WF ADCC Neuropathology Core

**Leader:** T. Montine, MD, PhD  
**Co-Leaders:** C.D. Keene, MD, PhD, R. Mott, MD

**Neuropathology Service**  
C.D. Keene MD, PhD  
R. Mott, MD, PhD  
T. Montine, MD, PhD  

*Autopsy:*  
P. Lantz, MD  
K. Stogner-Underwood, MD  

*Virtual Microscopy:*  
S. Qasem, MD

**Biospecimen Service**  
T. Register, PhD  
A. Molina, PhD  
D. Diz, PhD  
J. Parks, PhD  
C. Furdui, PhD  
C. Milligan, PhD

**Pre-Clinical Service**  

*NHP:*  
C. Shively, PhD  
T. Register, PhD  
M. Jorgensen, PhD  
M. Cline, DMV, PhD  
J. Kaplan, PhD  
K. Kavanagh, VMS, MS, MPH  
R. Hampson, PhD

*Rodent:*  
T. Ma, MD, PhD  
D. McClain, MD, PhD

*Imaging:*  
A. Mintz, MD, PhD  
C. Whitlow, MD, PhD  
J. Maldjian, MD  
Y. Jung, PhD

**Genotyping & Molecular Genetics Service**  
D. Bowden, PhD  
G. Hawkins, PhD
Neuropathology Core

**Aim 1**: Develop and manage a repository of brain tissue, CSF, DNA, and blood from Clinical and MESA Core participants of the Wake Forest ADC using state-of-the-art methods;

~84 brains will be collected from the MESA and Clinical Cores

~1000 ante-mortem collections of plasma, DNA, and CSF over next 2 years will add to the existing repository from over 1100 well characterized participants
Neuropathology Core

- **Aim 2**: Distribute data and/or tissue to Wake ADCC and ADC network investigators, NCRAD, and AD researchers world-wide

**Resources Available:**
- Wake Forest ADCC (under development)
  - [http://www.wakehealth.edu/Alzheimers/](http://www.wakehealth.edu/Alzheimers/)
- University of Washington ADRC (under development)
  - [http://depts.washington.edu/adrcweb/](http://depts.washington.edu/adrcweb/)
- National Alzheimer’s Disease Coordinating Center
  - [https://www.alz.washington.edu/](https://www.alz.washington.edu/)

**Other National Resources:**
- NCRAD: National Cell Repository for Alzheimer's Disease
  - [https://ncrad.iu.edu/accessing_data.html](https://ncrad.iu.edu/accessing_data.html)
- ADGC: Alzheimer's Disease Genetics Consortium
  - [http://alois.med.upenn.edu/adgc/index.html](http://alois.med.upenn.edu/adgc/index.html)
Neuropathology Core

**Aim 3:** Conduct rigorous neuropathological diagnostic evaluations and clinical-pathological investigations of decedent Clinical and MESA Core participants

- Neuropathologic evaluations performed according to NIA-AA guidelines, on 20+ regions using histochemical and/or immunohistochemical stains
- Diagnostic evaluations following consensus guidelines for AD, microvascular brain injury, Lewy body disease, frontotemporal lobar degeneration, hippocampal sclerosis.
**Aim 4:** Facilitate measurement of key biomarkers of AD pathology & innovative markers of metabolic/vascular function

- **All participants**: Plasma glucose, insulin, hemoglobin A1C
- **MESA participants**: Epigenetic/transcriptomic measures of oxidative phosphorylation and metabolic pathways available for all MESA participants.
- **Clinical Core participants**: Monocytes & PBMCs
- **Clinical and Mesa Core Subsets**: panels of specialized assays: mitochondrial function, CSF inflammatory/vascular markers, targeted epigenetic & transcriptomic panels
- All available to WF investigators
- **Molecular Genetics/Genomics** support provided by the WF Genomics Core

**Table 2. Example Assays Available to ADCC**

<table>
<thead>
<tr>
<th>AD / Synaptic Biomarkers</th>
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<tbody>
<tr>
<td>Aβ40, Aβ42, APP, sAPP, Tau, P-Tau, Neurogranin</td>
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<table>
<thead>
<tr>
<th>Metabolic</th>
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<tbody>
<tr>
<td>Glucose, HbA1c, Insulin, C-peptide, GLP-1, Leptin, Resistin, Cortisol, Adiponectin, Apelin, GH, Thyroid Hormone, Neprilysin</td>
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<thead>
<tr>
<th>Vascular</th>
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<tbody>
<tr>
<td>ICAM-1, VCAM-1, ET-1, E-selectin, P-selectin, L-selectin, E-cadherin, ICAM-3, MCP-1, MMP-9, Angiotensinogen, Angiotensin II, Angiotensin (1-7), Aldosterone, Plasma Renin Activity, Total Renin, ACE 1 &amp; 2</td>
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<thead>
<tr>
<th>Inflammatory/Immune/Oxidative Stress</th>
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<tbody>
<tr>
<td>CRP, IL-1β, IL-6, IL-1RA, IL-1R, TGF-β1, TNF-α, Heat Shock Proteins (Hsp70), F2-Isoprostanes (8-Isoprostane)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Lipid/Lipoprotein</th>
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</thead>
<tbody>
<tr>
<td>LDL, HDL, TG, Total Chol, VLDL, Apo-AI - AII, -B, -E, Lp(a), fatty acid and cholesterol quantification, ABCA1</td>
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<table>
<thead>
<tr>
<th>Mitochondrial</th>
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<tbody>
<tr>
<td>Mitochondrial mass quantification, ETC Complex Activity (ATP Synthase, NADH Dehydrogenase), Citrate Synthase Activity, PGC-1α expression</td>
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<table>
<thead>
<tr>
<th>Omics</th>
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</thead>
<tbody>
<tr>
<td>Proteomics, Lipidomics, Metabolomics (discovery/targeted)</td>
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<tr>
<th>Other Measures</th>
</tr>
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<tbody>
<tr>
<td>Estradiol, Estrone, SHBG, Testosterone, Progesterone</td>
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</table>
Aim 5: To establish preclinical models of AD and pathological brain aging in NHPs using procedures analogous to human protocols thus:

- creating a repository of brain tissue, CSF, DNA, biospecimens, and neuroimaging data; and
- providing NHP cohorts and rodent models that can be used for pivotal mechanistic and therapeutic studies.

NHP Neuropathology
A: Aβ in older NHP brain
B: Aβ in vascular wall
C: Neurofibrillary tangles
D: Dystrophic neurites
F: Hyperphosphorylated tau
Neuropathology Core

- Please consider contributing NHP brain, CSF, blood, images to repository
- Core will help collect and store tissue for the parent project
- Expert characterization of AD pathology will be available to donor PI
- Future collaborative projects honor intellectual property of donor PI
- Many studies with archived data and tissue available (selection below)

<table>
<thead>
<tr>
<th>Data and Tissues</th>
<th>PI/Contact</th>
<th>N, Years Follow-up</th>
<th>Manipulation &amp; Species</th>
<th>MRI</th>
<th>Blood</th>
<th>CSF</th>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vervet Research Colony Biomedical Resource</td>
<td>Jorgensen</td>
<td>150, 6</td>
<td>Age Female/Male Vervet</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Depression &amp; Coronary Artery Atherosclerosis in Cynomolgus Monkeys</td>
<td>Shively</td>
<td>44, 5</td>
<td>Depression, tx Female Cynomolgus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Atherosclerosis, Estrogen Receptors, and Vascular Responses to Estrogens</td>
<td>Register</td>
<td>24, 5</td>
<td>Hormone tx Female Cynomolgus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Age, Body Composition, Functional Status, &amp; Immune Function</td>
<td>Shively, Register Jorgensen</td>
<td>16, 2</td>
<td>Immune &amp; Physical Function Female Vervet</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Bazedoxifene Acetate and Estrogens Effects on Atherosclerosis</td>
<td>Clarkson Appt</td>
<td>100, 2</td>
<td>Hormone tx Female Cynomolgus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Genetic Studies of CSF Biomarkers of AD</td>
<td>Coppola Jorgenson</td>
<td>315</td>
<td>Age, genetics Female Vervet</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Radiation Countermeasures Center of Research Excellence Radiation Survivor Core (NIAID)</td>
<td>Cline</td>
<td>100, 1-11</td>
<td>Prior radiation, Rhesus</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>RADCCORE- Prospective Studies Core D (NIAID)</td>
<td>Cline</td>
<td>20/year</td>
<td>Radiation, mitigators Rhesus</td>
<td>X</td>
<td></td>
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<td>X</td>
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<tr>
<td>Modulation of Radiation-induced Brain Injury in the Nonhuman Primate (NCI)</td>
<td>Deadwyler Cline</td>
<td>26</td>
<td>Radiation, mitigators Rhesus</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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Neuropathology Core Contacts

Main ADCC Contact: Nora Shively
nshively@wakehealth.edu
336-713-4037

NP Contacts:
NHP Service Leader: Carol Shively
cshively@wakehealth.edu
Biomarker Service Leader: Tom Register
register@wakehealth.edu
Neuroimaging Service Leader: Akiva Mintz
amintz@wakehealth.edu