The Hospital for Sick Children
Division of Neurology – Neuromuscular Department
Neuromuscular Teaching Program

Introducción:

The Paediatric Neuromuscular Fellowship Program at The Hospital for Sick Children is a one-year fellowship, with the possibility of extension to a second year. The program is designed to provide excellence in diagnosis and management of paediatric neuromuscular disorders. At the conclusion of the fellowship, trainees will have acquired profound knowledge in genetics/molecular biology, EMG/NCVs, Neuromuscular imaging (MRI, CT), pathology, and rehabilitation in neuromuscular disorders. The fellowship will also provide an opportunity to be part of different clinical trials, with a focus in gene therapy.

We have a variety of different specialized multidisciplinary clinics such as the Spinal Muscular Atrophy clinic and a joint genetics-neuromuscular clinic. Trainees will be also be exposed to adult neuromuscular clinics since we consider it especially important to have exposure to the whole spectrum of this group of disorders. Upon completion the trainee will be eligible to take the CSCN EMG board examination.

Our neuromuscular program has a strong educational commitment as well as a strong clinical and translational research collaboration with different departments across the hospital. Although this is mainly a clinical fellowship, we will encourage the trainee to be involved in clinical or translational research as well. We strongly believed that the combination with translational research provides a unique vision that will enhance the knowledge and understanding of the diagnosis and treatment on neuromuscular disorders.

Our patient population varies but around 70% of them has a genetic condition and the rest are acquired. Thus, our fellowship has a strong genetics component. We currently are running a multi-disciplinary SMA clinic coordinate by Eugenia Law and Elisa Nigro that we expect the trainee will be participate.

Fellows Duties and Responsibilities

During each week, fellows will be participating in 3 neuromuscular clinics supervised by Dr. James J Dowling, Jiri Vajsar and Hernan D. Gonorazky. There is a monthly joint genetics neuromuscular clinic run but Dr. Dowling and Dr. Grace Yoon. After mastering the basic principles of EMG, each fellow will be expected to run their own supervised EMG clinic (once a week). Trainees will be participating in biweekly EMG rounds, alternate with neuromuscular pathology learning sessions. We hold bimonthly neuromuscular pathology rounds with all the neuromuscular staff where we review and discuss different pediatric cases. Fellows will be encouraged to prepared monthly journal clubs and teaching sessions that includes weekly meeting with our genetic counselor Kim Amburgey for interpretation of genetics results.

Trainees will have the opportunity to rotate in adult EMG clinic under the supervision of Dr. Aaron Izenberg, at Sunnybrook Hospital, Neuromuscular rehabilitation clinic supervised by Dr. Laura Mcadam at Bloorview Rehabiliation Center, Neurogenetic rotations with Dr Grace Yoon, Genetic laboratory at SickKids Hospital with Dr James Strapovolous for interpretation of genetic studies, Neuropathology rounds with Dr. Lili Naz Harati .

Trainees are expected to attend and give presentations at Sickkids grand rounds and at National and International meetings.

Evaluation of the fellows will done every three months in person and in writing by the program director with the guidance and feedback of the rest of the neuromuscular team.

There are **two** positions per year with different start dates (July to June and January to December).

The successful candidate must demonstrate:

1. Completion of residency in neurology/child neurology or PhD in relevant field.

3. Fluency in both spoken and written English

4. Completion of a successful interview with the neuromuscular team (face to face or online)

Qualified applicants are encouraged to obtain funding to secure a spot in the fellowship program. Interested candidates should email a curriculum vitae, a letter of interest, three reference letters with names and contact information to **abigail.tungul@sickkids.ca.** A neuromuscular fellowship curriculum is available upon request.

Objective: Neuromuscular medicine didactic lectures series encompasses knowledge of the pathophysiology, pathology, diagnosis, and treatment of these disorders At the end of this session, participants will be able to acquire knowledge of the basic science and clinical diagnosis and management of the following neuromuscular disorders with focus on the pathophysiology of the different disorders and understanding their relation with genotypic and phenotypic forms. Students must understand the normal function of molecules and how its alteration affects the normal functioning of the neurons in the peripheral nervous system, the nerves, the neuromuscular junction or in the muscle.

Neuromuscular Team
Dr. Hernan D. Gonorazky Neurology, Neuromuscular Fellowship Program Director Hospital for Sick Children
Dr. James J. Dowling Neurology, Translational Research PI Hospital for Sick Children
Dr. Jiri Vajsar Neurology Hospital for Sick Children
Dr. Grace Yoon Staff Neurogenetics Hospital for Sick Children
Kim Amburgey Genetic Counsellor Hospital for Sick Children
Lynn Macmillan nurse coordinator Hospital for Sick Children
Eugenia Law Nurse, Coordinator SMA program Hospital for Sick Children
Elisa Nigro, Nurse practitioner, SMA program Hospital for Sick Children
Dr. James Stavropoulos Clinical Lab Director Genetics
Dr. Lili-Naz Hazrati Neuropathology Hospital for Sick Children
Dr. Cynthia Hawkins Neuropathology Hospital for Sick Children
Dr. Aaron Izemberg Adult Neurology Sunnybrook Hospital
Dr. Laura Mcadam Physiatrist Bloorview rehabilitation Center

Length of the Teaching Program: Beside the activates previously describe, we will be running a 1 year teaching program that will be given in weekly basis by the fellows for the fellows with master classes given by the staff. .

Schedule: appointment every Monday from 12:00 to 13:30 pm. Lectures will be assigned one month before.

Lectures structure: it is recommended that every talk begin with an introduction, a historical and epidemiology overview of the disease, follow by a thoughtful explanation of the biochemical, the molecular basis and the pathophysiology of the disease, beginning with the normal functioning and correlating the genotype with its phenotype in the genetic disorders.
In the module of the motor neuron disorders students must describe the genetics forms and sporadic disorders. A comprehensive description of the genetic mechanisms in Spinal Muscular Atrophy must be made in order to understand the different phenotypes and new therapeutic targets.
In the module of neuropathies, we will focus in the dysimmune neuropathies, its underlying autoimmune mechanism and its association with the antibodies described so far. In the hereditary neuropathies, describe the different genetic forms and how they should be interpreted in the context of the nerve conduction studies.
In the neuromuscular junction disorders the students should understand why different locations of alterations on the neuromuscular plate are associated with different clinical pictures and therapeutic responses.
In the myopathies lectures the student should focus on specifically about the function of the affected protein and how it affects the normal muscle resulting in a structural or functional alteration. The clinical description and prognosis of the different phenotypes of neuromuscular diseases should be explained from the understanding of the physiopathology, as well as the complementary tests required in each case. Finally, there will be a review of conventional treatments and new therapeutics that will be of clinical relevance in the future.

Module 1: Introduction

1) EMG and NCS approach.
2) Neuromuscular imaging.
3) Introduction to Neuropathology.
4) Introduction to Neuromyogenetics.
5) Floppy baby. Arthogryposis.
6) Approach to the infant and adolescent patient with NMD.

Module 2: Anterior horn cell and cranial motor neuron diseases

7) Classical 5q-SMA. (SMN1 gene, SMN2 gene, molecular basis, diagnosis, clinical features, classification and prognosis).
8) New therapies in 5q SMA (Nusinersen, Zolgensma, Risdiplam, others).
9) Atypical forms SMA. X linked bulbospinal muscular atrophy (Kennedy disease).
10) Hereditary bulbar palsy (with/without deafness - Fazio Londe Syndrome and Brown–Vialetto–Van Laere syndrome). Others LMN disorders (Hexosaminidase deficiency (Tay Sachs disease), MMN, post-polio syndrome, Hopkin´s syndrome, monomelic SMA, post-irradiation syndrome). UMN disorders (PLS, HSP, Neurolathyrism, Konzo).
11) ALS sporadic and hereditary forms (adult onset and juvenil onset).

Module 3: Disorders of peripheral nerves and spinal nerve roots

12) Dysimmune neuropathies (AIDP and variants, CIDP).

13) Toxic and metabolic neuropathies (heavy metals, drugs, diabetes). Small fibers neuropathies (Fabry disease and FAP).
14) Hereditary motor and sensory neuropathy I.
15) Hereditary motor and sensory neuropathy II.
16) Focal neuropathies. Acquired plexopathies.

Module 4: Neuromuscular junction disorders

17) Congenital Myasthenic Syndrome (CMS) I. Development and physiology of the neuromuscular junction.
18) CMS II (presynaptic and synaptic disorders: ChAT, COLQ).
19) CMS III (postsynaptic disorders: CHRNE or RAPSN, DOK7).
20) Acquired neuromuscular junction disorders (Myasthenia gravis, neonatal myasthenia gravis, botulism, Lambert-Eaton syndrome).

Module 5: Muscle ion channels and calcium disorders

21) Membrane potential at rest. Chanelopathies / Non dystrophy myotonic syndromes (myotonia congenita, paramyotonia congenita, sodium cannel myotonias).
22) Myotonic dystrophies (DM1/Steinert and DM2/PROMM).
23) Calcium metabolism and release. Excitation contraction coupling (RYR1, SERCA1, DHPR1, MTM1, DNM).
24) Calcium homeostasis - Tubular aggregate myopathy (SEPN1, STIM1, ORAI1)

Module 7: Metabolic myopathies

25) Metabolic myopathies I (glycogen metabolism disorders).
26) Metabolic myopathies II (lipid metabolism disorders).
27) Mitochondrial disorders I.
28) Mitochondrial disorders II.

Module 6: Sarcomere myopathies and muscle fiber cytoskeleton

29) Thick filaments (myosin myopathies and titinopathy myopathies).
30) Thin filaments (actin, tropomyosin, troponins, and nebulin).
31) Muscle fiber cytoskeleton I (vinculin, talin, α-actinin, and β1 integrins). Myofibrillar myopathies (desmin, myotilin, CRYAB, filament C, BAG3, FHL1, DNAJB6, plectin, ZASP).
32) Muscle fiber cytoskeleton II Z-line alterations (ACTN, LIM, NEB).

Module 6: Structural myopathies, sarcolemma and extracellular space

33) Extracellular matrix and sarcolemma proteins (merosin deficency / laminin-2, sarcoglycanopathies, dystroglicanopathies (FKRP, POMT1, Fukutin, POMT2, POMGnT1), collagenopathies (COL-XII, COL-VI).
34) Dystrophinopathies I (DMD gene and dystrophin, molecular basis, related proteins, revertant fibers, clinical features and conventional treatment).
35) Dystrophinopathies II (new treatments and future perspectives).
36) Sarcolemma repair (caveolin-3, anocatamin-5, dysferlin, myotubularin, dynamin-2, amphiphysin-2). Proteins associated with lysosomes and autophagic vacuoles (LAMO-2).

Module 7: Nuclear envelope myopathies

37) Emery-Dreifuss (Lamine A-C, emerin, nesprin, FLH1).

Module 10: Other distrophies, miscellaneous and inflamatory myopathies

38) Facioscapulohumeral (FSHD 1 and 2). Oculopharyngeal muscular dystrophy (OPMD).
39) Inflammatory myopathies (Polymyositis (PM), dermatomyositis (DM), (immune mediated) necrotizing myopathy (NM), overlap syndrome with myositis (overlap myositis, OM) including anti-synthetize syndrome (ASS), and inclusion body myositis (IBM)).
40) Myoglobinopathy
41) Autosomal recessive spinocerebellar ataxia.
42) Autosomal dominant spinocerebellar ataxia.

Module 11 Appendix: Comprehensive classification and general care of NMD.

43) Congenital muscular dystrophies. Congenital myopathies.
44) LGMD 2018. Distal myopathies.
45) Cardiomyology.
46) Management of respiratory complications. Formation pnm recycle ach y union ach/r activation.
47) Orthopedic complications and surgery indications.
48) Nutritional support.
49) Motor measurements and scales in NMD.