# **BIOGRAPHICAL SKETCH**

NAME: Grinberg, Lea					
eRA COMMONS USER NAME (agency login):	leagrin				
POSITION TITLE: Associate Professor of Neur	ology/co-leader l	JCSF Neurode	egenerative Disease Brain Bank		
EDUCATION/TRAINING (Begin with baccalaur	reate or other initi	ial professiona	l education, such as nursing,		
include postdoctoral training and residency training if applicable.)					
INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY		
Faculdade de Ciências Médicas da Santa Casa de São Paulo - Sao Paulo - Brazil	MD	11/2001			
University of São Paulo Medical School, Sao Paulo, Brazil	PHD	06/2006	age-related neuropathology		
Federal University of Rio de Janeiro, Rio de Janeiro	Other training	10/2004	Neurobiophysics		
University of São Paulo Medical School	Resident	02/2005	residence in pathology		
Washington University in St. Louis	Fellow	04/2006	Clinical aspects and neuropathology of dementia		
University of São Paulo Medical School	Fellow	02/2007	neuropathology		
Albert Einstein Research and Education Institute, Sao Paulo	Postdoctoral Fellow	08/2007	histology-neuroimaging correlation		
University of Wuerzburg	Postdoctoral Fellow	08/2009	human neuroanatomy		

## A. Positions and Honors

## **Positions and Employment**

2002 2005	Tagahar aid University of Cão Davie Medical Cahool, Cao Davie			
2002 - 2005	Teacher aid, University of Sao Paulo Medical School, Sao Paulo			
2003 - 2010	Director, Brazilian Aging Brain Bank, University of Sao Paulo Medical School			
2009 - 2012	Co-chairwoman, Human Brain Proteome Project, Human Proteome Organization			
2009 - 2015	Assistant Professor of Neurology, University of California, San Francisco, CA			
2010 -	Deputy Director, Brazilian Aging Brain Bank, University of Sao Paulo Medical School			
2012 -	Assistant Professor of Pathology (on leave), University of Sao Paulo Medical School			
2013 -	Chairwoman, Human Brain Proteome Project, Human Brain Organization			
2013 - 2015	Assistant Professor of Pathology, University of California, San Francisco			
2014 -	Co-leader, Neuropathology Core, Memory and Aging Center, UCSF			
2015	Associate Professor of Neurology and Pathology, University of California, San Francisco			
Other Experience and Professional Memberships				
2009 -	Member of Scientific Advisory board, International Congress on Vascular Dementia			
2009 -	Editorial Board, Cell and Tissue Banking			
2010 -	Associate Editor, Frontiers on Aging Neuroscience			
2011 -	Reviewer for grant applications, Alzheimer Association			
2012 -	Member of Scientific Advisory board, Conference "Controversies in Neurology."			
2012 - 2015	Reviewer for Review panel - AD Research Awards, California Department of Public Health			
2014 -	Member, American Association of Neuropathologists			
2014 - 2017	Member - Senate Committee on Research, University of California, San Francisco			
2015 -	Member, California Medical Board			
2015 -	Editorial Board, BMC Medicine			

### <u>Honors</u>

- 2005 Honor Award, XX FESBE Congress of the Brazilian Societies of Experimental Biology
- 2005 PhD. Scholarship , FAPESP, Brazil
- 2005 PhD. Scholarship abroad, CAPES Foundation, Brazil
- 2006 Post-doctorate scholarship, UNIEMP Institute. Brazil
- 2006 1st prize 2nd Aging Research Award, Brazilian Society of Geriatrics and Gerontology
- 2007 Travel award, FAPESP, Brazil
- 2007 Post-doctorate scholarship abroad, CAPES, Brazil
- 2007 Best study on medical genetics, Neurology Annual Meeting, University of São Paulo
- 2008 Georg Foster Scholarship, Alexander von Humboldt Foundation
- 2008Travel Scholarship to International Congress on Alzheimer's Disease, Alzheimer Association2009"For Women in Science," Unesco/L'oreal
- 2010 Distinguished Research Scholar Award, John Douglas French Alzheimer Foundation
- 2014 Special Honor Award 1st award "Diaspora Brazil", Brazilian Federal Government

## **B.** Contribution to Science

### Most relevant to the current application

- 1. Theofilas P, Polichiso L, Wang X, Lima LC, Alho AT, Leite RE, Suemoto CK, Pasqualucci CA, Jacob-Filho W, Heinsen H. A novel approach for integrative studies on neurodegenerative diseases in human brains. J Neurosci Methods. 2014 Apr 15; 226:171-83. PMID: 24503023. PMCID: PMC4083099
- Seidel K, Mahlke J, Siswanto S, Krüger R, Heinsen H, Auburger G, Bouzrou M, Grinberg LT, Wicht H, Korf HW, den Dunnen W, Rüb U. The brainstem pathologies of Parkinson's disease and dementia with lewy bodies. Brain Pathol. 2015 Mar; 25(2):121-35. PMID: 24995389. PMCID: PMC4397912
- Di Lorenzo Alho AT, Suemoto CK, Polichiso L, Tampellini E, de Oliveira KC, Molina M, Santos GA, Nascimento C, Leite RE, de Lucena Ferreti-Rebustini RE, da Silva AV, Nitrini R, Pasqualucci CA, Jacob-Filho W, Heinsen H, Grinberg LT. Three-dimensional and stereological characterization of the human substantia nigra during aging. Brain Struct Funct. 2015 Sep 19. PMID: 26386691
- 4. Grinberg LT, Jimenez CR, Li KW. Neuroproteomics: Applications in Neuroscience and Neurology. Biochim Biophys Acta. 2015 Jul; 1854(7):703-704. PMID: 25858468
- Schrötter A, Magraoui FE, Marcus K, Park YM, Meyer HE, Grinberg LT. New Milestones in the Development of Characterization Tools for Neurodegenerative Diseases in Proteomics: 22nd HUPO BPP Workshop 7 October 2014, Madrid, Spain. Proteomics. 2015 Feb; 15(4):627-9. PMID: 25676247
- Stratmann K, Heinsen H, Korf HW, Del Turco D, Ghebremedhin E, Seidel K, Bouzrou M, Grinberg LT, Bohl J, Wharton SB, den Dunnen W, Rüb U. Precortical phase of Alzheimer's disease (AD)-related tau cytoskeletal pathology. Brain Pathol. 2015 Jul 20. PMID: 26193084
- 7. Theofilas P, Ehrenberg EJ, Dunlop S, et al. Locus coeruleus volume and cell population changes during Alzheimer's disease progression: a stereological study in human postmortem brains with potential implication for early-stage biomarker discovery. *Alzheimers Dement.* 2016: *In press.*

#### Additional recent publications of importance to the field (in chronological order)

- Grinberg LT, Wang X, Wang C, Sohn PD, Theofilas P, Sidhu M, Arevalo JB, Heinsen H, Huang EJ, Rosen H, Miller BL, Gan L, Seeley WW. Argyrophilic grain disease differs from other tauopathies by lacking tau acetylation. Acta Neuropathol. 2013 Apr; 125(4):581-93. PMID: 23371364. PMCID: PMC3692283
- Farfel JM, Nitrini R, Suemoto CK, Grinberg LT, Ferretti RE, Leite RE, Tampellini E, Lima L, Farias DS, Neves RC, Rodriguez RD, Menezes PR, Fregni F, Bennett DA, Pasqualucci CA, Jacob Filho W. Very low levels of education and cognitive reserve: a clinicopathologic study. Neurology. 2013 Aug 13; 81(7):650-7. PMID: 23873971. PMCID: PMC3775692
- Andrade-Moraes CH, Oliveira-Pinto AV, Castro-Fonseca E, da Silva CG, Guimarães DM, Szczupak D, Parente-Bruno DR, Carvalho LR, Polichiso L, Gomes BV, Oliveira LM, Rodriguez RD, Leite RE, Ferretti-Rebustini RE, Jacob-Filho W, Pasqualucci CA, Grinberg LT, Lent R. Cell number changes in Alzheimer's disease relate to dementia, not to plaques and tangles. Brain. 2013 Dec; 136(Pt 12):3738-52. PMID: 24136825. PMCID: PMC3859218

- Teipel S, Heinsen H, Amaro E, Grinberg LT, Krause B, Grothe M. Cholinergic basal forebrain atrophy predicts amyloid burden in Alzheimer's disease. Neurobiol Aging. 2014 Mar; 35(3):482-91. PMID: 24176625. PMCID: PMC4120959
- Sanders DW, Kaufman SK, DeVos SL, Sharma AM, Mirbaha H, Li A, Barker SJ, Foley AC, Thorpe JR, Serpell LC, Miller TM, Grinberg LT, Seeley WW, Diamond MI. Distinct tau prion strains propagate in cells and mice and define different tauopathies. Neuron. 2014 Jun 18; 82(6):1271-88. PMID: 24857020. PMCID: PMC4171396
- 6. Leite RE, Grinberg LT. Closing the gap between brain banks and proteomics to advance the study of neurodegenerative diseases. Proteomics Clin Appl. 2015 Jun 9. PMID: 26059592
- Corradini BR, Iamashita P, Tampellini E, Farfel JM, Grinberg LT, Moreira-Filho CA. Complex networkdriven view of genomic mechanisms underlying Parkinson's disease: analyses in dorsal motor vagal nucleus, locus coeruleus, and substantia nigra. Biomed Res Int. 2014; 2014:543673. PMID: 25525598. PMCID: PMC4261556
- Madeira C, Lourenco MV, Vargas-Lopes C, Suemoto CK, Brandão CO, Reis T, Leite RE, Laks J, Jacob-Filho W, Pasqualucci CA, Grinberg LT, Ferreira ST, Panizzutti R. d-serine levels in Alzheimer's disease: implications for novel biomarker development. Transl Psychiatry. 2015; 5:e561. PMID: 25942042. PMCID: PMC4471283
- 9. Kovacs GG, Ferrer I, Grinberg LT, et al.Aging-related tau <u>astrogliopathy</u> (<u>ARTAG</u>): harmonized evaluation strategy. Acta Neuropathol. 2016 Jan;131(1):87-102. PMID: 26659578. <u>PMCID:PMC4879001</u>
- 10. Fredericks CA, Koestler M, Seeley W, Miller B, Boxer A, Grinberg LT. Primary chronic traumatic encephalopathy in an older patient with late-onset AD phenotype. Neurol Clin Pract. 2015 Dec;5(6):475-479. <u>PMCID: PMC4684670</u>.
- 11. Rodriguez RD, Suemoto CK, Molina M, et al. Argyrophilic grain disease: demographics, clinical, and neuropathological features from a large autopsy study. J Neuropathol Exp Neurol. 2016: [Epub 9 June 2016]
- 12. Alegro M, Amaro-Jr E, Loring B, et al. Multimodal Whole Brain Registration: MRI and <u>High Resolution</u> Histology. *WBIR.* 2016: In press.

#### C. Research Support

#### **Ongoing Research Support**

*R01AG040311 (Grinberg) NIH/ NIA (21321)	09/30/2011 - 05/31/2016	\$206,019		
Brainstem as an early site in AD and FTLD. To determine the chronology, severity, inter changes in the isodendritic core in AD and Role: Principal Investigator	closing the etiopathogenic gap dependence, and symptom-relevar FTLD vs. healthy elderly controls.	nce of neuropathological		
P50 AG023501 (Miller) NIH/NIA (29042)	04/01/2014 - 03/31/2019	\$180,133 (Core D only)		
Alzheimer's <u>disease</u> Research Center Core D: Neuropathology <u>This is</u> a neuropathology core to characterize postmortem brain tissue of subjects enrolled in this project Role: Co-Investigator (4.04 cal mos)				
P01AG019724 (Miller) NIH/ NIA (29322)	09/01/2012 - 05/31/2017	\$1,348,531		
Frontotemporal Dementia: Genes, Images and Emotions This is a neuropathology core to characterize postmortem brain tissue of subjects enrolled in this project Role: Co-Investigator (0.92 cal mos)				
18F-AB-1451-A13 (Grinberg) Veterans Affairs	03/01/2015 – 08/31/2016	\$362,405		
A Pilot Study Evaluating the Relationship of 18F-AV-1451 PET Imaging and Tau Pathology at Autopsy Major goal: to validate 18F-AV-1451 PET Imaging using high-resolution point-to-point histology				

Rainwater Foundation/ aFTD (Rabinovici) 07/01/15-06/30/17 \$10,000.00 Neurological basis of AV1415 PET in frontotemporal dementia This is a clinicopathological study to identify the histological counterpart of tau PET-tracer signal in FTD Role: Co-Investigator Rainwater Foundation (Grinberg) 07/01/15-07/30/16 \$120.000.00 Neurobiology of sleep disturbances in PSP This is a study to better identify patterns of phospho-tau burden in nuclei belonging to the sleep/wake network Role: Principal Investigator **Pending Research Support** P0512565 (Grinberg) 02/01/2017 - 02/01/2019 NIH Exploratory/Developmental Research Grant \$150.000 Histology-based MRI template of the locus ceruleus for Alzheimer's Disease Goals: To develop a histology-based MRI template to identify the LC in clinical MRI Role: Principal Investigator 07/01/2016 - 06/30/2021 P0512565 (Grinberg) \$152,685. NIH National Institute Neurological Discord & Stroke Neuropathological changes underlying clinical heterogeneity in Alzheimer disease Goals: to investigate the neuropathology underlying AD variability in humans **Role: Principal Investigator** P0512347 (Grinberg) 02/01/2016 - 01/31/2018 Alzheimer's Association \$54,545.00 Caspases and the proteasome as determinants of opposite neuronal fate in AD Goals: To map the interdependence of aCasp-6, CHIP, Asp421- and p-tau inclusions in postmortem brain tissue across AD progression in an extremely vulnerable brain area. Role: Principal Investigator \$120,000.00 Rainwater Foundation (Grinberg) 08/01/16-07/30/17 Neurobiology of sleep disturbances in PSP This is a study to better identify patterns of phospho-tau burden in nuclei belonging to the sleep/wake network **Role: Principal Investigator** 09/01/16-08/30/21 P0516825 (Gan) \$200,000 (Human Core only) Linking tau proteostasis with neuronal activity in FTD" Center Without Walls for the Identification and Validation of Molecular Mechanisms Contributing to Tau Pathogenesis and Associated Neurodegereration in Frontotemporal Degeneration (FTD)

Goals: this is a core to validate the project findings in humans Role: Core Leader

Role: Principal Investigator