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Stanford Neuromuscular Research Program Newsletter: Issue 9

November 2023, Message from Dr. John W. Day

We thank you for participating in Stanford's Neuromuscular Database. Our newsletter addresses updates on progress during the last year and preparations for future advances. The Database is essential for research studies, drug trials, and community conferences. Over the years we have enrolled more than 2200 people affected by neuromuscular disorders, run ~150 studies, and contributed to the community with annual conferences, educational sessions, and support groups. Stanford's Division of Neuromuscular Medicine has published more than 21 articles this year and presented scientific findings at many national and international conferences. Progress in neuromuscular research is only possible with your ongoing participation - we greatly appreciate your continued involvement and support.

The last year created excitement throughout the neuromuscular world as the FDA followed-up on the success of antisense technology initially proven effective in Spinraza for treating SMA, by approving the related treatment, Qalsody, for ALS, and also built on another success for SMA, Zolgensma, the first systemic Gene Therapy, by approving Elevidys for Duchenne muscular dystrophy. Skyclarys, the first FDA-approved treatment for Friedreich's ataxia, works differently and may benefit other neuromuscular disorders. We are excited to use these successes as guides for ongoing trials of comparably revolutionary treatments that will stop the progression of many other neuromuscular disorders.

Furthermore, the impact of the SMA model continues to lay the groundwork for other neuromuscular disorders as we work to conquer unmet needs in patients who have had progression of their disease halted. We are identifying causes of residual weakness and fatigue and developing complementary treatments that rebuild strength and stamina in patients treated with Spinraza, Zolgensma, or Evrysdi. In order to explore and validate optimal use of these supplementary treatments we are developing novel methods to characterize muscle structure and function in every muscle of the body.

Contributions to the Stanford Neuromuscular Biobank help support and participate in explorations at Stanford and around the world using Stanford Neuromuscular Biobank samples many of you donated. Many labs are using muscle, blood and spinal fluid specimens, which we continue to collect, to better define neuromuscular conditions and identify therapeutic targets. Esteemed researchers at Stanford and around the world are expanding knowledge of neuromuscular conditions and identifying treatments. If you want to learn more about the Neuromuscular Biobank and how to contribute, please contact us at:

Website: med.stanford.edu/day-lab/biobank
Phone: 650.497.9807
Email: StanfordBiobank@lists.stanford.edu

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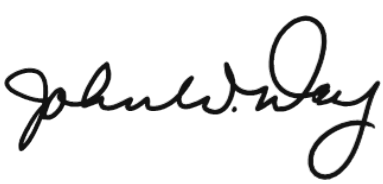
November 2023 Message from Dr. John W. Day (continued)

We are thrilled to update you on investigator-initiated studies led by Dr. Tina Duong, Director of Clinical Outcomes Research and Development. These studies are at the forefront of our commitment to advancing the understanding of neuromuscular diseases through innovative approaches.

- **Quantification of Physical Activity and Kinematics of Movement**: Our collaboration with Dr. Scott Delp's engineering team has yielded significant progress, with valuable kinematic insights gained in FSHD, DM, SMA, and other disorders thus far
- **Measurement of Aerobic Capacity and Fatigue**: Having developed a method to assess endurance in non-ambulatory and ambulatory individuals in collaboration with Drs. Euan Ashley's and Matt Wheeler's labs, we are now exploring recovery and biomarkers of physical fitness and cardiorespiratory health and response to exercise and treatment
- **Wearable Technology to Measure Movement and Physical Activity**: Our collaboration with Syde and Actigraph technology continues, aiming to establish correlations with timed function tests and develop specific algorithms that better reflect patients' daily lives
- **Hand Myotonia Assessment**: Ongoing assessments of hand myotonia measures will soon be published, comparing wearable and video technology to traditional video hand opening tests
- **Muscle Imaging and Histology for Disease Characterization and Treatment Discovery**: An exciting collaboration with Springbok on whole-body imaging enables a deeper understanding of muscle architecture changes that are then being characterized with biopsies that are processed with new microscopic imaging methods
- **Brain Imaging and Neuropsychological Testing**: Brain MRIs and new machine learning approaches are being employed to identify unique connections between neurological changes in the brain and cognition

These endeavors mark significant strides in the field of neuromuscular research. We extend our appreciation to all involved, from researchers and collaborators to the invaluable patients contributing to the progress of medical science.

Sincerely,



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Research programs organized by condition:

The following is a list of active studies, with many additional studies about to be initiated or in late stages of planning to start in the very near future

All Neuromuscular Conditions

- Recruitment Database: Enrolling people with neuromuscular conditions into a database for recruitment to upcoming studies (recruiting)
- Biobank: Enrolling people with neuromuscular conditions who are interested in donating biological samples (recruiting)
- Exercise tolerance study: Observational study to assess aerobic capacity for people ≥9 years old with Neuromuscular Disorders (recruiting)
- MDA MOVR registry of an expanding number of neuromuscular conditions (recruiting in clinic soon)
- A6Mct: Testing the feasibility and efficacy of the 6 minute assisted cycle test in non-ambulatory neuromuscular patients (recruiting)
- ATEND: Adapted motor scale to assess individuals in wheelchairs (recruiting in clinic)
- OpenCAP: Video technology to assess timed function tests and gait movement quality (recruiting)

Amyotrophic Lateral Sclerosis (ALS)

- Biogen ALSpire: Drug trial testing safety and efficacy of BIIB105 adults with ALS (enrollment closed)
- CReATe CAPTURE: Observational study of patients with ALS (recruiting in clinic)
- Ionis: Testing safety and efficacy of ION363 in people with FUS ALS ages 12-65 years old (recruiting)

Charcot-Marie Tooth (CMT)

- Observational study of symptoms, progression, and genetics of CMT (recruiting in clinic)
- CMT4J natural history study leading toward Elpidatx genetic trial (recruiting soon)

Cystinosis Myopathy

- Natural history and MRI studies of adults with Cystinosis myopathy (recruiting)

Duchenne Muscular Dystrophy (DMD)

- PPMD registry (recruiting in clinic)
- Avidity EXPLORE 44: Drug trial testing safety and efficacy of AOC1044 males ages 7-24 with specific DMD mutations (recruiting)
- REGENXBIO AFFINITY DUCHENNE: Gene therapy trial testing safety and efficacy of RGX-202 in ambulatory boys ages 4-11 with DMD (recruiting soon)
- Sarepta ENDEAVOR: Gene therapy trial testing safety and efficacy of SRP-9001 in boys age 8-18 (enrollment closed)
- Sarepta EMBARK: Gene therapy trial testing safety and efficacy of SRP-9001 in boys with DMD (enrollment closed)
- Sarepta ENVISION: Gene therapy trial testing safety and efficacy of SRP-9001 in boys with DMD (recruiting)
- Stanford: Wearable Technology to Assess Gait Function in SMA and DMD (recruiting in clinic)

Facioscapulohumeral Dystrophy (FSHD)

- MOVE-FSHD: Observational study of natural history (recruiting)
- Avidity FORTITUDE: Testing safety and efficacy of AOC-1020 in adults with FSHD (recruiting)

GNE Myopathy

- Observational and MRI study of adults with GNE myopathy preparing for genetic trial (recruiting)

Limb Girdle Muscular Dystrophies (LGMD)

- COS2: Observational study of adults with LGMD2B (enrollment closed)

Myasthenia Gravis (MG)

- Janssen: Drug trial testing safety and efficacy of Nipocalimab in children with gMG (recruiting)

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Research programs organized by condition: (continued)

Myotonic Dystrophy (DM)

- AMO: Drug trial testing safety and efficacy of Tideglusib in children with congenital DM (enrollment closed)
- Avidity MARINA: Open label extension of AOC1001-CS1 trial (enrollment closed)
- END-DM1: Observational study of symptoms and biomarkers in adults with DM1 (recruiting paused)
- END-DM1 Actigraphy substudy to assess physical activity in DM1 (recruiting paused)
- END-DM1 Covid substudy (recruiting paused)
- Stanford MYOCAP: Digital wearables study to assess walking and hand myotonia (recruiting)
- Stanford: 10 year longitudinal follow-up study of neurological changes in DM1 (invitation only)
- Stanford: Spinal fluid studies to define new measures of neurological change (recruiting soon)

Pompe Disease (PD)

- Audentes FORTIS: Drug trial testing safety and efficacy of AT845, an AAV8 genetic treatment in Late Onset PD (enrollment closed)
- Pompe Registry: Observational study tracking outcomes of people with PD (recruiting in clinic)

Spinal and Bulbar Muscular Atrophy (SBMA)

(also known as Kennedy's Disease)

- AnnJi: Drug trial testing safety and tolerability of AJ201 in adults with SBMA (recruiting)

Spinal Muscular Atrophy (SMA)

- AveXis: Long term extension of gene therapy trials (enrollment closed)
- Biogen ASCEND: Drug trial testing safety and efficacy of higher dose nusinersen in patients previously receiving risdiplam (recruiting)
- Biogen DEVOTE: Drug trial testing safety and efficacy of high dose of nusinersen (enrollment closed)
- Biogen ONWARD: Drug trial testing high dose safety and efficacy (invitation only)
- Biogen RESPOND: Drug trial testing safety and efficacy of nusinersen in patients who previously received Zolgensma (recruiting)
- CureSMA registry (recruiting in clinic)
- iSMAC/PNCR: Observational study of patients with SMA, collecting samples, medical history, and tracking progression (recruiting in clinic)
- Roche: Drug trial of RO7034067 SUNFISH (age 2 to 25) and JEWELFISH (ages 6 mo to 60 yrs) (enrollment closed)
- Scholar Rock ONYX: Long term extension study of SAPPHIRE and TOPAZ participants (recruiting by invitation only)
- Scholar Rock TOPAZ: Drug trial testing safety and efficacy of SRK-015 in SMA (enrollment closed)
- Stanford Adult SMA exploratory ("ASE") study: Observational study and MRI of adults with SMA clinically treated with nusinersen or risdiplam (recruiting in clinic)

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