FSHD 101 AND OVERVIEW OF RESEARCH IN CANADA

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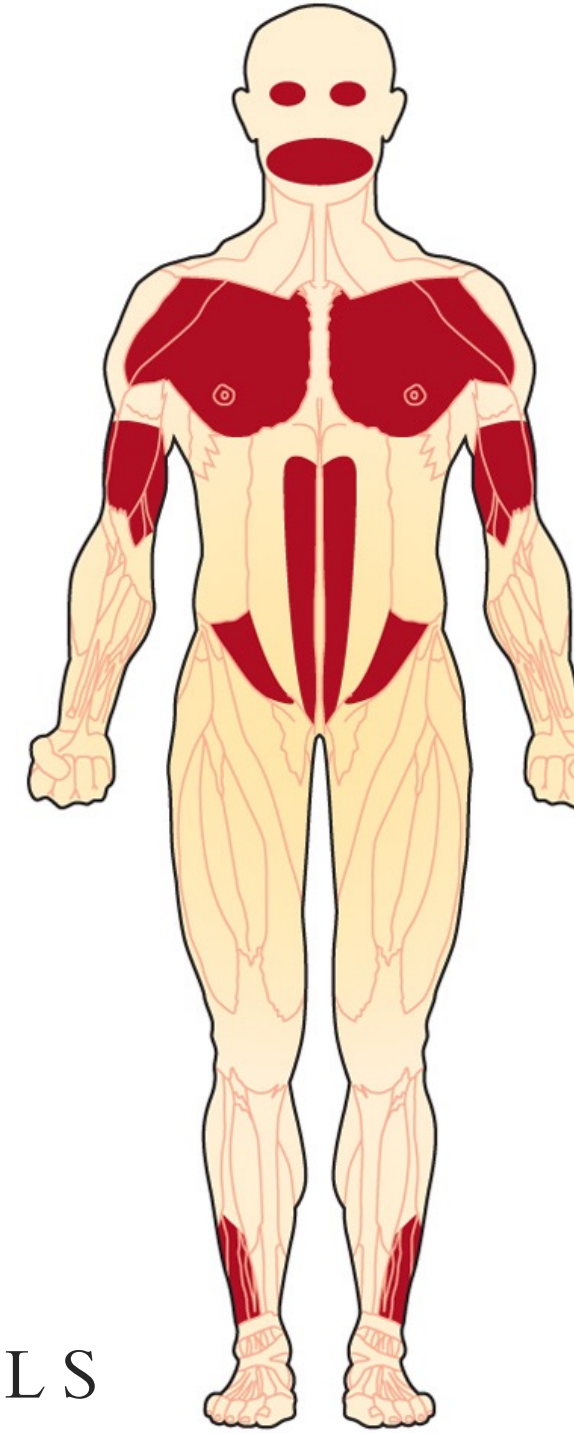
COMMON SIGNS AND SYMPTOMS OF FSHD

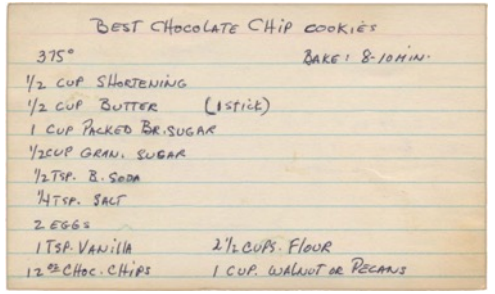
- Decreased or flattened facial expression
- Scapular (shoulder blade) winging
- Inability to lift arms overhead
- Excessive curvature of the low back (lumbar hyperlordosis)
- Inability to lift feet up (foot drop)
- Difficulty walking
- Fatigue

LESS COMMON SIGNS AND SYMPTOMS OF FSHD

- Hearing impairment (usually affecting high pitch sounds)
- Quiet or unclear speech
- Pain
- Vision problems (rare)
- Breathing concerns (rare)
- Heart problems (rare)



Molecular Biology 101



Chromosome → **DNA** → **RNA** → **Protein**

Epigenetic-controlled access → Transcription → Translation

Ways to treat FSHD

Correct the DNA sequence (D4Z4 shortening or mutation)

Block or remove DUX4 RNA

Block or remove DUX4 protein

Chromosome → **DNA** → **RNA** → **Protein**

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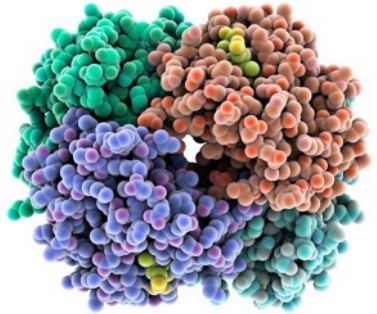
Re-repress access to DUX4 DNA

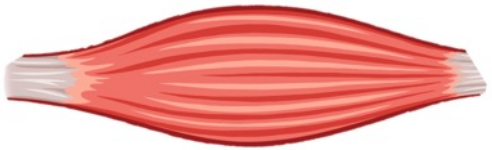
Interfere with DUX4 transcription

Interfere with DUX4 translation

Ways to treat FSHD



DUX4 Protein



Muscle Cell Loss

Stop muscle cell loss

Helps muscles grow or regenerate

FSHD SOCIETY
LIGHTING THE WAY TO A CURE

The CNDR: Who We Are

A Multi-centre, National Collaborative Study

- Clinic-based recruitment & prospective data collection
- Over **5800 patients** registered across all neuromuscular disease
- Initiated 2010; continual growth & expansion

38 NM clinics
14 ALS clinics

136 investigators

Partnership

Bringing together the whole rare disease community

PROJECT MERCURY

GLOBAL TASK FORCE MEETING

BANFF, CANADA

FSHD SOCIETY
LIGHTING THE WAY TO A CURE

fshdcanada.org

PROJECT MERCURY
The Global Initiative to Speed the Delivery of Therapies for FSHD

Acceleron Clinical Trial in FSHD

We had the highest number of participants globally

Leadership Team

Dr. Toshifumi Yokota, PhD
Chief Scientific Officer
Co-Founder

Dr. Lawrence Korngut, MD
Chief Medical Officer
Co-Founder

Dr. Rika Maruyama, PhD
Chief Development Officer
Co-Founder

Jeff Miller
Chief Executive Officer

Dr. Toshifumi Yokota, PhD & Dr. Rika Maruyama, PhD – Yokota Labs

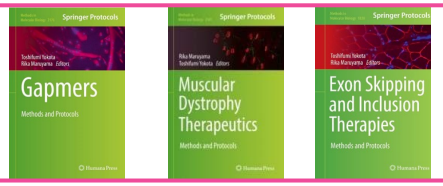
- Pioneering research has led to significant advancements in the treatment of muscular dystrophy including the development of viltolarsen, an FDA-approved ASO drug for the treatment of Duchenne Muscular Dystrophy (DMD)
- Lead Yokota Labs at the University of Alberta, where their team has published >100 papers in respected scientific journals including a recent DMD breakthrough that made international headlines
- Co-edited three books addressing therapeutic approaches to treating muscular dystrophies
- Prolific in fundraising, attaining >60 research grants and >CAD$30 million in competitive funding
- Honored with several awards, notably as a Fellow of the Canadian Academy of Health Sciences (FCAHS) — one of Canada's pinnacle recognitions for researchers. Also bestowed with the Alberta Scientific Achievement and Innovation Award, NIH's Ruth L. Kirschstein NRSA, and entrusted with prominent research chairs like the Friends of Garrett Cumming Research & Muscular Dystrophy Canada Endowed Research Chair, and HM Toupin Neurological Science Endowed Research Chair

Dr. Lawrence Korngut, MD

- Neurologist with extensive experience in clinical trial execution and design, having participated in >90 trials over the course of his career
- Specializes in design of clinical development programs/conduct of clinical trials for new therapies in different muscle and nerve diseases
- Has >60 publications in peer-reviewed journals and has advised a multitude of pharmaceutical companies in the clinical development process from pre-clinical through to regulatory and health technology assessment
- Expert review panel member for Health Canada and Canadian Agency for Drug & Health Technology (CADTH)
- Assists SOLVE FSHD, an organization focused on the development, validation and clinical evaluation of biomarkers that predict clinically meaningful outcomes measures for clinical trials in FSHD

Viltepso® (viltolarsen) injection

bio alberta 1998-2023 25
Association for Life Sciences Industry



OligomicsTx Addresses Key Unmet Needs

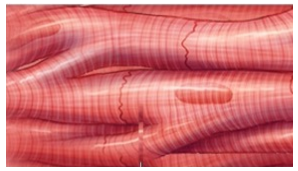
Current RNA-targeted therapies are inefficient due to unoptimized treatment sequences and lack of delivery conjugates;
Result: lack of efficacy and target tissue penetration, leading to accumulation of ASOs in the liver and kidneys

For diseases with high unmet needs, OligomicsTx delivers innovative, optimized drugs (sequences) combined with optimized novel delivery vehicles, enabling drug delivery to critical parts of the body - leading to transformational health outcomes

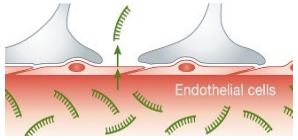
Existing RNA-targeted therapies are not optimized. Unoptimized sequences lack effectiveness, don't address disease progression, interfere with other treatments, lack safety and tolerability, and require highly invasive procedures

Ineffective delivery in RNA-targeted therapies hinder efficient transport, compromise stability, limit cellular penetration, result in non-specific delivery, and ultimately reduce the therapeutic efficacy of the treatments

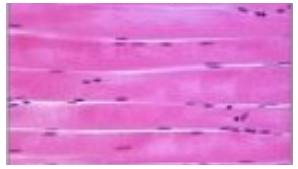
Heart
Lack of penetration, almost 0%



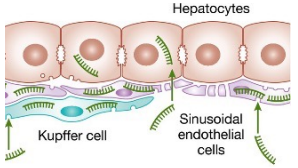
Brain
ASO cannot penetrate blood-brain barrier



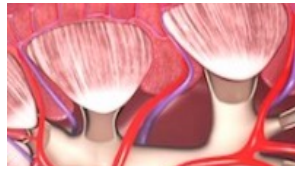
Skeletal Muscles
Lack of penetration in skeletal muscles



Liver
Up to 40-50% of ASOs accumulate in the liver



Kidney
Up to 40-80% of ASOs accumulate in the kidneys



Network Grant

2023-2028

NMD4C

NEUROMUSCULAR DISEASE NETWORK FOR CANADA 2023–2028

Addressing the Translational Research Pathway

DISCOVERY SCIENCE
Grow pre-clinical research capacity by sharing research protocols and expertise, improving access to biomaterials, and training in cutting-edge technologies across cell and animal models.

TRANSLATION TO HUMANS
Build a Canadian neuromuscular clinical trial network to improve trial and recruitment infrastructure, working with trial sites to share and develop clinical trial resources.

TRANSLATION TO PATIENTS
Improve efficacy of trials by standardizing outcome measures that allow demonstration of therapeutic efficacy, working with patient registries to collect data, and collating natural history study research.

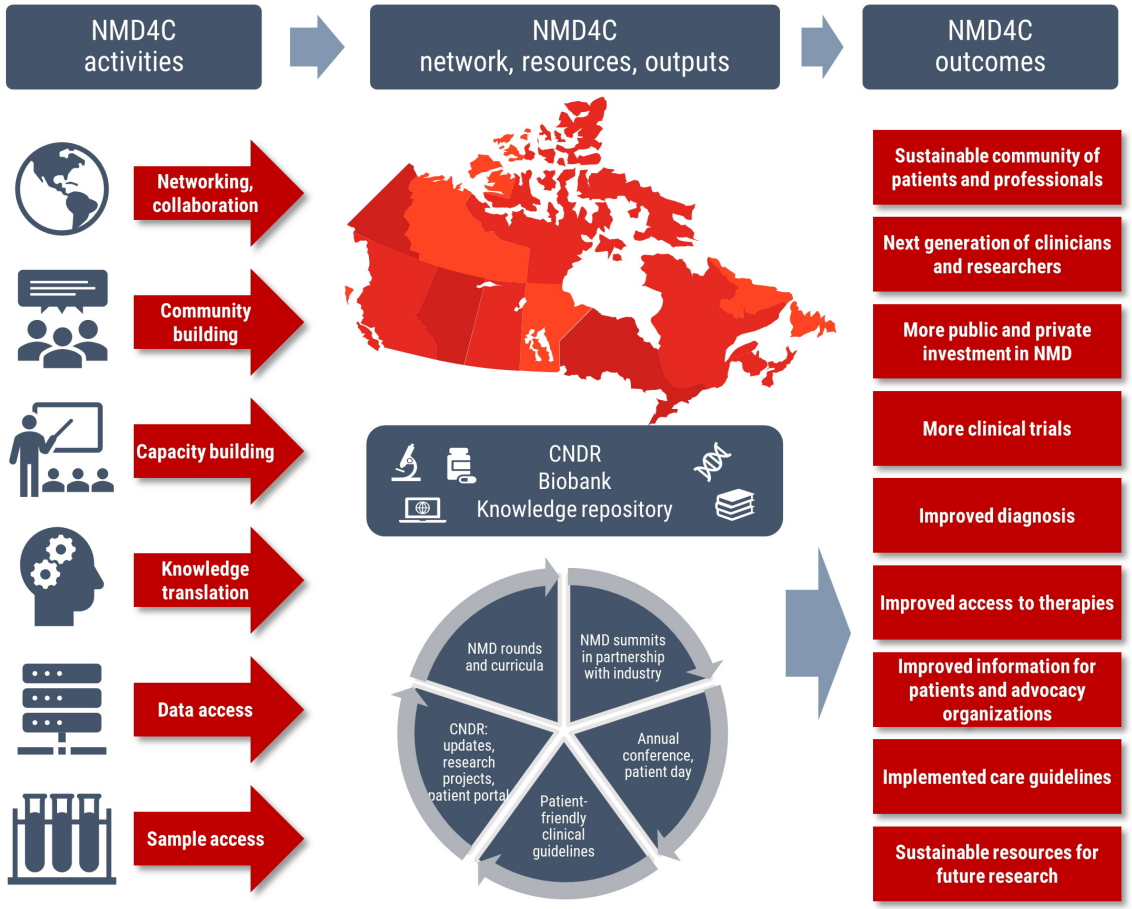
TRANSLATION INTO PRACTICE
Facilitate a community of practice for best-practice sharing for all members of the NMD clinical care community and provide education on emerging knowledge and tools to NMD specialists.

TRANSLATION TO COMMUNITY
Provide guidance on real-world evidence on NMDs for health policy and funding decision-makers by leveraging clinical and research outcomes to advocate for data-driven access to novel therapies.

MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

CIHR IRSC | Institute of Musculoskeletal Health and Arthritis | Institut de l'appareil locomoteur et de l'arthrite

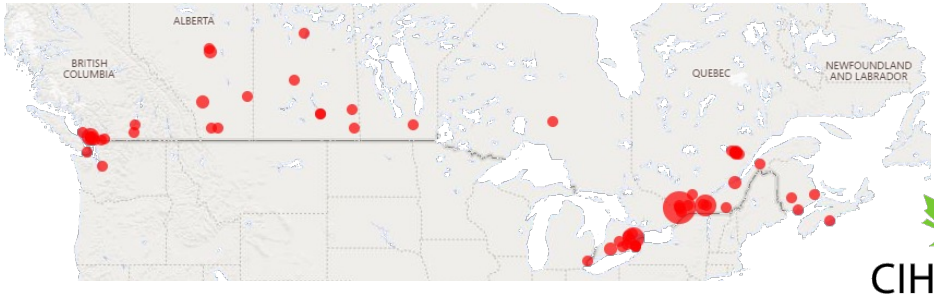
Neuromuscular Disease Network for Canada (NMD4C)



- A pan-Canadian network that brings together the country's leading clinical, scientific, technical, and patient expertise to improve care, research, and collaboration in neuromuscular disease
- Launched in January 2020 with funding from the CIHR and Muscular Dystrophy Canada

478 members

377 clinicians & researchers
58 patients & family
24 industry



MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Unwilling to Let Muscular Dystrophy Beat Him, Lululemon Founder Commits $100M to Research

Published: Mar 09, 2022 | By Vanessa Doctor, RN

BioSpace®

- $100M commitment from Chip & Summer Wilson
- Commitment focused on innovative new approaches to treat FSHD
- Embracing a Team Science approach

  Example: Collaborative Research Awards

Plan

Remove barriers and accelerate development of novel therapies for FSHD.