BIOGRAPHICAL SKETCH

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NAME: Farida Sohrabji

eRA COMMONS USER NAME (credential, e.g., agency login): sohrabjf

POSITION TITLE: Joseph Shelton Professor of Neuroscience

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
St. Xaviers College, Bombay, India	B.A.	1982	Psychology
Bombay University, Bombay, India	M.A.	1984	Clinical Psychology
University of Rochester, Rochester, NY	M.S.	1989	Neurobiology
University of Rochester, Rochester, NY	Ph.D.	1991	Biopsychology/Neurobiology
Columbia University Medical Center, NY, NY	Postdoctoral	1991-1994	Neurobiology/MolecularBiology/Tissue Culture

A. Personal Statement

My research program focuses on brain-immune interactions regulated by age and sex hormones and its implications for neuro-inflammatory diseases such as stroke in women. Our current studies use an animal model to examine age and sex differences in recovery from stroke, focusing at the cellular level on the endothelium and astrocytes, which are the principal components of the blood brain barrier. At the molecular level, we are examining sex and age differences in microRNA and epigenetic markers, with a view to developing biomarkers for diseases and uncovering new therapeutic targets. Below are recent invited book chapters that I have authored on sex and age differences in stroke.

1. Sohrabji, F (2015) The impact of aging on ischemic stroke. In *Advances in Geroscience* Ed. F. Sierra and Ronald Kohanski Springer International Publishing pp 161-196.
2. Sohrabji, F. (2015) Cerebrovascular Stroke: Sex differences and the impact of estrogen. In Estrogen's effects on traumatic brain injury: Mechanisms of Neuroprotection and Repair. Edited by K. Duncan Elsevier Press, pp 125-141.
3. Sohrabji, F, Welsh, C.J and Reddy, DS (2015) Sex differences in neurological diseases. Chapter 12 in *Sex differences in the central nervous system*, edited by Rebecca M Shansky, Academic Press, London UK Pages 297-323.

B. Positions and Honors

1990-1994	Postdoctoral Fellow/Associate Research Scientist, Columbia University College of Physicians and Surgeons.
1995-1998	Associate Research Scientist, Human Anatomy and Neurobiology, Texas A&M HSC
1998-2003	Assistant Professor, Human Anatomy and Neurobiology, Texas A&M Health Science Center
2003- 2009	Associate Professor, Human Anatomy and Neurobiology (reorganized as Neuroscience and Experimental Therapeutics) Texas A&M Health Science Center
2009-present	Professor, Neuroscience and Experimental Therapeutics Texas A&M Health Science Center

Other positions:

2017-	Presidential Impact Fellow, Texs A&M University
2016-	Fellow of the American Heart Association (FAHA) Stroke Council
2012-	Joseph H. Shelton Professor of Neuroscience
2011-present	Vice-Chair, Texas A&M Institute of Neuroscience
2007- present	Director, Women's Health in Neuroscience Program
2007- present	Associate Department Chair, Neuroscience and Experimental Therapeutics
2006- present	Adjunct Faculty, Department of Psychology, TAMU
2005- present	Texas Brain and Spine Institute (Research Director, 2010-present)
1997- present	Faculty of Neuroscience/Texas A&M Institute of Neuroscience/Faculty of Reproductive Biology

Professional Service:
NNRS study section: 2007-2012 (Chartered member 2008)
ICER study section: 2014-2018 (Chartered member 2015)
Special Emphasis Panels: MDCN2, 2002; BDCN 2009
NIA/NIH PPG Review: 2002; 2003; 2004; 2005; 2006; 2011; 2015
AHA 1A Study Section Brain/Renal 2005-2009; Co-Chair 2008-2009
Advisory Committee for Research on Women's Health (OD-ORWH) 2009-2013
Ad hoc review: NSF (Endocrinology), Alzheimer's Association 1997, 1999-2009
External Advisory Committee, Oklahoma Reynolds Center on Aging, 2009
Editorial Board, Endocrinology 2010-2013
Frontiers in Aging Neuroscience, Editorial Board, 2009-present
Organization for the Study of Sex Differences (OSSD), Treasurer, 2012-2015
Texas Alzheimer's Research Consortium and Care (TARCC): Steering committee member 2013-2016

C. Contribution to Science

1. Development of a female reproductive aging model:
My research program over the last 20 years has centered on the effects of estrogen on neuroinflammation and stroke. Our earlier studies were performed in young ovariectomized females, which mimics a surgical menopause. About 15 years ago, I made a critical decision to study a more clinically valid animal model to study hormone replacement. We selected 10-12 month old (Sprague Dawley) female rats. These rats are acyclic (as determined by daily vaginal smears), have undetectable levels of estrogen, low levels of progesterone and elevated levels of FSH. This hormonal profile more closely mimics menopausal females. We reported that this middle aged acyclic female differs dramatically from normally cycling adult females in its response to inflammatory stimuli and, more importantly, the effects of estrogen are dependent on the reproductive age of the animal. Thus while estrogen is neuroprotective and anti-inflammatory in young females, it is diametrically opposite in middle-aged acyclic females.

a. Jezierski, M.K. and F. Sohrabji (2001) Neurotrophin expression in the reproductively senescent forebrain is refractory to estrogen stimulation. Neurobiology of Aging, 22: 311-321.
b. Nordell, V.L, M.M. Scarborough and F. Sohrabji (2003) Estrogen regulation of cytokine expression in the injured forebrain is dependent on reproductive age. Neurobiology of Aging 24: 733-743.
c. Johnson AB and Sohrabji F (2005) Estrogen's inflammatory effects on central and circulating immune cells vary with reproductive age. Neurobiology of Aging, 26: 1365-1374.

2. Stroke and reproductive aging: Stroke occurs more often in the elderly, and within that demographic, stroke occurs more often, and is more severe, in women. Our preclinical studies have shown that stroke is more severe in middle-aged females as compared to younger females and that estrogen treatment is not neuroprotective in this older population. Our studies have focused aggressively on identifying new therapeutics for this older group. We have reported an age-related decline in circulating and parenchymal levels of the peptide hormone, IGF-1 and further shown that post stroke IGF-1 treatment is neuroprotective in this older female group. We are currently focused on IGF-1 dependent mechanisms (inflammation, maintenance of the blood brain barrier), as well as epigenetic regulators that can increase IGF-1 availability.

a. Selvamani A. and Sohrabji F. (2010) Reproductive age modulates the impact of focal ischemia on the forebrain as well as the effects of estrogen treatment in female rats. Neurobiology of Aging, 31: 1618-1628, Epub 2008. PMID: 18829137
b. Selvamani A. and Sohrabji F. (2010) The neurotoxic effects of estrogen on ischemic stroke in older female rats is associated with age-dependent loss of IGF-1. J. Neurosci., 30: 6852-61.
c. Bake S, Selvamani A, Cherry J. Sohrabji F. (2014) Blood Brain Barrier and Neuroinflammation Are Critical Targets of IGF-1-Mediated Neuroprotection in Stroke for Middle-Aged Female Rats. PLoS One, e91427. PMID: 24618563

3. Blood brain barrier in aging and ischemia: We were among the first lab to show that the blood brain barrier is more permeable in middle-aged female rats as compared to younger females. Furthermore, while estrogen treatment improves barrier function in young females, hormone treatment, paradoxically, increases barrier permeability in middle aged females. This observation provides a mechanistic clue as to why older animals have worse stroke outcomes.

a. Bake S. and Sohrabji F. (2004) 17b-estradiol differentially regulates blood brain barrier permeability in young and aging female rats. Endocrinology, 145: 5471-5475.
b. Bake S, Friedman J, Sohrabji F (2009) Reproductive age-related changes in the blood brain barrier: Expression of IgG and tight junction proteins. Microvascular Research, 78(3):413-24. PMID: 19591848.
c. Bake, S., A. K. Okoreeh, R. C. Alaniz and F. Sohrabji (2016). "Insulin-Like Growth Factor (IGF)-I Modulates Endothelial Blood-Brain Barrier Function in Ischemic Middle-Aged Female Rats." Endocrinology **157**(1): 61-69.

4. Astrocytes as a critical target of aging: At a mechanistic level, our studies have led us to consider the possibility that cellular components of the blood brain barrier (astrocytes and endothelial cells) may be critical mediators of the stroke response. Post stroke, astrocytes provide trophic support for ischemic neurons and clearance of cytotoxic compounds. Our studies have shown that in the aging astrocyte, these repair mechanisms are inefficient, and may be associated with epigenetic alterations in this cell with aging.

a. Lewis DK, Thomas KT, Selvamani A, Sohrabji, F. (2012) Age-related severity of focal ischemia in female rats is associated with impaired astrocyte function. Neurobiol of Aging, 33: 1123.e1-16. PMID: 22154819
b. Chisholm NC, Henderson ML, Selvamani A, Park MJ, Dindot S, Miranda RC, Sohrabji F. 2015. Histone methylation patterns in astrocytes are influenced by age following ischemia. Epigenetics 10:142-52. PMID 25565250
c. Okoreeh, A, Bake, S, Sohrabji F (2017) Astrocyte-specific Insulin-like Growth Factor-1 Gene Transfer in aging female rats improves stroke outcomes. Glia, *In press*.

5. In vivo experiments with miRNA therapeutics:
Our recent work focuses on epigenetic changes in aging and innovative therapeutic strategies involving small non-coding RNA and histone modifying agents for stroke neuroprotection. Our first strategy was a 'targeted' approach, based on miRNA that would elevate endogenous levels of IGF-1. Thus, miRNA with consensus sites on the IGF-1 UTR were targeted with antagomirs in a stroke model. Although this approach proved successful in young females it was not effective in middle-aged females. In order to identify a neuroprotectant for older groups, we are profiling age and sex differences in circulating miRNA and age differences in histone methylation, to identify novel epigenetic modifiers.

a. Selvamani A, Sathyan P, Miranda R.C. **Sohrabji, F.** (2012) An antagomir to microRNA Let7f promotes neuroprotection in an ischemic stroke model. PLoS ONE 7(2): e32662. PMID: 22393433
b. Selvamani A, Williams M, Miranda RC, Sohrabji F. (2014) Circulating miRNA profiles provide a biomarker for severity of stroke outcomes associated with age and sex in a rat model. Clin Sci, 127:77-89. PMID: 24428837
c. Selvamani A, Sohrabji F. 2016. Mir363-3p improves ischemic stroke outcomes in female but not male rats. Neurochem Int. Oct 20. pii: S0197-0186(16)30179-6. doi: 10.1016/j.neuint.2016.10.008.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=sohrabji

D. Research Support
Ongoing:

1R01AG042189 (F. Sohrabji) Role: PI 9/15/11-8/31/17
NIH (NIA/NINDS/ORWH)
Epigenetics of the Aging Astrocyte: Implications for Stroke

Major goals: The overall goal of this application is to identify aging- and stroke-related epigenomic changes in astrocytes (in response to RFA ES 10-002).

1R01NS074895 Role: PI 9/01/2011- 08/30/2017
NIH/NINDS
Neuroprotection in the Aging Female Brain

Synopsis: The overall goal of this application is determine the interaction of estrogen and IGF-1 in the context of stroke and neuroprotection in middle age females, using an animal model.

R01AA024659 (Miranda) Role: Co-I 10/03/2016-28/2/2021
NIH/NIAAA
Prenatal microRNA neuro-therapeutics for fetal alcohol exposure.

Synopsis: The overall goal of this application is to develop epigenetic therapies for individuals exposed to fetal alcohol exposure.

Discovery Foundation, Dallas, TX Role: PI 1/1/15-12/31/17
The impact of IGF-1 on post-stroke depression and neuroinflammation in a preclinical model

Synposis: This application examines the neuroinflammatory response to stroke and longterm consequences of stroke on depression in an animal model.

SCIRP160225 (PI: Hook; Co-PI: Sohrabji) 04/01/17-03/31/20 0.6 calendar mos
Department of Defense

Derivation of the Mechanisms Mediating the Adverse Effects of Morphine in a Rodent Model of SCI: Functional Recovery and Neuron Loss

Synopsis: This application examines the effects of morphine on neuroinflammatory response after spinal cord injury and its impact on cell survival and behavioral recovery. No overlap with present proposal

State Contract:
Development of TARCC Investigator Grant Program **Role**: PI 9/26/14-9/25/2016
Texas Council on Alzheimer's Disease and Related Disorders

Completed (in the last 5 years):

1R01AG041360 (PI Griffith) Role: Co-I 4/1/11-3/31/16
NIH/NIA
Estrogens, Ovarian Aging and Calcium Channel Modulation

Synopsis: The overall goal of this project is to examine sex differences and the effect of estrogen on calcium currents in basal forebrain cholinergic neurons in young and middle aged rats.

#14GRNT18370013 (PI: Earnest) Role: Co-I 1/1/14-12/31/15
AHA

Circadian Clocks and Neuroprotection in Response to Stroke during Reproductive Aging

Synopsis: The overall goal is to examine whether alterations in circadian patterns will impact the severity of stroke in middle-aged females. No overlap with present proposal.

5R01AG027684 Role: PI 05/01/2006 – 04/30/2012
NIA/NIH
Impact of Endocrine Aging on Brain and Immune Response

Synopsis: This proposal will investigate the hypothesis that the timing of estrogen replacement is critical for its neuroprotective effects.

5R01AG028303 Role: PI (16% effort) 08/01/2006 – 07/31/2011