HIV and Aging:
Overview and Future Opportunities

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Disclosures

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HIV+ Adults Are Aging but Survival Has Not Yet Normalized

~9 years shorter life expectancy even among those with no comorbidity

Smit, Lancet Inf Dis 2015, 15(7):810-8

Legarth et al, JAIDS 2016, 71(2):213-8

Graphs Courtesy Sara Gianella & Peter Hunt
Aging and HIV Affect the Immune System in Similar Ways

• **Aging associated with:**
  – Loss of thymus tissue
  – Decrease in the number of naive T-cells
  – Reduced T-cell responsiveness
  – B cell dysfunction

• **Immune senescence** in the general population has been linked to some of the same end-organ disorders that occur in aging HIV+ adults

Unifying Hypothesis of Premature Aging of HIV+ Adults

Deeks, Tracy, & Douek, Immunity 2013, 39: 633-45
Evidence of Premature Aging Has Been Found in Nearly Every Organ System

• **Nervous System**
  – Cognitive Disorders
  – Depression
  – Neuropathy
  – Sleep Disorders

• **Vascular System**
  – Cardiovascular
  – Cerebrovascular

• **Endocrine/Metabolic**
  – Diabetes
  – Hypogonadism

• **Liver**
  – ↓ Drug Metabolism
  – ↓ Synthetic Function

• **Kidney**
  – ↓ Drug Elimination

• **Musculoskeletal**
  – Osteoporosis
  – Frailty

• **Pulmonary**

• **Hematopoietic**

• **(Cancer)**

HIV+ Adults are at Greater Risk for Multiple Diseases than the General Population

Schouten, IAC 2012, Abstract THAB0205

Schouten et al, Clin Infect Dis 2014; 59(12):1787–97

Adapted from Todd Brown, Johns Hopkins
Successful Aging is a Multidimensional Construct

- **Typical elements of successful aging**
  - Avoidance of disease and disability
  - Maintenance of high physical and cognitive function
  - Sustained engagement in social and productive activities

- **Subjective quality of life** may be more important than the absence of disease

36% of the Population Age Successfully: May be Lower in HIV+ Adults

Most frequent correlates of SA: Nonsmoking and absence of disability, arthritis, and diabetes

Higher self-rated SA in PLWH was associated with better physical and emotional functioning but not HIV disease or negative life events

Depp & Jeste, American Journal of Geriatric Psychiatry. 2006; 14: 6-20
Moore et al, J Clinical Psychiatry 2013, 74: e417-23
HIV and Inflammation Associated with Shorter Telomere Length

Leeansyah et al, JID 2013; 207:1157

Srinivasa et al, JAIDS 2014; 67: 414
Telomere Data from 2 UCSD Cohorts

**Graphs**

- **TMARC**
  - Telomere Length vs. Age (Years) for HIV- and HIV+ groups with a p-value of 0.059.
  - Interaction effect p = 0.16.

- **SIRA**
  - Telomere Length vs. Age (Years) for HIV- and HIV+ groups with a p-value of 0.79.
HIV Accelerates Aging of Blood Cells by ~5 Years by DNA Methylation

Horvath & Levine, J Infect Dis 2015, 212:1563–73
Multiple Mechanisms of Brain Injury

• Comorbidities
  – Vascular disease
  – Metabolic syndrome
  – Frailty and sarcopenia
  – Anemia and iron metabolism
  – Other neurodegenerative diseases

• Cellular senescence
  – Immune senescence
  – Telomere length

• Neuronal vulnerability
  – Mitochondria and oxidative stress

• Polypharmacy and Drug interactions

• Drug metabolism and distribution
  – Reduced elimination
  – Reduced drug binding proteins
  – Altered blood-brain barrier permeability and molecular drug transporter functioning
HIV may Accelerate Aging to a Greater Extent in the Brain

Levine et al, J Neurovirol 2015, Epub ahead of print
HIV May Cause Premature Neurocognitive Decline

Modified from Valcour et al, Neurology 2004;63:822–827

HIV May Accelerate White Matter Injury in the Brain

22:201–212
Recent Longitudinal Data Do Not Support Premature Brain Aging

Cole et al, CROI 2017, Abstract 352LB
Other Biomarkers May Be More Sensitive to Accelerated Aging


*Graph Courtesy Jean-Pierre Routy, McGill University*

Immune Responses to CMV Are Associated with Atherosclerosis & HAND

Hsue et al, AIDS 2006, 20: 2275-83

Multiple Studies Have Identified Increased Risk of Vascular Disease

- HIV+ adults have greater 10-year risk of cardiovascular events (CVEs) and higher rates of atherosclerosis than HIV- adults
- HIV disease itself is associated with greater risk of atherosclerosis independent of viral load, type of ART, or severity of immunodeficiency
- Whether the increased risk of cardiovascular disease can be modified by ART remains uncertain
  - We still need randomized clinical trial data

Acute Myocardial Infarctions Are More Common in HIV+ Adults

- 871 acute MIs in ~80,000 veterans over ~6 years
- Across 3 decades of age, mean acute MIs per 1000 person-years was consistently higher for HIV+ than HIV- adults
- Hazard ratio for acute MI: 1.5 after adjusting for Framingham risk factors, comorbidities, and substance use


UC San Diego
Stroke Risk is Also Higher in HIV+ Adults

Using a hospital database of 9,664,892 people, US stroke hospitalizations declined 7% while stroke hospitalizations with HIV rose 60%.

- 4,308 people with HIV and 32,423 people without HIV
- Incidence rate of ischemic stroke was 40% higher in people with HIV
  - HIV: 5.27 per 1,000 PY
  - Non-HIV: 3.75 per 1,000 PY

Chow, et al. JAIDS 2012; 60:351–358
Persistently Increased Ischemic Stroke Risk in HIV-Infected Women

Model A: Unadjusted
Model B: Demographics
Model C: +Traditional Risk Factors
Model D: +Sex-specific Risk Factors

1,212 HIV+, 12,040 HIV- women

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>HIV-infected</th>
<th>HIV-uninfected</th>
<th>Incidence rate ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard ratio</td>
<td>2.09</td>
<td>4.36</td>
<td>1.86</td>
<td>2.34 (1.60-3.35)</td>
</tr>
</tbody>
</table>

Chow et al, CROI 2016, Abstract 638
Mechanisms of Premature Aging May Differ Between Women and Men

- Estrogen has neuroprotective effects so its loss may increase neuronal vulnerability
  - Wallace et al, Synapse 2006, 59: 51-60

- Insulin resistance linked to cognitive impairment in women

- Lower antioxidants in women

- Women more likely to have altered iron metabolism, which can affect the CNS
Women May Have Different Exposure of Some Antiretrovirals Than Men

- Reviews of ART pharmacokinetics indicate that women can have higher drug exposure
- Difference exists for:
  - Zidovudine
  - Lamivudine
  - Ritonavir-Boosted PIs
- Mixed data for non-nucleoside RTIs

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Ofotokun et al, Gender Medicine, 4(2):106-
### Meta-Analysis of Prevalence of Metabolic Syndrome in HIV

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Sample Size</th>
<th>Prevalence Off ART</th>
<th>Prevalence On ART</th>
</tr>
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<tbody>
<tr>
<td>Awotedu 2010</td>
<td>South Africa</td>
<td>83</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Ayodele 2012</td>
<td>Nigeria</td>
<td>55</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>Berger 2006</td>
<td>Norway</td>
<td>56</td>
<td>7</td>
<td>34</td>
</tr>
<tr>
<td>Bonfanti 2010</td>
<td>Italy</td>
<td>292</td>
<td>1</td>
<td>89</td>
</tr>
<tr>
<td>Bonfanti 2007</td>
<td>Italy</td>
<td>186</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Calza 2011</td>
<td>Italy</td>
<td>99</td>
<td>9</td>
<td>27</td>
</tr>
<tr>
<td>Da Silva 2009</td>
<td>Brazil</td>
<td>69</td>
<td>8</td>
<td>49</td>
</tr>
<tr>
<td>Fourie 2010</td>
<td>South Africa</td>
<td>300</td>
<td>46</td>
<td>115</td>
</tr>
<tr>
<td>Hansen 2009</td>
<td>Denmark</td>
<td>78</td>
<td>11</td>
<td>144</td>
</tr>
<tr>
<td>Jerico 2005</td>
<td>Spain</td>
<td>84</td>
<td>11</td>
<td>144</td>
</tr>
<tr>
<td>Maloberti 2013</td>
<td>Italy</td>
<td>36</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Mbunkah 2014</td>
<td>Cameroon</td>
<td>61</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>Muhammad 2013</td>
<td>Nigeria</td>
<td>100</td>
<td>7</td>
<td>21</td>
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<tr>
<td>Samaras 2007</td>
<td>Multicountry</td>
<td>56</td>
<td>1</td>
<td>21</td>
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<tr>
<td>Schillaci 2008</td>
<td>Italy</td>
<td>39</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>Tesfaye 2014</td>
<td>Ethiopia</td>
<td>188</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Wand 2007</td>
<td>Multicountry</td>
<td>881</td>
<td>75</td>
<td>21</td>
</tr>
</tbody>
</table>

**Overall prevalence varied by definition:**

- **16.7% - 31.3%**

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*Nguyen et al, PLOS ONE 2016, 11(3):e0150970*
Metabolic and Vascular Disease Increase Risk for Neurocognitive Impairment

**CHARTER**

<table>
<thead>
<tr>
<th>Risk</th>
<th>OR</th>
<th>p</th>
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<tbody>
<tr>
<td>AIDS</td>
<td>Yes</td>
<td>49.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>17.6</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>Larger</td>
<td>1.3</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Lower</td>
<td>0.32</td>
</tr>
<tr>
<td>BMI</td>
<td>Smaller</td>
<td>0.69</td>
</tr>
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</table>

McCutchan et al. Neurology 2012. 78: 485

**SMART**

<table>
<thead>
<tr>
<th>Risk</th>
<th>OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior CVD</td>
<td>Yes</td>
<td>6.2</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Higher</td>
<td>1.1</td>
</tr>
<tr>
<td>AIDS</td>
<td>No</td>
<td>0.41</td>
</tr>
<tr>
<td>Race</td>
<td>Black</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Wright et al, HIV Medicine 2015, 16 (S1), 97–108

**WIHS**

Wright et al. Neurology 2010; 75: 864

Path Analysis of Risk for Neurocognitive Impairment

- Highest Tertile CSF sCD40L
- IL-6
- Neurocognitive Impairment
- Model Lack of Fit $p = 0.82$

- Waist Circumference
- sCD14
- Gut dysbiosis
- Microbial translocation
- Macrophage activation

- Insulin resistance
- Hypertension
- Dyslipidemia
- Visceral adiposity

Sattler et al, JAIDS 2014, PMID: 25469522
Embellishment courtesy of Jordan Lake, M.D.
Persistent Inflammation
Dyslipidemia
Visceral Fat
Insulin Resistance
Steatohepatitis
Liver Fibrosis
Brain Disease
Vascular Disease
Gut Microbiome, sCD14, and HAND

Perez Santiago et al, CROI 2017, Abstract 390
Neurocognitive Decline Associated with Evidence of Insulin Resistance

Khuder et al, CROI 2018, Submitted
White Matter Abnormalities and Glucose Metabolism


Vaishnavi et al, PNAS 2010; 107(41): 17757–17762

Non et al, Translational Research 2017;183:41–56
Interactions Between Insulin Resistance, Amyloid, & Neurodegeneration

Verdile et al, Neurobiology of Disease 2015, 84: 22–38

Campos Peña et al, Antioxidants & Redox Signaling 2017, 26 (10): 542-60
Metabolic Syndrome Components Influence BBB Permeability

1. LDL Cholesterol, Serum (mg/dL) vs. CSF-Serum Albumin Ratio ($\log_{10}$)
   - $r = 0.21$
   - $p = 0.01$

2. HDL Cholesterol, Serum ($\log_{10}$ mg/dL) vs. CSF-Serum Albumin Ratio ($\log_{10}$)
   - $r = -0.23$
   - $p = 0.0032$

3. Glucose, Serum ($\log_{10}$ mg/dL) vs. CSF-Serum Albumin Ratio ($\log_{10}$)
   - $r = 0.22$
   - $p = 0.0042$

4. Diastolic Blood Pressure (mmHg) vs. CSF-Serum Albumin Ratio ($\log_{10}$)
   - $r = 0.20$
   - $p = 0.0032$

5. Multivariate Regression Predicted Value vs. CSF-Serum Albumin Ratio ($\log_{10}$)
   - $r = 0.40$
   - $p < 0.0001$

6. CSF-Serum Albumin Ratio ($\log_{10}$) vs. CSF-Plasma Lopinavir ($\log_{10}$)
   - $r = 0.57$
   - $p < 0.0001$

7. CSF-Serum Albumin Ratio ($\log_{10}$) vs. CSF-Plasma Efavirenz ($\log_{10}$)
   - $r = 0.33$
   - $p = 0.02$
Higher Concentrations of ART Drugs Can Injure Neurons \textit{in vitro}

Robertson et al, J Neurovirol 2012, 18: 388-299

Hinckley et al, CROI 2016, Abstract 395
DTG and CNS Adverse Events

**N=565**
DTG Only

**N=1,950**
InSTIs Only

**N=6,347**
DTG or 3 Others

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**Adverse drug reaction n (%)**

- Sleep disturbance, insomnia: 31 (5.6)
- Gastrointestinal complaints: 21 (3.8)
- Joint, tendon and/or muscle pain: 13 (2.0)
- Psychological/psychiatric symptoms: 14 (2.5)
- Neurologic symptoms: 10 (1.8)
- General malaise (headache and severe fatigue): 24 (4.3)
- Respiratory tract complaints: 5 (0.9)
- Other: 9 (1.6)

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**de Boer et al, AIDS 2016, 30:2831–2834**

**Hoffmann et al, HIV Medicine 2017, 18, 56--63**

**Fettiplace et al, J AIDS 2017;74:423–431**

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**Psychiatric event**

**Depression**
ART Drugs May Alter Other Aging-Related Biological Processes

EFV Reduces Microglial Phagocytosis of Aβ₁₋₄₂

Leeansyah et al, J Infect Dis 2013; 207:1157

Increasing Polypharmacy in Aging HIV+ Adults

Smit, Lancet Inf Dis 2015, 15(7):810-8
Concomitant Medications May Also Influence Risk for Metabolic Syndrome

<table>
<thead>
<tr>
<th>Metabolic variable</th>
<th>MAP</th>
<th>TG(^a)</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA</td>
<td>0.28(^***) (0.08, 0.49)</td>
<td>0.28(^**) (0.06, 0.50)</td>
<td>2.28(^***) (1.29, 4.02)</td>
</tr>
<tr>
<td>Age(^b)</td>
<td>0.11(^***) (0.04, 0.19)</td>
<td></td>
<td>1.62(^***) (1.30, 2.03)</td>
</tr>
<tr>
<td>Male</td>
<td>0.28(^***) (0.13, 0.44)</td>
<td>0.28(^***) (0.12, 0.44)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity(^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>-0.26(^***) (-0.40, -0.12)</td>
<td>0.36(^***) (0.22, 0.51)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>-0.36(^***) (-0.55, -0.18)</td>
<td>0.50(^***) (0.31, 0.69)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>-0.40(^**) (-0.73, -0.06)</td>
<td>0.22 (-0.15, 0.60)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C virus status(^d)</td>
<td></td>
<td></td>
<td>1.97(^**) (1.23, 2.15)</td>
</tr>
<tr>
<td>Estimated HIV duration (years)(^d)</td>
<td>0.05(^*) (0, 0.10)</td>
<td>-0.05(^*) (-0.1, 0)</td>
<td></td>
</tr>
<tr>
<td>CD4 Nadir(^d)</td>
<td></td>
<td>0.04(^***) (0.02, 0.06)</td>
<td>1.06(^*) (1.00, 1.13)</td>
</tr>
<tr>
<td>CD4(^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detectable plasma viral load</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protease inhibitor-based regimen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifetime substance dependence diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SGA = Second generation antipsychotic, BMI = Body mass index, MAP = Mean arterial pressure, TG = Triglycerides, DM = Diabetes mellitus

\(^*\) \(p < 0.10\), \(^**\) \(p < 0.05\), \(^***\) \(p < 0.01\)

Ferrara et al, Psychiatry Research 2014, 218: 201–208
Polypharmacy
Stimulant &
Opiate Use
ART
Toxicity
Drug-
Related
CMV
Viral
Proteins
Advanced
Immune
Suppression
Persistent HIV
Replication
Viral
Proteins
ART
Toxicity
Stimulant &
Opiate Use
Poly
pharmacy
Genetic
Comorbidities
Behavior
Host-
Related
Protein
Processing
Innate and
Adaptive
Immunity
Insulin
Resistance
Unsuccessful
Aging
Coagulation
Imbalance
Mitochondria
& Oxidative
Stress
Other
Pathogen-
Related
Gut
Microbiome
Viral
Hepatitis
CMV
HIV-
Related
Unsuccessful
Aging
Possible Interventions

• “Lifestyle” modification
  – Exercise, Weight loss
  – Smoking Cessation
  – Moderate Alcohol Use
  – Alter Microbiome
• Modify Existing Medications
• Target components of the metabolic syndrome
  – Pitavastatin (REPRIEVE)
  – Metformin
• Treat coinfections
  – HCV
• Adjunctive therapy
  – Tesamorelin
  – Intranasal insulin
  – Intranasal IGF-1

Graphic courtesy of Peter Hunt, UCSF (and ulead.org)
Benefits of Exercise, Diabetes Management, & Probiotics

- OR 0.38 for Global NCI
- DSST = Digit Symbol Substitution Test
- TBV = Total Brain Volume

- Dufour et al, J Neurovirol 2013, 19(5):410-7
- Vrieze et al, Gastroenterology 2012;143:913–916
- Weitzman et al, Circulation. 2005;112:862-869

- d’Ettorre et al, PLoS ONE 2015, 10(9): e0137200
Tesamorelin

- Synthetic growth hormone releasing factor analogue (GHRH) that stimulates in the pituitary production and pulsatile release of endogenous GH, which also stimulates IGF-1 production
- Selectively reduces visceral fat, intima media thickness and triglycerides, and improves cognitive function in older persons

Mangili et al, PLoS ONE 2015, 10(10): e0140358
Sattler F. Best Practice & Research Clinical Endocrinology & Metabolism 27 (2013) 541–555
Metformin

• Oral biguanide that has multiple effects on IR:
  – Activates AMPK in liver, brain, and other tissues
  – Decreases hepatic gluconeogenesis production
  – Decreases intestinal absorption of glucose, increases peripheral glucose uptake, and reduces weight
• Improves endothelial function

• Neurologic effects:
  – Reduces BACE1 activity and amyloid β production
  – Antioxidant and anti-inflammatory effects in brain
  – May reduce acetylcholinesterase activity
  – May promote tau dephosphorylation

• May also improve gut dysbiosis

Lake & Currier, Lancet Infect Dis 2013; 13: 964–75
G. Verdile et al., Neurobiology of Disease 84 (2015) 22–38
Markowicz-Piasecka et al, Pharm Res, 2017, DOI 10.1007/s11095-017-2199-y
Questions Guiding Future Research

• Is premature aging a biological condition or an artifact of study design?
  – Is evidence of premature aging from cross-sectional studies confirmed in longitudinal ones?

• Is there a unifying hypothesis of the pathogenesis of premature aging?
  – Immune senescence/inflammation, microbiome, coinfections, coagulation, genetic
  – Is it due to HIV, associated conditions, or both?

• What are the best methods for assessing aging?
  – Successful aging, Frailty, Multimorbidity, Quality of life
  – Ecological momentary assessment
  – Biological indicators of aging
  – NP testing, mood, imaging, CSF biomarkers
Questions Guiding Future Research

• What are the best approaches for managing premature aging in the clinic?
  – Antiretroviral therapy
  – Treatment of multimorbid conditions
    • Metabolic syndrome, dyslipidemia, vascular disease, depression, addictive drugs
  – Limit polypharmacy
  – Nutrition, Microbiome, Exercise, Smoking cessation

• What support structures do aging people living with HIV require?
  – Case managers, Housing, Healthcare, Social
Funding Opportunities

• PAR-17-321: Multidisciplinary Studies of HIV-AIDS and Aging (R01)

• Encourages applications at the intersection of HIV and aging by addressing two overarching objectives:

  1) To improve understanding of biological, clinical, and sociobehavioral aspects of aging through the lens of HIV infection and its treatment;

  2) To improve approaches for testing, prevention, and treatment of HIV infection, and management of HIV-related comorbidities, co-infections, and complications in different populations and cultural settings by applying our current understanding of aging science.
Funding Opportunities

• PAR-17-321: Multidisciplinary Studies of HIV-AIDS and Aging (R01)

• Encourages applications with the following characteristics:
  1) Clinical orientation
  2) Focus on aging or the aged
  3) Attention to geriatric outcomes
  4) Leveraging existing resource where possible
  5) Selection of appropriate controls
  6) Characterization of phenotypes
Funding Opportunities

• PA-17-088: Secondary Analyses of Existing Cohorts, Data Sets, and Stored Biospecimens to Address Clinical Aging Research Questions (R01)

• Invites applications to address clinically related issues on aging changes influencing health across the lifespan, or on diseases and disabilities in older persons.
  – Use of cohorts that are linked to electronic health record systems or Centers for Medicare and Medicaid Services (CMS) administrative data are especially welcome.
Funding Opportunities

• PA-17-088: Secondary Analyses of Existing Cohorts, Data Sets, and Stored Biospecimens to Address Clinical Aging Research Questions (R01)

• … to address clinically related issues on aging…:
  – Will support activities addressing specific hypotheses in clinical aging research or to inform the design and implementation of future epidemiologic or human intervention studies, or current geriatric practice in maintenance of health, management of disease, and prevention of disability.
  – Existing data sets may also be used to develop and test new analytical approaches.
  – Costs for archiving of data to be made publicly available and those associated with data harmonization or assay refinement/validation may be included in the budget…
Funding Opportunities

• RFA-AG-023: Pathogenesis of Age-Related HIV Neurodegeneration (R01)
• Due 9 February 2018

• Encourages basic and clinical research to study the molecular and cellular mechanisms underpinning neurodegenerative diseases, particularly Alzheimer's disease, and neurological disorders associated with HIV infection and AIDS.

  – Particularly encourages research to explore the causal role of Alzheimer's and other related proteinopathies in HIV+ older adults.
  – Envisages cross-disciplinary, multi-PI, and integrative approaches. It will encourage development of both animal and human research to study whether, and how, different neuropathological processes interact with one another, as well as to understand how these interactions lead to neurodegeneration.
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- Gabe Wagner
- Connie Benson
- Chip Schooley
- Doug Richman

NIH
- …Mental Health
- …Drug Abuse
- …Allergy and Infectious Diseases

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- Justin McArthur
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- Ann Collier
- Christina Marra
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- David Simpson
- Ben Gelman
- Howard Fox

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- Qing Ma (Buffalo)
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- Micol Ferrara
- Josue Perez Santiago