Roadmap 2 Rare

Muscle Disorders Panel – Roadmap2Rare Diagnostics Program

As part of Sanofi Canada's sponsored Roadmap2Rare Diagnostic Program, an expanded **122-gene** muscle disorders (MD) panel is available at **no charge** to facilitate differential diagnosis of various muscular and neuromuscular diseases, including Pompe disease. This testing is made available in collaboration with PerkinElmer Genomics.

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This next-generation sequencing (NGS) testing is offered at no-charge and with complimentary genetic consultation/results interpretation for clinicians; genetic counselling for patients is also available. Clinicians can collect specimens with complimentary saliva swab kits or have PerkinElmer mail kits directly to patients for self-collection.

Genetic testing criteria

To be eligible for testing on the panel, patients need to show laboratory evidence suggestive of a muscle pathology (i.e. EMG, CK, muscle biopsy, MRI), in addition to at least one of the following:

- Muscle weakness, or
- Unexplained respiratory insufficiency, or
- Other symptom(s) suggesting muscle involvement (i.e. exercise intolerance, rhabdomyolysis, myalgia)

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The Muscle Disorders Panel includes the following groups of disorders:

- Muscular dystrophies with predominant limb-girdle weakness patterns,
- Congenital muscular dystrophies,
- Rigid spine syndrome,
- Congenital myopathies,
- Inclusion myopathies,
- Congenital myasthenic syndromes,
- Scapuloperoneal syndromes,
- Metabolic myopathies

For more information about the Roadmap2Rare Diagnostic Program services, and to access the MD panel, please visit PerkinElmer Genomics (www.perkinelmergenomics.com/roadmap2rare).

Patient and physician identifying information provided to PerkinElmer Genomics remains confidential and is not shared with Sanofi.

Limb-girdle muscular dystrophy (LGMD) is a heterogeneous group of genetic disorders characterized by progressive muscle weakness involving the shoulder and pelvic girdles.[1] Pompe disease is a life-threatening, progressive neuromuscular disorder that causes progressive, irreversible muscle damage.[2]

From a similar Canadian panel, of all diagnosed patients, more than 36% of patients were diagnosed with an LGMD.[3]

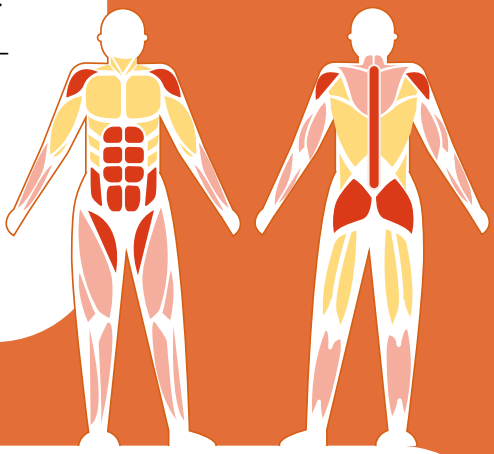
For information about Sanofi Canada's Roadmap2Rare initiatives, visit roadmap2rare.ca.

Proximal muscle weakness

Progressive proximal muscle weakness: the hallmark symptom of Pompe disease[4]

Progressive proximal muscle weakness affects the majority of late-onset Pompe patients.[5]

1. Progressive proximal muscle weakness – especially in lower limbs.[4,5]
2. Respiratory insufficiency because of diaphragm weakness.[6]
3. Mild-to-moderate hyperckemia levels.[6]



>80% of patients 50-80% of patients <50% of patients

Distribution of skeletal muscle weakness in 94 adults with Pompe disease. Adapted from van der Beek.[5]

Though symptoms vary, progressive proximal muscle weakness, with or without respiratory insufficiency or hyperckemia, should raise suspicion of Pompe disease.[6]

Genes included in the Muscle Disorders Panel

GENE
ACTA1
ACTN2
AGRN
ANO5
ATP2A1
B3GALNT2
B4GAT1
BAG3
BIN1
BVES
CACNA1S
CAPN3
CASQ1
CAV3
CCDC78
CFL2
CHAT
CHKB
CHRNA1
CHRNB1
CHRND
CHRNE
COL12A1
COL13A1
COL6A1
COL6A2
COL6A3
COLQ
CPT2
CRYAB
DAG1

GENE
DES
DMD
DNAJB6
DNM2
DOK7
DPAGT1
DPM3
DYSF
EMD
FHL1
FKBP14
FKRP
FKTN
FLNC
GAA
GFPT1
GMPPB
GNE
HNRNPDL
INPP5K
ISPD/CRPPA
ITGA7
KBTBD13
KLHL40
KLHL41
KY
LAMA2
LAMP2
LARGE1
LDB3
LMNA

GENE
LMOD3
LRP4
MEGF10
MTM1
MUSK
MYBPC1
MYF6
MYH2
MYH7
MYO18B
MYOT
MYPN
NEB
ORAI1
PABPN1
PAX7
PFKM
PHKA1
PLEC
PNPLA2
POGLUT1
POMGNT1
POMGNT2
POMK
POMT1
POMT2
PYGM
RAPSN
RBCK1
RXYLT1/TMEM5
RYR1

GENE
SCN4A
SELENON
SGCA
SGCB
SGCD
SGCG
SLC18A3
SLC25A1
SLC5A7
SPEG
STAC3
STIM1
SYNE1
SYNE2
SYT2
TCAP
TMEM43
TNNT1
TNPO3
TOR1AIP1
TPM2
TPM3
TRAPPC11
TRIM32
TRIP4
TTN
VAMP1
VCP
VMA21

For more information about Sanofi Canada's Roadmap2Rare initiatives, and for the full list of genes and associated disorders, visit roadmap2rare.ca.

Or scan the QR code on the right.

References: **1.** Limb-Girdle Muscular Dystrophy. Muscular Dystrophy Canada website. https://muscle.ca/discovermd/types-of-neuromuscular-disorders. Accessed Jan 20, 2020. **2.** Hagemans MLC et al. *Neurology*. 2005;64(12):2139-2141. **3.** Thuriot et al. *Neurol Genet*. 2020;6(2):e408. **4.** Hirschhorn R et al. Glycogen storage disease type II: acid alpha-glucosidase (acid maltase) deficiency. In: Scriver CR et al, eds. *The Metabolic & Molecular Bases of Inherited Disease.* 8th ed. New York, NY: McGraw-Hill; 2001:3389-3420. **5.** van der Beek N et al. *Orphanet J Rare Dis.* 2012;7:88. **6.** American Association of Neuromuscular & Electrodiagnostic Medicine. *Muscle Nerve.* 2009;40(1):149-160.

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