BIOGRAPHICAL SKETCH

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NAME: Nicole Schupf

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

POSITION TITLE: Professor of Epidemiology at CUMC

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
Bryn Mawr College, Bryn Mawr, PA	B.A.	1960-1964	Psychology
New York, University, New York, NY	Ph.D.	1964-1970	Physiological Psychology
University of California-Berkeley, Berkeley CA	M.P.H.	1983-1984	Epidemiology
Columbia University, New York, NY	Dr.P.H.	1988-1995	Epidemiology

A. Personal Statement

A. I have a broad background in physiological psychology and epidemiology and extensive experience in the analysis of longitudinal data in community based cohorts. I have conducted studies of antecedent factors related to onset and risk of MCI and Alzheimer's disease, both in the Washington Heights- Inwood (WHICAP) cohort and in cohorts of high risk adults with Down syndrome. In studies of adults with Down syndrome, we have shown that Aß1-42 and Aß1-40 levels are significantly higher in adults with DS than in controls from the general population and that Aß1-42 levels are selectively increased in demented adults with DS and developed a blood based proteomic profile that can predict onset of MCI and dementia. A major focus of current work on Down syndrome is the investigation of blood based, genetic and host factors that increase ß -amyloid load or accelerate the accumulation of fibrillized amyloid plaques and tau neurodegenrqation. I am one of the three lead PIs on the U01 study of Biomarkers of Alzheimer's Disease in Adults with Down syndrome. This work is focused on the role of biomarkers of risk for Alzheimer's disease in adults with Down syndrome and includes studies of the contribution of proteomic and metabolomics profiles, beta amyloid levels, genetic factors, and imaging markers of Alzheimer's disease. We will enroll 400 adults with Down syndrome and collect and analyze clinical profiles, blood based biomarkers and imaging data every 16 months over 3 assessment cycles. I work closely with co-investigators to coordinate follow-up of the cohort, and oversee linkage of laboratory data with clinical, imaging and genetic information and consult with all investigators on data analysis and publications.

B. B. Positions and Honors

Positions and Employment

1969-1971 Research Associate, Laboratory of Biochemical Genetics, Rockefeller University, N.Y.
1974-1977 Instructor, Department of Neurology, New York University Medical Center, N.Y.,
1977-1986 Assistant (1977-1883), Associate Professor of Psychology, Manhattanville College, N.Y.
1984-1990 Associate Research Scientist, Gertrude H. Sergievsky Center, Columbia University, NY
1990-1993 Scholar in the Gertrude H. Sergievsky Center
1988-2002 Research Scientist VI, Laboratory of Epidemiology, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, N.Y.
2002 Associate Research Scientist, Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University, N.Y.

2003- Associate Professor of Epidemiology at CUMC, Mailman School of Public Health, Columbia University, N.Y.
2009- Professor of Epidemiology at CUMC, Mailman School of Public Health, Columbia University, N.Y.

Other Experience and Professional Memberships

Editorial Staff, American Journal of Public Health
Assistant Editor, 1992-1993
Associate Editor, 1993-1995

Consulting Editor, Mental Retardation, 2000-2004

Associate Editor, Journal of Alzheimer's Disease, 2012-2013

Reviewer for American Journal of Public Health, Biological Psychiatry, PloS, Neurobiology of Aging, Lancet Neurology, Neurology, Neuroepidemiology, Neuroscience Letters, Dementia & Geriatric Cognitive Disorders, Journal of Alzheimer's Disease and Related Disorders, International Journal of Epidemiology, American Journal on Mental Retardation, Mental Retardation, Journal of Intellectual Disability Research,

Grant Reviewer for Alzheimer's Association, NWO, Netherlands, Special review panels for NIH/NIA, Special Review Panel on Genetics for NIH GO grants, British MRC review Panel, Canadian IHRC review

Invited working group member, CDC National Center on Birth Defects and Developmental Disabilities, and the National Down Syndrome Society (NDSS) special meeting on "Setting a Public Health Research Agenda for Down Syndrome". November 8-9, 2007

Working Group Member and Invited Speaker. NIH Workshop on "Advancing Treatments in Alzheimer's Disease in Individuals with Down Syndrome" April 16-17, 2013

Member, Executive Committee, Down Syndrome Professional Interest Area (Alzheimer's Association): Chair, Epidemiology and Genetics Subcommittee. (2013-2017)

Member, NIH Working Group on Outcomes Measures for Clinical Trials in Down Syndrome: Medical/Physical Work Group 2015

Member, Scientific Advisory Board and member, Program Committee, Trisomy 21 Research Society, 2015-

Honors

1964. B.A. Cum Laude with Honors in Psychology
1970 Ph.D. New York University Founder's Day Award for outstanding academic achievement
1995 Dr.P.H. Anna C. Gelman Award for Excellence in Epidemiology, Columbia University
2000 The Blake Marsh Lecture. Genetic and host factors for accelerated ageing and dementia in Down syndrome. Royal College of Psychiatry Annual Meeting, Edinburgh, Scotland, July 7,
2001 Fellow, American Association on Mental Retardation,
2014 Invited Speaker Welcome Trust Scientific Conference. Alzheimer's disease in Down syndrome: from molecules to cognition. Cambridge, UK. March 27-29,
2016 Invited Speaker, Keystone Symposia on Biology of Down syndrome: Impact throughout Biomedicine. January 2016, Santa Fe, New Mexico.

Fellowships

Sergievsky Scholar, Gertrude H. Sergievsky Center, 1990-1993

C. Contributions to Science.

1. Identifying blood-based biomarkers of risk and determining which individuals are at the highest risk can provide insights into AD pathogenesis, are critical to the early diagnosis of dementia, and can guide the development of effective intervention. Our initial biomarker studies focused on the role of beta amyloid peptides in the pathogenesis of AD and their utility as a screening tool to identify high risk individuals and early detection of disease onset.

a. R. Mayeux, L.S. Honig, MX Tang, J. Manly, Y. Stern, N, Schupf, P. D. Mehta (2003). Plasma Amyloid Aβ40 and Aβ42 and Alzheimer's Disease (AD). Relation to Age and Mortality. Neurology 61 (9): 1185-1190

b. N. Schupf, B.N. Patel, D. Pang, W.B. Zigman, W. Silverman. P.D. Mehta, R. Mayeux (2007). Elevated plasma amyloid β-peptide Aβ42, incident dementia and mortality in Down syndrome. Archives of Neurology 64(7):1007-13

c. N. Schupf, MX Tang, H Fukuyama, JJ Manly, H Andrews, P Mehta, J Ravetch, R Mayeux (2008). Peripheral Aβ subspecies as risk biomarkers of Alzheimer's disease. Proceedings of the National Academy of Sciences 105(37):14052-14957 PMCID: PMC2544577

d. N, Schupf, W. Zigman, M-X Tang, D Pang, R Mayeux, P Mehta, W Silverman, Change in Plasma Aβ peptides and Onset of Dementia in Adults with Down Syndrome Neurology 2010; 75: 1639-1644. PMCID: PMC3385463

2. I have conducted studies of the familial aggregation of Down syndrome (DS) and Alzheimer's disease (AD). Most of the non-disjunction events in DS are of maternal origin. I hypothesized that a shared genetic susceptibility to DS and AD would be associated with an increased frequency of AD among mothers, but not fathers, of individuals with DS. I further hypothesized that the shared susceptibility could involve an accelerated aging process, leading to the birth of a child with DS to a relatively young mother and to an increased risk of dementia in mothers who were young when their child with DS was born compared with mothers who were older at the birth of a child with DS. The risk of dementia among mothers who were 35 or younger when their DS children were born was 5 times that control mothers, while there was no increase in risk of dementia among mothers who were older (> 35 years) at the proband's birth.

a. N. Schupf, D. Kapell, J.H. Lee, R. Ottman and R. Mayeux (1994) Increased risk of Alzheimer's disease in mothers of adults with Down syndrome. Lancet 334:353-356.

b. N. Schupf, D. Kapell, B. Nightingale, J.H Lee, J. Mohlenhoff, S. Bewley, R. Ottman, R. Mayeux (2001). Specificity of the five-fold increase in AD in mothers of adults with Down syndrome. Neurology, 57:979-984

3. We have been interested in understanding the role of hormonal risk factors for AD in women with DS and in women in the general population, in order to identify risk factors and determinants of the higher risk of AD in women than in men. Among women with DS, younger age at menopause and lower levels of bioavailable estradiol in postmenopausal women were associated with a 3-4 fold increased risk of AD. In both women with DS and women in the general population, polymorphisms in genes involved in estrogen biosynthesis and in estrogen receptor activity were associated with earlier onset and an increased risk of AD. These findings support an important neuroprotective role for estrogen.

a. N. Schupf, D. Pang, BN Patel, W. Silverman, R. Schubert, F. Lai, JK Kline, Y Stern, M. Ferin, B. Tycko, R. Mayeux (2003). Onset of dementia is associated with age at menopause in women with Down syndrome. Annals of Neurology 54:433-438. PMID: 14520653

b. N. Schupf , S Winsten, B Patel, D. Pang, M. Ferin, WB Zigman, W Silveman, R. Mayeux (2006). Bioavailable estradiol and age at onset of Alzheimer's disease in postmenopausal women with Down syndrome. Neuroscience Letters 406(3) 298-302 PMID: 16926067

c. C. Chace, D Pang, C. Weng, A. Temkin, S. Lax W. Silverman, WB. Zigman, M. Ferin, JH Lee, B Tycko, N. Schupf (2012): Variants in CYP17 and CYP19 cytochrome p450 genes are associated with onset of Alzheimer's disease in women with Down syndrome. J Alzheimer's Disease 28(3):601-12, PMCID: PMC3276705

d. N. Schupf, JH Lee, D. Pang WB Zigman, B Tycko, S, Krinsky-McHale, W. Silverman (2018). Epidemiology of estrogen and dementia in women with Down syndrome. Free Radic Biol Med. 2018 Jan;114:62-68. PMID: 28827423.

4. We have examined a range of other risk factors for AD and for mortality in the multi-ethnic WHICAP cohort.

a. Brickman AM, Schupf N, Manly JJ, Stern Y, Luchsinger JA, Provenzano FA, Narkhede A, Razlighi Q, Collins-Praino L, Artero S, Akbaraly TN, Ritchie K, Mayeux R, Portet F (2014). APOE epsilon4 and risk for Alzheimer's disease: Do regionally distributed white matter hyperintensities play a role?

Alzheimer's Dement;10(6):619-29. PMID:25304991 PMCID: PMC4252241

b. Golub JS, Luchsinger JA, Manly JJ, Stern Y, Mayeux R, Schupf N. (2017) , Observed hearing loss and incident dementia in a multiethnic population. J. Am Geriatr Soc, 65 (8) 1691-1697. PMID: 28323321; PMCID: PMC5555781

c. Noble JM, Schupf N, Manly JJ, Andrews H, Tang MX, Mayeux R. (2017). Secular trends in the incidence of dementia in a Multi-Ethnic Community J. Alzheimer's disease 60 (3) 1065-1075 PMID: 28984588

d. Gu Y, Gutierrez J, Meier IB, Guzman VA, Manly JJ, Schupf N, Brickman AM, Mayeux R. Circulating inflammatory biomarkers are related to cerebrovascular disease in older adults. Neurol Neuroimmunol Neuroinflamm. 2018 Nov 14;6(1):e521. doi: 10.1212/NXI.0000000000000521. eCollection 2019

e. Avila JF, Vonk JMJ, Verney SP, Witkiewitz K, Arce entería M, **S**chup**f** N, Mayeux R, Manly JJ. Sex/gender differences in cognitive trajectories vary as a function of race/ethnicity. Alzheimers Dement. 2019 Dec;15(12):1603-1611. doi: 10.1016/j.jalz.2019.07.013. Epub 2019 Oct 3. PMID: 31587996

5. The Long Life Family Study is a family study of longevity and exceptional survival traits among 546 families with multiple family members with long life spans. In population-based cohorts of the elderly, those with mild as well as severe cognitive impairment have been found to have an increased risk of death We and others have documented a significant association between preserved cognitive function, successful aging and longevity. It is likely that cognitive traits, such as exceptional memory, might represent one of the several endophenotypes contributing to exceptional survival. Our work has focused on the contribution of preserved and exceptional cognition to healthy aging and longevity.

a. Schupf. N, Barral S, Perls T, Newman A, Christensen K, Thyagarajan B, Province M, Rossi WK. Mayeux R (2012) Apolipoprotein E and Familial Longevity Neurobiology of Aging PMCID: PMC3545094

b. Cosentino S, Schupf N, Christensen K, Andersen SL, Newman A, Mayeux R, (2013) Reduced prevalence of cognitive impairment in families with exceptional longevity. JAMA Neurology.Jul;70(7):867-74. PMCID: PMC4151346

c. Barral S, Singh J, Fagan E, Cosentino S, Andersen-Toomey SL, Wojczynski MK, Feitosa M, Kammerer CM, Schupf N (2017) Age-related biomarkers in LLFS families with exceptional cognitive abilities. J. Gerontol A Bio Sci Med Sci 72 (10) 1411-1416 PMID:28329324

For a complete bibliography of N. Schupf see

http://www.ncbi.nlm.nih.gov/sites/myncbi/nicole.schupf.1/bibliography/44391571/public/?sort=date&direction=ascending

D. Ongoing Research Support

U01AG051412 (Schupf, Lott & Silverman) 09/30/2015 – 04/30/2020 2.88 calendar
NIH/NIA $3,369,595
Biomarkers of Alzheimer's Disease in Adults with Down Syndrome This study will examine blood based proteomic and lipidomic, imaging and genetic biomarkers of risk for Alzheimer's disease in adults with Down syndrome. Participating sites include Columbia University; University of California, Irvine; the Kennedy Krieger Institute and Johns Hopkins University Schools of Medicine and Public Health, Massachusetts General Hospital, the New York State Institute for Basic Research in Developmental Disabilities, and the University of North Texas Health Science Center.

3U01AG051412-03S1 (Schupf, Lott & Silverman) 05/01/2017 – 04/30/2020 0.48 calendar
NIH Administrative Supplement $1,683,555

Biomarkers of Alzheimer's Disease in Adults with Down Syndrome The objectives of this administrative supplement are to increase the number of amyloid- Positron Emission Tomography (PET) scans and to initiate tau-PET scans as part of our parent grant focusing on biomarkers associated with the progression of Alzheimer's disease (AD) in adults with Down syndrome (DS).

3U01AG051412-04S1 (Schupf, Lott & Silverman) 09/15/2018 – 04/30/2020 0.24 calendar
NIH/NIA Administrative Supplement $205,891
Biomarkers of Alzheimer's Disease in Adults with Down Syndrome This study focuses on a multidisciplinary determination of key risk as well as protective biomarkers that are likely to affect AD progression, including blood-based, CSF-based and imaging-based biomarkers, and polymorphisms in AD-related genes. This administrative supplement is to expand the parent grant to conduct untargeted proteomic analyses. Role: MPI

3U01AG051412-04S2 (Schupf, Lott & Silverman) 09/30/2018 – 04/30/2020 0.48 calendar
NIH/NIA Administrative Supplement $632,382
Biomarkers of Alzheimer's Disease in Adults with Down Syndrome This study focuses on a multidisciplinary determination of key risk as well as protective biomarkers that are likely to affect AD progression, including blood-based, CSF-based and imaging-based biomarkers, and polymorphisms in AD-related genes. This administrative supplement is to expand the parent grant to conduct untargeted metabolomic analyses.

3U01AG051412-05S1 (MPIs: Schupf*/Silverman/Lott) 09/30/2019 – 04/30/2020 0.01 calendar
NIH/NIA $355,477
Outcome Measures for use with adults with DS and Severe or Profound ID Biomarkers of Alzheimer disease in adults with Down syndrome (Parent study) This administrative supplement study examines neuropsychological profile in adults with DS and severe or profound ID. Role: MPI

R01AG049810 (Bondi) 03/15/2016 – 02/28/2021 0.36 calendar
NIH $58,299 (Subaward-UCSD)
Re-visiting Methods for MCI Diagnosis to Improve Biomarker and Trial Findings Subcontract site is to provide collaborative support for the aims and goals of the UCSD-based research project.

1RF1AG054070-01 (Manly/Brickman) 09/01/2016 – 06/30/2021 2.40 calendar
NIH/NIA $5,771,857
Offspring Study of Mechanisms for Racial Disparities in Alzheimer's Disease The overall aim of this study is to identify biological and sociocultural mechanisms of racial/ethnic disparities in cognitive function among middle-aged people with and without a parent with Alzheimer's Disease.

RF1AG054023 (Mayeux) 08/01/2016 – 06/30/2021 0.60 calendar
NIH $5,500,508
Genetic Epidemiology of Cerebrovascular Factors in Alzheimer's Disease The overall goal of this project is to test hypotheses concerning how genetic variants, cardiovascular risk factors, and cerebrovascular disease predispose to Late Onset Alzheimer's disease and whether these relationships differ by ethnic group.

5P50AG008702-30 (Andrews) 06/01/2019 – 05/31/2020 0.36 calendar
Alzheirmer's Disease Research Center $132,040
Diagnostics and assessment of patients with Alzheimer's Disease

1R56AG061837-01 (Lee & Krinsky-McHale) 09/30/2018 – 08/31/2020 0.01 calendar
NIH/NIA NCE Identification of protective factors for cognitive resilience in adults with Down Syndrome: A multi-omic study The overall aim of this study is to investigate multi-omic profiles for successful cognitive aging in adults with Down syndrome (DS).
U19AG063893 (Province) 08/15/2019 – 03/31/2024 3.0 calendar
NIH $14,578,813
The Long Life Family Study We will continue to follow the unique Long Life Family Study of families exhibiting exceptional survival and healthy aging to discover the secrets of their protection. We will generate "Big Data" from their blood and DNA to discover the protective biological mechanisms, which could lead to new therapies and prevention approaches.