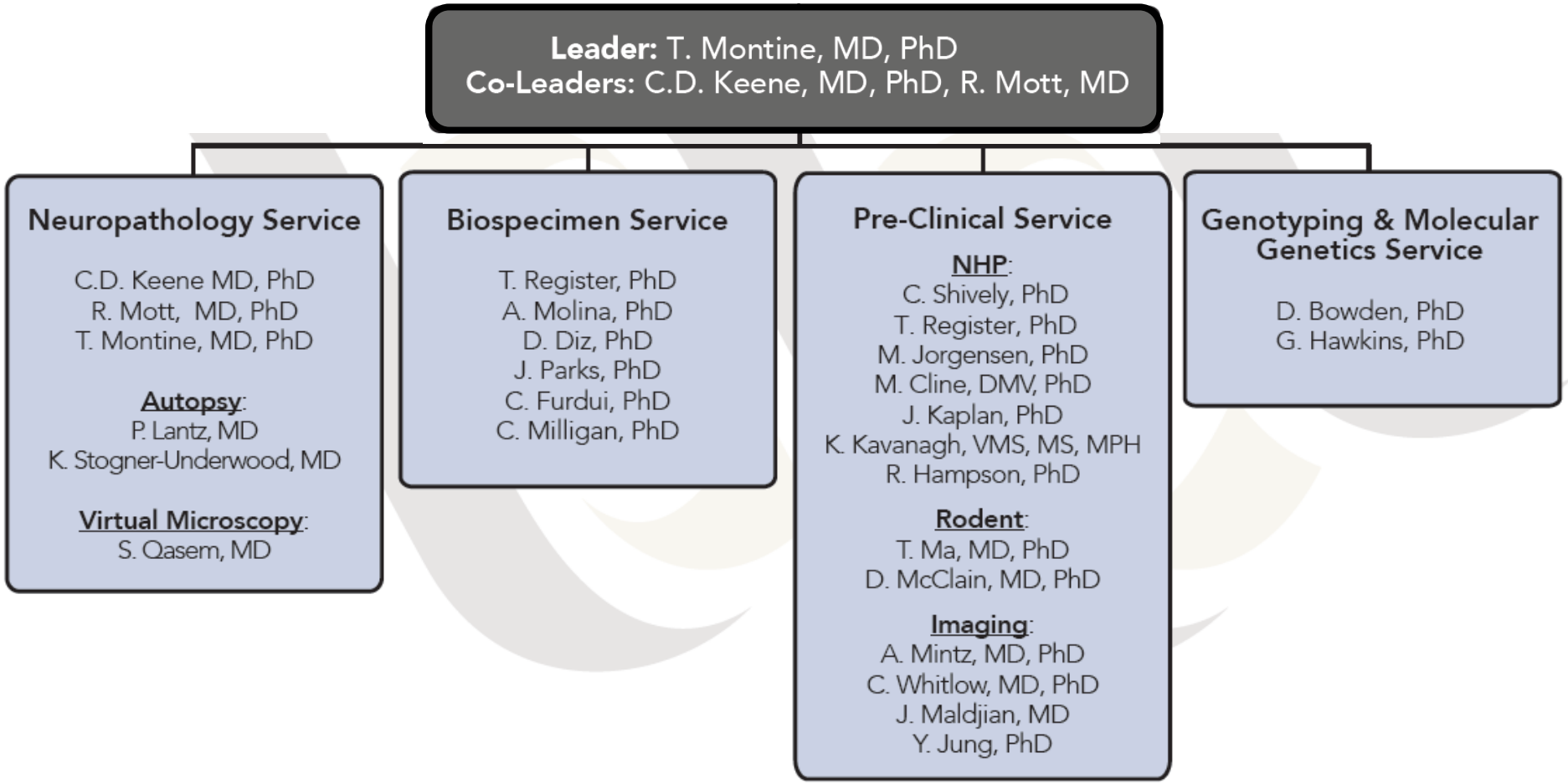
Wake Forest®
School of Medicine

Wake Forest Alzheimer's Disease Core Center

Neuropathology Core

WF ADCC Neuropathology Core

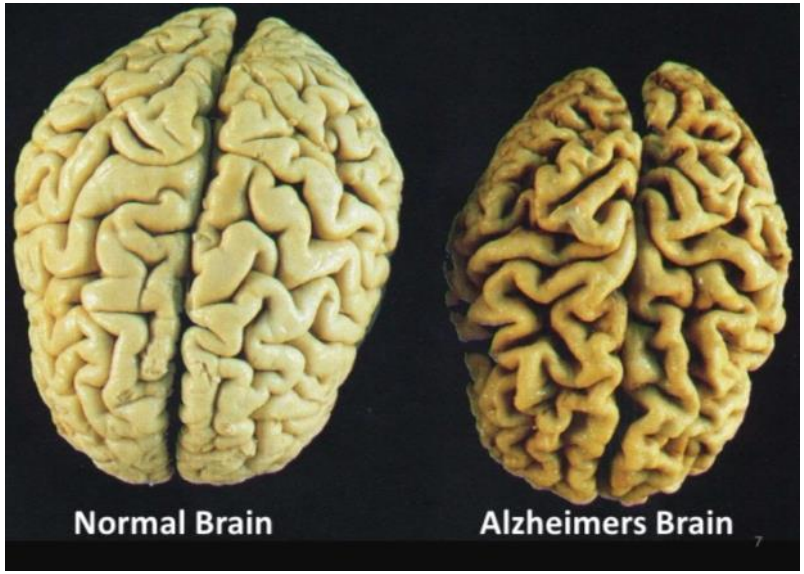


Neuropathology Core

- **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

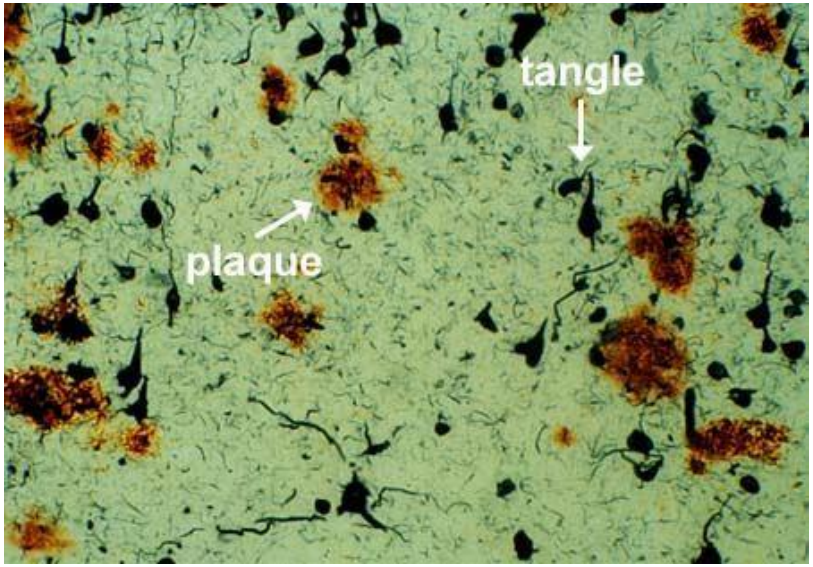
Resources Available:
Wake Forest ADCC (under development)
http://www.wakehealth.edu/Alzheimers/
University of Washington ADRC (under development)
http://depts.washington.edu/adrcweb/
National Alzheimer's Disease Coordinating Center
https://www.alz.washington.edu/

Other National Resources:
NCRAD: National Cell Repository for Alzheimer's Disease
https://ncrad.iu.edu/accessing_data.html
ADGC: Alzheimer's Disease Genetics Consortium
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.



Neuropathology Core

Aim 4: Facilitate measurement of key biomarkers of AD pathology & innovative markers of metabolic/ vascular function

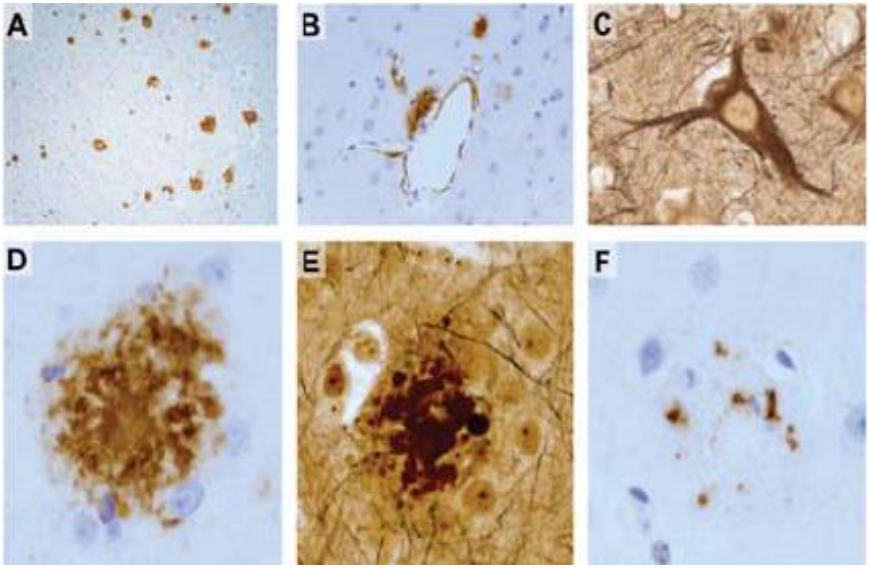
- **All participants**: Plasma glucose, insulin, hemoglobin A1C
- **MESA participants**: Epigenetic/ transcriptomic measures of oxidative phosphorylation and metabolic pathways available for all MESA participants.
- **Clinical Core participants**: Monocytes & PBMCs
- **Clinical and Mesa Core Subsets**: 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
AD / Synaptic Biomarkers
Aβ40, Aβ42, APP, sAPP, Tau, P-Tau, Neurogranin
Metabolic
Glucose, HbA1c, Insulin, C-peptide, GLP-1, Leptin, Resistin, Cortisol, Adiponectin, Apelin, GH, Thyroid Hormone, Neprilysin
Vascular
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 & 2
Inflammatory / Immune / Oxidative Stress
CRP, IL-1β, IL-6, IL-1RA, IL-1R, TGF-β1, TNF-α, Heat Shock Proteins (Hsp70), F2-Isoprostanes (8-Isoprostane)
Lipid/Lipoprotein
LDL, HDL, TG, Total Chol, VLDL, Apo-AI - AII, -B, -E, Lp(a), fatty acid and cholesterol quantification, ABCA1
Mitochondrial
Mitochondrial mass quantification, ETC Complex Activity (ATP Synthase, NADH Dehydrogenase), Citrate Synthase Activity, PGC-1α expression
Omics
Proteomics, Lipidomics, Metabolomics (discovery/targeted)
Other Measures
Estradiol, Estrone, SHBG, Testosterone, Progesterone

Neuropathology Core

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)

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

Neuropathology Core Contacts

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