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
Tapscott, Stephen Justice	Member
eRA COMMONS USER NAME (credential, e.g., agency login) STAPSCOTT	

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
Hampshire College, Amherst, MA	BA	1975	Physiological Psych.
University of Pennsylvania, Philadelphia, PA	MD/PhD	1982	Anatomy
University of Pennsylvania, Philadelphia, PA	Internship	1983	Medicine
University of Pennsylvania, Philadelphia, PA	Residency	1986	Neurology
Fred Hutchinson Cancer Res Ctr, Seattle, WA	Staff Sci	1991	Molecular Biology

A. PERSONAL STATEMENT

Dr. Tapscott has expertise in clinical neurology and neuromuscular disease. He has contributed to understanding the molecular pathology of FSHD, including identification of candidate molecular biomarkers. He also has expertise in the transcriptional regulation of myogenesis and neurogenesis in normal development and disease.

B. POSITIONS AND HONORS

Professional Positions:

1991 – date Assistant Member / Associate Member / Full Member, Human Biology Division; and, Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA.

1994 – date Assistant Professor / Associate Professor / Professor, Department of Neurology; and, Adj. Professor, Dept of Pathology, University of Washington School of Medicine, Seattle, WA.

Honors, Awards**:** 1980-1982 Insurance Medical Scientist Scholarship Fund Fellowship / 1981 Flexnor Award, Institute of Neurological Sciences, University of Pennsylvania / 1982 William A. Jeffers Prize for Graduate Research, University of Pennsylvania / 1986 – 1991 Clinical Investigator Development Award, NINCDS, NIH / 1989 – 1993 McDonnell Fellow in Molecular Medicine in Cancer Research.

Advisory Positions**:** Fellowship Review Subcommittee, Muscular Dystrophy Association / 1993 – 1995; Task Force on Therapy for Genetic Diseases, Muscular Dystrophy Association / 1995 – 1998; Scientific Advisory Committee, Muscular Dystrophy Association / 1996 – 2008; Advisory Council, The Emily Dorfman Foundation for Children / 2000 – 2005; Scientific Advisory Council, American Brain Tumor Association / 2000 – date; Scientific Advisory Committee, National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members / 2001 – date; Co-chair (2004) and Chair (2007) Gordon Conference on Myogenesis; Translational Research Advisory Committee, Muscular Dystrophy Association / 2003 – 2008; Scientific Advisory Board, Hereditary Disease Foundation / 2003 – 2009; Co-director, Paul D. Wellstone Muscular Dystrophy Cooperative Research Center, University of Washington and Fred Hutchinson Cancer Research Center / 2003 – 2009.

Editorial Boards: Developmental Cell; Muscle & Nerve

C. SELECTED PEER-REVIEWED PUBLICATIONS *(selected from >100 publications)*

Snider L, Asawachaicharn A, Tyler AE, Geng LN, Petek LM, Maves L, Miller DG, Lemmers RJ, Winokur ST, Tawil R, van der Maarel SM, Filippova GN, Tapscott SJ. RNA Transcripts, miRNA-sized Fragments, and Proteins Produced from D4Z4 Units: New Candidates for the Pathophysiology of Facioscapulohumeral Dystrophy. *Hum Mol Genet* 18(13): 2414-2430, 2009. PMCID: PMC2694690.

Wang Z, Storb R, Lee D, Kushmerick MJ, Chu B, Berger C, Arnett A, Allen J, Chamberlain JS, Riddell SR, Tapscott SJ. Immune Responses to AAV in Canine Muscle Monitored by Cellular Assays and Noninvasive Imaging. *Mol Ther* 2010 Mar; 18(3):617-24. Epub 2009 Dec 29. PMCID: PMC2839426.

Lemmers RJ, vander Vliet PJ, Klooster R, Sacconi S, Camano P, Dauwerse JG, Snider L, Straasheijm KR, Jan van Ommen G, Padberg GW, Miller DG, Tapscott SJ, Tawil R, Frants RR, van der Maarel SM. A Unifying Genetic Model for Facioscapulohumeral Muscular Dystrophy. *Science* 2010 Sep 24;329(5999):1650-3. Epub 2010 Aug 19. PMID:20724583.

Snider L, Geng LN, Lemmers RJ, Kyba M, Ware CB, Nelson AM, Tawil R, Filippova GN, van der Maarel SM, Tapscott SJ, Miller DG. Facioscapulohumeral dystrophy: incomplete suppression of a retrotransposed gene. *PLoS Genet.* 2010 Oct 28;6(10):e1001181. PMCID: PMC2965761.

van der Maarel SM, Tawil R, Tapscott SJ. Facioscapulohumeral muscular dystrophy and DUX4: breaking the silence. *Trends Mol Med.* 2011 May;17(5):252-8. Epub 2011 Feb 1. PMCID: PMC3092836.

Balog J, Miller D, Sanchez-Curtailles E, Carbo-Marques J, Block G, Potman M, de Knijff P, Lemmers RJ, Tapscott SJ, van der Maarel SM. Epigenetic regulation of the X-chromosomal macrosatellite repeat encoding for the cancer/testis gene CT47. *Eur J Hum Genet.* 2011; 20:185-91. PMID: 21811308.

Wang Z, Tapscott SJ, Chamberlain JS, Storb R. Immunity and AAV-Mediated Gene Therapy for Muscular Dystrophies in Large Animal Models and Human Trials. Front Microbiol. 2011;2:201. Epub 2011 Sep 26. PubMed PMID: 21980317; PMCID: PMC3180173.

Wang Z, Storb R, Tapscott SJ, Riddell S. Analyzing cellular immunity to AAV in a canine model using ELISPOT assay. Methods Mol Biol. 2012;792:65-74. PMID: 21956501.

Geng LN, Yao Z, Snider L, Fong AP, Cech JN, Young JM, van der Maarel SM, Ruzzo WL, Gentleman RC, Tawil R, Tapscott SJ. DUX4 activates germline genes, retroelements, and immune mediators: implications for facioscapulohumeral dystrophy. Dev Cell. 2012 Jan 17;22(1):38-51. Epub 2011 Dec 29. PMID: 22209328; PMCID: PMC3264808.

Fong AP, Yao Z, Zhong J-W, Cao Y, Ruzzo WL, Gentleman RC, Tapscott SJ. Genetic and epigenetic determinants of neurogenesis and myogenesis. Dev Cell. 2012; 22:721-735. PMID: 22445365; PMCID: PMC3331915

Balog J, Thijssen PE, de Greef JC, Shah B, van Engelen BG, Yokomori K, Tapscott SJ, Tawil R, van der Maarel SM. Correlation analysis of clinical parameters with epigenetic modifications in the DUX4 promoter in FSHD. Epigenetics. 2012 Jun 1;7(6). PubMed PMID: 22522912; PMCID: PMC3398987.

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 Jun 12. doi: 10.1038/mt.2012.111. PubMed PMID: 22692496; PMC3412492.

Krom YD, Dumonceaux J, Mamchaoui K, den Hamer B, Mariot V, Negroni E, Geng LN, Martin N, Tawil R, Tapscott SJ, van Engelen BG, Mouly V, Butler-Browne GS, van der Maarel SM. Generation of isogenic D4Z4 contracted and noncontracted immortal muscle cell clones from a mosaic patient: A cellular model for FSHD. AM J Pathol. 2012 Oct 18; 181(4):1387-401. PubMed PMID:22871573

Van der Maarel SM, Miller DG, Tawil R, Filippova GN, Tapscott SJ. Facioscapulohumeral muscular dystrophy: consequences of chromatin relaxation. Curr Opin Neurol. 2012 Oct 25 (5):614-20 PubMed PMID: 22892954

Lemmers RJ, Tawil R, Petek LM, Balog J, Block GJ, Santen GW, Amell AM, van der Vliet PJ, Almomani R, Straasheijm KR, Krom YD, Klooster R, Sun Y, den Dunnen JT, Helmer Q, Donlin-Smith CM, Padberg GW, van Engelen BG, de Greef JC, Aartsma-Rus AM, Frants RR, de Visser M, Desnuelle C, Sacconi S, Filippova GN, Bakker B, Bamshad MJ, Tapscott SJ, Miller DG, van der Maarel SM. Digenic inheritance of an SMCHD1 mutation and an FSHD-permissive D4Z4 allele causes facioscapulohumeral muscular dystrophy type 2. Nat Genet. 2012 Dec;44(12):1370-4. doi: 10.1038/ng.2454. Epub 2012 Nov 11. PubMed PMID: 23143600.

D. RESEARCH SUPPORT: *Ongoing*

NIH/NINDS 5 P01 NS069539-03 (PI: Tapscott) The Pathogenesis of Facioscapulohumeral Muscular Dystrophy
Role: PI 4/15/2010 – 3/31/2015

- The studies proposed under this program project grant combine genetic, epigenetic, transcriptional and developmental approaches to defining the epigenetic modifications associated with FSHD and will provide a basis for developing therapies.

NIH/NIAMS 5 R01 AR045203-13 (PI: Tapscott) D4Z4 Coding Transcripts and FSHD

Role: PI 2/01/2010 – 1/31/2015

- The major goal of this research is to identify the coding transcripts that might cause facioscapulohumeral dystrophy (FSHD).

NIH/NIAMS 5 R01 AR045113-15 (PI: Tapscott) Lineage Determination in Muscle
Role: PI 5/01/2013 – 4/30/2018

- The major goal of this project is to apply the knowledge gained from studies of gene regulation in myogenesis to identify the mechanisms of lineage specification and differentiation.

NIH/NIAMS 5 R01 AR056949-04 (PI: Tapscott) Preclinical Gene Therapy Studies in Canine Muscular Dystrophy
Role: PI 7/01/2009 – 6/30/2014

- The overall goal of this proposal will be to develop AAV mediated gene therapy strategies in *cxmd* dogs that can be applied to human patients with DMD.

NIH/NINDS 5 P01 NS046788-09 (PI: Froehner) Molecular and Cellular Therapies for Muscular Dystrophy.
Project 2: Muscle Cell Transplantation in Canine DMD
Role: Project 2 Leader 6/01/2009 – 3/31/2014

- This program project explores therapeutic options for the muscular dystrophies. The overall objective for Project 2 is to establish which cell populations and modulating factors most successfully restore dystrophin expression to diseased muscle using both the immune tolerant cxmd model and canine-to-mouse xenotransplant model.

NIH/NIGMS R01 GM088277-03 (PI: Bradley) Predicting Protein-DNA Interactions with Structural Models
Role: Co-Investigator 8/10/2009 – 7/31/2014

- Interactions between proteins and DNA molecules are central to a wide range of genetic and regulatory processes. This research project will lead to improved tools for computationally predicting protein-DNA structures and interactions using only protein sequence data (such as that generated by the human genome project).

Friends of FSH Research (PI: Tapscott) Modulators of Epigenetic Disease
Role: PI 11/01/2011 – 10/31/2015

- This application will support new projects that use our current knowledge of the mechanisms of FSHD to develop and validate biological platforms for screening for agents that will support the development of therapies for FSHD.

Glaxo Smith Kline (PI: Tapscott) Inhibitors of DUX4 Mediated Transcription as a Treatment for FSH
Role: PI 9/7/2012 – 3/5/2016

- Research agreement with GSK to provide reagents to support identification of small molecules that inhibit DUX4 protein activity as a transcription factor. Concurrent with Friends of FSH research because the reagents developed under Friends funding will be modified and validated for the GSK agreement.

RESEARCH SUPPORT: *Completed during the last 3 years*

FHCRC-Synergy Fund (PI: Bradley, Gentleman, Tapscott) The Evolution and Engineering of Cell Diversity
Role: co-PI 8/01/2008 – 6/30/2010

- A collaborative research project to identify the computational and engineering principles that can assign functional values to DNA binding sites on the basis of primary DNA sequence.

NIH/NICHD 3 P30 HD002274-43S1 (PI: Guralnick / Director: Laird) Fragile X Res Ctr – Supplement
Role: Co-Investigator 7/01/2008 – 6/30/2013

- The proposed study assesses: 1) the molecular mechanisms underlying fragile X syndrome (FXS); 2) how the molecular variations affect the clinical phenotype of FXS; and, 3) the treatment of FXS, specifically the use of sertraline. Advances based on this research will lead to molecular interventions and will improve the understanding of psychopharmacological interventions.

NIH/NIGMS 5 R01 GM057070-13 (PI: Tapscott) Variation, Functions, and Dynamics of Human Subtelomeres.
Role: PI 9/01/2007 – 8/31/2012

- The goal of this project is to determine the structure, function, evolution and somatic dynamics of subtelomeric regions of human chromosomes and the role these regions play in the evolution of gene families.

*Under a no cost extension without additional funds through 11/30/2012