

# ADNI and DIAN Neuropathology Core



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**Nigel Cairns, PhD, FRCPath**

**Knight ADRC  
Neuropathology Core Leader**

# ADNI Participants Autopsied per Funding Period

Autopsy rates for ADNI 1, ADNI GO, and ADNI 2				
ADNI	ADNI-NPC	Deaths	Autopsies	Autopsy Rate (%)
Funding Period				
9-1-05 to 8-31-07	NO	6	0	0
9-1-07 to 8-31-08	YES	7	2	28
9-1-08 to 8-31-09	YES	8	8	100
9-1-09 to 8-31-10	YES	4	1	25
9-1-10 to 8-31-11	YES	13	6	46
9-1-11 to 8-31-12	YES	4	3	75
9-1-12 to 8-31-13	YES	15	8	53
9-1-13 to 8-31-14	YES	20	13	65
9-1-14 to 8-31-15	YES	17	11	65
9-1-15 to 8-31-16	YES	16	12	75
Total (2005-2016)	-	110	64	58
Total since NPC established	-	104	64	62

**Note:** The ADNI-NPC was established on 9/1/2007.

# ADNI and DIAN Participating Sites

## Brain Procurement at ADC/ADRC Neuropathology Cores

Site	Core Leader
OHSU	Randy Woltjer
USC	Carol A. Miller *
UCSD	Lawrence Hansen/ Eliezer Masliah **
COLUMBIA	Jean Paul Vonsattel #
WUSTL	Nigel J. Cairns **##
Mt SINAI	Vahram Haroutunian
RUSH	Julie A. Schneider **
J HOPKINS	Juan Troncoso
NYU	Thomas Wisniewski
UPENN	John Q. Trojanowski
UK	Peter Nelson **
UPITT	Julia Kofler **#
UCI	Ronald Kim **
UTSW	Charles L. White III **

Site	Core Leader
Yale	Angus Narin (outside pathologist) *
Stanford	Tony Wyss-Coray (outside pathologist) **
NWU	Eileen Bigio
UCSF	William Seeley *
BWH	Matthew P. Frosch ##
SHRI	Thomas G. Beach **
BUSM	Ann C. McKee
UCD	Lee-Way Jin **
UWI	Michael Hart *
EMORY	Johnathan Glass/Marla Gearing **
KANSAS	Kathy Newell **
MAYO-J	Dennis W. Dickson
IU	Bernadino Ghetti *##

\*1 ADNI, \*\*≥2 ADNI cases; #1 DIAN, ##≥2 DIAN cases.

Donations from additional 9 ADNI /8 DIAN sites not affiliated with an ADNI/DIAN site.

# ADNI: Clinical and Neuropathologic Diagnosis at Expiration

Clinical Diagnosis at Expiration	Neuropathologic Diagnosis [N (%)]											
	AD	AD + DLB	AD + TDP	AD + DLB + TDP	AD + DLB + TDP + AGD	AD + ALB	AD + AGD	AD + HS	AD + TDP + Infarcts	AGD	Pending	TOTAL (%) ^
DAT	18*	12**	2	2		2	1	3†	1	2¶		43 (83)
DAT + DLB				1	1	2‡						4 (8)
Pending											5	5 (10)
TOTAL (%) ^	18 (35)	12 (23)	2 (4)	3 (6)	1 (2)	4 (8)	1 (2)	3 (6)	1 (2)	2 (4)	5 (9)	52 (100)

AD, Alzheimer disease (NIA-AA score: A1, B0, C0 or greater); ALB, AD with amygdala Lewy bodies; DAT, Dementia a of the Alzheimer's type; DLB, dementia with Lewy bodies; AGD, argyrophilic grain disease; TDP, AD with TDP-43 proteinopathy in medial temporal lobe; HS, hippocampal sclerosis.

Notes: \*One case had additional infarcts; \*\*One case had additional AGD and two cases had additional ARTAG; †One case had additional AGD and one case had additional TDP-43 proteinopathy; ‡One case had additional TDP-43 proteinopathy; ¶Both cases had additional PART. ^Figures are rounded and may not equal 100%. Small vessel disease (arteriolosclerosis and cerebral amyloid angiopathy) was a feature of all cases.

The clinical diagnostic accuracy of DAT is high: 45/47 (95.7%)

## Neuropathologic Assessment of 11 DIAN Participants (2 assessments pending)

Mutation	P	PMI (h)	Brain wt. (g)	Clin. Dx.#	NPath. Dx.	A <sup>^</sup> (A $\beta$ )	B <sup>^</sup> (NFT)	C <sup>^</sup> (NP)	SYN* *
PSEN1 I143T	P	18	1,330	ADD	AD+DLB	3	3	3	6
PSEN1 M146L	P	38	1,070	ADD	AD+DLB	3	3	3	6
PSEN1 H163R	P	9	1,130	ADD	AD	3	3	3	0
PSEN1 G206V	P	15	1,095	ADD	AD	3	3	3	0
PSEN1 I229F	P	23	1,220	ADD	AD	3	3	3	0
PSEN1 I229F	P	24.5	1,080	ADD	AD	3	3	3	0
PSEN1 T245P	P	6.5	1,050	ADD	AD+DLB	3	3	3	5
PSEN1 N135S	P	20	1,580	ADD	AD+DLB	3	3	3	5
PSEN1 S169L	P	41.8	1,051	ADD	AD+DLB	3	3	3	4
PSEN1 S169L	P	33	1,245	ADD	AD+DLB	3	3	3	5
PSEN1 I439V	P	41	1,200	ADD	AD+ALB	3	3	3	ALB
Mean	N=11	24.5	1,186	-	AD (100%)				
Range	-	6.5-41.8	1,050-1,580	-	AD+DLB/ALB (64%)				

P, participant; # ADD, Alzheimer disease dementia ; ^NIA-AA criteria for AD neuropathologic change: A, (A $\beta$  plaque score); B, (Braak neurofibrillary tangle score); and C, (CERAD neuritic plaque score). \*\*SYN,  $\alpha$ -synucleinopathy; Braak Parkinson's disease Lewy body stage. PMI, postmortem interval (hours). DLB, dementia with Lewy bodies. ALB, amygdala Lewy bodies. Note: all cases also had small vessel disease with moderate to severe cerebral amyloid angiopathy (CAA) and arteriolosclerosis; but none had infarcts. TDP-43 proteinopathy was not detected in any case. na, not available.

## Neuropathologic Assessment of 15 DIAN Family Members

Mutation	P/F	PMI (h)	Brain wt. (g)	Clin. Dx.#	Npath. Dx.	A <sup>^</sup> (A $\beta$ )	B <sup>^</sup> (NFT)	C <sup>^</sup> (NP)	SYN* *
PSEN1 H163R	F	4.5	1,300	ADD	AD+ALB	3	3	3	ALB
PSEN1 H163R	F	9	1,490	ADD	AD	3	3	3	0
PSEN1 H163R	F	6	1,210	ADD	AD+DLB	3	3	3	6
PSEN1 G206A	F	na	na	ADD	AD	3	3	3	0
PSEN1 G217R	F	15	1,040	ADD	AD+DLB	3	3	3	6
PSEN1 L226R	F	16	1,124	ADD, PD	AD+ALB	3	3	3	ALB
PSEN1 S290C	F	60	1,144	ADD	AD	3	3	3	0
PSEN1 C410Y	F	21	1,224	ADD	AD	3	3	1	0
PSEN1 A431E	F	5	720	ADD	AD+DLB	3	3	3	6
PSEN2 A141I	F	6	1,100	ADD	AD+ALB	3	3	3	ALB
APP K670N,M671L	F	6	1,210	ADD	AD	3	3	3	0
APP V717I	F	15	1,150	ADD	AD	3	3	3	0
APP V717I	F	26.5	1,370	ADD	AD	3	3	3	0
APP V717I	F	10	1,110	ADD	AD+ALB	3	3	3	ALB
APP V717I	F	na	980	ADD	AD+ALB	3	3	3	ALB
Mean	N=15F	15.4	1,155	-	AD (100%)				
Range	-	4.5-60	720-1,490	-	AD+DLB/ALB (53%)				

F, family member; # ADD, Alzheimer disease dementia ; <sup>^</sup>NIA-AA criteria for AD neuropathologic change: A, (A $\beta$  plaque score); B, (Braak neurofibrillary tangle score); and C, (CERAD neuritic plaque score). \*\*SYN,  $\alpha$ -synucleinopathy; Braak Parkinson's disease Lewy body stage. PMI, postmortem interval (hours). DLB, dementia with Lewy bodies. ALB, amygdala Lewy bodies. Note: all cases also had small vessel disease with moderate to severe cerebral amyloid angiopathy (CAA) and arteriolosclerosis; but none had infarcts. TDP-43 proteinopathy was not detected in any case. na, not available.

# Comorbidities in LOAD (ADNI) and ADAD (DIAN) Participants

Neuropathologic Diagnoses		LOAD (ADNI)		ADAD (DIAN)	
Primary	Comorbidities <sup>^</sup>	N=50*	%	N=24**	%
ADNC	None	18	36.0	11	46
ADNC	DLB/ALB	22	44.0	13†	54
ADNC	TDP-43	10	20.0	0	0
ADNC	AGD	4	8.0	0	0
ADNC	ARTAG	3	6.0	0	0
ADNC	Hippocampal sclerosis	3	6.0	0	0
ADNC	Infarcts	2	4.0	0	0
AGD	PART	2	4.0	0	0

\*6 cases pending; \*\*2 cases pending; ^more than one comorbidity may be present in a single case; †, one case had additional *glioblastoma*.

**Average age at death = 81.9 y (ADNI) and 51.6 y (DIAN).**

Of 42 ADNI cases with expiration CDRs, 5 were CDR 0.5, 3 were CDR 1, 8 were CDR 2, and 26 were CDR 3.

Of 9 DIAN participant cases with completed assessments, all were CDR 3.

*Produced with data as of 3/2016*

# Acknowledgements

## The Participants

<http://www.adni-info.org/>

<http://dian-info.org/>

**DIAN PI: Randall J. Bateman (John C. Morris)**

**ADNI PI: Michael W. Weiner**

**DIAN Sites (17): USA, Australia, Germany, Argentina**

**ADNI Sites (57): USA, Canada**



**DIAN/ADNI Neuropathology Core**

**Nigel Cairns**

**Erin Franklin**

**Benjamin Vincent**

**Michael Baxter**

**Washington University**

**Division of Neuropathology**

**Robert Schmidt**

**Joseph Corbo**

**Sonika Dahiya**

**Richard Perrin**



**Dominantly Inherited  
Alzheimer Network**

