BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Childers, Martin Kent	Professor
eRA COMMONS USER NAME (credential, e.g., agency login) CHILDERSMK	

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
Seattle Pacific University	BA	05/80	Music Performance
Western University	DO	05/90	Medicine
University of Missouri	PhD	05/02	Physiology and Pharmacology

A. Personal Statement

The goal of our primary research is to address the hurdles required for systemic gene replacement delivery for patients with X-Linked Myotubular Myopathy (XLMTM). This step is necessary to rapidly translate findings from the XLMTM dog to a clinical trial in XLMTM patients suffering from respiratory dysfunction and certain death. As the lead in this investigation, I command a broad background in medical physiology, with specific training and expertise in key research areas for this application. About 20 years ago as a medical resident at the University of Missouri, I trained under the mentorship of Joe Kornegay, the world's leading authority in the canine model of Duchenne muscular dystrophy. A subsequent KO8 award provided me the opportunity to study dystrophic dog skeletal muscle mechanics at the whole muscle and single fiber levels. As a faculty member, I conducted pivotal multicenter drug trials in patients, and am currently lead investigator in a preclinical gene therapy trial for XLMTM, a study that will lead to generating data needed for application for an investigative new drug (IND) to the FDA. The current R01 proposal to test systemic gene therapy in the dog model builds logically upon the initial success in our first preclinical trial to test regional limb delivery. I have chosen complementary co-investigators/collaborators (Drs Beggs, Lawlor, Grange, Moullier, Buj-Bello, and Storb). Together, our team provides expertise in genetics, gene therapy, pathology, physiology, and immunology – all working together to tackle a challenging and exciting approach to execute a pre-clinical gene therapy trial for patients with a deadly disease.

B. Positions and Honors.

Positions and Employment

1990-1991	Intern, Department of Internal Medicine; Sun Coast Hospital, Largo, FL
1991-1994	Emergency Physician, Still Regional Medical Center, Jefferson City, MO
1991-1994	Resident Physician, Dept. of Physical Medicine & Rehabilitation (PM&R), University of Missouri-Columbia
1994-2000	Assistant Professor, Dept. of PM&R, University of Missouri-Columbia
2000-2006	Associate Professor, Dept. of PM&R, University of Missouri-Columbia
2006-2009	Associate Professor, Dept. of Neurology, Wake Forest University Health Sciences
2009-2012	Professor (with tenure), Dept. of Neurology, and Institute for Regenerative Medicine, Wake Forest University Health Sciences
2012-present	Professor, Department of Rehabilitation Medicine, University of Washington School of Medicine

Editorial Boards

Board Member:

2011 – Present *TheScientificWorldJOURNAL*
2010 – Present *Frontiers in Integrative Pharmacology*
2008 – Present *PM & R Journal*
2004 – 2009 *American Journal of Physical Medicine & Rehabilitation*

Other editorial work
Ad Hoc Reviewer:
2012 _ Present *Science Translational Medicine*
2012 _ Present *Molecular Medicine*
2010 – Present *PLOS One*
2011 – Present *Journal of Urology*
2010 – Present *Human Molecular Genetics*
2010 – Present *Recent Patents on Regenerative Medicine*
2009 – Present *Neuromuscular Disorders*
2008 – Present *Journal of Tissue Engineering & Regenerative Medicine*
2004 – Present *Journal of Applied Physiology*
2000 – 2004 *Brain Injury*
2002 – Present *Pain*
2001 – Present *Muscle and Nerve*
1999 – Present *Archives of Physical Medicine and Rehabilitation*

Study sections and other grant review committees
2011 – Distinguished Editor, Musculoskeletal, Oral and Skin Sciences (MOSS) study section special emphasis panel (ZRG1 MOSS-C90)
2006 – 2012 Intramural Research Support Committee, Wake Forest University School of Medicine
2004 – 2009 NIH (NIAMS, NINDS) Skeletal muscle exercise physiology (SMEP) study section (ad hoc)
2002 – 2011 US Army, American Institute of Biological Sciences (annual review of DMD programs)
2002 – 2006 Advisory Board for the Spinal Cord Injuries or Acquired Disease Processes Research Program, Office of the President of the University of Missouri
2001 – 2006 Roger S. Williams Fund Board of Trustees, School of Health Professions, University of Missouri

C. Selected peer-reviewed publications (from 55)
Relevant to this proposal

1. **Childers MK***, Okamura CS, Bogan DJ, Bogan JR, Sullivan MJ, Kornegay JN. Myofiber injury and regeneration in a canine homologue of Duchenne muscular dystrophy. Am J Phys Med Rehabil 2001;80(3):175-81.
2. **Childers MK***, Okamura CS, Bogan DJ, Bogan JR, Petroski GF, McDonald K, Kornegay JN. Eccentric contraction injury in dystrophic canine muscle. Arch Phys Med Rehabil 2002;83(11):1572-8.
3. **Childers MK***, McDonald KS. Regulatory light chain phosphorylation increases eccentric contraction-induced injury in skinned fast-twitch fibers. Muscle Nerve 2004;29:313-7.
4. Liu JM, Okamura CS, Bogan DJ, Bogan JR, **Childers MK***, Kornegay JN. Effects of prednisone in canine muscular dystrophy. Muscle Nerve 2004 Dec;30(6):767-73.
5. **Childers MK***, Staley JT, Kornegay JN, McDonald KS. Skinned single fibers from normal and dystrophin-deficient dogs incur comparable stretch-induced force deficits. Muscle Nerve 2005;25;31(6):768-771.
6. Markert C, Ning, J, Staley J, Heinzke L, Childers CK, Ferreira J, Brown M,, Stoker A, Okamura C, **Childers MK***. TCAP knockdown by RNA interference inhibits myoblast differentiation in cultured skeletal muscle cells. Neuromuscular Disorders, 2008;18(5):413-22.
7. Markert C, Atala A, Cann JK, Christ G, Furth M, Ambrosio F, **Childers MK***. Mesenchymal stem cells: emerging therapy for Duchenne muscular dystrophy. PM R. 2009 Jun;1(6):547-59. PMID: 19627945.
8. Marsh AP, Eggebeen JD, Kornegay JN, Markert CD, **Childers MK***. Kinematics of gait in golden retriever muscular dystrophy. Neuromuscul Disord. 2010 Jan;20(1):16-20. PubMed PMID: 19932618.

9. Markert CD, Meaney MP, Voelker KA, Grange RW, Dalley HW, Cann JK, Ahmed M, Bishwokarma B, Walker SJ, Yu SX, Brown M, Lawlor MW, Beggs AH, **Childers MK***. Functional muscle analysis of the Tcap knockout mouse. Hum Mol Genet. 2010 Jun1;19(11):2268-83. PMID: 20233748; PMCID: PMC2865379.
10. Tegeler C, Grange RW, Bogan DJ, Markert CD, Case D, Kornegay JN, **Childers MK***. Eccentric contractions induce rapid isometric torque drop in dystrophin-deficient dogs. Muscle Nerve 2010 Jul;42(1):130-2.PMID: 20544944.
11. Beggs AH, Böhm J, Snead E, Kozlowski M, Maurer M, Minor K, **Childers MK**, Taylor SM, Hitte C, Mickelson JR, Guo LT, Mizisin AP, Buj-Bello A, Tiret L, Laporte J, Shelton GD. MTM1 mutation associated with X-linked myotubular myopathy in Labrador Retrievers. Proc Natl Acad Sci U S A. 2010 Aug 17;107(33):14697-702. PMID: 20682747.
12. **Childers MK***, Grange R, Kornegay J. In Vivo Canine Muscle Function Assay. J Vis Exp (2011) (50) pp. e2623 PubMed PMID: 21494224
13. Shively CA, Willard SL, Register TC, Bennett AJ, Pierre PJ, Laudenslager ML, Kitzman DW, **Childers MK**, Grange RW, Kritchevsky SB. Aging and physical mobility in group-housed Old World monkeys. Age (Dordr). 2011 Dec 28. PubMed PMID: 22203457.
14. **Childers MK***, Bogan JR, Bogan DJ, Greiner H, Holder M, Grange R and Kornegay JN (2011). Chronic administration of a leupeptin-derived calpain inhibitor fails to ameliorate severe muscle pathology in a canine model of Duchenne muscular dystrophy. *Front. Pharmacol.* **2:**89. doi: 10.3389/fphar.2011.00089
15. Goddard MA, Smith BK, Mitchell E, **Childers MK***. Establishing clinical endpoints of respiratory function in dogs for clinical translation. In: Carter GT (ed). Recent Advancements in Neuromuscular Medicine. Phys Med Rehabil Clin N Am 23 (2012) 75-94; doi:10.1016/j.pmr.2011.11.014.
16. **Childers MK*.** Invited Perspective: Increasing need for academic leadership in clinical trials, *PM R* 2012 Jun;4:391-3.
17. Moghadaszadeh B, Rider BE, Lawlor MW, **Childers MK**, Grange RW, Gupta K, Boukedes SS, Owen CA, Beggs AH. Selenoprotein N deficiency in mice is associated with abnormal lung development. FASEB J. 2013 Jan 16. [Epub ahead of print] PubMed PMID: 23325319.
18. Lawlor MW, Armstrong D, Viola MG, Widrick JJ, Meng H, Grange RW, **Childers MK**, Hsu CP, O'Callaghan M, Pierson CR, Buj-Bello A, Beggs AH. Enzyme replacement therapy rescues weakness and improves muscle pathology in mice with X-linked myotubular myopathy. Hum Mol Genet. 2013 Apr 15;22(8):1525-38. doi: 10.1093/hmg/ddt003. Epub 2013 Jan 9. PubMed PMID: 23307925; PubMed Central PMCID: PMC3605830.
19. Grange RW, Doering J, Mitchell E, Holder MN, Guan X, Goddard M, Tegeler C, Beggs AH, **Childers MK***. Muscle function in a canine model of X-linked myotubular myopathy. Muscle Nerve. 2012 Oct;46(4):588-91. doi: 10.1002/mus.23463. PubMed PMID: 22987702; PubMed Central PMCID: PMC3448125.

*corresponding author

D. Research Support

Ongoing Research Support

MDA Academic Translational Grant Childers (PI) 05/01/11 – 04/30/14
Gene therapy in canine myotubular myopathy Childers (PI)
The goal is to test efficacy and safety of AAV-MTM1 in a canine model of X-linked myotubular myopathy

Association Francaise contre les Myopathies (AFM)
Research Grant Childers (PI) 05/01/11 – 04/30/14
Gene therapy in canine myotubular myopathy (Matching funds to MDA Academic Translational Grant)
The goal is to test efficacy and safety of AAV-MTM1 in a canine model of X-linked myotubular myopathy

MDA201127 Childers (PI) 08/1/11 – 07/31/14
MDA Research Grant: Dystrophin-deficient Cardiomyocytes for High Throughput Screening
The goal is to produce iPS cell lines from patients with Duchenne muscular dystrophy (DMD), isolate cardiac lineage progenitors derived from these stem cells, and screen DMD cardiomyocytes to discover new drugs.

1R21AR064503-01A1 Childers (PI) 09/12/12 – 08/31/14
NIH/NIAMS
Establishing endpoints in canine myotubular myopathy for clinical translation
The goal is to study the natural history of disease progression in the dog model of XLMTM

Industry Funding Childers (PI) 04/01/13 – 03/30/16
Audentes Therapeutics
Gene replacement therapy in a canine model of X-linked myotubular myopathy
The goal is to study is to generate preclinical pharmacodynamic data using AAV8-MTM in the dog model of XLMTM

1R01HL115001-01A1 Childers (PI) 05/01/13 – 04/30/18
NIH/NHLBI
Gene therapy in canine myotubular myopathy for clinical translation
The goal of this preclinical study in XLMTM dogs is to determine efficacy of various AAV constructs carrying MTM1.

Completed Research Support

K18HL102884-01 Childers (PI) 05/01/10 – 04/30/12
NIH/NHLBI
Induced Pluripotent Stem Cells in Canine Muscular Dystrophy
The goal is to produce iPS cell lines from dystrophic dogs, isolate cardiac lineage progenitors derived from these stem cells, and assess effects of dystrophin mutation on cardiomyocyte development and function.
Role: PI

U01NS052476-01A2 Stedman HH (PI) 09/01/07-08/31/09
NIH/NINDS
Translational Program for Molecular Therapeutics in DMD
This study addresses a series of critical steps in the translational process for molecular therapy for Duchenne muscular dystrophy. It is meets the needs for AAV-mediated gene therapy for DMD, and the experimental plan in the submission of an investigational new drug application to the FDA.
Role: PI on the subcontract to Wake Forest University.

R21NS050135 Childers (PI) 07/01/05-05/31/08
NIH/NINDS
Leupeptin in a Canine Model of Duchenne Muscular Dystrophy
This project examines functional and pathological response to a calpain inhibitor in dogs with muscular dystrophy.