BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Chamberlain, Jeffrey S.	Professor of Neurology, Biochemistry and Medicine McCaw Endowed Chair in Muscular Dystrophy
eRA COMMONS USER NAME (credential, e.g., agency login) Chamberl	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Rice University, Houston, TX	BS	1978	Biochemistry
University of Washington, Seattle, WA	PhD	1985	Biochemistry
Baylor College of Medicine, Houston, TX	Post-doc	1990	Molecular Genetics

A. Personal Statement

I began working on DMD ~25 years ago, with a focus on DNA diagnostics, then on the murine dystrophin gene and the *mdx* mouse. Our group was the first to assemble full-length dystrophin cDNAs, first from mice and then humans, and we used those clones to make a series of transgenic *mdx* mice to explore structure-function relationships in the dystrophin protein and in the DGC, and how dystrophin affected muscle physiology and mechanics. Much of our recent work has focused on gene therapy using recombinant AAV vectors (rAAV), as these vectors show a remarkable ability to deliver genes to cardiac and skeletal muscle when administered *via* the vasculature. We were the first group to publish a method for whole body systemic gene transfer, which was based on the rAAV6 system (Nat Med, 2004). We have gone on to show that striated muscles of canines can also be transduced with similar efficiency, but route of administration is a key limitation. Our lab is now focused on optimizing AAV delivery to large animals and initiating human clinical trials for gene therapy of muscular dystrophy. Our first trial involves IM administration in the presence of immune suppression, and a second planned trial will focus on regional limb delivery using the outcomes of the proposed ECC testing.

B. Positions and Honors

Positions and Employment

1990-1994 Assistant Professor, Dept. of Human Genetics, U. Michigan Medical School, Ann Arbor, MI.
1994-1999 Associate Professor, Department of Human Genetics, U. Michigan Medical School, Ann Arbor, MI
1999-2000 Interim Director, Center for Gene Therapy, U. Michigan Medical School, Ann Arbor, MI
1999-2000 Professor, Dept. of Human Genetics, U. Michigan Medical School, Ann Arbor, MI
2001- Professor, Dept. of Neurology, University of Washington School of Medicine, Seattle, WA
2002- Professor, Dept. of Medicine, Division of Medical Genetics, University of Washington
2003- Professor, Dept. of Biochemistry, University of Washington

Awards and Other Professional Activities

1991 Basil O'Conner Starter Scholar Research Award, March of Dimes Birth Defects Foundation
1994 Leadership Award, Service Merchandise Inc.
1995 Gift of Hope Award, Jones Intercable Inc.
1995- Scientific Advisory Committee, Muscular Dystrophy Association
1995 Faculty Recognition Award, University of Michigan
1996- Scientific Review Board, National Gene Vector Laboratory
1999-2002 Board of Directors, American Society of Gene Therapy
1998-2001 Cell Development and Function-5 study section, NIH
2000-2005 Biological Response Modifiers Advisory Committee, CBER, FDA, *ad hoc member*
2001 Advisory committee on skeletal muscle biology, NIH, CSR
2001-2003 ZRG(1) multiple special emphasis review panels, chair, NIH

2002-2003 Muscular dystrophy task force member, NIH
2003-2006 Translational Research Advisory Committee member, Muscular Dystrophy Association
2004 Skeletal muscle and exercise physiology study section, NIH, *ad hoc member*
2005-2009 Cellular, Tissue and Gene Therapies Advisory Committee, Center for Biologics Evaluation and Research, Food and Drug Administration
2006 NIH MERIT Award, NIAMS
2007- Gene Therapy Resource Program, Scientific Review Board, NHLBI
2008-2012 Skeletal Muscle and Exercise Physiology study section member, NIH
2013- ZRG-1 Special emphasis review panels (2), NIH
2012- Fondazione Telethon, Milan, Italy, Scientific Advisory Committee
2012-2015 American Society for Cell and Gene Therapy, Board of Directors
Editorial Boards: *J Gene Med, Molec Therapy, J Neurodegen Regen, Skeletal Mus*

C. Selected peer-reviewed publications or manuscripts in press (from >230)

1. Chamberlain JS, Pearlman JA, Muzny DM, Gibbs RA, Ranier JE, Reeves AA and Caskey CT: Expression of the murine Duchenne muscular dystrophy gene in muscle and brain. Science 1988; 239:1416-18.
2. Chamberlain JS, Gibbs RA, Ranier JE, Nguyen PN and Caskey CT: Deletion screening of the Duchenne muscular dystrophy locus *via* multiplex DNA amplification. Nucleic Acids Res 1988; 16:11141-56.
3. Cox GA, Cole N, Matsamura K, Phelps SF, Hauschka SD, Campbell KP, Faulkner JA, Chamberlain JS: Overexpression of dystrophin in transgenic *mdx* mice eliminates dystrophic symptoms without toxicity. Nature 1993; 364:725-729.
4. Cox GA, Sunada Y, Campbell KP, Chamberlain JS: Dp71 can form a stable dystrophin-associated glycoprotein complex in muscle but fails to prevent dystrophy. Nature Genet 1994; 8:333-338.
5. Phelps SF, Hauser MA, Cole NM, Rafael JA, Hinkle RT, Faulkner JA, Chamberlain JS: Expression of full-length and truncated dystrophin mini-genes in transgenic *mdx* mice. Hum Mol Genet 1995; 4:1251-1258.
6. Kumar-Singh R, and Chamberlain JS: Encapsidated adenovirus mini-chromosomes allow delivery and expression of a 14 kb dystrophin cDNA to muscle cells. Hum Mol Genet 1996; 5:913-921.
7. Rafael JA, Cox GA, Jung D, Campbell KP, and Chamberlain JS: Forced expression of dystrophin deletion constructs reveals structure-function correlations. J Cell Biol. 1996; 134:93-102.
8. Crawford GE, Faulkner J, Crosbie R, Campbell K, Froehner S, and Chamberlain J: Assembly of the dystrophin associated protein complex does not require the dystrophin COOH-terminal domain. J Cell Biol 2000; 150:1399-1410.
9. Harper S, Hauser M, DelloRusso C, Duan D, Crawford RW, Phelps SF, Harper HA, Robinson AS, Engelhardt JF, Brooks SV, and Chamberlain JS. Modular flexibility of dystrophin: Implications for gene therapy of Duchenne muscular dystrophy. Nature Med 2002; 8:253-261.
10. Gregorevic P, Blankinship MJ, Allen J, Crawford RW, Meuse L, Miller D, Russell DW and Chamberlain JS: Systemic delivery of genes to striated muscles using adeno-associated viral vectors. Nature Med 2004; 10:828-834. PMC1365046.
11. Gregorevic P, Blankinship MJ, Minami E, Allen JA, Haraguchi M, Meuse L, Finn E, Adams M, Froehner SC, Murry CE and Chamberlain JS: Systemic delivery of rAAV6-microdystrophin preserves muscle function and extends lifespan in a murine model of severe muscular dystrophy. Nature Med 2006; 12:787-789.
12. Odom G, Gregorevic P, Doremus C, Allen J and Chamberlain JS: Microutrophin delivery *via* rAAV6 increases lifespan and improves muscle function in dystrophic dystrophin/utrophin deficient mice. Mol Ther 2008; 16:1539-1545. PMC2643133.
13. Gregorevic P, Schultz B, Allen JM, Halldorson JB, Blankinship M, Meznarich NAK, Kuhr CS, Doremus C, Finn E, Liggitt HD and Chamberlain JS: Evaluation of methodologies to enhance rAAV6-mediated gene transfer to canine striated musculature. Mol Ther 2009; 17: 1427-1433. PMC2788962.
14. Banks G, Judge L, Doremus C, Finn E, Allen J and Chamberlain JS: The polyproline site in hinge 2 influences the functional capacity of truncated dystrophins. PLoS Genetics 2010; 6:e1000958. PMC2873924.

15. Odom GL, Gregorevic P, Allen JA, Finn E and Chamberlain JS: Gene therapy of *mdx* mice with large truncated dystrophins generated by recombination using rAAV6. Mol Ther 2011; 19:36-45. PMC3017440.
16. Judge LM, Arnett ALH, Banks G and Chamberlain JS: Expression of the dystrophin isoform Dp116 preserves functional muscle mass and extends lifespan without preventing dystrophy in severely dystrophic mice. Hum Molec Genet 2011; 20: 4978-4990. DDR433. PMC3221536 Free PMC Article
17. Winbanks CE, Weeks KL, Thomson RE, Sepulveda PV, Beyer C, Qian H, Chen JL, Allen JM, Lancaster GI, Febbraio MA, Harrison CA, McMullen JR, Chamberlain JS and Gregorevic P: Follistatin-mediated skeletal muscle hypertrophy is regulated by Smad3 and mTOR independently of myostatin. J Cell Biol 2012; 197:997-1008. PMC3384410 Free PMC Article.
18. Wang Z, Storb R, Halbert CL, Banks GB, Butts TM, Finn EE, Allen JM, Miller AD, Chamberlain JS, Tapscott SJ. Successful regional delivery and long-term expression of a dystrophin gene in canine muscular dystrophy: a preclinical model for human therapies. Mol Ther 2012; 20:1501-1507. PMC3412492 Free PMC Article.
19. Arnett AL, Beutler L, Quintana A, Allen J, Finn E, Palmiter R and Chamberlain JS: Heparin-binding correlates with increased efficiency of AAV1- and AAV6-mediated transduction of striated muscle, but negatively impacts CNS transduction. Gene Therapy 2013; 20:497-503. doi: 10.1038/gt.2012.60. PMC Journal – in process.
20. Chamberlain, JS: A Genetic Intervention Stands a Skip Away from Clinical Tests. Science 2012; 338:1431-1432. PMID: 23239725.
21. Konieczny P, Boyle K and Chamberlain JS: Gene and Cell-Mediated Therapies for Muscular Dystrophies. Muscle Nerve 2013; 47:649-663. PMC Journal – in process.

D. Research Support

NIH R01 AR44533-18 Chamberlain (PI) 04/01/1996 – 03/31/2017
Assembly of the dystrophin-glycoprotein complex
The goals of this project are to examine the relationship between defective assembly of the dystrophin-glycoprotein complex (DGC) and the structural, mechanical and signaling functions of dystrophin and the DGC.

NIH R37 AR40864-24 (MERIT Award) Chamberlain (PI) 04/01/1991 – 03/31/2015
Dystrophin replacement in mdx mice
The goals of this project are to develop and optimize methods for systemic delivery of genes using adeno-associated viral vectors. The aims include optimization of infusion methods, vector preparation, capsid modification and testing in mice and large animal models.

NIH P01 NS046788-10 Froehner (PI) 05/01/2004 - 04/30/2014
Molecular and cellular therapies for muscular dystrophy
Project 1: Dystrophin delivery to muscle *via* myogenic precursors
This is a program project application to explore therapeutic options for the muscular dystrophies. My Project explores the use of stem cells for *ex vivo* gene therapy of muscular dystrophy. Role: PI of Project 1.

NIH R01 AG033610-05 Chamberlain (PI) 04/01/2009 – 03/31/2014
Genetic modification of aging and diseased striated muscles
This is a project to study gene transfer in aging. The goals are to develop new adeno-associated viral vector serotypes and to explore their use in gene transfer to aging and diseased muscles. We also propose designing new micro-dystrophins, using AAV to generate new disease models in mice and to develop synergistic therapies using dual gene transfer methodologies.