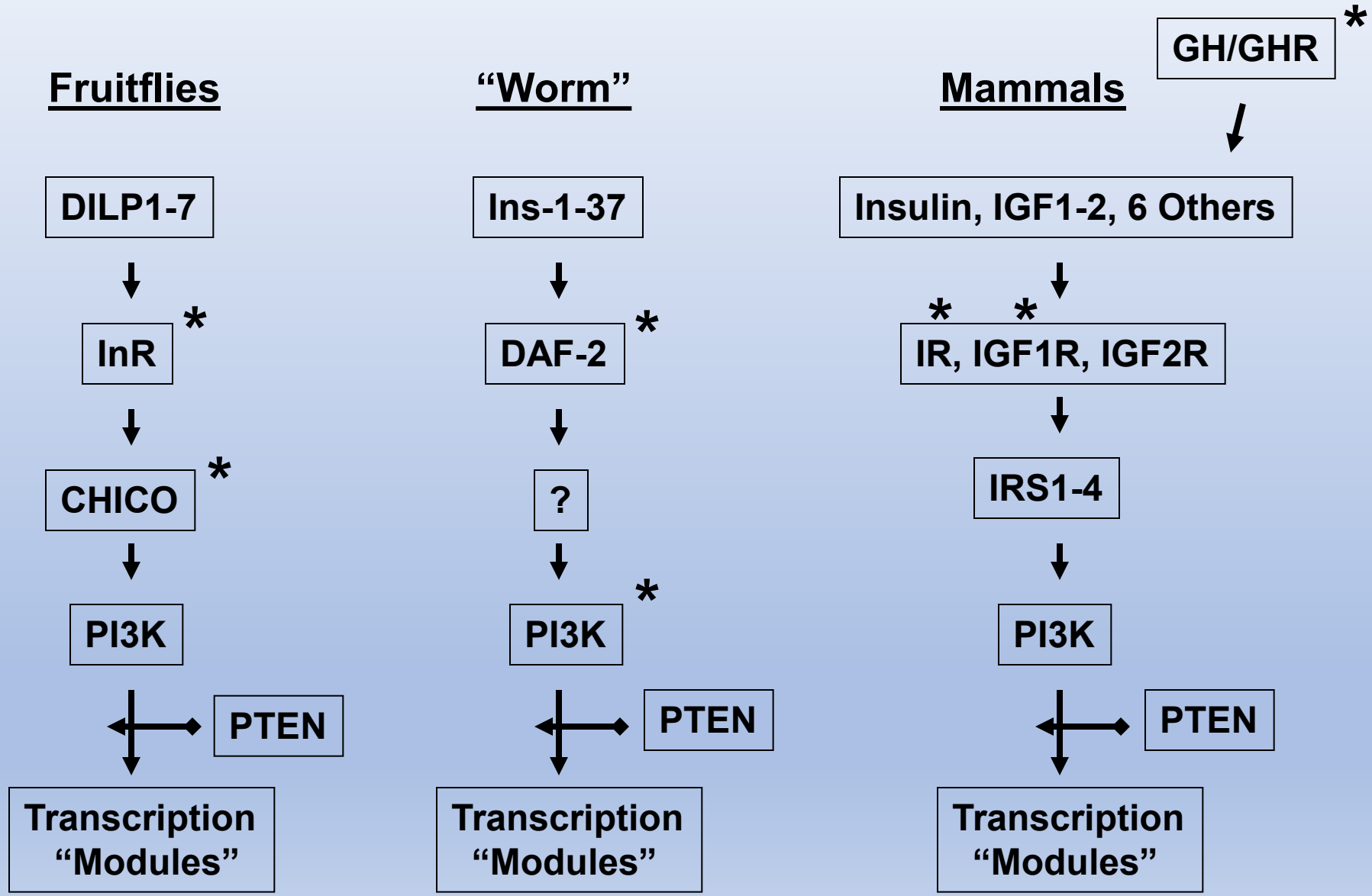


Johnson disc.
age-1 mutant
(1988)

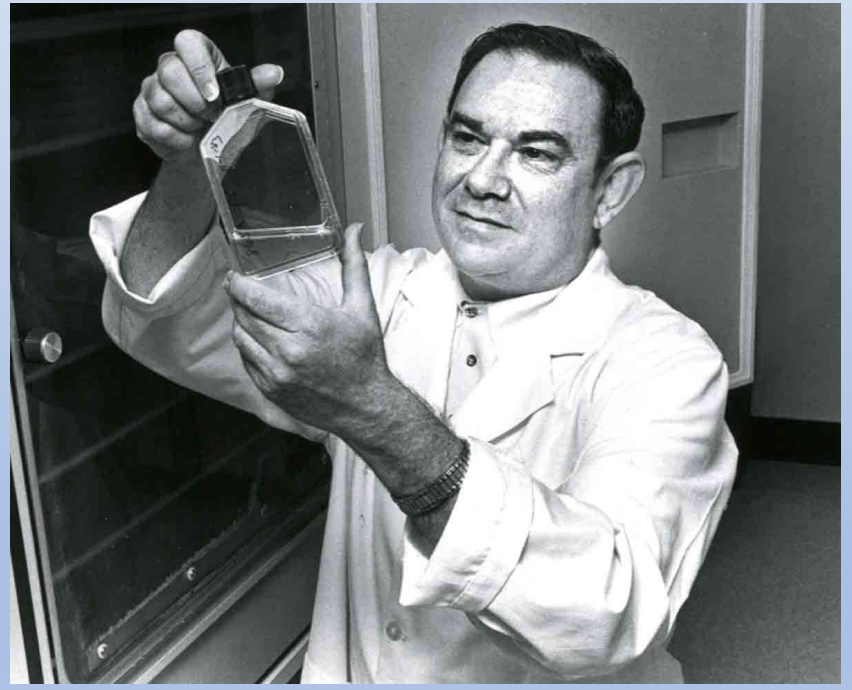


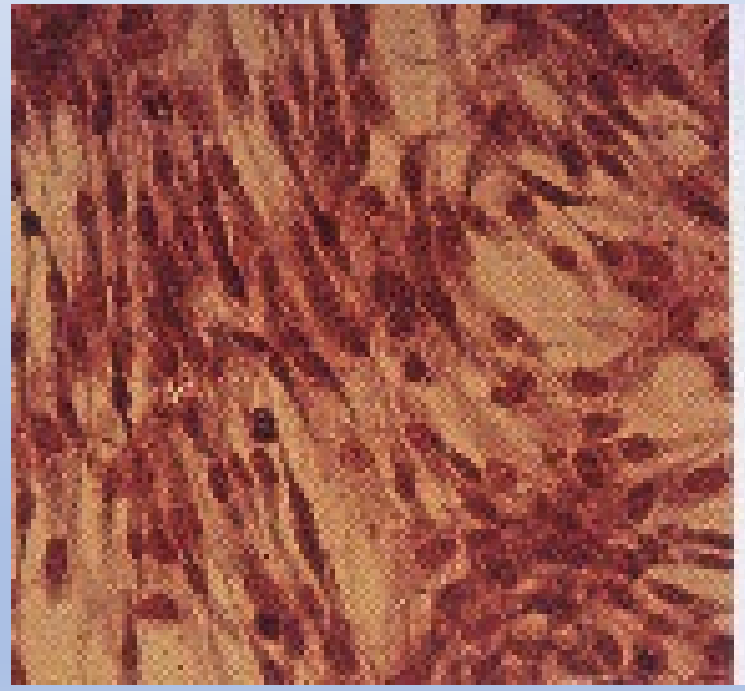


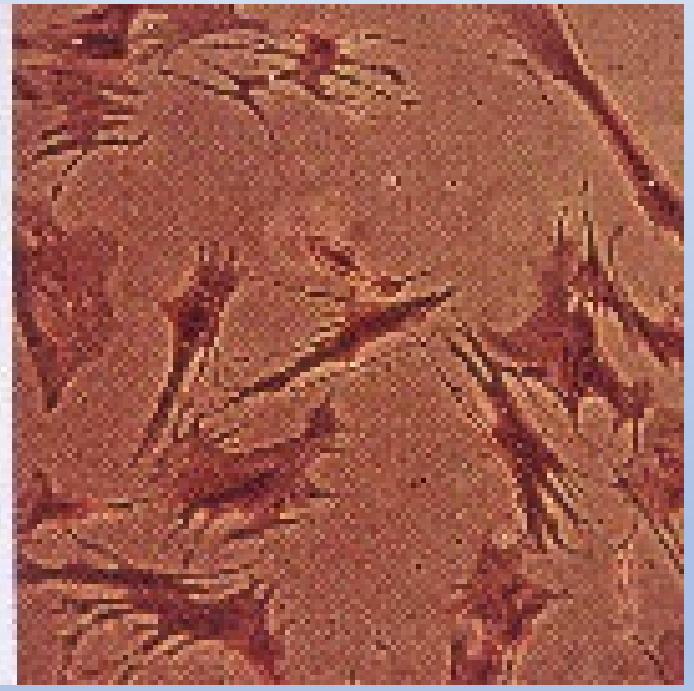
Conserved Insulin/IGF Longevity-Enhancing Pathways



Hayflick (1961) discovers normal cells (in culture) eventually stop dividing ("senescent" cells)







Can senescent cells be distinguished?

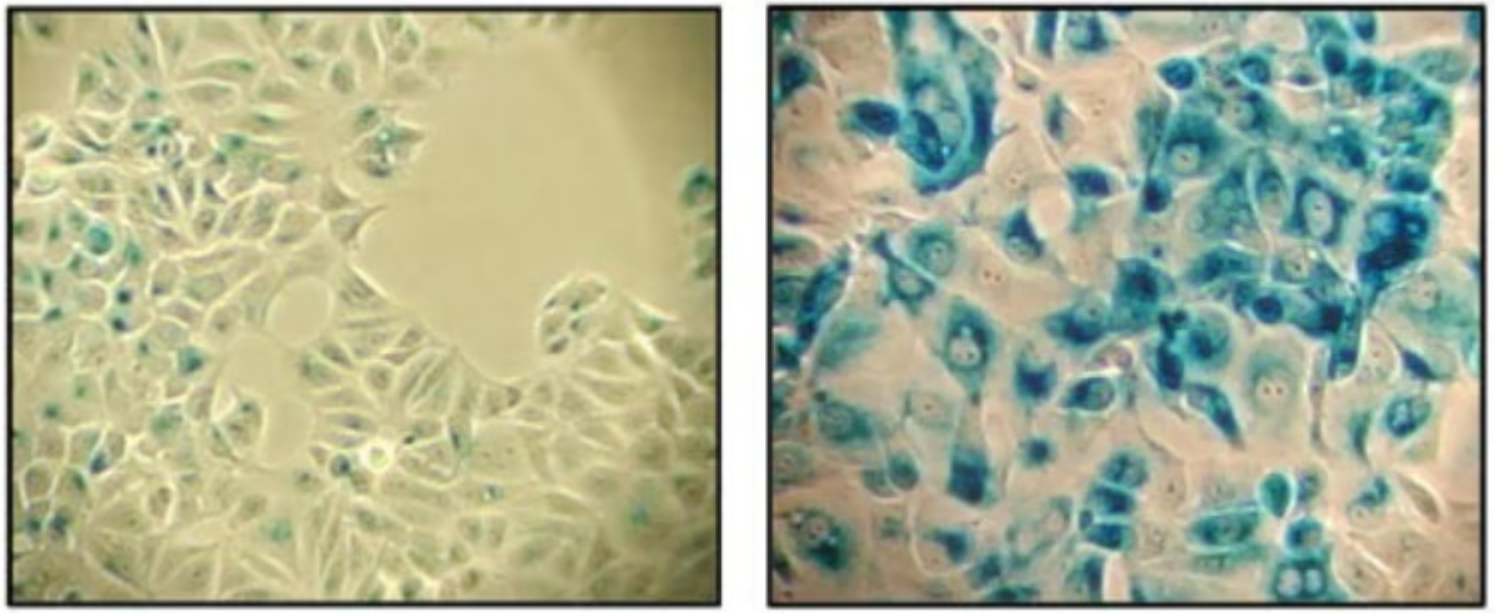
A biomarker that identifies senescent human cells in culture and in aging skin *in vivo*

(replicative senescence/tumor suppression/β-galactosidase)

PNAS 1995

GOBERDHAN P. DIMRI*, XINHUA LEE†, GEORGE BASILE*, MEILEEN ACOSTA*, GLYNIS SCOTT‡, CALVIN ROSKELLEY*, ESTELA E. MEDRANO§, MAARTEN LINSKENS¶, IVICA RUBELJ‖, OLIVIA PEREIRA-SMITH‖, MONICA PEACOCKE†, AND JUDITH CAMPISI*,**

SA β-gal Staining

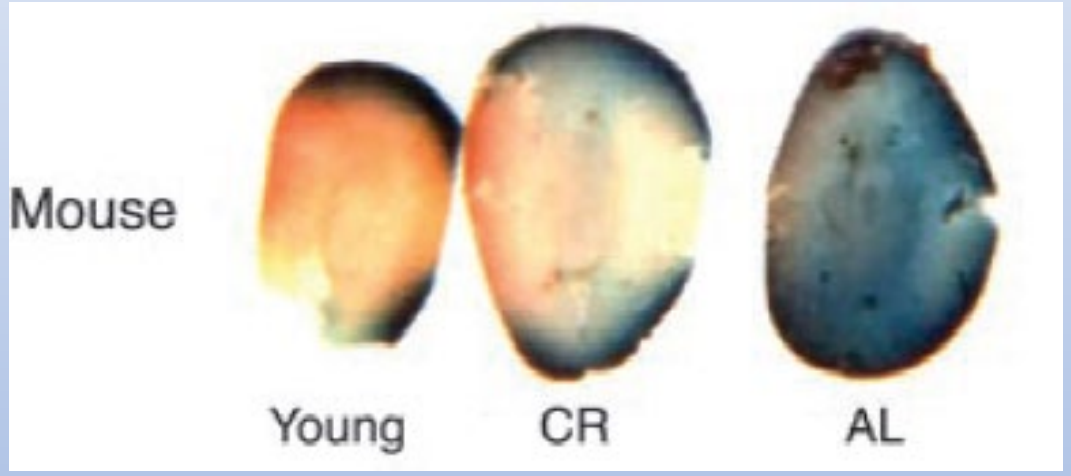


Judith Campisi



Does cellular senescence occur *in vivo*?

3 mo 28 mo

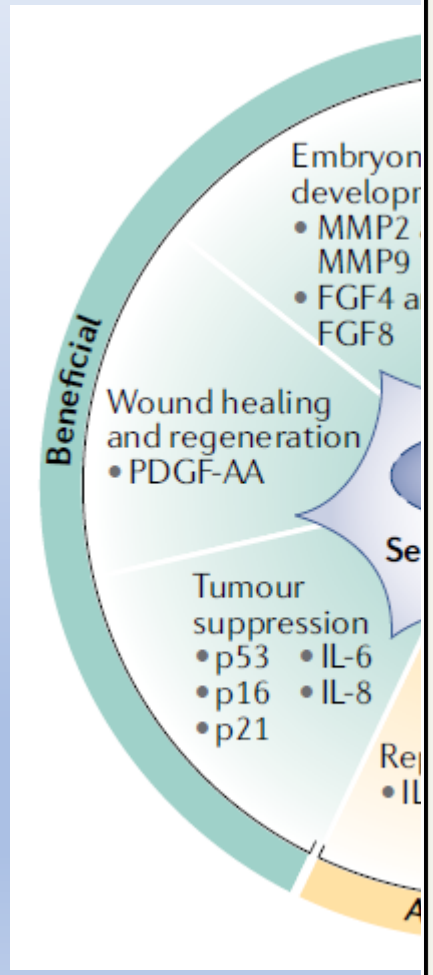


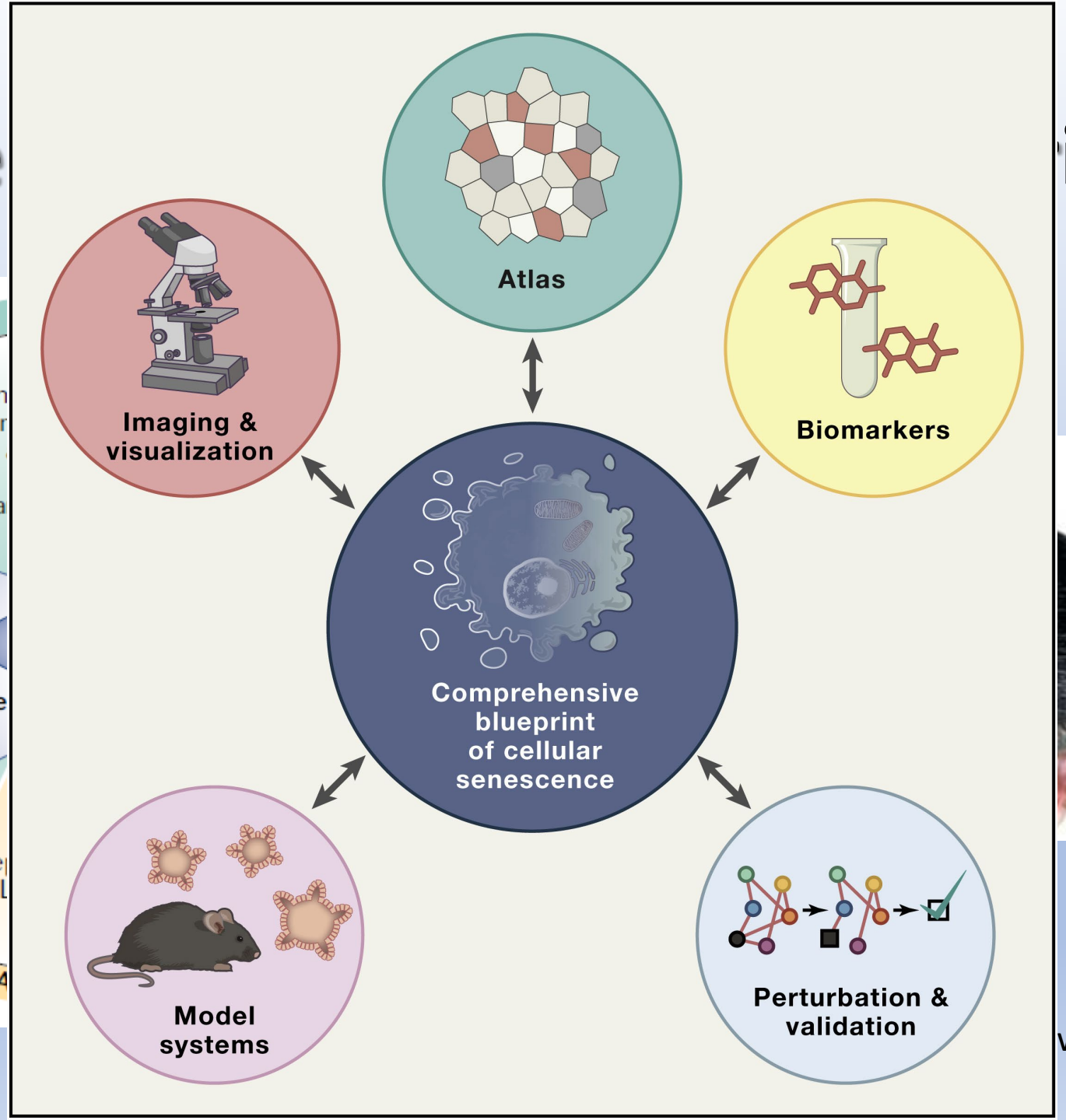


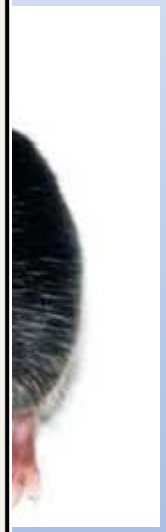
CR = calorie restricted

AL = ad lib fed

Are sene imental?







ws Molecular Cell Biology

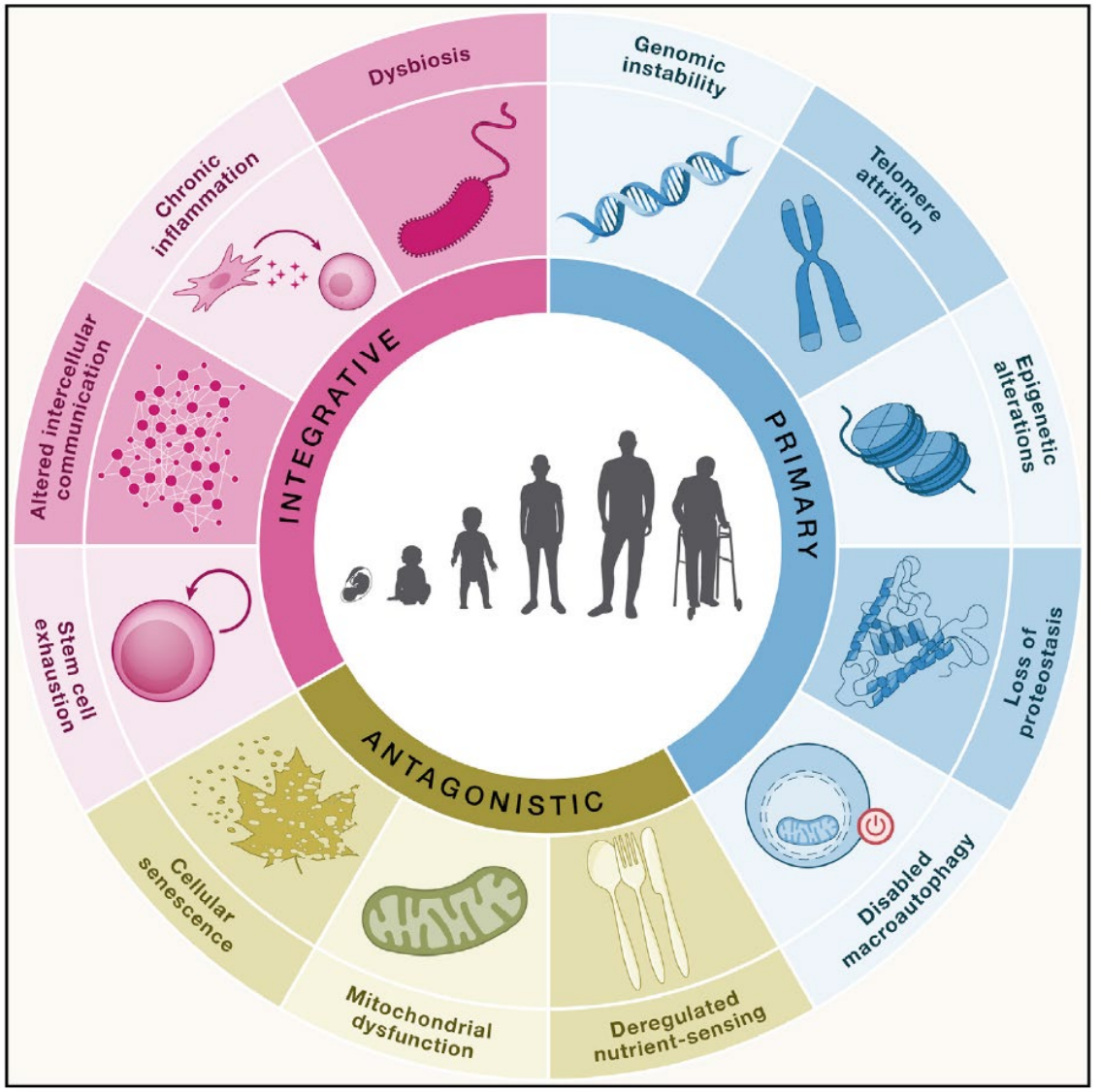
Cell
Leading Edge

CellPress

Review

Hallmarks of aging: An expanding universe

Carlos López-Otín,[1,2,3,*] Maria A. Blasco,[4] Linda Partridge,[5,6] Manuel Serrano,[7,8,9] and Guido Kroemer[10,11,12,*]
[1]Departamento de Bioquímica y Biología Molecular, Instituto Universitario de Oncología (IUOPA), Universidad de Oviedo, Oviedo, Spain
[2]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain
[3]Centro de Investigación Biomédica en Red de Cáncer (CIBERONC), Madrid, Spain
[4]Telomeres and Telomerase Group, Molecular Oncology Program, Spanish National Cancer Centre (CNIO), Madrid, Spain
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[6]Max Planck Institute for Biology of Ageing, Cologne, Germany
[7]Institute for Research in Biomedicine (IRB Barcelona), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
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[9]Altos Labs, Cambridge, UK
[10]Centre de Recherche des Cordeliers, Equipe labellisée par la Ligue contre le cancer, Université de Paris, Sorbonne Université, INSERM U1138, Institut Universitaire de France, Paris, France
[11]Metabolomics and Cell Biology Platforms, Gustave Roussy, Villejuif, France
[12]Institut du Cancer Paris CARPEM, Department of Biology, Hôpital Européen Georges Pompidou, AP-HP, Paris, France
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https://doi.org/10.1016/j.cell.2022.11.001



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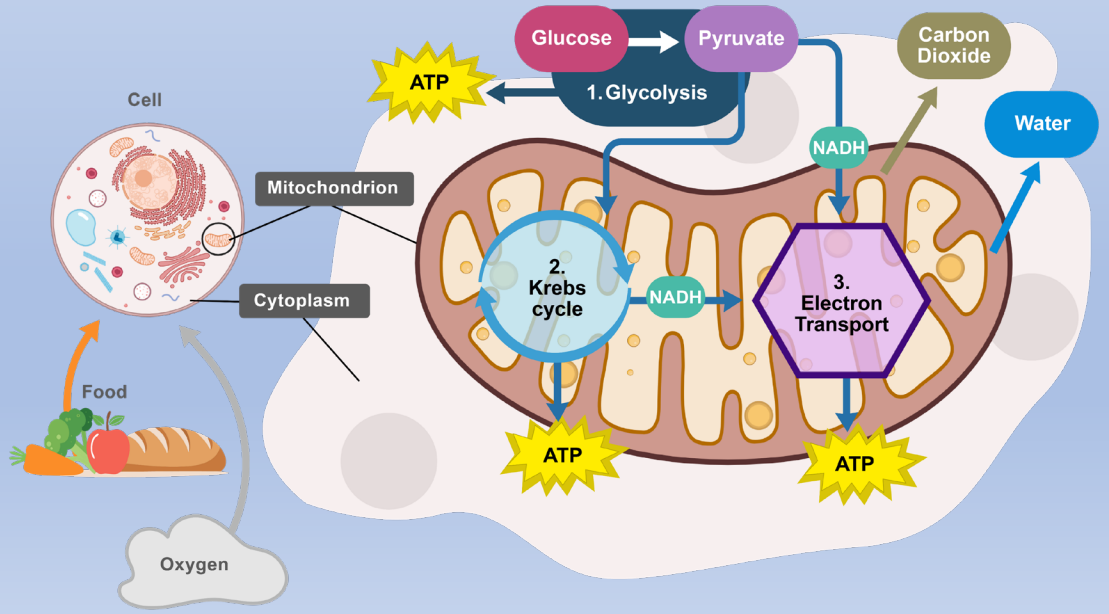
1. ~~Translation~~
2. Targets (IIS, senescent cells)
3. **Tools**







One of many new tools (thanks to mice)



Resource

SOURCE DATA | TRANSPARENT PROCESS | OPEN ACCESS

THE EMBO JOURNAL

A novel approach to measure mitochondrial respiration in frozen biological samples

Rebeca Acin-Perez[1,2,*,†], Ilan Y Benador[1,2,3], Anton Petcherski[1,2], Michaela Veliova[1,2,4], Gloria A Benavides[5], Sylviane Lagarrigue[6], Arianne Caudal[7], Laurent Vergnes[2,8], Anne N Murphy[9], Georgios Karamanlidis[10], Rong Tian[7], Karen Reue[2,8], Jonathan Wanagat[2,11], Harold Sacks[1,2], Francesca Amati[6], Victor M Darley-Usmar[5], Marc Liesa[1,2,4,12], Ajit S Divakaruni[2,4], Linsey Stiles[1,2,†,**] & Orian S Shirihai[1,2,3,4,12,†,***]

The EMBO Journal e104073 | 2020

Think about how animal use can expand and deepen your study

