Paul J. Hagerman, M.D., Ph.D.

Hagerman, Paul J., M.D., Ph.D., Professor, Department of Biochemistry and Molecular Medicine, School of Medicine; Director, NeuroTherapeutics Research Institute (NTRI)

Education
B.A., Chemistry, University of Oregon, 1971
M.D., Ph.D., Medicine and Biochemistry, Stanford University, 1977

Biography
Paul J. Hagerman, M.D., Ph.D. is a professor in the Department of Biochemistry and Molecular Medicine and a MIND Institute investigator at the University of California, Davis, School of Medicine. He obtained both his M.D. and Ph.D. degrees from Stanford University School of Medicine. Following a three-year Leukemia Society Fellowship at UC San Diego, Dr. Hagerman joined the faculty of Biochemistry and Molecular Biology at the University of Colorado School of Medicine, where he remained for twenty years prior to joining the UC Davis faculty in 2001. Dr. Hagerman is a molecular geneticist with a principal interest in understanding the basis for neurodevelopmental and neurodegenerative diseases. In particular, the Hagerman lab has made a number of important observations related to the mechanism of gene expression of the fragile X (FMR1) gene, mutations of which are responsible for fragile X syndrome, the leading heritable form of mental impairment and leading known cause of autism. In 2001, Dr. Hagerman and his wife, Dr. Randi Hagerman (Medical Director of the MIND Institute), reported their discovery of a neurological disorder involving tremor and gait ataxia, which they later named fragile X-associated tremor/ataxia syndrome (FXTAS). They also discovered that FXTAS represents a new class of inclusion disorder, with numerous intranuclear inclusions found throughout the brains of affected individuals. FXTAS is now known to be one of the most common single-gene forms of neurodegeneration. Since it has features of both Parkinsonism and dementia, FXTAS represents a model system for understanding the pathogenesis of those more common, sporadic disorders. Remarkably, FXTAS is caused by smaller CGG-repeat expansions of the same gene (FMR1) that gives rise to fragile X syndrome, albeit by an entirely separate mechanism: excess “toxic” FMR1 mRNA for FXTAS; gene silencing and absence of FMR1 protein in fragile X syndrome. Dr. Hagerman is currently on the scientific advisory board of the National Fragile X Foundation and is Director of the NeuroTherapeutics Research Institute (NTRI), which is funded through the “Roadmap Initiative” from the National Institutes of Health. Dr. Hagerman’s other NIH support has been through the National Institute on Aging and the National Institute of Child Health and Development. He is most grateful for the support he has received from families for his work on fragile X disorders.

Publications (selected)

The MIND Institute


**Presentations**

*Everything you wanted to know about FXTAS but were afraid to ask*, Family-friendly panel presenter, National Fragile X Foundation, 11th International Fragile X Conference, St. Louis MO, July 2008.


*Molecular Aspects of FXTAS*, Invited Speaker, Agrupación SXF de Chile, Santiago Chile, January 2009.

*Molecular basis of FXTAS*, Session speaker, Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS): A Novel Dementia Syndrome, American Association for Geriatric Psychiatry (AAGP), Honolulu, HI, March 2009.

*An Aging Face of the Fragile X Gene*, Invited Speaker, Brain Awareness Week Symposium, Neuroscience Research: the road to clinical breakthroughs, Saint Louis University, St. Louis, MO, March 2009.


*FXTAS - Recent developments*, Invited Speaker, 14th XLMR Workshop, Praia do Forte, Bahia, Brazil, September 2009.

*Aspectos moleculares de las patologías asociadas a la premutación (Falla ovárica prematura y Síndrome de Ataxia y temblor asociado a X frágil – POF y FXTAS)*, Invited Speaker, Jornadas Argentinas Sobre Síndrome X Frágil, Buenos Aires, Argentina, September 2009.

*Avances moleculares*, Invited Speaker, Jornadas Argentinas Sobre Síndrome X Frágil,

**FXTAS as a model for understanding neurogenetic disorders.** Invited Speaker with Hessl, D. Translational Grand Rounds, Department of Psychiatry and Behavioral Sciences, UC Davis. April 2010.


**NeuroTherapeutics Research Institute (NTRI) Consortium: A model for interdisciplinary collaboration.** Invited Speaker, School of Medicine Council of Chairs’ Meeting, UC Davis, July 2010.

RNA toxicity in premutation carriers leading to FXTAS. Invited Speaker, Symposium on Mental Retardation and Autism. Diponegoro University, Semarang, Indonesia. August 2010.


**Molecular basis of FXTAS and other Fragile X associated disorders,** Invited Speaker, 15th International Congress of Parkinson’s Disease and Movement Disorders, Parallel Session: Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS), Toronto, Ontario Canada. July 2011.


**Sequencing the Unsequenceable: Expanded CGG Repeats in the Human FMR1 Gene,** Invited Speaker, AGBT Pacific Biosciences® Workshop, 2012 Advances in Genome Biology & Technology, Marco Island, FL. February 2012.


Research Funding

**Principal Investigator**: NeuroTherapeutics Research Consortium (1 of 6), NIDCR, 09/30/07 - 06/30/12, $530,000 annual direct. The principal objective of the Research Consortium is implementation of a highly integrated, interdisciplinary approach to develop targeted molecular therapeutics for neurogenetic disorders, using the late-onset neurodegenerative disorder fragile X-associated tremor/ataxia syndrome (FXTAS) as its principal research paradigm. The fundamental challenge addressed by the Consortium is how to develop and integrate the various components required to achieve (and measure) a targeted therapeutic response to a CNS disorder.

**Principal Investigator**: Development of Targeted Therapeutic Agents for the Treatment of FXTAS (2 of 6), NIA, 9/30/07 - 06/30/12, $564,000 annual direct. The principal objective of this project will be the identification and assessment of various candidate therapeutic agents that might attenuate the effects of the pathogenic RNA in FXTAS. Research will also involve further study of neural cell models of FXTAS.

**Investigator**: Social-Affective Bases of Word Learning in Fragile X Syndrome and Autism, NIA, 03/08/08 - 2/28/13, $464,000 annual direct. The overall focus of this UC Davis and University of Wisconsin Waisman Institute collaboration is the study of the behavioral and cognitive phenotype of fragile X syndrome (FXS) with autism, and to investigate the neurological and molecular basis of this phenotype.

**Principal Investigator**: Expression of the Fragile X Gene, NICHD, 01/01/12-12/31/16, $220,000 annual direct. This is the second competing continuation of the original grant. This project is designed to identify the origins of altered expression of the gene (low protein, fragile X syndrome; elevated RNA, FXTAS) to facilitate the development of targeted therapeutic approaches to these disorders.

Community Service (most recent and ongoing)

Faculty Member, Biochemistry, Molecular, Cellular & Developmental Biology Graduate Group
Faculty Member, Neurosciences Graduate Group
Faculty Member, Genetics Graduate Group
Advisor, Physician-Scientist Training Program (2002-2010)
Steering Committee, Physician-Scientist Training Program (2002-2010)
Mentor, NTRI Interdisciplinary Postdoctoral Training Program in Neurogenetic Disorders
Academic Affairs Ad Hoc Review Committee
Health System Research Award Committee (UCDHSRA)
Search and Selection Advisory Committee for Director of the Center for Neuroscience (2008-2010)
MIND Institute Director Search Committee (2010)
Biochemistry & Molecular Medicine – Recruitment and Executive Committees (2010-2011)
College of Biological Sciences Vision Committee (2010-2011)
Committee on Human Genetics and Genomics
Scientific Advisory Board, National Fragile X Foundation
Permanent Reviewers Reserve, National Institutes of Health
Chair of the FXTAS Work Group, National Institutes of Health Fragile X Research Coordinating Group (FXRCG) (2008)
National Institutes of Health Special Emphasis Panel (2011)
Editorial Advisory Board, Biochemistry (1998-2010)
Awards and Honors
School of Medicine Research Award, UC Davis School of Medicine (2011)
William Rosen Award for Fragile X Research
Stallone Fund for Autism Research