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Stanford Neuromuscular Research Program Newsletter: Issue 8

December 2022, Message from Dr. John W. Day

We thank you for joining our Neuromuscular Database and are writing to update you on our progress during the last year. The Database is essential for research studies, drug trials, and community conferences. Over the years we have enrolled more than 2000 people affected by neuromuscular disorders, run ~142 studies, currently have 58 active studies, and continue with community outreach through annual conferences, educational session, and support groups. The Stanford neuromuscular research division has published more than 25 articles this year and presented scientific findings at many national and international conferences. Progress in neuromuscular research is impossible without the ongoing support of participants and their families, and we greatly appreciate your continued involvement in our research.

The previous year held a lot of excitement for our clinic and research teams as we increased use of FDA-approved drugs for various neuromuscular conditions, as well as welcomed new FDA approvals of Vyvgart, Ultomiris, and Soliris for generalized myasthenia gravis, and Relyvrio for ALS. As our understanding of neuromuscular conditions, and their response to newly available treatments grows, so too does our focus on optimizing each individual's abilities. Complementary and supplementary experimental treatments are being explored, including regenerative approaches working in concert with FDA-approved treatments. The next generation of treatments are also being explored in conditions currently without treatments available, including next-generation antisense approaches using novel antisense chemistries and ligand-conjugated antisense, AAV gene replacement, novel monoclonal antibodies and small molecule therapeutics directed at novel genetic mechanisms.

Additionally, our repository of specimens from SMA, myotonic dystrophy, Duchenne, ALS and other neuromuscular disorders continues to provide a unique resource for investigators around the world to better understand disorders, develop outcome measures and biomarkers, generate and validate novel forms of treatment and characterize the clinical effects of genetic treatments. Requests for repository specimens have greatly increased from academicians and industry during the last year, and we are now working with Dr. Jody Hooper, recently recruited from Johns Hopkins University to be Director of Stanford Autopsy Services, to grow our available resources and learn more about these conditions and the response to novel treatments. We invite anyone with a neuromuscular condition themselves, or in their family, to please check out our Biobank website and then to call us, or email us for more information about how to donate biological tissues for research.

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December 2022 Message from Dr. John W. Day (continued)

We are also excited to share updates on investigator-initiated studies led by our new director of clinical outcomes research and development, Tina Duong. We are integrating novel technology and statistical modeling to characterize neuromuscular disease through a deeper understanding of motor function, muscle imaging and histology to advance trial readiness and design.

- Quantification of physical activity and kinematics of movement: Collaborating with Dr. Scott Delp's team to determine feasibility of video technology to measure muscle force and movement quality
- Measurement of aerobic capacity and fatigue: We have developed a method to measure cardiopulmonary exercise capacity for individuals across the spectrum of muscle weakness to understand exercise capacity. This allows us to better understand physical activity and exercise, and provide more precise exercise recommendations
- Wearable technology to measure movement and physical activity: We are using actimyo and actigraph technology to determine correlations of movement with timed function tests in the clinic and at home
- Hand Myotonia Assessment: We are refining current measures of hand myotonia with video technology using novel machine learning approaches to quantify hand opening time
- Muscle imaging and histology for characterization of disease and treatment discovery: We are performing whole body imaging and muscle biopsies alongside extensive motor function assessments and exercise testing for a more personalized approach to understanding disease progression
- Brain imaging and neuropsychological testing: We are performing brain MRIs and applying new machine learning approaches to identify unique connections between neurological changes in the brain and cognition

Thank you for joining the Stanford Neuromuscular Recruitment Database, and best wishes to you and your family for a safe and productive year.

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 with Neuromuscular Disorders (recruiting)
- MDA MOVR registry of some neuromuscular conditions (recruiting in clinic)
- 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 the wheelchair (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 (recruiting)
- CReATe CAPTURE: Observational study of patients with ALS (recruiting in clinic)
- Cytokinetics COURAGE: Drug trial testing safety and efficacy of Reldesemtiv in patients with ALS (recruiting)
- Ionis: Drug trial testing safety and efficacy of ION363 in people ages 12-65 with FUS ALS mutations (recruiting)
- Stanford: Collecting blood or saliva DNA from clinic patients with ALS from Stanford and other local participating clinics (recruiting in clinic)

Charcot-Marie Tooth (CMT)

- Observational study of symptoms, progression, and genetics of CMT (recruiting in clinic)

Duchenne Muscular Dystrophy (DMD)

- PPMD registry (recruiting in clinic)
- 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 soon)
- Stanford: Wearable Technology to Assess Gait Function in SMA and DMD (recruiting in clinic)

Facioscapularhumeral Dystrophy (FSHD)

- MOVE-FSHD: Observational study of natural history (recruiting paused)

GNE Myopathy

- Observational study of adults with GNE myopathy (recruiting)

Limb Girdle Muscular Dystrophies (LGMD)

- COS2: Observational study of adults with LGMD2B, measuring symptom progression (enrollment closed)

Myasthenia Gravis (MG)

- Alexion: Drug trial testing safety and efficacy of ALXN2050 in adults with generalized MG (recruiting)
- Janssen: Drug trial testing safety and efficacy of Nipocalimab in children with gMG (recruiting)
- Momenta: Drug trial testing safety and efficacy of Nipocalimab in adults with gMG (recruiting)
- Momenta: Open label extension of Nipocalimab trial (enrollment closed)

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Research programs organized by condition: (continued)

Myotonic Dystrophy (DM)

- ASPIRE: Observational study of infants with congenital DM (recruiting soon)
- AMO: Drug trial testing safety and efficacy of Tideglusib in children with congenital DM (enrollment closed)
- Avidity MARINA: Drug trial testing safety and efficacy of AOC1001-CS1 in adults with DM1 (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: 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-Delivered Gene Transfer Therapy in Patients With Late Onset PD (recruiting paused)
- Pompe Registry: Observational study tracking outcomes of people with PD (recruiting in clinic)

Stanford MYOCAP study examining new technologies to measure hand myotonia in individuals with myotonic dystrophy

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 soon)

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 soon)
- Biogen DEVOTE: Drug trial testing safety and efficacy of higher doses of nusinersen (recruiting only cohort B <7 months old)
- Biogen ONWARD: Drug trial extension testing safety and efficacy of nusinersen (recruiting of previous DEVOTE enrollees, by invitation)
- 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 FIREFISH (age <7 months) and SUNFISH (age 2 to 25) and JEWELFISH (ages 6 mo to 60 yrs) (enrollment closed)
- Scholar Rock TOPAZ: Drug trial testing safety and efficacy of SRK-015 in SMA (enrollment closed)
- Scholar Rock SAPPHIRE: Drug trial testing safety and efficacy of SRK-015 in later-onset SMA receiving background nusinersen or risdiplam therapy (recruiting)
- Stanford Adult SMA exploratory ("ASE") study: Observational study of efficacy and exploratory endpoints and biomarkers in clinically treated nusinersen patients (recruiting in clinic)