Objectives

The New Directions in Biology and Disease of Skeletal Muscle Conference will be held in Charleston, SC on June 28-July 1, 2021. This meeting brings together scientists working to understand mechanisms and develop new therapies for muscle disease, especially the muscular dystrophies. The “New Directions” meeting differs from other topically related meetings because of its focus on bringing together industry and academic attendees with a focus on evaluating laboratory based observations and assessing or testing suitability for therapy in the preclinical and clinical setting. This meeting was developed in response to MD Care Act and the recognition that devising and testing therapy for rare neuromuscular disorders requires organization and coordinated efforts among all stakeholders. In addition to the focus on identifying and testing therapeutic pathways, the New Directions meeting places a high emphasis on inclusion of trainees and young investigators, as it is recognized that the challenges of these medical problems will require a diverse and prolonged effort to realize cures for these devastating disorders.

Objective 1: The presentation and sharing of cutting edge research. This meeting specifically emphasizes the presentation of unpublished work through oral and poster presentations. Early access to information allows for new collaborations to form moving scientific discovery forward faster into translation.

Objective 2: Promotion of collaboration between industry and academic investigators. With rigorous mechanistic understanding of the disease processes and moving targets towards development, preclinical and clinical testing, the interaction and partnership between industry and academia is increasingly important. The first session of this meeting is designed to promote industry and advocacy group participation.

Objective 3: Identify both common and unique targets for among muscle diseases. This meeting provides a format where multiple different mechanisms of muscle disease are covered providing a backdrop to identify common elements that can be manipulated therapeutically.

Objective 4: Provide trainees and young investigators a forum in which to present data and to encourage trainees to remain studying neuromuscular disease. Trainees are expected to present posters, and senior and junior investigators are engaged by evaluating these presentations.

Conference Organizers
Elizabeth McNally, Northwestern University
H. Lee Sweeney, University of Florida

Coordinators
Christa Stout, University of Florida

Program Committee
Mary Baylies, Memorial Sloan Kettering Cancer Center
Alexis Demonbreun, Northwestern University
Jim Dowling, SickKids
Angela Lek, Yale University
Doug Millay, Cincinnati Children’s
Ben Prosser, University of Pennsylvania
April Pyle, University of California, Los Angeles
DeWayne Townsend, University of Minnesota
KEYNOTE SPEAKER

Bruce Spiegelman, Ph.D.
Harvard University Medical School

Irisin and Its Receptor: Therapeutic Potential in Neuromuscular Diseases

Bruce M. Spiegelman, Ph.D.
Stanley J. Korsmeyer Professor of Cell Biology and Medicine
Dana-Farber Cancer Institute, Harvard Medical School
Director, Center for Metabolism and Chronic Disease, Dana-Farber Cancer Institute

Bruce M. Spiegelman is the Stanley J. Korsmeyer Professor at Harvard Medical School and Dana-Farber Cancer Institute. Spiegelman received a B.S. with highest honors from the College of William and Mary, his PhD in biochemistry from Princeton University, and completed postdoctoral work at MIT. He then joined Harvard Medical School and Dana-Farber Cancer Institute. His research focuses on fat cell biology, diabetes and muscular diseases.

Bruce Spiegelman and his trainees discovered many of the most important regulators in adipose development and muscle adaptation to exercise. In the muscle area Spiegelman is best known for the discovery of PGC1a, a dominant regulator of mitochondrial biogenesis and the adaptation of muscle to exercise. Further studies have shown that molecules regulated by PGC1a such as irisin and meteorin-like are secreted and carry some of the benefits of exercise to muscle cells themselves, as well as distal tissues including bone and brain.

Spiegelman has published over 300 scientific articles that have been widely cited in the scientific literature. He is a member of the U.S. National Academy of Sciences, the American Academy of Arts and Sciences, the National Academy of Medicine and EMBO. His major awards include the Heinrich Wieland Prize in Lipid Research; the Bristol-Myers Squibb Award for Distinguished Achievement in Metabolic Research; the Rolf Luft award in Endocrinology; the Eliot P. Joslin Medal; the Transatlantic Medal (British Endocrine Society); the Frederick Banting Medal of the American Diabetes Association (their highest award); the Manpei Suzuki Prize for Diabetes Research, Japan; the Inbev Baillet-Latour Health Prize in 2015; the Helmholtz Prize for Diabetes Research, Munich, Germany and the 2021 Albert Renold Award of the American Diabetes Association. He has served as Chair of the Section on Metabolism and Medical Physiology of the National Academy of Sciences.
Monday, June 28, 2021

Industry Workshop, Crystal Ballroom
(all registered conference attendees are welcomed and encouraged to attend)

12:00 – 12:10PM  Welcome and Introductions

12:10 – 12:40  Alan Russell, Edgewise Therapeutics
Selective Inhibition of Fast Skeletal Muscle Myosin as a Novel Therapeutic Strategy for Muscular Dystrophy

12:40 – 1:10  Anthony Accorsi, Fulcrum Therapeutics
Unraveling the complexity of the dystrophic microenvironment to unlock a new future for patients with devastating muscle diseases

1:10 – 1:40  Patrick Gonzalez, Solid Biosciences
SGT-001: AAV Microdystrophin Gene Therapy for Duchenne Muscular Dystrophy

1:40 – 2:10  Olivier Danos, RegenxBio Inc.
RGX:202, a novel investigational microdystrophin gene therapy for Duchenne Muscular Dystrophy

2:10 – 2:40PM  COFFEE BREAK

2:40 – 3:10  Dan Levy, Pfizer
Fordaistrogene Movaparvovec for the potential treatment of DMD

3:10 – 3:40  Rachael Potter, Sarepta Therapeutics, Inc.
Sarepta Gene Therapy Engine: Investigating therapies for Duchenne and Limb Girdle Muscular Dystrophies

3:40 – 4:10  Arthur Levin, Avidity Biosciences
Engineering Antibody Oligonucleotide Conjugates (AOCs): Taking Receptor-Mediated Uptake One Step Further

4:10 – 4:30PM  BREAK

4:30 - 5:30PM  Keynote Speaker: Bruce Spiegelman, Harvard University Medical School
Irisin and Its Receptor: Therapeutic Potential in Neuromuscular Diseases
Tuesday, June 29, 2021

7:30AM  Continental breakfast served in Crystal Ballroom Foyer

Session I:  Novel Findings in Neuromuscular Disorders

All sessions in Crystal Ballroom

Chair: Jim Dowling

8:00 – 8:20AM  Alan Beggs, Boston Children’s Hospital, Harvard Medical School
Modeling of Nemaline Myopathy associated Autosomal Dominant TNNT1 variants in zebrafish

8:20 – 8:40  Anastasia Gromova, University of California, Irvine, University of California, San Diego
Disease Modeling of Spinal and Bulbar Muscular Atrophy Using iPSC-derived Skeletal Muscle and Motor Neurons

8:40 – 9:00  Jim Dowling, Sick Kids
New adventures in neuromuscular genetics

9:00 – 9:20  Monkol Lek, Yale University
High throughput assays for resolving variants of uncertain significance in Neuromuscular disease genes

9:20 – 9:40  Raquel Gomez Oca, Institut de Génétique et de Biologie Moléculaire et Cellulaire
Muscle-specific dynamin 2 isoform and its potential therapeutic interest in X-linked centronuclear myopathy

9:40 – 10:10AM COFFEE BREAK

Session II:  Muscle Adaptation in Normal and Diseased Muscle

Chair: Mary Baylies

10:10 – 10:30AM  Charlotte Peterson, University of Kentucky
Satellite cell-mediated myonuclear domain flexibility in muscle adaptation

10:30 – 10:50  Mary Baylies, Memorial Sloan Kettering Cancer Center
Nuclei, Position, Activity: Decoding Cell Size Regulation in Muscle Development and Disease

10:50 – 11:10  Edgar Gomes, University of Lisbon
The role of nuclear positioning in muscle function

11:10 – 11:30  Michael Hicks, University of California, Irvine
In Vivo Satellite Cell Niche Emergence from Human Pluripotent Stem Cells

11:30 – 11:50  Paul Rosenberg, Duke University School of Medicine
Desmin-STIM1 interaction influences Ca2+ store refilling in skeletal muscle that impacts muscle performance

11:50AM – 2:00PM LUNCH BREAK (on your own)
Data Blitz Session I, Data Blitz from abstract submissions
Pre and Post-Doctoral Trainees; 5 minute presentations (1 minute Q&A):

Collin Douglas, University of Florida
Loss of skeletal muscle circadian clock results in z-line structural disruptions and attenuation of sarcomere TCAP

Steve Guzman, University of Michigan
Neuromuscular junction regeneration after nerve injury in Sod1-/- mice

Cora Hart, University of Florida
Impact of gene therapy treatment age and duration on the functional recovery of D2.mdx skeletal muscle

Erynn Johnson, University of Minnesota
Kynurenine pathway dysregulation in Duchenne muscular dystrophy

Swathy Krishna, Iowa State University
Diet induced insulin resistance in mdx mice

Alessandra Norris, University of Florida
Regulation of Intramuscular Fat through the Hedgehog Pathway

Joseph O’Brien, Northwestern University
Modifiers of cardiomyopathy in muscular dystrophy

Maria Paz Ramirez Lopez, University of Minnesota
Dystrophin missense mutations associated with Duchenne and Becker muscular dystrophy impair C2C12 myoblast focal adhesion tension and migration via altered YAP activation

Yichi Zhang, UT Southwestern Medical Center
The nuclear envelope protein Net39 is required for skeletal muscle maintenance and function through regulation of Mef2c activity

3:00 – 3:30PM  BREAK

Session III: Screening For Novel Drugs And Targets
Chair: Angela Lek

3:30 – 3:50PM  Angela Lek, Yale University
Using CRISPR screens to identify drug targets for FSHD

3:50 – 4:10  Eric Wang, University of Florida
RNA processing and transport in healthy and diseased muscle

4:10 – 4:30  Vandana Gupta, Brigham and Women’s Hospital, Harvard Medical School
Uncovering the Power of Protein Degradation in Skeletal Muscle Diseases

4:30 – 4:50  Nicolas Wein, Nationwide Children’s Hospital
Viral Delivery of Exon Skipping Construct to Treat Duchenne Muscular Dystrophy

4:50 – 5:10PM  Matthias Lambert, Boston Children’s Hospital
Downregulation of the genetic modifier PITPNA as means of therapy in Duchenne Muscular Dystrophy
**Wednesday, June 30, 2021**

7:30AM  Continental breakfast served in Crystal Ballroom Foyer

**Session IV: Muscle Growth In Normal And Diseased Muscles II**
*All sessions in Crystal Ballroom*

Chair: Doug Millay

8:00 – 8:20AM  **Doug Millay**, Cincinnati Childrens  
*Defining the role of nuclei accrual during muscle development and growth*

8:20 – 8:40  **Sakthivel Sadayappan**, University of Cincinnati  
*Ablation of slow myosin binding protein-C results in perinatal lethality and skeletal muscle dysfunction in mice postnatally*

8:40 – 9:00  **David Hammers**, University of Florida  
*Filopodia powered by class X myosin promote fusion of mammalian myoblasts*

9:00 – 9:20  **Foteini Mourkioti**, University of Pennsylvania  
*Dynamics of skeletal muscle-resident stem cells during regeneration in fibrodysplasia ossificans progressiva*

9:20 – 9:40  **Yifan Li**, The University of South Dakota  
*Pro-BDNF-p75NTR pathway is involved inflammation in denervated skeletal muscle*

9:40 – 10:10AM  **COFFEE BREAK**

**Session V: Engineered Muscles As Models**

Chair: April Pyle

10:10 – 10:30AM  **April Pyle**, University of California, Los Angles  
*Skeletal Muscle Progenitor and Stem Cell states in Development and Disease*

10:30 – 10:50  **Kristen Stearns-Reider**, University of California, Los Angles  
*Myo-scaffolds reveal laminin scarring is detrimental for stem cell function while sarcospan induces compensatory fibrosis*

10:50 – 11:10  **Genevieve Wilson**, Fulcrum Therapeutics  
*Targeting Dystrophic Muscle Remodeling in Fibro-Adipogenic Progenitor Cells (FAPs)*

11:10 – 11:30  **Nenad Bursac**, Duke University  
*3D Myobundles for Studies of Human Muscle Biology, Disease, and Regeneration*

11:30 – 11:50  **Mina Gouti**, Max-Delbrück Center for Molecular Medicine  
*Generation of human neuromuscular organoids to study development and disease*

11:50AM – 2:00PM  **LUNCH BREAK (on your own)**
2:00 – 3:00PM  **Data Blitz Session II**, *Data Blitz from abstract submissions*
Clinical Trial Updates, 12 minute presentations (3 minutes Q&A):

2:00 – 2:15PM  **Perry Shieh**, UCLA Medical Center
*A Phase 2 clinical trial evaluating the safety and efficacy of SRP-9001 for treating patients with Duchenne muscular dystrophy*

2:15 – 2:30  **Louise Rodino-Klapac**, Sarepta Therapeutics, Inc.
*Safety, β-Sarcoglycan Expression, and Functional Outcomes From Systemic Gene Transfer of rAAVrh74.MHCK7.hSGCB in LGMD2E/R4*

**Additional Blitz Presentations, 10 minute presentations (2 minutes Q&A):**

2:30 – 2:42  **Marcela Cataldi**, Atrium Health
*Combined Ribitol and FKRP therapy for FKRP dystroglycanopathy*

2:42 – 2:54  **Atsushi Asakura**, University of Minnesota
*Inhibition of FLT1 ameliorates muscular dystrophy phenotype by increased vasculature in a mouse model of Duchenne muscular dystrophy*

2:54 – 3:06  **Laura Hagerty**, ReveraGen BioPharma
*Double-blind placebo- and prednisone-controlled clinical trial of vamorolone in DMD*

3:06 – 3:30PM  **BREAK**

**Session VI:**  **Muscle Inflammation In Disease And Therapy**
Chair: Alexis Demonbreun

3:30 – 3:50PM  **Alexis Demonbreun**, Northwestern University
*Annexins in muscle membrane repair*

3:50 – 4:10  **Armando Villalta**, University of California, Irvine
*Regulatory T cells suppress a novel population of fibrogenic macrophages*

4:10 – 4:30  **Melissa Spencer**, University of California, Los Angles
*Cell specific sources of osteopontin/SPP1 drive different target cell responses in the dystrophic niche*

4:30 – 4:50  **Thomas Rando**, Stanford University
*Regulation and prevention of fibroadipogenic degeneration of muscle in aging and disease*

4:50 – 5:10  **Chady Hakim**, University of Missouri
*Local and systemic AAV CRISPR therapy induces Cas9-specific immune responses in the canine model of Duchenne muscular dystrophy*
Thursday, July 1, 2021

7:30AM  Continental breakfast served in Crystal Ballroom

Session VII:  Hypoxia And Metabolism As Drivers Of Disease

All sessions in Crystal Ballroom

Chair: DeWayne Townsend

8:00 – 8:20AM  DeWayne Townsend, University of Minnesota
Effects of hypoxia in dystrophic cardiomyopathy

8:20 – 8:40  Jackie McCourt, University of California, Los Angeles
Extracellular matrix remodeling and cell-matrix interactions in DMD-associated cardiomyopathy

8:40 – 9:00  Mattia Quattrocelli, Cincinnati Children’s Hospital Medical Center
Chrono-pharmacology of bioenergetics in the aged muscle

9:00 – 9:20  Giuseppina Caretti, University of Milan
BETs inhibition preserves muscle integrity in a mouse model of Duchenne Muscular Dystrophy

9:20 – 9:40  Clara Bien Peek, Northwestern University
Circadian clock control of muscle stem cell metabolism and muscle regeneration

9:40 – 10:10AM  COFFEE BREAK

Session VIII:  Novel Mechanisms Of Muscle Dysfunction

Chair: Ben Prosser

10:10 – 10:30AM  Jan Lammerding, Cornell University
Myonuclear damage as disease driver of LMNA-related muscular dystrophy and cardiomyopathy

10:30 – 10:50  Pietro Spitali, Leiden University Medical Center
Premature termination codons in the DMD gene cause reduced local mRNA synthesis

10:50 – 11:10  Ben Prosser, University of Pennsylvania
Microtubules orchestrate local translation to enable cardiac growth

11:10 – 11:30  Orna Halevy, The Hebrew University of Jerusalem
Halofuginone enantiomers in muscle fibrosis and histopathology in Duchenne muscular dystrophy

11:30 – 11:50  Jeffery Molkentin, Cincinnati Children’s Hospital
Deletion of skeletal muscle satellite cells attenuates muscular dystrophy pathogenesis

11:50 – 12:00  Closing Remarks

12:00PM  Adjourn

Thank you for your participation in our program, we look forward to seeing you in Ft. Lauderdale, FL June 20-23, 2022 for the next New Directions Conference!