BIOGRAPHICAL SKETCH

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NAME: Edwin M. Stone, M.D., Ph.D.

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

POSITION TITLE: Professor

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
Rice University	BA	1978	Biology and English
Baylor College of Medicine	PhD	1983	Cell Biology
Baylor College of Medicine	MD	1985	Medicine

A. Personal Statement

My research seeks to understand how small variations in the genes of human beings can result in large variations in their vision. I am especially interested in finding and characterizing genes that are involved in three classes of human eye disease: macular degeneration, glaucoma, and heritable photoreceptor degeneration. I am also very interested in strategies for bringing new genetic discoveries to the clinic as rapidly as possible and in so doing I have been very active in removing the technical, legal and financial barriers between genetic discoveries and the patients who could benefit from them by creating a nonprofit genetic testing laboratory that provides low cost clinical genetic tests for more than 20 different inherited eye diseases on an international scale.

I am a fellowship-trained vitreoretinal surgeon with a special interest in hereditary diseases of the retina. I am also the director of the Institute for Vision Research, which consists of 29 faculty and 60 staff. I and my collaborators at the University of Iowa, have mapped and/or cloned dozens of human disease genes including: three glaucoma genes (MYOC, FOXC1, and familial cavitary optic disk anomaly), five genes for macular disease (Best disease, pattern dystrophy, Stargardt-like dominant macular dystrophy, malattia Leventinese, and fibulin-5-associated age-related macular degeneration), dominant stromal corneal dystrophy, Wagner disease, erosive vitreoretinopathy, the enhanced S cone syndrome, and achromatopsia.

a) Stone, EM. Leber congenital amaurosis - a model for efficient genetic testing of heterogeneous disorders: LXIV Edward Jackson Memorial Lecture. Am J Ophthalmol 144, 791-811, doi:10.1016/j.ajo.2007.08.022 (2007).
b) Sheffield, VC, Stone, EM. Genomics and the eye. N Engl J Med 364, 1932-1942, doi:10.1056/NEJMra1012354 (2011).
c) Tucker BA, Mullins RF, Stone EM. Stem cells for investigation and treatment of inherited retinal disease. Hum Mol Genet. 2014 23(R1):R9-R16. doi: 10.1093/hmg/ddu124. PMID: 24647603.
d) Tucker BA, Mullins RF, Streb LM, Anfinson K, Eyestone ME, Kaalberg E, Riker MJ, Drack AV, Braun TA, Stone EM. Patient-specific iPSC-derived photoreceptor precursor cells as a means to investigate retinitis pigmentosa. Elife. 2013 Aug 27;2:e00824. doi: 10.7554/eLife.00824.

B. Positions and Honors

Positions and Employment

Intern (Transitional) St. Joseph Hospital, Houston 7/85-6/86
Resident (Ophthalmology) The University of Iowa 7/86-12/89
Fellow (Ophthalmology Research/Vitreoretinal Surgery) The University of Iowa 1/90-2/92
Assistant Professor of Ophthalmology The University of Iowa 7/90-7/94
Associate Professor of Ophthalmology The University of Iowa 7/94-7/97
Professor of Ophthalmology The University of Iowa 7/97-present
Investigator The Howard Hughes Medical Inst. 8/02-8/15

Honors and Awards

Sigma Xi Award for Ph.D. Thesis Excellence, 1983
The DeBakey Scholar, 1984
Alpha Omega Alpha, 1985
Outstanding Intern, Department of Medicine, St. Joseph Hospital, 1986
P. J. Leinfelder Award for Ophthalmology Resident Research, 1989, 1990
Research to Prevent Blindness Dolly Green Scholar, 1993
Alcon Research Institute Award, 1995
The Chibret Award (Switzerland), 1995
Prix Porphyrogenis and Prix Tissiéres (Switzerland), 1996
Lew Wasserman Merit Award (Research to Prevent Blindness), 1997
Rosenthal Award (The Macula Society), 1998
Cogan Award (Association for Research in Vision and Ophthalmology, ARVO), 1998
Louis Rudin Glaucoma Prize (New York Academy of Sciences), 1999
The Gregg Lecture (The Royal Australian College of Ophthalmology), 1999
The Inaugural Davson Lecture (The Institute for Ophthalmology, London), 2000
The Doyne Lecture (The Oxford Congress), 2000
The Alex Krill Memorial Lecture (The Chicago Ophthalmological Society) 2000
Investigator, Howard Hughes Medical Institute, 2002
Humanitarian Award (Heart Sight; Miami, Florida) 2003
Trustee Award (Foundation Fighting Blindness) 2003
Distinguished Alumnus (Baylor College of Medicine) 2004
Seamans-Hauser Endowed of Molecular Ophthalmology 2006
Jackson Memorial Lecture (American Academy of Ophthalmology) 2007
John Kearney Rodgers Physician of the Year Award (New York Eye & Ear Infirmary) 2008
Llura Liggett Gund Award (Foundation Fighting Blindness) 2012
Franceschetti Lecture and Medal (International Society of Genetic Eye Disease) 2013
Secretariat Award (American Academy of Ophthalmology) 2013
Association of American Physicians 2016
Carver College of Medicine Faculty Service Award 2016
Board of Reagents Award for Faculty Excellence 2017
Marshall Parks Lecture (American Academy of Ophthalmology) 2017
Future Vision Award (Future Vision Foundation) 2020

C. Contributions to Science

1. By studying families that I have cared for in my clinic, my laboratory has mapped and identified more than a dozen disease genes, including genes responsible for macular degeneration, glaucoma, corneal dystrophies, retinal development, retinitis pigmentosa, Leber congenital amaurosis (LCA), and uveitis. I have collected over 60,000 DNA samples from patients with various inherited eye diseases and have developed high-throughput methods for screening these patients for disease-causing mutations in candidate genes.

a) Stone EM, Fingert JH, Alward WLM, Polansky JR, Nguyen TD, Sunden SLF, Nishimura D, Nysteun A, Nichols BE, Mackey DA, Ritch R, Kalenak JW, Craven ER, Sheffield VC. Identification of a gene that causes primary open angle glaucoma. Science, 1997, 275:668-670.

b) Stone EM, Lotery AJ, Munier FL, Héon E, Piguet B, Guymer RH, Vandenburgh K, Cousin P, Nishimura D, Swiderski RE, Silvestri G, Mackey DA, Hageman GS, Bird AC, Sheffield VC, Schorderet DF A single EFEMP1 mutation associated with both Malattia Leventinese and Doyne honeycomb retinal dystrophy. Nat Genet 22, 199-202, doi:10.1038/9722 (1999).
c) Fingert JH, Oh K, Chung M, Scheetz TE, Andorf JL, Johnson RM, Sheffield VC, Stone EM. Association of a novel mutation in the retinol dehydrogenase 12 (RDH12) gene with autosomal dominant retinitis pigmentosa. Archives of Ophthalmology. 2008;126(9):1301-1307.
d) Fingert JH, Robin AL, Stone JL, Roos BR, Davis LK, Scheetz TE, Bennett SR, Wassink TH, Kwon YH, Alward WL, Mullins RF, Sheffield VC, Stone EM. Copy number variations on chromosome 12q14 in patients with normal tension glaucoma. Hum Mol Genet. 2011 Jun 15;20(12):2482-94. doi: 10.1093/hmg/ddr123. Epub 2011 Mar 29.

2. My laboratory has been at the forefront of understanding how genetic variations contribute to quantifiable phenotypes in Mendelian retinal diseases as well as complex diseases. We have performed genotype-phenotype correlations for LCA, retinitis pigmentosa, cone rod dystrophy, Usher syndrome, Stargardt disease, age-related macular degeneration, Best disease, Bardet-Biedl syndrome, glaucoma, and cataract. This information has been used to guide the medical care of patients with inherited eye diseases.

a) Nichols BE, Sheffield VC, Vandenburgh K, Drack AV, Kimura AE, Stone EM. Butterfly-shaped pigment dystrophy of the fovea caused by a point mutation in codon 167 of the RDS gene. Nat Genet 3, 202-207, doi:10.1038/ng0393-202 (1993). PMID: 8485574.
b) Alward WL, Fingert JH, Coote MA, Johnson AT, Lerner SF, Junqua D, Durcan FJ, McCartney PJ, Mackey DA, Sheffield VC, Stone EM. Clinical features associated with mutations in the chromosome 1 open-angle glaucoma gene (GLC1A). N Engl J Med 338, 1022-1027, doi:10.1056/NEJM199804093381503 (1998).
c) Schindler EI, Nylen EL, Ko AC, Affatigato LM, Heggen AC, Wang K, Sheffield VC, Stone EM. Deducing the pathogenic contribution of recessive ABCA4 alleles in an outbred population. Hum Mol Genet 19, 3693-3701, doi:10.1093/hmg/ddq284 (2010).
d) Stone EM, Andorf JL, Whitmore SS, DeLuca AP, Giacalone JC, Streb LM, Braun TA, Mullins RF, Scheetz TE, Sheffield VC, Tucker BA. Clinically Focused Molecular Investigation of 1000 Consecutive Families with Inherited Retinal Disease. Ophthalmology. 2017 Sep;124(9):1314-1331. PMID: 28559085.

3. My laboratory has elucidated the mechanisms of a number of inherited disorders of vision, including retinitis pigmentosa, Stargardt disease, achromatopsia, LCA, Usher syndrome, ADNIV, age-related macular degeneration, glaucoma, and Bardet Biedl syndrome.

a) Tucker BA, Scheetz TE, Mullins RF, DeLuca AP, Hoffmann JM, Johnston RM, Jacobson SG, Sheffield VC, Stone EM. Exome sequencing and analysis of induced pluripotent stem cells identify the cilia-related gene male germ cell-associated kinase (MAK) as a cause of retinitis pigmentosa. Proc Natl Acad Sci U S A 108, E569-576, doi:10.1073/pnas.1108918108 (2011).
b) Mullins RF, Kuehn MH, Radu RA, Enriquez GS, East JS, Schindler EI, Travis GH, Stone EM Autosomal recessive retinitis pigmentosa due to ABCA4 mutations: clinical, pathologic, and molecular characterization. Invest Ophthalmol Vis Sci 53, 1883-1894, doi:10.1167/iovs.12-9477 (2012).
c) Braun TA, Mullins, RF, Wagner AH, Andorf JL, Johnston RM, Bakall BB, Deluca, AP, Fishman GA, Lam BL, Weleber RG, Cideciyan AV, Jacobson SG, Sheffield VC, Tucker BA, Stone EM. Nonexomic and synonymous variants in ABCA4 are an important cause of Stargardt disease. Human Molecular Genetics. (2013) 22(25)5136-5145.
d) Sharma TP, Wiley LA, Whitmore SS, Anfinson KR, Cranston CM, Oppedal DJ, Daggett HT, Mullins RF, Tucker BA, Stone EM. Patient-specific induced pluripotent stem cells to evaluate the pathophysiology of TRNT1-associated Retinitis pigmentosa. Stem Cell Res. (2017) May;21:58-70.

4. A major goal of my research is the development and evaluation of novel therapies, including gene augmentation and stem cell replacement therapies, as well as novel outcome measures for inherited retinal diseases including retinitis pigmentosa, Stargardt disease, LCA, X-linked retinoschisis, and glaucoma.

a) Burnight ER, Wiley LA, Drack AV, Braun TA, Anfinson KR, Kaalberg EE, Halder JA, Affatigato LM, Mullins RF, Stone EM, Tucker BA. CEP290 gene transfer rescues Leber congenital amaurosis cellular phenotype. Gene Ther. (2014) Jul;21(7):662-72. doi: 10.1038/gt.2014.39. PMID: 24807808.
b) Walia S, Fishman GA, Molday RS, Dyka FM, Kumar NM, Ehlinger MA, Stone EM. Relation of response to treatment with dorzolamide in X-linked retinoschisis to the mechanism of functional loss in retinoschisin. Am J Ophthalmol. (2009) 147(1):111-115.e1. doi: 10.1016/j.ajo.2008.07.041. PMID: 18834580 [PubMed - indexed for MEDLINE] PMCID: PMC2668603.
c) Giacalone JC, Andorf JL, Zhang Q, Burnight ER, Ochoa D, Reutzel AJ, Collins MM, Sheffield VC, Mullins RF, Han IC, Stone EM, Tucker BA. Development of a molecularly stable gene therapy vector for the treatment of RPGR-associated x-linked retinitis pigmentosa. *Human Gene Therapy*. 2019 PMID:31106594.
d) Stone EM. Progress toward effective treatments for human photoreceptor degenerations. Curr Opin Genet Dev. 2009 Jun;19(3):283-9. doi: 10.1016/j.gde.2009.03.006. PMID: 19414246.