

BIOGRAPHICAL SKETCH

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NAME Beggs, Alan H.		POSITION TITLE Associate Professor of Pediatrics	
eRA COMMONS USER NAME abeggs			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Cornell University, Ithaca, NY	A.B.	1982	Biology
Johns Hopkins University, Baltimore, MD	Ph.D.	1987	Human Genetics
Johns Hopkins University, Baltimore, MD	Fellowship	1987-8	Molecular Genetics
Children's Hospital, Harvard Med. Sch. Boston	Fellowship	1988-92	Medical Genetics

A. Positions and Honors

- 1988-91 Associate, Howard Hughes Medical Institute
 1992- Research Associate in Medicine (Genetics), Children's Hospital, Boston, MA
 1992-94 Charles H. Hood Foundation Fellow
 1992-93 Instructor in Pediatrics, Harvard Medical School, Boston, MA
 1993-03 Board Certification, in Clinical Molecular Genetics, American Board of Medical Genetics
 1993-99 Assistant Professor of Pediatrics, Harvard Medical School, Boston, MA
 2000- Associate Professor of Pediatrics, Harvard Medical School, Boston, MA
 2000-01 Consultant to the NICHD: 5 Year Planning Committee for SIDS Research
 2003 NIH Special Emphasis Panel member, "Skeletal Muscle Biology 50"
 2005-6 NIH Skeletal Muscle Biology and Exercise Physiology Study Section, temporary member
 2006-10 NIH Skeletal Muscle Biology and Exercise Physiology Study Section, standing member

B. Publications (Selected from 118 total published or in press)

- Migeon BR, Axelman J, Beggs AH. Effect of aging on reactivation of the human X-linked HPRT locus. *Nature* 1988; 335:93-96.
- Beggs AH, Hoffman EP, Synder JR, Arahata K, Specht L, Shapiro F, Angelini C, Sugita H, Kunkel LM. Exploring the molecular basis for variability among patients with Becker muscular dystrophy: Dystrophin gene and protein studies. *Am J Hum Genet* 1991; 49:54-67.
- Beggs AH, Neumann PE, Arahata K, Arikawa E, Nonaka I, Anderson MD, Kunkel LM. Possible influences on the expression of X chromosome-linked dystrophin abnormalities by heterozygosity for autosomal recessive Fukuyama congenital muscular dystrophy. *Proc Natl Acad Sci* 1992; 89:623-627.
- Beggs AH, Byers TJ, Knoll JHM, Boyce F, Bruns G, Kunkel L. Cloning and characterization of two human skeletal muscle alpha-actinin genes located on chromosomes one and eleven. *J Bio Chem* 92;267:9281-8
- Engle EC, Kunkel LM, Specht LA, Beggs AH. Mapping a gene for congenital fibrosis of the extraocular muscles to the centromeric region of chromosome 12. *Nature Genetics* 1994; 7:69-73.
- Wyszynski M, Lin J, Rao A, Nigh E, Beggs AH, Craig AM, Sheng M. Competitive binding of α -actinin and calmodulin to the NMDA receptor. *Nature* 1997; 385:439-442.
- Engle EC, Gumerov BC, McKeown CA, Schatz M, Johns DR, Porter JD, Beggs AH. Oculomotor nerve and muscle abnormalities in congenital fibrosis of the extraocular muscles. *Ann Neurol* 1997; 41:314-325.
- Duggal P, Vesely MR, Wattanasirichaigoon D, Villafane J, Kaushik V, Beggs AH. Mutation of the gene for IsK associated with both Jervell and Lange-Nielsen and Romano Ward forms of long QT syndrome. *Circulation* 1998; 97:142-146.
- Pelin K, Hilpelä P, Donner K, Sewry C, Akkari PA, Wilton SD, Wattanasirichaigoon D, Centner T, Hanefeld H, Odent S, Fardeau M, Urtizberea JA, Muntoni F, Dubowitz V, Beggs AH, Laing NG, Labeit S, de la Chapelle A, Wallgren-Pettersson C. Mutations in the nebulin gene associated with autosomal recessive nemaline myopathy. *Proc Natl Acad Sci, USA* 1999; 96:2305-2310.

10. North KN, Yang N, Wattanasirichaigoon D, Mills M, Easteal S, Beggs AH. A common nonsense mutation results in α -actinin-3 deficiency in the general population. *Nature Genetics* 1999; 21:353-354.
11. Nowak KJ, Wattanasirichaigoon D, Goebel HH, Wilce M, Pelin K, Donner K, Jacob RL, Hubner C, Oexle K, Anderson JR, Verity CM, North KN, Iannaccone ST, Muller CR, Nurnberg P, Muntoni F, Sewry C, Hughes I, Stuphen R, Lacson AG, Swoboda KJ, Vigneron J, Wallgren-Pettersson C, Beggs AH, Laing NG. Mutations in the skeletal muscle α -actin gene in patients with actin myopathy and nemaline myopathy. *Nature Genetics* 1999; 23:208-212.
12. Kaplan JM, Kim SH, North KN, Rennke H, Correia LA, Mathis B, Rodriguez-Perez J-C, Tong H-Q, Allen PG, Beggs AH, Pollak MR. Alpha-actinin-4 mutations in familial focal segmental glomerulosclerosis. *Nature Genetics*, 2000; 24:251-256.
13. Takada F, Vander Woude DL, Tong H-Q, Thompson TG, Watkins S, Kunkel L, Beggs AH. Myozenin: An α -actinin and γ -filamin-binding protein of skeletal muscle Z lines. *Proc Natl Acad Sci* 2001; 98:1595-1600.
14. Mills M, Yang N, Weinberger R, Vander Woude DL, Beggs AH, Easteal S, North K. Differential expression of the actin binding proteins, α -actinin-2 and -3 in different species: implications for the evolution of functional redundancy. *Hum Molec Genet*, 2001, 10:1335-1346.
15. Ryan MM, Schnell C, Strickland CD, Shield LK, Morgan G, Iannaccone ST, Laing NG, Beggs AH, North KN. Nemaline myopathy: a clinical study of 143 cases. *Annal Neurol*, 2001, 50:312-320.
16. Splawski I, Timothy KW, Tateyama M, Clancy CE, Malhotra A, Beggs AH, Cappuccio FP, Sagnella GA, Kass RS, Keating MT. Variant of SCN5A sodium channel implicated in risk of cardiac arrhythmia. *Science*, 2002; 297:1333-1336.
17. Wattanasirichaigoon D, Swoboda KJ, Takada F, Tong H-Q, Lip V, Iannaccone ST, Wallgren-Pettersson C, Laing NG, Beggs AH. Mutations of the slow muscle α -tropomyosin gene, *TPM3*, are a rare cause of nemaline myopathy. *Neurology*, 2002; 59:613-617.
18. Haslett JN, Sanoudou D, Kho AT, Bennett RR, Greenberg SA, Kohane IS, Beggs AH, Kunkel LM. Gene expression comparison of biopsies from Duchenne muscular dystrophy (DMD) and normal skeletal muscle. *Proc Natl Acad Sci USA* 2002; 99:15000-15005.
19. Ryan MM, Ilkovski B, Strickland SD, Schnell C, Sanoudou D, Midgett C, Houston R, Muirhead D, Dennett X, Shield LK, De Girolami U, Iannaccone ST, Laing NG, North KN, Beggs AH. Clinical course correlates poorly with muscle pathology in nemaline myopathy. *Neurology* 2002; 60:665-673.
20. Sanoudou D, Haslett JN, Kho AT, Guo S, Gazda HT, Greenberg SA, Lidov HGW, Kohane IS, Kunkel LM, Beggs AH. Expression profiling reveals altered satellite cell numbers and glycolytic enzyme transcription in nemaline myopathy muscle. *Proc Natl Acad Sci, USA* 2003; 100:4666-4671.
21. Yang N, MacArthur D, Gulbin JP, Hahn AG, Beggs AH, Easteal S, North KN. *ACTN3* genotype is associated with human elite athletic performance. *Am J Hum Genet* 2003; 73:627-631.
22. Tomczak KT, Marinescu VD, Ramoni MF, Sanoudou D, Montanaro F, Han M, Kunkel LM, Kohane IS, Beggs AH. Expression profiling and identification of novel genes involved in myogenic differentiation. *FASEB J* 2004, 18; 403-5. Full article at: FASEB J Express Article 10.1096/fj.03-0568fj
23. Sanoudou D, Kang PB, Haslett JN, Han M, Kunkel LM, Beggs AH. Transcriptional profile of postmortem skeletal muscle. *Physiological Genomics*, 2004; 16:222-8
24. Sanoudou D, Frieden LA, Haslett JN, Kho AT, Greenberg SA, Kohane IS, Kunkel LM, Beggs AH. Molecular classification of nemaline myopathies: "non-typing" specimens exhibit unique patterns of gene expression. *Neurobiol Dis* 2004; 15:590-600.
25. Agrawal PB, Strickland CD, Midgett CM, Morales A, Newburger D, Poulos MA, Tomczak KK, Ryan M, Iannaccone ST, Crawford TO, Laing NG, Beggs AH. Heterogeneity of nemaline myopathy cases with skeletal muscle actin gene (*ACTA1*) mutations. *Annal Neurol* 2004, 56:86-96.
26. Liadaki K, Kho AT, Sanoudou D, Schienda J, Flint A, Beggs AH, Kohane IS, Kunkel LM. Side population cells isolated from different tissues share transcriptome signatures and express tissue-specific markers. *Exper Cell Res* 2005; 303:360-74.
27. Splawski I, Tomothy KW, Decher N, Kumar P, Sachse FB, Beggs AH, Sanguinetti MC, Keating MT. Severe arrhythmia disorder caused by cardiac L-type calcium channel mutations. *Proc Natl Acad Sci, USA* 2005; 102:8089-8096.
28. Kang P, Kho A, Sanoudou D, Haslett J, Dow C, Han M, Blasko J, Lidov H, Beggs A, Kunkel L. Variations in gene expression among different types of human skeletal muscle. *Muscle Nerve* 2005; 32:483-91.
29. Pierson CR, Tomczak K, Agrawal P, Moghadaszadeh B, Beggs AH. X-linked myotubular and centronuclear myopathies. *J Neuropathol Exp Neurol* 2005; 64:555-564.

30. Bitoun M, Maugenre S, Jeannet PY, Lacene E, Ferrer X, Laforet P, Martin JJ, Laporte J, Lochmuller H, Beggs AH, Fardeau M, Eymard B, Romero NB, Guicheney P. Mutations in dynamin 2 cause dominant centronuclear myopathy. *Nature Genetics* 2005; 37:1207-9.
31. Haslett JN, Kang PB, Han M, Kho AT, Sanoudou D, Volinski JM, Beggs AH, Kohane IS, Kunkel LM. The influence of muscle type and dystrophin deficiency on murine expression profiles. *Mammalian Genome* 2005; 16:739-748.
32. Barnes CM, Huang S, Kaipainen A, Sanoudou D, Chen EJ, Eichler GS, Guo Y, Yu Y, Ingber DE, Mulliken JB, Beggs AH, Folkman J, Fishman SJ. Evidence by molecular profiling for a placental origin of infantile hemangioma. *Proc Natl Acad Sci, USA* 2005; 102:19097-19102.
33. Gazda HT, Kho AT, Sanoudou D, Zaucha JM, Kohane IS, Sieff CA, Beggs AH. Defective Ribosomal Protein Gene Expression Alters Transcription, Translation, Apoptosis And Oncogenic Pathways In Diamond-Blackfan Anemia. *Stem Cells* 2006; 24:2034-2044.
34. Cerletti M, Molloy MJ, Tomczak KK, Yoon S, Ramoni MF, Kho AT, Beggs AH, Gussoni E. Melanoma Cell Adhesion Molecule is a novel marker for human fetal myogenic cells and affects myoblast fusion. *J Cell Sci* 2006; 119:3117-3127.
35. Sanoudou D, Corbett MA, Han M, Ghodusi M, Nguyen MT, Vlahovich N, Hardeman, Beggs AH. Skeletal muscle repair in a mouse model of nemaline myopathy. *Human Mol Genet* 2006; 15:2603-2612.
36. Paterson DS, Trachtenberg FL, Thompson EG, Belliveau RA, Beggs AH, Darnall RA, Chadwick AE, Krous HF, Kinney HC. Multiple serotonergic brainstem abnormalities in the sudden infant death syndrome. *JAMA* 2006; 296:2124-2132.
37. Gazda HT, Grabowska A, Merida-Long LB, Latawiec E, Schneider HE, Lipton JM, Vlachos A, Atsidaftos E, Ball SE, Orfali KA, Niewiadomska E, Da Costa L, Tchernia G, Niemeyer C, Meerpohl JJ, Stahl J, Schratz G, Glader B, Backer K, Wong C, Nathan DG, Beggs AH, Sieff CA. Ribosomal protein S24 is mutated in Diamond-Blackfan anemia. *Am J Hum Genet* 2006; 79:1110-1118.
38. Agrawal PB, Greenleaf RS, Tomczak KK, Lehtokari V-L, Wallgren-Pettersson C, Wallefeld W, Laing NG, Darras BT, Maciver SK, Dormitzer PR, Beggs AH. Nemaline myopathy with minicores caused by mutation of the *CFL2* gene encoding the skeletal muscle actin-binding protein, cofilin-2. *Am J Hum Genet* 2007; 80:162-167.

C. Research Support

Ongoing Research Support

R01 AR44345-10 Beggs (PI) 12/15/96-11/30/11

NIH, NIAMS

“Alpha-actinins in normal and diseased muscle.”

The major goals of this project are to understand the structures, functions, and protein interactions of muscle-specific sarcomeric proteins and to apply this information to the study of human neuromuscular disorders, particularly nemaline myopathy.

Role: PI

1 P01 NS40828-02 Kunkel (PI) 9/25/01 – 8/31/07

“Gene expression and biochemical analysis of muscle development in myotubular myopathy.”

NIH, NINDS and NIAMS

The major goal of this project is to understand the molecular basis for myotubular myopathy (MTM) and its defect in muscle differentiation and to use this information to develop therapies for patients with this disorder.

Role: Project PI

1 P01 NS40828-02 Kunkel (PI) 9/25/01 – 8/31/07

“Gene expression and bioinformatics core.”

NIH, NINDS and NIAMS

Type: Research grant/Program Project Period: 9/25/01 – 8/31/06

The major Aim of this Core is to provide expression arrays of muscle mRNAs to examine differential mRNA expression in various developmental states of unaffected individuals and muscle disease states and differences between stem cell populations at different stages of differentiation.

Role: Microarray biologist

Research grant Beggs (PI) 7/1/05-6/30/08

Muscular Dystrophy Association of USA

“Molecular genetics of congenital myopathies”

This project focuses on ascertainment and collection of data and specimens from patients with congenital myopathies and on molecular genetic studies to understand the molecular basis for these disorders.

Role: PI

Research grant Beggs (PI) 12/1/01-ongoing

Joshua Frase Foundation

“Genetics and therapy for myotubular myopathy”

The goals of this project are to understand the pathogenesis of myotubular myopathy and develop cell-based myoblast therapy using the *Mtm1* knockout mouse model.

Role: PI

Completed Research Support

Research grant Beggs (PI) 7/1/02-6/30/05

Muscular Dystrophy Association of USA

“Molecular genetics of congenital myopathies”

The major goal of this project was to elucidate the molecular genetics of nemaline myopathy. Specific aims included study of the *TPM3* and nebulin genes as well as identification of new nemaline myopathy genes and correlation with clinical and histopathological phenotypes.

Role: PI

K02 AR02026 Beggs (PI) 06/23/97-08/31/01

NIH, NIAMS

“Sarcomeric proteins in normal and diseased muscle.”

The major goals of this project were to understand the structures, functions, and protein interactions of muscle-specific alpha-actinins and other sarcomeric proteins and to apply this information to the study of human neuromuscular disorders. Specific aims include identification and characterization of novel alpha-actinin binding proteins and study of their role(s) in human neuromuscular disease.

Role: PI

Research grant Beggs (PI) 12/1/98-11/30/01

Joshua Frase Foundation and the Muscular Dystrophy Association of USA

“Genetics and therapy of myotubular myopathy, Project 1.”

This subproject, of which Dr. Beggs is PI, was directed at understanding the genetics and pathophysiology of myotubular myopathy and using this information to develop improved therapies. Specific aims included the genetic analysis of patients with myotubular myopathy and characterization of global patterns of gene expression using microarray-based methods.

Role: PI

R01 NS043471-01A1 Beggs (subcontract PI) 12/15/02-11/30/03

NIH, NINDS

“Gene expression in inflammatory myopathies.”

Overall project goals were to characterize gene expression patterns in skeletal muscle from patients with inflammatory myopathies. This subcontract was to perform all the laboratory-related activities on this grant. The PI, Dr. Greenberg, conducted subsequent bioinformatic analysis.

Role: Subcontract PI