BIOGRAPHICAL SKETCH

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NAME: Diego Fraidenraich, PhD, FAHA

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

POSITION TITLE: Assistant Professor, Director of human iPS cell

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
University of Buenos Aires, Argentina	Ph.D.	05/1994	Biochemistry
New York University School of Medicine, NY		12/2000	Pew Fellow, Developmental Biology
Memorial Sloan-Kettering Cancer Center, NY		12/2003	Postdoctoral Fellow, Stem Cells
Memorial Sloan-Kettering Cancer Center, NY		12/2006	Senior Research Scientist, Stem Cells

A. POSITIONS AND HONORS

Positions and Employment

2007-2013 Assistant Professor, Dept. of Cell Biology and Molecular Medicine, UMDNJ-NJMS.
2009-2011 Director, Stem Cell Research, Dept. of Cell Biology and Molecular Medicine,UMDNJ-NJMS.
2013- Assistant Professor, Dept. of Cell Biology and Molecular Medicine, Rutgers-NJMS.
2014- Director, human iPS cell Core, Cell Biology and Molecular Medicine, Rutgers-NJMS.
2014- Member, Stem Cell Program, Human Genetics Institute of NJ

Honors

1988-1990 Undergraduate Student Fellowship, University of Buenos Aires, Argentina.
1990-1994 Graduate Student Fellowship, National Council for Research and Technology
'Leloir' award for the Best Thesis of the Year, University of Buenos Aires.
1996-1998 Postdoctoral Fellowship, Pew Latin American Fellows Program in Biomedical Sciences, San Francisco, CA.
2007 Searle Scholars Program Award nomination to young investigators
2007 Travel Grant Award, AHA Scientific Sessions, Orlando, FL.
2007- Member, Hispanic Center of Excellence-New Jersey Medical School
2007-2011 Member, NHLBI-sponsored Heart, Lung and Blood Summer Student Research Program, to mentor underrepresented summer students.
2013- Fellow of the AHA (FAHA)

Membership in Scientific Societies

2003- International Society for Stem Cell Research (ISSCR).
2007- American Heart Association (AHA).

Editorial Board, Reviewer in Journals and Study Sections

2007 National Science Foundation-Animal Developmental Mechanisms Study Section.
2009-2013 UMDNJ Foundation Dean's Biomedical Research Support Program Review Committee.
2009- Reviewer in journals: Tissue Engineering, FEBS, Muscle and Nerve, PLoS ONE, Stem Cells and Development, AJP-Heart and Circulatory Physiology (participation in an editorial Podcast), Gene Therapy, International Journal of Biochemistry and Cell Biology.
2010 Ontario Research Fund-Global Leadership in Genomics and Life Sciences Cancer & Stem Cells Peer-Review Panel.

2010 US Army Medical Research and Materiel Command (USAMRMC), CDMRP Review Panel.
2011 Telethon Italy – Grant study section - external reviewer.
2011 Ad hoc reviewer for the Muscular Dystrophy Association (MDA) and for the MDA Venture Philanthropy
2014- New Jersey Health Foundation Review Committee.
2012-2014 Regular member, AHA Basic Cell GE 3 Study Section
2014- Regular member, AHA Basic Cell GE 1 Study Section
2012- Academic Editor, PLOS ONE

Patents

2014 Corrective roles of insulin-like growth factor-binding protein-3 in pathological conditions. US Patent 8,802,629 B1 (8-2014). Inventors: Drs. D. Fraidenraich and Q. Zhao.

B. CONTRIBUTION TO SCIENCE

Stem cells

As lead author and subsequently as senior PI, I injected PSCs into pre-implantation embryos predisposed to develop disease, but the PSCs rescued disease from occurring. We discovered that the PSCs secrete paracrine factors that correct the mutant environment. Some of these factors are not normally expressed in the embryo or adult tissue due to a "neomorphic" effect of the PSCs. This is the first time that the PSCs have been seen as vehicles of the factors responsible for their therapeutic effects (see comment in Perspectives in *Science* by Kenneth Chien)(http://www.ncbi.nlm.nih.gov/pubmed/15472069). *As leading expert in the pluripotent stem cell field, I participate in podcasts http://ajpheart.podbean.com/2011/11/09/electrophysiology-of-hipsc-derived-cardiomyocytes/) and as Academic Editor for PLOS ONE. I am Director of the newly established human Pluripotent Stem Cell Core.*

1. Fraidenraich, E. Stillwell, D. Wilkes, C. Basson and R. Benezra. "Rescue of cardiac defects in Id knockout embryos by injection of embryonic stem cells. *Science* (2004) 306: 247-252. PMCID: PMC1351017.
2. D. Fraidenraich and R. Benezra. "Embryonic stem cells prevent developmental cardiac defects in mice". *Nat Clin Pract Cardiovasc Med. (*2006) Suppl 1:S14-7.
3 S. Yamada, T. Nelson, A. Behfar, R. Crespo-Diaz, D. Fraidenraich and A. Terzic. "Stem cell transplant into Pre-implantation embryo yields myocardial infarction-resistant adult phenotype". *Stem Cells* (2009); 27(7):1697-705. PMCID: PMC2800943
4. A. Ziegler, J. Schneider, M. Qin, W. Tyler, J. Pintar, D. Fraidenraich, T. Wood, S. Levison. "IGF-II promotes stemness of neural restricted precursors" *Stem Cells* (2012) 30(6):1265-76.
5. J. Schneider, X. Cheng, Q. Zhao, C. Underbayev, JP. Gonzalez, E. Raveche, D. Fraidenraich and A. Ivessa. Reversible mitochondrial DNA accumulation in nuclei of pluripotent stem cells. *Stem Cells Dev. (*2014) 23(22):2712-9. doi: 10.1089/scd.2013.0630.
6. Q Zhao, C Chang, JP Gonzalez, K Alzahrani, JL Button, D. Fraidenraich. "Combined Id1 and Id3 Deletion Leads to Severe Erythropoietic Disturbances"; under review
7. C Underbayev, M Batish, S Kasar, W Ruezinsky, H Degheidy, JS Schneider, G Marti, S Bauer, D Fraidenraich, E Raveche. "Role of miR-15A/16-1 in early B cell development in a mouse model of chronic lymphocytic leukemia"; submitted

Muscular dystrophy and cardiomyopathy.

In my postdoctoral training as a PEW fellow I acquired extensive background in developmental biology (myogenesis and cardiogenesis). We discovered several pathways that are required for proper cardiac and skeletal muscle development. Some of these pathways can be used therapeutically in disease states like muscular dystrophy and cardiomyopathy. We are particularly interested in cell-cell communication, or paracrine interaction between the target tissue and outside tissues (i.e. epicardium, endocardium, bone marrow, adipose tissue). Our studies led to one patent (http://www.google.com/patents/US8802629) and one recent paper in Nature Sci Rep and Neuromusc Disord. As expert in these fields, I serve as reviewer for the AHA.

1. Q. Zhao, A. Beck, J. Vitale, J Schneider, S. Gao, C. Chang, Y. Yeon, B. Tian, G. Elson, S. Leibovich, H. Nam and D. Fraidenraich. "Developmental ablation of Id1 and Id3 genes in the vasculature leads to postnatal cardiac phenotypes". *Dev. Biol.* (2011) 349(1):53-6; Journal Cover. PMCID: PMC2993814

2. E. Stillwell, J. Vitale, Q. Zhao, A. Beck, J. Schneider, F. Khadim, G. Elson, A. Altaf, G. Yehia, J. Liu, J. Dong, M., W. Mark, Bhaumik, R. Grange and D. Fraidenraich. "Blastocyst injection of wild type embryonic stem cells induces global corrections in mdx mice." *PLoS ONE* (2009) 4(3): e4759. PMCID: PMC2653195
3. J. Vitale, J. Schneider, A. Beck, Q. Zhao, C. Chang, R. Gordan, J. Michaels, M. Bhaumik and D. Fraidenraich."Dystrophin-compromised sarcoglycan-δ knockout diaphragm requires full wild type embryonic stem cell reconstitution for correction." *J. Cell Sci.* (2012) 125:1807-13. PMCID: PMC3346830
4. J. Ramachandran, J. Schneider, P. Crassous, R. Zheng, J. Gonzalez, L. Xie, A. Beuve, D. Fraidenraich and R. Peluffo. Nitric Oxide Signaling Pathway in Duchenne Muscular Dystrophy Mice: Upregulation of L-Arginine Transporters, *Biochem J.* (2013) 449(1):133-42 PMID: 23009292.
5. J. Schneider, M. Shanmugam, J. Gonzalez, H. Lopez, R. Gordan, D. Fraidenraich and G. Babu. Increased sarcolipin expression and decreased sarco(endo)plasmic reticulum Ca2+ uptake in skeletal muscles of mouse models of Duchenne muscular dystrophy. (Epub ahead of print), *J Muscle Res Cell Motil. (2013) Dec;34(5-6):349-56.*
6. JP Gonzalez, J Ramachandran, LH Xie, JE Contreras and D Fraidenraich. Selective Connexin43 Inhibition Prevents Isoproterenol-Induced Arrhythmias and Lethality in Muscular Dystrophy Mice. *Nature Sci Rep. (2015) 27;5:13490. doi: 10.1038/srep13490.*
7. JP Gonzalez, PA Crassous, J Schneider, A Beuve and D Fraidenraich. nNOS Localizes to Utrophin Expressing Intercalated Discs and Stabilizes Their Structural Integrity. *Neuromuscul Disord. (2015); pii: S0960-8966(15)00738-5 [Epub ahead of print]*

Signaling transduction mechanisms of *T. cruzi* differentiation.
As a PhD student, I discovered that the Latin American endemic bloodborn parasite T. cruzi turned into infective forms using breakdown products of the globin in the hindgut of the invertebrate vector. This work was published in PNAS, and communicated by the Nobel laureate Dr. James D. Watson.

1. D. Fraidenraich, C. Pena, E. Isola, E. Lammel, O. Coso, A. Diaz Anel, S. Pongor, A. Baralle, H. Torres and M. Flawia. "Stimulation of *Trypanosoma cruzi* adenylyl cyclase by an α^{D}-globin fragment from *Triatoma* hindgut. Effect on differentiation of epimastigote to trypomastigote forms". *Proc. Natl. Acad. Sci. USA*. (1993) 90: 10140-10144. PMCID: PMC47729

A list of peer-reviewed publications can be seen at: http://www.ncbi.nlm.nih.gov/pubmed/?term=fraidenraich+d

C. RESEARCH SUPPORT

Active

Grant-in-Aid 15GRNT25140001 (Fraidenraich, PI) 07/01/2015-06/30/2018
American Heart Association
Mechanisms of endomyocardial fibrosis caused by loss of extracardiac Id
We seek to study the role of Id in the endothelium and bone marrow on cardiac disease.

Team Science Initiative (Fraidenraich PI, col: Tao, Shirokova, Soteropoulos, Bhaumik, Sadoshima)
New Jersey Health Foundation 07/01/2014-06/30/2016
Epigenetic memory of embryonic stem cells in adult tissue.
We seek to understand why the cardiomyocytes derived from embryonic stem cells exert a dominant phenotype in mouse chimeras.

Predoctoral Fellowship 1F31HL117621 (Gonzalez, PI; Fraidenraich, sponsor) 7/1/2013-6/30/2016
NIH/NHLBI
Nitric oxide pathway requirement for the correction of cardiomyopathy in muscular dystrophy carrier mice
We seek to study the role of the nitric oxide pathway in duchenne muscular dystrophy carrier mice

Completed
1R21HL09490501 (Fraidenraich, PI) 08/01/09-7/31/12

NIH/NHLBI
Role of murine induced pluripotent stem cells on the correction of cardiac and skeletal muscle defects
The study will test if wild-type iPS cells injected into mdx or Id knockout mice correct muscular dystrophy and cardiomyopathy from occurring

Stem Cell Research Grant NJ0749 (Fraidenraich, PI) 08/01/2007-07/31/2009
New Jersey Commission on Science and Technology
Stem cell-based therapy in Mst1 transgenic mice, a mouse model of cardiomyopathy
The study will determine whether injection of stem cells (embryonic or adult) into Mst1 mice before or near the onset of the disease will prevent cardiomyopathy from occurring by secretion of paracrine factors

Grant-in-Aid 0755909T (Fraidenraich, PI) 07/01/2007-06/30/2010
American Heart Association
Correction of vascular defects in Id knockout hearts by Wnt5a-induced compensatory mechanisms
The study will characterize hearts from mice with conditional ablation of Id in the vasculature and the potential corrective effect of Wnt5a

K01 HL076568 (Fraidenraich, PI) 06/01/2004-05/31/2010
NIH/NHLBI
Role of Id genes during cardiac development
The study will address the role and the molecular mechanisms underlying the mode of action of Id (inhibitor of DNA binding) genes during cardiac formation.

Research Grant 68648 (Fraidenraich, PI) 01/012008-12/31/2010
Muscular Dystrophy Association
Embryonic stem cells prevent Duchenne muscular dystrophy in mdx mice
We seek to prevent muscular dystrophy from occurring by supplying wild type embryonic stem cells before the muscle forms.

UMDNJ-NJMS Single Investigator Award (Fraidenraich, PI) 07/01/08-06/30/09
UMDNJ Foundation
Derivation of mutant induced pluripotent stem cells from mice predisposed to develop muscular dystrophy
We seek to derive iPS cells from mouse embryonic fibroblasts.

UMDNJ Research Grant (Fraidenraich, PI) 1/1/10-12/31/11
UMDNJ Dean's Biomedical Research Support Program
Non-canonical Wnt Signaling Protection of Muscular Dystrophy
The goal is to study a potential link between non-canonical Wnt signaling and dystrophin stability

UMDNJ Bridge Grant (Fraidenraich, PI) 1/1/11-12/31/11
UMNDJ Foundation
Induced Pluripotent Stem Cell Correction of Muscular Dystrophy-Associated Cardiomyopathy
The goal is to enrich for a dystrophin-expressing fraction from mdx+/- cardiomyocytes derived *in vitro* from iPSCs to ultimately test engraftment into adult hearts and therapeutic potential.

Predoctoral Fellowship 12PRE1207008 (Chang, PI; Fraidenraich, sponsor) 07/01/2012-06/30/2014
American Heart Association
Paracrine effects of Id genes on cardiac disease
We seek to examine roles of Id genes in cardiac disease at a distance

Seed Grant (Fraidenraich, PI) 05/01/2013-04/30/2015
New Jersey Health Foundation
Insulin like growth factor-1 mediates cardiac defects triggered by Id-deficient bone marrow
We seek to examine the distal role of bone marrow on the production of a fibrotic heart.

Research Grant 200037 (Fraidenraich, PI) 08/01/2011-01/31/2015

Muscular Dystrophy Association
Pluripotent stem cell-induced corrections in muscle and fat of mdx mice
We seek to study fat/muscle interconversion in WT/mdx mosaic mice