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Listes de gènes nationales consensuelles pour le diagnostic génétique de myopathies par NGS établies par la filière FILNEMUS et Répertoire national des laboratoires effectuant l'analyse des listes de gènes par portes d'entrée cliniques/anatomopathologiques respectives

Commission Outils diagnostiques - Sous-groupe Génétique Moléculaire

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Référence bibliographique: "A National French consensus on gene lists for the diagnosis of myopathies using Next Generation Sequencing" European Journal of Human Genetics, 2018

Martin Krahn[1,2 *], Valérie Biancalana[3#], Mathieu Cerino[1,2#], Aurélien Perrin[4,5#], Laurence Michel-Calemard[6], Juliette Nectoux[7], France Leturcq[7], Céline Bouchet-Séraphin[8], Cécile Acquaviva-Bourdain[9], Emmanuelle Campana-Salort[1,10], Annamaria Molon[10], Jon Andoni Urtizberea[11], Frédérique Audic[1,10], Brigitte Chabrol[10], Jean Pouget[1,10], Roseline Froissart[9], Judith Melki[12], John Rendu[13,14,15], François Petit[16], Corinne Metay[17], Nathalie Seta[8], Damien Sternberg[17], Julien Fauré[13,14,15] and Mireille Cossée[4,5]

[1]Aix Marseille Univ, Inserm, MMG, Marseille Medical Genetics - Translational Neuromyology, Marseille, France;
[2]APHM, Hôpital Timone Enfants, Département de Génétique Médicale, Marseille, France;
[3]Laboratoire Diagnostic Génétique, Faculté de Médecine, CHRU, Nouvel Hôpital Civil, Strasbourg, France;
[4]CHRU Montpellier, Laboratoire de Génétique moléculaire, Montpellier, France;
[5]Université Montpellier, Laboratoire de Génétique de maladies rares, Montpellier, France.
[6]HCL, Centre de Biologie et Pathologie Est, UM Pathologies Endocriniennes, Rénales, Musculaires et Mucoviscidose, Bron, France;
[7]APHP, Service de Biochimie et Génétique Moléculaire, Cochin Hospital, Paris, France;
[8]APHP, Hôpital Bichat Claude Bernard, Département de Génétique, Paris, France;
[9]Service Maladies Héréditaires du Métabolisme et Dépistage Néonatal, Centre de Biologie et de Pathologie Est - CHU de Lyon, Lyon, France;
[10]APHM, Hôpital Timone, Centre de référence des maladies neuromusculaires et de la SLA, Marseille, France;
[11]APHP, Hôpital Marin, Centre de compétence neuromusculaire Hendaye, France;
[12]Inserm UMR-1169, Université Paris Sud, Paris, France;
[13]Centre Hospitalier Régional Universitaire de Grenoble, Hôpital Michallon, Biochimie Génétique et Moléculaire, Grenoble, France;
[14]Univ Grenoble Alpes, Grenoble Institut des Neurosciences, GIN, Grenoble, France;
[15]Inserm U1216, Grenoble, France;
[16]Laboratoire de Génétique moléculaire, APHP - GH Antoine Béclère, Clamart, France;
[17]Centre de génétique moléculaire et chromosomique AP-HP, Hôpital Pitié-Salpêtrière, Paris, France.
[#] Contribution égale

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Bilan du travail initié en 2015 pour la structuration des listes de gènes nationales consensuelles, pour le diagnostic génétique de myopathies par Séquençage de Nouvelle Génération

Un objectif majeur fixé dès 2015 par le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques de FILNEMUS a été la mise en place de listes homogènes de gènes pour le diagnostic génétique des myopathies.
Effectivement, l'état des lieux réalisé à l'automne 2015 avait mis en évidence une **grande disparité dans l'offre de diagnostic génétique, complexifiant la visibilité pour les cliniciens prescripteurs**.
Certains laboratoires avaient mis en place l'analyse de **listes restreintes** de gènes, alors que d'autres avaient mis en place l'analyse de **listes étendues**.
Ce choix était lié également à la **disparité dans les équipements et moyens disponibles pour les différentes plates-formes hospitalières** impliquées dans le diagnostic génétique de myopathies, telle qu'elle avait été mise en évidence par l'état des lieux.
Le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques a fait le choix consensuel de **prendre en compte l'état actuel des plates-formes et des listes de gènes existantes comme point de départ pour l'évolution vers des listes nationales consensuelles**.
De ce fait, une stratégie possible qui aurait consisté à établir des listes uniques très larges et exhaustives de gènes impliqués dans les myopathies ou maladies neuromusculaires, n'a pas été retenue, et ceci également en raison de la complexité de l'analyse systématique de listes larges de gènes qui y aurait été associée (très nombreux variants identifiés et à interpréter pour de telles listes extensives, avec un impact sur le délai de rendu de résultat).
Le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques a établi de manière consensuelle des listes de gènes pour les principaux groupes phénotypiques / les principales portes d'entrée cliniques et/ou anatomopathologiques.
Selon les portes d'entrée cliniques et/ou anatomopathologiques il s'agit de :
- « listes de gènes principales » et « listes de gènes exhaustives »
- « listes de gènes uniques exhaustives».

- **« Listes de gènes principales » et « listes de gènes exhaustives » :**

Lorsqu'il existe, pour une porte d'entrée clinique et/ou anatomopathologique donnée, certains gènes fréquemment impliqués (gènes « majeurs », ou « core genes »), ces gènes ont été retenus pour constituer une « liste de gènes principale » (« core gene list »).
Dans cette situation, le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques recommande d'effectuer une démarche d'analyse séquentielle.
L'analyse NGS sera effectuée :

- dans un premier temps en utilisant cette **« liste de gènes principale »**, qui constitue une liste de gènes « majeurs » à analyser en première intention ;
- puis dans un deuxième temps [en l'absence de variant(s) identifié(s) classé(s) comme pathogène(s) ou probablement pathogène(s) suite à l'analyse de la « liste de gènes principale »], sur une **« liste de gènes exhaustive »** (panel large de gènes, correspondant à l'ensemble des gènes impliqués dans la porte d'entrée clinique et/ou anatompathologique respective, selon la Gene Table of Neuromuscular Disorders, www.musclegenetable.fr).

  NB : Les laboratoires ayant la possibilité d'analyser, pour une porte d'entrée donnée, directement une « liste de gènes exhaustive » pourront proposer, selon la situation clinique, soit une stratégie de rendu de résultat séquentiel (premier rendu de résultat sur la liste principale, puis le cas échéant deuxième rendu de résultat sur la liste exhaustive) ; soit une stratégie de rendu de résultat unique (rendu de résultat directement sur la liste exhaustive).
  Ce choix stratégique sera basé sur une discussion préalable avec le clinicien prescripteur et/ou en réunion de concertation plurisdisciplinaire.

Ceci permet aux laboratoires de mettre en place de manière relativement aisée l'analyse de listes « principales ». D'autre part, pour des laboratoires impliqués dans une thématique donnée, cette démarche séquentielle permet d'étendre le champ thématique en mettant en place dans un premier temps l'analyse de listes principales, en coordination avec des laboratoires spécialistes respectifs pour poursuivre les analyses le cas échéant sur les listes exhaustives.

Des « listes de gènes principales » et « listes de gènes exhaustives » ont été établies pour les portes d'entrée cliniques et/ou anatomopathologiques suivantes :
- Dystrophies musculaires des ceintures (7 gènes/40 gènes)
- Dystrophies musculaires congénitales hors alpha-dystroglycanopathies (8 gènes/17 gènes)
- Alpha-dystroglycanopathies (13 gènes/18 gènes)
- Myasthenies congénitales (9 gènes/32 gènes)
- Myotonies non-dystrophiques (2 gènes/7 gènes)
- Myopathies métaboliques (5 gènes/35 gènes)

- **« Listes de gènes uniques exhaustives » :**

Lorsqu'il n'existe **pas**, pour une porte d'entrée clinique et/ou anatomopatholgique donnée, certains gènes fréquemment impliqués (gènes « majeurs », ou « core genes »), une « liste de gènes unique exhaustive » a été constituée, correspondant à l'ensemble des gènes impliqués dans la porte d'entrée clinique et/ou anatompathologique respective, selon la Gene Table of Neuromuscular Disorders, www.musclegenetable.fr).

Dans cette situation, le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques recommande d'effectuer une analyse complète de cette « liste de gènes unique exhaustive » consensuelle.

Des « listes de gènes uniques exhaustives » ont été établies pour les portes d'entrée cliniques et/ou anatomopathologiques suivantes :

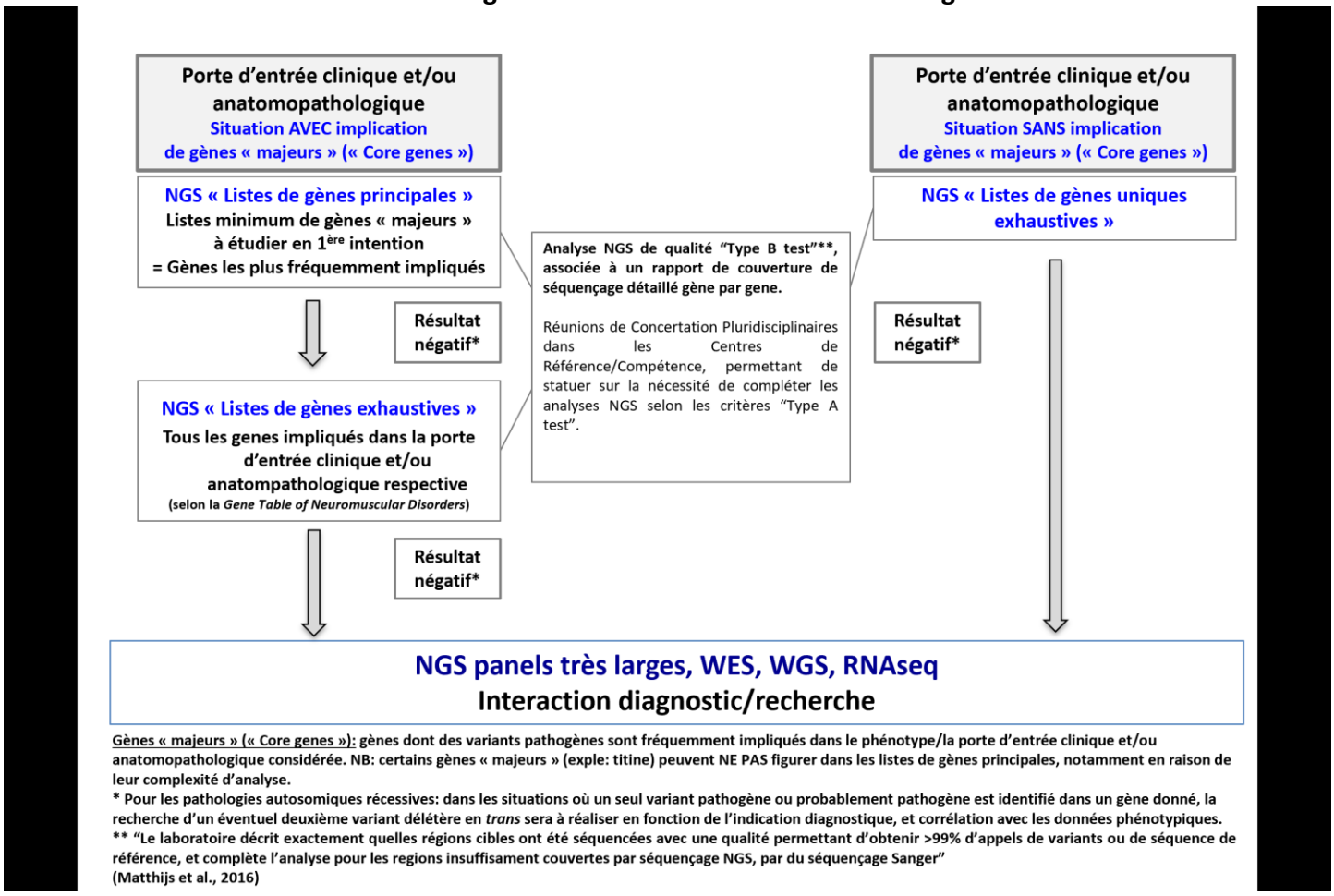
- **Myopathies congénitales à némaline (12 gènes)**
- **Myopathies congénitales « némaline-négatives » (32 gènes)**
- **Arthrogryposes fœtales et néonatales (37 gènes)**
- **Myopathies distales et scapulopéronières (24 gènes)**
- **Myopathies rétractiles (29 gènes)**
- **Myopathies myofibrillaires et Myopathies à inclusions (15 gènes)**
- **Paralysies périodiques (3 gènes)**

NB : Il est prévu que les laboratoires associent à l'avenir un rapport détaillé de couverture de séquençage gène par gène, afin de permettre facilement l'identification de régions cibles insuffisamment séquencés par l'analyse en NGS, qui pourraient nécessiter un complément d'analyse, par exemple en séquençage Sanger (selon discussion avec le prescripteur et/ou en réunion de concertation pluridisciplinaire).

Les variants de séquence identifiés sont classés selon les recommandations du Réseau NGS-DIAG « Homogénéisation de l'interprétation de variants de séquence générés par les analyses en NGS » auxquelles le Sous-groupe Génétique Moléculaire de la Commission Outils Diagnostiques de FILNEMUS a contribué
http://ffgh.net/index.php/presentation/les-reseaux-partenaires/reseau-ngs-diagnostic/182-reseaux/ngs/354-recommandations-professionnelles-du-reseau-ngs-diag

Stratégie consensuelle nationale pour le diagnostic génétique de myopathies par NGS

NB : les listes consensuelles seront intégrées dans les arbres décisionnels diagnostics



Gènes « majeurs » (« Core genes »): gènes dont des variants pathogènes sont fréquemment impliqués dans le phénotype/la porte d'entrée clinique et/ou anatomopathologique considérée. NB: certains gènes « majeurs » (exple: titine) peuvent NE PAS figurer dans les listes de gènes principales, notamment en raison de leur complexité d'analyse.

* Pour les pathologies autosomiques récessives: dans les situations où un seul variant pathogène ou probablement pathogène est identifié dans un gène donné, la recherche d'un éventuel deuxième variant délétère en *trans* sera à réaliser en fonction de l'indication diagnostique, et corrélation avec les données phénotypiques.

** "Le laboratoire décrit exactement quelles régions cibles ont été séquencées avec une qualité permettant d'obtenir >99% d'appels de variants ou de séquence de référence, et complète l'analyse pour les regions insuffisament couvertes par séquençage NGS, par du séquençage Sanger"
(Matthijs et al., 2016)

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Répertoire des laboratoires effectuant l'analyse des listes de gènes nationales consensuelles pour le diagnostic génétique de myopathies par NGS

NB : les laboratoires s'engagent à analyser tous les gènes pour les listes principales déclarées ; et si possible l'intégralité, sinon quasiment tous les gènes pour les listes uniques ou exhaustives (avec une actualisation dans les meilleurs délais), avec dans ce cas une information dans le compte-rendu d'analyse détaillant les gènes qui n'ont pas été analysés pour les listes concernées, permettant une éventuelle poursuite des investigations.

REPERTOIRE NATIONAL FILNEMUS DES LABORATOIRES EFFECTUANT LES ANALYSES GENETIQUES DE MYOPATHIES PAR NGS A VISEE DIAGNOSTIQUE
CATALOGUE DES LISTES DE GENES PROPOSEES

Intitulé du laboratoire	*Chef de service* , Généticien référent myopathie	LGMD Liste de gènes principale	LGMD Liste de gènes exhaustive	Myopathies congénitales à némaline Liste de gènes UNIQUE	Myopathies congénitales « némaline négatives » Liste de gènes	Arthrogryposes fœtales et néonatales Liste de gènes UNIQUE	Dystrophies musculaires congénitales hors a-DGpathies Liste de gènes principale	Dystrophies musculaires congénitales hors a-DGpathies Liste de gènes exhaustive	Alpha-Dystroglycanopathies Liste de gènes principale	Alpha-Dystroglycanopathies Liste de gènes exhaustive
Département de Génétique Médicale, APHM, Marseille	*Pr Nicolas Levy* Pr Martin Krahn Dr Rafaëlle Bernard Pr Béroud Christophe	X	X				X		X	
Laboratoire de génétique moléculaire, département de génétique moléculaire, CHU Montpellier	*Pr Michel Koenig* Dr Mireille Cossée		X	X	X		X	X		
LABORATOIRE de BIOLOGIE MEDICALE MULTI SITES du CHU de LYON – Service de Biochimie et Biologie Moléculaire Grand Est-UM Pathologies Endocriniennes Rénales Musculaires et Mucoviscidose	*Dr Véronique Tardy-Guidollet* Dr Laurence Michel-Calemard Dr Rita Menassa	X	X				X	X	X	X
Biochimie et Biologie Moléculaire Grand Est, UF Maladies Héréditaires du Métabolisme, CHU Lyon	*Dr Christine Vianey-Saban* Dr Cécile Acquaviva-Bourdain Dr Roseline Froissart									
Laboratoire de génétique et biologie moléculaires, HUPC Cochin, Paris	*Pr Michel Vidaud* Dr France Leturcq Dr Juliette Nectoux	X	X							
Unité Fonctionnelle de Cardiogénétique et Myogénétique Hopital Pitié-Salpêtrière APHP Paris	*Dr Pascale Richard* Dr Damien Sternberg Dr Corinne Métay									
Laboratoire de génétique moléculaire, hôpital Antoine Béclère, Clamart	*Pr Christian Pous* Dr François Petit									
Laboratoire de Biologie Moléculaire, Grenoble	*Dr Julien Fauré* Dr John Rendu Dr Nathalie Roux-Buisson			X	X	X				
Laboratoire Diagnostic Génétique, Nouvel Hopital Civil, Strasbourg	*Pr Jamel Chelly* Dr Nadège Calmels Dr Valérie Biancalana	X	X	X	X	X	X	X	X	X
Département de génetique , APHP - HUPNVS Hopital Bichat Claude Bernard, Paris	*Pr Nathalie Seta* Dr Celine Bouchet-Seraphin Dr Sandrine Vuillaumier-Barrot	X							X	X

REPERTOIRE NATIONAL FILNEMUS DES LABORATOIRES EFFECTUANT LES ANALYSES GENETIQUES DE MYOPATHIES PAR NGS A VISEE DIAGNOSTIQUE
CATALOGUE DES LISTES DE GENES PROPOSEES

Intitulé du laboratoire	*Chef de service* , Généticien référent myopathie	Myopathies distales et scapulopéronières Liste de gènes	Myopathies rétractiles Liste de gènes UNIQUE	Myopathies myofibrillaires et Myopathies à inclusions Liste de gènes	Myasthénies congénitales Liste de gènes principale	Myasthénies congénitales Liste de gènes exhaustive	Paralysies périodiques Liste de gènes UNIQUE	Myotonies non dystrophiques Liste de gènes principale	Myotonies non dystrophiques Liste de gènes exhaustive	Myopathies métaboliques Liste de gènes principale	Myopathies métaboliques Liste de gènes exhaustive
Département de Génétique Médicale, APHM, Marseille	*Pr Nicolas Levy* Pr Martin Krahn Dr Rafaëlle Bernard Pr Béroud Christophe	X		X							
Laboratoire de génétique moléculaire, département de génétique moléculaire, CHU Montpellier	*Pr Michel Koenig* Dr Mireille Cossée	X		X							
LABORATOIRE de BIOLOGIE MEDICALE MULTI SITES du CHU de LYON – Service de Biochimie et Biologie Moléculaire Grand Est-UM Pathologies Endocriniennes Rénales Musculaires et	*Dr Véronique Tardy-Guidollet* Dr Laurence Michel-Calemard Dr Rita Menassa	X		X							
Biochimie et Biologie Moléculaire Grand Est, UF Maladies Héréditaires du Métabolisme, CHU Lyon	*Dr Christine Vianey-Saban* Dr Cécile Acquaviva-Bourdain Dr Roseline Froissart									X	X
Laboratoire de génétique et biologie moléculaires, HUPC Cochin, Paris	*Pr Michel Vidaud* Dr France Leturcq Dr Juliette Nectoux										
Unité Fonctionnelle de Cardiogénétique et Myogénétique Hopital Pitié-Salpêtrière APHP Paris	*Dr Pascale Richard* Dr Damien Sternberg Dr Corinne Métay	X	X	X	X	X	X	X	X		
Laboratoire de génétique moléculaire, hôpital Antoine Béclère, Clamart	*Pr Christian Pous* Dr François Petit									X	X
Laboratoire de Biologie Moléculaire, Grenoble	*Dr Julien Fauré* Dr John Rendu Dr Nathalie Roux-Buisson	X	X	X	X	X	X	X	X		
Laboratoire Diagnostic Génétique, Nouvel Hopital Civil, Strasbourg	*Pr Jamel Chelly* Dr Nadège Calmels Dr Valérie Biancalana	X		X	X	X		X	X	X	
Département de génetique , APHP - HUPNVS Hopital Bichat Claude Bernard, Paris	*Pr Nathalie Seta* Dr Celine Bouchet-Seraphin Dr Sandrine Vuillaumier-Barrot										

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Listes de gènes nationales consensuelles pour le diagnostic génétique de myopathies par NGS

(Version adaptée de l'article "A National French consensus on gene lists for the diagnosis of myopathies using Next Generation Sequencing" European Journal of Human Genetics, 2018)
*la colonne "Pathologies" spécifie tous les phenotypes connus de pathologies touchant le tissu musculaire squelettique sur la base d'entrées OMIM répertoriées, pour les 13 portes d'entrée cliniques et/ou anatomopathologiques retenues, en excluant d'autres phenotypes éventuels (par exemple cardiaques).

RefSeq NM_DIAG: séquence codante de référence consensuelle.
AD: autosomique dominant; **AR:** autosomique récessif; **CDG:** Congenital Disorders of Glycosylation
LGMD: Limb Girdle Muscular Dystrophy; **MDC:** Muscular Dystrophy Congenital; **XLD:** dominant lié à l'X; **XLR:** récessif lié à l'X.

Dystrophies musculaires des ceintures - Liste de gènes principale (7 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
CAV3	Caveolin 3	NM_033337	- LGMD1C / - Distal myopathy, Tateyama type / - Rippling muscle disease	AD / AD / AD	21496630[1] 15580566[3]	15888488[2]
CAPN3	Calpain 3	NM_000070	- LGMD2A	AR (AD)	15725583[4] 9771675[5]	15961411[6]
DYSF	Dysferlin	NM_003494	- LGMD2B / - Miyoshi muscular dystrophy 1 / - Distal myopathy with anterior tibial onset	AR / AR / AR	17562833[7] 17698709[8]	21522182[9]
SGCG	Gamma sarcoglycan	NM_000231	- LGMD2C	AR	16832103[10] 18285821[11]	10942431[12]
SGCA	Alpha sarcoglycan	NM_000023	- LGMD2D	AR	8069911[13] 7663524[14]	8226900[15]
FKRP	Fukutin-related protein	NM_024301	- LGMD2I / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 5 / - Muscular dystrophy-dystroglycanopathy (congenital with or without mental retardation), type B, 5	AR / AR / AR	11592034[16] 12666124[17]	12471058[18]
ANO5	Anoctamin 5	NM_213599	- LGMD2L / - Miyoshi muscular dystrophy 3 (Early onset calf distal myopathy)	AR / AR	20096397[19] 23670307[20]	22946059[21]

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Dystrophies musculaires des ceintures - Liste de gènes exhaustive (40 gènes):

(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
MYOT	Myotilin	NM_006790	- LGMD1A / - Myopathy, myofibrillar, 3 / - Myopathy, spheroid body	AD / AD / AD	10958653[22] 16380616[23]	12499399[24]
LMNA	Lamin A/C	NM_170707	- LGMD1B / - Emery-Dreifuss muscular dystrophy 2 / - Emery-Dreifuss muscular dystrophy 3 / - Congenital muscular dystrophy due to LMNA defect (L-CMD)	AD / AD / AR / AD	10814726[25] 17377071[26]	14749366[27]
(CAV3)	Caveolin 3	NM_033337	- LGMD1C / - Distal myopathy, Tateyama type / - Rippling muscle disease	AD / AD / AD	21496630[1] 15580566[3]	15888488[2]
DNAJB6	DNAJ/HSP40 homolog, subfamily B, member 6	NM_058246	- LGMD1D	AD	22366786[28] 26205529[29]	11896048[30]
DES	Desmin	NM_001927	- LGMD1E / - LGMD2R / - Myopathy, myofibrillar, 1 / - Scapuloperoneal syndrome, neurogenic, Kaeser type	AD / AR / AD, AR / AD	22275259[31] 10717012[33]	16217025[32]
TNPO3	Transportin 3	NM_012470	- LGMD1F	AD	23667635[34] 23543484[35]	23632945[36]
HNRNPDL	Heterogeneous nuclear ribonucleoprotein D-like protein	NM_001207000 NM_031372	- LGMD1G	AD	24647604[37] 15367920[38]	
(CAPN3)	Calpain 3	NM_000070	- LGMD2A	AR (AD)	15725583[4] 9771675[5]	15961411[6]
(DYSF)	Dysferlin	NM_003494	- LGMD2B / - Miyoshi muscular dystrophy 1 / - Distal myopathy with anterior tibial onset	AR / AR / AR	17562833[7] 17698709[8]	21522182[9]
(SGCG)	Gamma sarcoglycan	NM_000231	- LGMD2C	AR	16832103 [10] 18285821[11]	10942431[12]
(SGCA)	Alpha sarcoglycan	NM_000023	- LGMD2D	AR	8069911[13] 7663524 [14]	8226900[15]
SGCB	Beta sarcoglycan	NM_000232	- LGMD2E	AR	10662809[39] 10678176[40]	10942431[12]
SGCD	Delta sarcoglycan	NM_000337	- LGMD2F	AR	10735275[41] 8841194[42]	10481911[43]
TCAP	Titin-CAP (Telethonin)	NM_003673	- LGMD2G	AR	10655062[44] 16352453 [45]	19679566[46]
TRIM32	Tripartite motif-containing 32	NM_012210	- LGMD2H	AR	11822024[47] 25351777 [48]	17994549[49]

(FKRP)	Fukutin-related protein	NM_024301	- LGMD2I / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 5 / - Muscular dystrophy-dystroglycanopathy (congenital with or without mental retardation), type B, 5	AR / AR / AR	11592034[16] 12666124[17]	12471058[18]
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / AD / AR AR / AD	15728284[50] 20571043[52]	20634290[51]
POMT1	Protein O-mannosyltransferase 1	NM_007171	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 1 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 1 / - LGMD2K	AR / AR / AR	12369018[53] 15792865[55]	19299310[54]
(ANO5)	Anoctamin 5	NM_213599	- LGMD2L / - Miyoshi muscular dystrophy 3 (Early onset calf distal myopathy)	AR / AR	20096397 [19] 23670307[20]	22946059[21]
FKTN	Fukutin	NM_001079802	- LGMD2M / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 4 / - Muscular dystrophy-dystroglycanopathy (congenital without mental retardation), type B, 4	AR / AR / AR	17044012 [56] 14627679[57]	19342235[58]
POMT2	Protein O-mannosyltransferase 2	NM_013382	- LGMD2N / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 2 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 2	AR / AR / AR	17923109[59] 24183756 [60]	17878207[61]
POMGNT1	Protein O-mannose Beta-1,2-N-acetyl glucosaminyltransferase	NM_001243766	- LGMD2O / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 3 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 3	AR / AR / AR	18195152[62] 17878207[61]	22419172[63]
DAG1	Dystroglycan1	NM_001165928	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 9 / - LGMD2P (Recessive LGMD with primary alphaDG defect)	AR / AR	21388311 [64] 14678799[65]	25503980[66]
PLEC	Plectin	NM_000445	- Congenital myasthenic syndrome with epidermolysis bullosa / - Epidermolysis bullosa simplex with muscular dystrophy / - LGMD2Q	AR / AR / AR	8696340 [67] 10446808[68]	21109228[69]

TRAPPC11	Trafficking protein particle complex subunit 11	NM_021942	- LGMD2S	AR	23830518[70] 26322222[71]	26912795[72]
GMPPB	GDP-mannose pyrophosphorylase, beta subunit	NM_013334	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 14 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 14 / - LGMD2T	AR / AR / AR	23768512 [73] 26133662[74]	11082198[75]
ISPD	Isoprenoid synthase domain-containing protein	NM_001101426	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 7 / - LGMD2U (Limb-Girdle, Muscular dystrophy related to ISPD)	AR / AR	23390185[76]	22522420[77]
GAA	Glucosidase, Alpha, Acid	NM_000152 NM_001079803	- Glycogen storage disease Type II (Pompe disease) - GSDII / - LGMD2V (Adult onset LGMD2 related to GAA deficiency)	AR / AR	8558570[78] 16917947[79]	9668092[80]
LIMS2	LIM zinc finger domain containing 2	NM_001136037	- LGMD2W (Limb girdle muscular dystrophy with severe cardiomyopathy and triangular tongue)	AR	25589244[81]	12167643[82]
BVES [POPDC1]	Blood vessel epicardial substance	NM_147147	- LGMD2X	AR	26642364[83]	26642364[83]
TOR1AIP1 [LAP1B]	Torsin 1A interacting protein 1	NM_015602 NM_001267578	- LGMD2Y	AR	24856141[84]	24856141[84]
POGLUT1	Protein O-glucosyltransferase 1	NM_152305	- LGMD2Z	AR	27807076[85]	27807076[85]
LAMA2	Laminin alpha 2 (merosin, included)	NM_000426	- Muscular dystrophy, congenital merosin-deficient - MDC1A	AR	Not Applicable	Not Applicable
FHL1	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset / - Emery-Dreifuss muscular dystrophy 6, X-linked / - Myopathy, X-linked,with postural atrophy / - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	Not Applicable	Not Applicable
COL6A1	Collagen, type VI, alpha-1	NM_001848	- Bethlem myopathy / - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	Not Applicable	Not Applicable
COL6A2	Collagen, type VI, alpha-2	NM_001849	- Bethlem myopathy / - Ullrich congenital muscular dystrophy -UCMD / - Congenital myosclerosis	AD, AR/ AD, AR / AR	Not Applicable	Not Applicable
COL6A3	Collagen, type VI, alpha-3	NM_004369	- Bethlem myopathy / - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	Not Applicable	Not Applicable
GNE	UDP-N-acetylglucosamine-2- epimerase/N-acetylmannosamine kinase	NM_001128227	- Distal myopathy with rimmed vacuoles (Nonaka) and Hereditary inclusion body myopathy	AR	Not Applicable	Not Applicable
VCP	Valosin-containing protein	NM_007126	- Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia 1 / - Charcot-Marie-Tooth disease, type 2Y	AD / AD	Not Applicable	Not Applicable
DPM3	Dolichyl-phosphate mannosyltransferase 3	NM_153741	- DPM3-CDG (Congenital Disorder of Glycosylation)	AR	Not Applicable	Not Applicable

1 Gazzerro E, Bonetto A, Minetti C. Caveolinopathies: translational implications of caveolin-3 in skeletal and cardiac muscle disorders. *Handb Clin Neurol* 2011; **101**: 135–142.

2 Nixon SJ, Wegner J, Ferguson C *et al.* Zebrafish as a model for caveolin-associated muscle disease; caveolin-3 is required for myofibril organization and muscle cell patterning. *Hum Mol Genet* 2005; **14**: 1727–1743.

3 Fulizio L, Nascimbeni AC, Fanin M *et al.* Molecular and muscle pathology in a series of caveolinopathy patients. *Hum Mutat* 2005; **25**: 82–89.

4 Fanin M, Nascimbeni AC, Fulizio L, Angelini C. The frequency of limb girdle muscular dystrophy 2A in northeastern Italy. *Neuromuscul Disord NMD* 2005; **15**: 218–224.

5 Kawai H, Akaike M, Kunishige M *et al.* Clinical, pathological, and genetic features of limb-girdle muscular dystrophy type 2A with new calpain 3 gene mutations in seven patients from three Japanese families. *Muscle Nerve* 1998; **21**: 1493–1501.

6 Kramerova I, Kudryashova E, Venkatraman G, Spencer MJ. Calpain 3 participates in sarcomere remodeling by acting upstream of the ubiquitin-proteasome pathway. *Hum Mol Genet* 2005; **14**: 2125–2134.

7 van der Kooi AJ, Frankhuizen WS, Barth PG *et al.* Limb-girdle muscular dystrophy in the Netherlands: gene defect identified in half the families. *Neurology* 2007; **68**: 2125–2128.

8 Nguyen K, Bassez G, Krahn M *et al.* Phenotypic study in 40 patients with dysferlin gene mutations: high frequency of atypical phenotypes. *Arch Neurol* 2007; **64**: 1176–1182.

9 Cacciottolo M, Numitone G, Aurino S *et al.* Muscular dystrophy with marked Dysferlin deficiency is consistently caused by primary dysferlin gene mutations. *Eur J Hum Genet EJHG* 2011; **19**: 974–980.

10 Duncan DR, Kang PB, Rabbat JC *et al.* A novel mutation in two families with limb-girdle muscular dystrophy type 2C. *Neurology* 2006; **67**: 167–169.

11 Trabelsi M, Kavian N, Daoud F *et al.* Revised spectrum of mutations in sarcoglycanopathies. *Eur J Hum Genet EJHG* 2008; **16**: 793–803.

12 Crosbie RH, Lim LE, Moore SA *et al.* Molecular and genetic characterization of sarcospan: insights into sarcoglycan-sarcospan interactions. *Hum Mol Genet* 2000; **9**: 2019–2027.

13 Roberds SL, Leturcq F, Allamand V *et al.* Missense mutations in the adhalin gene linked to autosomal recessive muscular dystrophy. *Cell* 1994; **78**: 625–633.

14 Piccolo F, Roberds SL, Jeanpierre M *et al.* Primary adhalinopathy: a common cause of autosomal recessive muscular dystrophy of variable severity. *Nat Genet* 1995; **10**: 243–245.

15 Roberds SL, Anderson RD, Ibraghimov-Beskrovnaya O, Campbell KP. Primary structure and muscle-specific expression of the 50-kDa dystrophin-associated glycoprotein (adhalin). *J Biol Chem* 1993; **268**: 23739–23742.

16 Brockington M, Blake DJ, Prandini P *et al.* Mutations in the fukutin-related protein gene (FKRP) cause a form of congenital muscular dystrophy with secondary laminin alpha2 deficiency and abnormal glycosylation of alpha-dystroglycan. *Am J Hum Genet* 2001; **69**: 1198–1209.

17 Mercuri E, Brockington M, Straub V *et al.* Phenotypic spectrum associated with mutations in the fukutin-related protein gene. *Ann Neurol* 2003; **53**: 537–542.

18 Esapa CT, Benson MA, Schröder JE *et al.* Functional requirements for fukutin-related protein in the Golgi apparatus. *Hum Mol Genet* 2002; **11**: 3319–3331.

19 Bolduc V, Marlow G, Boycott KM *et al.* Recessive mutations in the putative calcium-activated chloride channel Anoctamin 5 cause proximal LGMD2L and distal MMD3 muscular dystrophies. *Am J Hum Genet* 2010; **86**: 213–221.

20 Witting N, Duno M, Petri H *et al.* Anoctamin 5 muscular dystrophy in Denmark: prevalence, genotypes, phenotypes, cardiac findings, and muscle protein expression. *J Neurol* 2013; **260**: 2084–2093.

21 Tian Y, Schreiber R, Kunzelmann K. Anoctamins are a family of Ca2+-activated Cl- channels. *J Cell Sci* 2012; **125**: 4991–4998.

22 Hauser MA, Horrigan SK, Salmikangas P *et al.* Myotilin is mutated in limb girdle muscular dystrophy 1A. *Hum Mol Genet* 2000; **9**: 2141–2147.

23 Foroud T, Pankratz N, Batchman AP *et al.* A mutation in myotilin causes spheroid body myopathy. *Neurology* 2005; **65**: 1936–1940.

24 Salmikangas P, van der Ven PFM, Lalowski M *et al.* Myotilin, the limb-girdle muscular dystrophy 1A (LGMD1A) protein, cross-links actin filaments and controls sarcomere assembly. *Hum Mol Genet* 2003; **12**: 189–203.

25 Muchir A, Bonne G, van der Kooi AJ *et al.* Identification of mutations in the gene encoding lamins A/C in autosomal dominant limb girdle muscular dystrophy with atrioventricular conduction disturbances (LGMD1B). *Hum Mol Genet* 2000; **9**: 1453–1459.

26 Benedetti S, Menditto I, Degano M *et al.* Phenotypic clustering of lamin A/C mutations in neuromuscular patients. *Neurology* 2007; **69**: 1285–1292.

27 Favreau C, Higuet D, Courvalin J-C, Buendia B. Expression of a mutant lamin A that causes Emery-Dreifuss muscular dystrophy inhibits in vitro differentiation of C2C12 myoblasts. *Mol Cell Biol* 2004; **24**: 1481–1492.

28 Sarparanta J, Jonson PH, Golzio C *et al.* Mutations affecting the cytoplasmic functions of the co-chaperone DNAJB6 cause limb-girdle muscular dystrophy. *Nat Genet* 2012; **44**: 450–455, S1-2.

29 Ruggieri A, Brancati F, Zanotti S *et al.* Complete loss of the DNAJB6 G/F domain and novel missense mutations cause distal-onset DNAJB6 myopathy. *Acta Neuropathol Commun* 2015; **3**: 44.

30 Chuang J-Z, Zhou H, Zhu M, Li S-H, Li X-J, Sung C-H. Characterization of a brain-enriched chaperone, MRJ, that inhibits Huntingtin aggregation and toxicity independently. *J Biol Chem* 2002; **277**: 19831–19838.

31 Greenberg SA, Salajegheh M, Judge DP *et al.* Etiology of limb girdle muscular dystrophy 1D/1E determined by laser capture microdissection proteomics. *Ann Neurol* 2012; **71**: 141–145.

32 Bär H, Mücke N, Kostareva A, Sjöberg G, Aebi U, Herrmann H. Severe muscle disease-causing desmin mutations interfere with in vitro filament assembly at distinct stages. *Proc Natl Acad Sci U S A* 2005; **102**: 15099–15104.

33 Dalakas MC, Park KY, Semino-Mora C, Lee HS, Sivakumar K, Goldfarb LG. Desmin myopathy, a skeletal myopathy with cardiomyopathy caused by mutations in the desmin gene. *N Engl J Med* 2000; **342**: 770–780.

34 Torella A, Fanin M, Mutarelli M *et al.* Next-generation sequencing identifies transportin 3 as the causative gene for LGMD1F. *PloS One* 2013; **8**: e63536.

35 Melià MJ, Kubota A, Ortolano S *et al.* Limb-girdle muscular dystrophy 1F is caused by a microdeletion in the transportin 3 gene. *Brain J Neurol* 2013; **136**: 1508–1517.

36 Peterle E, Fanin M, Semplicini C, Padilla JJV, Nigro V, Angelini C. Clinical phenotype, muscle MRI and muscle pathology of LGMD1F. *J Neurol* 2013; **260**: 2033–2041.

37 Vieira NM, Naslavsky MS, Licinio L *et al.* A defect in the RNA-processing protein HNRPDL causes limb-girdle muscular dystrophy 1G (LGMD1G). *Hum Mol Genet* 2014; **23**: 4103–4110.

38 Starling A, Kok F, Passos-Bueno MR, Vainzof M, Zatz M. A new form of autosomal dominant limb-girdle muscular dystrophy (LGMD1G) with progressive fingers and toes flexion limitation maps to chromosome 4p21. *Eur J Hum Genet EJHG* 2004; **12**: 1033–1040.

39 Barresi R, Di Blasi C, Negri T *et al.* Disruption of heart sarcoglycan complex and severe cardiomyopathy caused by beta sarcoglycan mutations. *J Med Genet* 2000; **37**: 102–107.

40 Durbeej M, Cohn RD, Hrstka RF *et al.* Disruption of the beta-sarcoglycan gene reveals pathogenetic complexity of limb-girdle muscular dystrophy type 2E. *Mol Cell* 2000; **5**: 141–151.

41 Duggan DJ, Manchester D, Stears KP, Mathews DJ, Hart C, Hoffman EP. Mutations in the delta-sarcoglycan gene are a rare cause of autosomal recessive limb-girdle muscular dystrophy (LGMD2). *Neurogenetics* 1997; **1**: 49–58.

42 Nigro V, de Sá Moreira E, Piluso G *et al.* Autosomal recessive limb-girdle muscular dystrophy, LGMD2F, is caused by a mutation in the delta-sarcoglycan gene. *Nat Genet* 1996; **14**: 195–198.

43 Coral-Vazquez R, Cohn RD, Moore SA *et al.* Disruption of the sarcoglycan-sarcospan complex in vascular smooth muscle: a novel mechanism for cardiomyopathy and muscular dystrophy. *Cell* 1999; **98**: 465–474.

44 Moreira ES, Wiltshire TJ, Faulkner G *et al.* Limb-girdle muscular dystrophy type 2G is caused by mutations in the gene encoding the sarcomeric protein telethonin. *Nat Genet* 2000; **24**: 163–166.

45 Bos JM, Poley RN, Ny M *et al.* Genotype-phenotype relationships involving hypertrophic cardiomyopathy-associated mutations in titin, muscle LIM protein, and telethonin. *Mol Genet Metab* 2006; **88**: 78–85.

46 Zhang R, Yang J, Zhu J, Xu X. Depletion of zebrafish Tcap leads to muscular dystrophy via disrupting sarcomere-membrane interaction, not sarcomere assembly. *Hum Mol Genet* 2009; **18**: 4130–4140.

47 Frosk P, Weiler T, Nylen E *et al.* Limb-girdle muscular dystrophy type 2H associated with mutation in TRIM32, a putative E3-ubiquitin-ligase gene. *Am J Hum Genet* 2002; **70**: 663–672.

48 Nectoux J, de Cid R, Baulande S *et al.* Detection of TRIM32 deletions in LGMD patients analyzed by a combined strategy of CGH array and massively parallel sequencing. *Eur J Hum Genet EJHG* 2015; **23**: 929–934.

49 Saccone V, Palmieri M, Passamano L *et al.* Mutations that impair interaction properties of TRIM32 associated with limb-girdle muscular dystrophy 2H. *Hum Mutat* 2008; **29**: 240–247.

50 Udd B, Vihola A, Sarparanta J, Richard I, Hackman P. Titinopathies and extension of the M-line mutation phenotype beyond distal myopathy and LGMD2J. *Neurology* 2005; **64**: 636–642.

51 Sarparanta J, Blandin G, Charton K *et al.* Interactions with M-band titin and calpain 3 link myospryn (CMYA5) to tibial and limb-girdle muscular dystrophies. *J Biol Chem* 2010; **285**: 30304–30315.

52 Pénisson-Besnier I, Hackman P, Suominen T *et al.* Myopathies caused by homozygous titin mutations: limb-girdle muscular dystrophy 2J and variations of phenotype. *J Neurol Neurosurg Psychiatry* 2010; **81**: 1200–1202.

53 Beltrán-Valero de Bernabé D, Currier S, Steinbrecher A *et al.* Mutations in the O-mannosyltransferase gene POMT1 give rise to the severe neuronal migration disorder Walker-Warburg syndrome. *Am J Hum Genet* 2002; **71**: 1033–1043.

54 Mercuri E, Messina S, Bruno C *et al.* Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. *Neurology* 2009; **72**: 1802–1809.

55 Balci B, Uyanik G, Dincer P *et al.* An autosomal recessive limb girdle muscular dystrophy (LGMD2) with mild mental retardation is allelic to Walker-Warburg syndrome (WWS) caused by a mutation in the POMT1 gene. *Neuromuscul Disord NMD* 2005; **15**: 271–275.

56 Godfrey C, Escolar D, Brockington M *et al.* Fukutin gene mutations in steroid-responsive limb girdle muscular dystrophy. *Ann Neurol* 2006; **60**: 603–610.

57 de Bernabé DB-V, van Bokhoven H, van Beusekom E *et al.* A homozygous nonsense mutation in the fukutin gene causes a Walker-Warburg syndrome phenotype. *J Med Genet* 2003; **40**: 845–848.

58 Puckett RL, Moore SA, Winder TL *et al.* Further evidence of Fukutin mutations as a cause of childhood onset limb-girdle muscular dystrophy without mental retardation. *Neuromuscul Disord NMD* 2009; **19**: 352–356.

59 Biancheri R, Falace A, Tessa A *et al.* POMT2 gene mutation in limb-girdle muscular dystrophy with inflammatory changes. *Biochem Biophys Res Commun* 2007; **363**: 1033–1037.

60 Saredi S, Gibertini S, Ardissone A *et al.* A fourth case of POMT2-related limb girdle muscle dystrophy with mild reduction of α-dystroglycan glycosylation. *Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc* 2014; **18**: 404–408.

61 Godfrey C, Clement E, Mein R *et al.* Refining genotype phenotype correlations in muscular dystrophies with defective glycosylation of dystroglycan. *Brain J Neurol* 2007; **130**: 2725–2735.

62 Clement EM, Godfrey C, Tan J *et al.* Mild POMGnT1 mutations underlie a novel limb-girdle muscular dystrophy variant. *Arch Neurol* 2008; **65**: 137–141.

63 Raducu M, Baets J, Fano O, Van Coster R, Cruces J. Promoter alteration causes transcriptional repression of the POMGNT1 gene in limb-girdle muscular dystrophy type 2O. *Eur J Hum Genet EJHG* 2012; **20**: 945–952.

64 Hara Y, Balci-Hayta B, Yoshida-Moriguchi T *et al.* A dystroglycan mutation associated with limb-girdle muscular dystrophy. *N Engl J Med* 2011; **364**: 939–946.

65 Dinçer P, Balci B, Yuva Y *et al.* A novel form of recessive limb girdle muscular dystrophy with mental retardation and abnormal expression of alpha-dystroglycan. *Neuromuscul Disord NMD* 2003; **13**: 771–778.

66 Dong M, Noguchi S, Endo Y *et al.* DAG1 mutations associated with asymptomatic hyperCKemia and hypoglycosylation of α-dystroglycan. *Neurology* 2015; **84**: 273–279.

67 Smith FJ, Eady RA, Leigh IM *et al.* Plectin deficiency results in muscular dystrophy with epidermolysis bullosa. *Nat Genet* 1996; **13**: 450–457.

68 Banwell BL, Russel J, Fukudome T, Shen XM, Stilling G, Engel AG. Myopathy, myasthenic syndrome, and epidermolysis bullosa simplex due to plectin deficiency. *J Neuropathol Exp Neurol* 1999; **58**: 832–846.

69 Gundesli H, Talim B, Korkusuz P *et al.* Mutation in exon 1f of PLEC, leading to disruption of plectin isoform 1f, causes autosomal-recessive limb-girdle muscular dystrophy. *Am J Hum Genet* 2010; **87**: 834–841.

70 Bögershausen N, Shahrzad N, Chong JX *et al.* Recessive TRAPPC11 mutations cause a disease spectrum of limb girdle muscular dystrophy and myopathy with movement disorder and intellectual disability. *Am J Hum Genet* 2013; **93**: 181–190.

71 Liang W-C, Zhu W, Mitsuhashi S *et al.* Congenital muscular dystrophy with fatty liver and infantile-onset cataract caused by TRAPPC11 mutations: broadening of the phenotype. *Skelet Muscle* 2015; **5**: 29.

72 DeRossi C, Vacaru A, Rafiq R *et al.* trappc11 is required for protein glycosylation in zebrafish and humans. *Mol Biol Cell* 2016; **27**: 1220–1234.

73 Carss KJ, Stevens E, Foley AR *et al.* Mutations in GDP-mannose pyrophosphorylase B cause congenital and limb-girdle muscular dystrophies associated with hypoglycosylation of α-dystroglycan. *Am J Hum Genet* 2013; **93**: 29–41.

74 Belaya K, Rodríguez Cruz PM, Liu WW *et al.* Mutations in GMPPB cause congenital myasthenic syndrome and bridge myasthenic disorders with dystroglycanopathies. *Brain J Neurol* 2015; **138**: 2493–2504.

75 Ning B, Elbein AD. Cloning, expression and characterization of the pig liver GDP-mannose pyrophosphorylase. Evidence that GDP-mannose and GDP-Glc pyrophosphorylases are different proteins. *Eur J Biochem* 2000; **267**: 6866–6874.

76 Tasca G, Moro F, Aiello C *et al.* Limb-girdle muscular dystrophy with α-dystroglycan deficiency and mutations in the ISPD gene. *Neurology* 2013; **80**: 963–965.

77 Willer T, Lee H, Lommel M *et al.* ISPD loss-of-function mutations disrupt dystroglycan O-mannosylation and cause Walker-Warburg syndrome. *Nat Genet* 2012; **44**: 575–580.

78 Kroos MA, Van der Kraan M, Van Diggelen OP *et al.* Glycogen storage disease type II: frequency of three common mutant alleles and their associated clinical phenotypes studied in 121 patients. *J Med Genet* 1995; **32**: 836–837.

79 Montalvo ALE, Bembi B, Donnarumma M *et al.* Mutation profile of the GAA gene in 40 Italian patients with late onset glycogen storage disease type II. *Hum Mutat* 2006; **27**: 999–1006.

80 Raben N, Nagaraju K, Lee E *et al.* Targeted disruption of the acid alpha-glucosidase gene in mice causes an illness with critical features of both infantile and adult human glycogen storage disease type II. *J Biol Chem* 1998; **273**: 19086–19092.

81 Chardon JW, Smith AC, Woulfe J *et al.* LIMS2 mutations are associated with a novel muscular dystrophy, severe cardiomyopathy and triangular tongues. *Clin Genet* 2015; **88**: 558–564.

82 Zhang Y, Chen K, Guo L, Wu C. Characterization of PINCH-2, a new focal adhesion protein that regulates the PINCH-1-ILK interaction, cell spreading, and migration. *J Biol Chem* 2002; **277**: 38328–38338.

83 Schindler RFR, Scotton C, Zhang J *et al.* POPDC1(S201F) causes muscular dystrophy and arrhythmia by affecting protein trafficking. *J Clin Invest* 2016; **126**: 239–253.

84 Kayman-Kurekci G, Talim B, Korkusuz P *et al.* Mutation in TOR1AIP1 encoding LAP1B in a form of muscular dystrophy: a novel gene related to nuclear envelopathies. *Neuromuscul Disord NMD* 2014; **24**: 624–633.

85 Servián-Morilla E, Takeuchi H, Lee TV *et al.* A POGLUT1 mutation causes a muscular dystrophy with reduced Notch signaling and satellite cell loss. *EMBO Mol Med* 2016; **8**: 1289–1309.

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Myopathies congénitales à némaline - Liste de gènes unique exhaustive (12 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
ACTA1	Actin, alpha, skeletal muscle 1	NM_001100	- Nemaline Myopathy 3- Actin congenital myopathy with cores / - Actin congenital myopathy with excess of thin myofilaments / - Congenital myopathy with fiber-type disproportion 1 / - Nemaline Myopathy 3	AD, AR / AD, AR / AD, AR / AD, AR	11333380[1] 255310[2] 11333380[1] 19562689[4]	22174871[3] 22825594[5]
TPM2	Tropomyosin type 2	NM_003289	- Nemaline Myopathy 4 / - CAP myopathy 2 / - Distal arthrogryposis multiplex congenita type 1 / - Distal arthrogryposis type 2B	AD / AD / AD / AD	24692096[6] 22832340[7]	29792862[8]
TPM3	Tropomyosin type 3	NM_152263	- Nemaline Myopathy 1 / - Congenital myopathy with fiber-type disproportion / - CAP myopathy 1	AD, AR / AD, AR / AD, AR	24692096[6] 2469209[9]	26307083[10]
TNNT1	Troponin T type 1 (skeletal, slow)	NM_003283	- Nemaline myopathy 5	AR	25430424[11] 26296490[12]	27429059[13]
NEB	Nebulin	NM_001271208 NM_001164507	- Nemaline myopathy 2	AR	12207937[14] 25205138 [15]	22159874[16]
KBTBD13	Kelch repeat and BTB (POZ) domain-containing protein 13	NM_001101362	- Nemaline myopathy 6	AD	21109227[17]	
KLHL40	Kelch-like family member 40	NM_152393	- Nemaline myopathy 8	AR	27528495[18] 23746549[19]	24960163[20]
KLHL41	Kelch-like family member 41	NM_006063	- Nemaline myopathy 9	AR	24268659[21] 28939701 [22]	24268659[21]
LMOD3	Leiomodin type 3	NM_198271	- Nemaline myopathy 10	AR	25250574[23]	25250574[23]
CFL2	Cofilin type 2	NM_138638	- Nemaline myopathy 7	AR	17160903[24] 22560515 [25]	22343409[26]
MYPN	Myopalladin	NM_032578	- Nemaline myopathy 11	AR	28017374[27] 28220527[28]	28017374[27]
MYO18B	Myosin XVIIIB	NM_032608	- Klippel-Feil syndrome 4 with myopathy and facial dysmorphism	AR	27858739[29] 25748484[30]	27879346[31]

1 Ilkovski B, Cooper ST, Nowak K *et al.* Nemaline myopathy caused by mutations in the muscle alpha-skeletal-actin gene. *Am J Hum Genet* 2001; **68**: 1333–1343.

2 Van Duyn RL, Folkerts TM. Concentrations of tylosin in blood and lung tissue from calves given single and repeated daily intramuscular doses. *Vet Med Small Anim Clin VM SAC* 1979; **74**: 375–377.

3 Ravenscroft G, Jackaman C, Sewry CA *et al.* Actin nemaline myopathy mouse reproduces disease, suggests other actin disease phenotypes and provides cautionary note on muscle transgene expression. *PloS One* 2011; **6**: e28699.

4 Laing NG, Dye DE, Wallgren-Pettersson C *et al.* Mutations and polymorphisms of the skeletal muscle alpha-actin gene (ACTA1). *Hum Mutat* 2009; **30**: 1267–1277.

5 Nowak KJ, Ravenscroft G, Laing NG. Skeletal muscle α-actin diseases (actinopathies): pathology and mechanisms. *Acta Neuropathol (Berl)* 2013; **125**: 19–32.

6 Marttila M, Lehtokari V-L, Marston S *et al.* Mutation update and genotype-phenotype correlations of novel and previously described mutations in TPM2 and TPM3 causing congenital myopathies. *Hum Mutat* 2014; **35**: 779–790.

7 Kubrak OI, Husak VV, Rovenko BM *et al.* Antioxidant system efficiently protects goldfish gills from Ni(2+)-induced oxidative stress. *Chemosphere* 2013; **90**: 971–976.

8 Avrova SV, Karpicheva OE, Rysev NA *et al.* The reason for the low Ca2+-sensitivity of thin filaments associated with the Glu41Lys mutation in the TPM2 gene is 'freezing' of tropomyosin near the outer domain of actin and inhibition of actin monomer switching off during the ATPase cycle. *Biochem Biophys Res Commun* 2018. doi:10.1016/j.bbrc.2018.05.145.

9 Byerley W, Mellon C, O'Connell P *et al.* Mapping genes for manic-depression and schizophrenia with DNA markers. *Trends Neurosci* 1989; **12**: 46–48.

10 Yuen M, Cooper ST, Marston SB *et al.* Muscle weakness in TPM3-myopathy is due to reduced Ca2+-sensitivity and impaired acto-myosin cross-bridge cycling in slow fibres. *Hum Mol Genet* 2015; **24**: 6278–6292.

11 Marra JD, Engelstad KE, Ankala A *et al.* Identification of a novel nemaline myopathy-causing mutation in the troponin T1 (TNNT1) gene: a case outside of the old order Amish. *Muscle Nerve* 2015; **51**: 767–772.

12 Abdulhaq UN, Daana M, Dor T *et al.* Nemaline body myopathy caused by a novel mutation in troponin T1 (TNNT1). *Muscle Nerve* 2016; **53**: 564–569.
13 Amarasinghe C, Hossain MM, Jin J-P. Functional Basis of Three New Recessive Mutations of Slow Skeletal Muscle Troponin T Found in Non-Amish TNNT1 Nemaline Myopathies. *Biochemistry (Mosc)* 2016; **55**: 4560–4567.
14 Wallgren-Pettersson C, Donner K, Sewry C *et al.* Mutations in the nebulin gene can cause severe congenital nemaline myopathy. *Neuromuscul Disord NMD* 2002; **12**: 674–679.
15 Lehtokari V-L, Kiiski K, Sandaradura SA *et al.* Mutation update: the spectra of nebulin variants and associated myopathies. *Hum Mutat* 2014; **35**: 1418–1426.
16 Telfer WR, Nelson DD, Waugh T, Brooks SV, Dowling JJ. Neb: a zebrafish model of nemaline myopathy due to nebulin mutation. *Dis Model Mech* 2012; **5**: 389–396.
17 Sambuughin N, Yau KS, Olivé M *et al.* Dominant mutations in KBTBD13, a member of the BTB/Kelch family, cause nemaline myopathy with cores. *Am J Hum Genet* 2010; **87**: 842–847.
18 Seferian AM, Malfatti E, Bosson C *et al.* Mild clinical presentation in KLHL40-related nemaline myopathy (NEM 8). *Neuromuscul Disord NMD* 2016; **26**: 712–716.
19 Ravenscroft G, Miyatake S, Lehtokari V-L *et al.* Mutations in KLHL40 are a frequent cause of severe autosomal-recessive nemaline myopathy. *Am J Hum Genet* 2013; **93**: 6–18.
20 Garg A, O'Rourke J, Long C *et al.* KLHL40 deficiency destabilizes thin filament proteins and promotes nemaline myopathy. *J Clin Invest* 2014; **124**: 3529–3539.
21 Gupta VA, Ravenscroft G, Shaheen R *et al.* Identification of KLHL41 Mutations Implicates BTB-Kelch-Mediated Ubiquitination as an Alternate Pathway to Myofibrillar Disruption in Nemaline Myopathy. *Am J Hum Genet* 2013; **93**: 1108–1117.
22 van Diemen CC, Kerstjens-Frederikse WS, Bergman KA *et al.* Rapid Targeted Genomics in Critically Ill Newborns. *Pediatrics* 2017; **140**. doi:10.1542/peds.2016-2854.
23 Yuen M, Sandaradura SA, Dowling JJ *et al.* Leiomodin-3 dysfunction results in thin filament disorganization and nemaline myopathy. *J Clin Invest* 2014; **124**: 4693–4708.
24 Agrawal PB, Greenleaf RS, Tomczak KK *et al.* Nemaline myopathy with minicores caused by mutation of the CFL2 gene encoding the skeletal muscle actin-binding protein, cofilin-2. *Am J Hum Genet* 2007; **80**: 162–167.
25 Ockeloen CW, Gilhuis HJ, Pfundt R *et al.* Congenital myopathy caused by a novel missense mutation in the CFL2 gene. *Neuromuscul Disord NMD* 2012; **22**: 632–639.
26 Agrawal PB, Joshi M, Savic T, Chen Z, Beggs AH. Normal myofibrillar development followed by progressive sarcomeric disruption with actin accumulations in a mouse Cfl2 knockout demonstrates requirement of cofilin-2 for muscle maintenance. *Hum Mol Genet* 2012; **21**: 2341–2356.
27 Miyatake S, Mitsuhashi S, Hayashi YK *et al.* Biallelic Mutations in MYPN, Encoding Myopalladin, Are Associated with Childhood-Onset, Slowly Progressive Nemaline Myopathy. *Am J Hum Genet* 2017; **100**: 169–178.
28 Lornage X, Malfatti E, Chéraud C *et al.* Recessive MYPN mutations cause cap myopathy with occasional nemaline rods. *Ann Neurol* 2017; **81**: 467–473.
29 Malfatti E, Böhm J, Lacène E, Beuvin M, Romero NB, Laporte J. A Premature Stop Codon in MYO18B is Associated with Severe Nemaline Myopathy with Cardiomyopathy. *J Neuromuscul Dis* 2015; **2**: 219–227.
30 Alazami AM, Kentab AY, Faqeih E *et al.* A novel syndrome of Klippel-Feil anomaly, myopathy, and characteristic facies is linked to a null mutation in MYO18B. *J Med Genet* 2015; **52**: 400–404.
31 Gurung R, Ono Y, Baxendale S *et al.* A Zebrafish Model for a Human Myopathy Associated with Mutation of the Unconventional Myosin MYO18B. *Genetics* 2017; **205**: 725–735.

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Myopathies congénitales « némaline-négatives » - Liste de gènes unique exhaustive (32 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
RYR1	Ryanodin receptor type 1	NM_000540	- Central core disease / - King-Denborough syndrome / - Minicore myopathy with external ophthalmoplegia / - Congenital neuromuscular disease with uniform type 1 fiber (RYR1-related congenital myopathy with fatigable weakness, responding to pyridostigimine)	AD, AR / AD / AR / AD, AR	17190947[1] 17376685[2] 18765655[4] 16163667[5] 18253926[7] 17376685[2] 19303294[9] 19734047[10]	7515481[3] 1774074[6] 23553787[8] 7515481[3]
STAC3	SH3 and cysteine-rich domains 3	NM_145064	- Congenital myopathy (Native American myopathy)	AR	28777491 [11] 28411587[12]	28003463 [13] 27621462[14]
ACTA1	Actin, alpha, skeletal muscle 1	NM_001100	- Actin congenital myopathy with cores / - Actin congenital myopathy with excess of thin myofilaments / - Congenital myopathy with fiber-type disproportion 1 / - Nemaline Myopathy 3	AD,AR / AD, AR / AD, AR / AD, AR	10508519[16] 19562689[17] 19562689[17] 15468086[18]	22174871[15] 22174871[15] 17387733[19] 22825594[20]
TPM2	Tropomyosin Type 2	NM_003289	- Nemaline Myopathy 4 / - CAP myopathy 2 / - Distal arthrogryposis multiplex congenita type 1 / - Distal arthrogryposis type 2B	AD / AD / AD / AD	19345583[21] 19047562 [22]	22084935[23]
TPM3	Tropomyosin Type 3	NM_152263	- Nemaline Myopathy 1 / - Congenital myopathy with fiber-type disproportion / - CAP myopathy 1	AD, AR / AD, AR / AD, AR	24692096[24] 18300303[25] 24239060[27] 24095155[28]	26307083[26]
SELENON [SEPN1]	Selenoprotein N (1)	NM_020451	- Rigid spine muscular dystrophy 1 / - Congenital myopathy with fiber-type disproportion	AR / AD, AR	11528383[29] 21670436[30]	19557870[31] 25452428[32]
MYH7	Myosin Heavy chain type 7, cardiac muscle, bêta	NM_000257	- Laing distal myopathy / - Congenital myopathy (myosin storage myopathy) / - Scapuloperoneal syndrome, myopathic type	AD / AD, AR / AD	24664454[33]	19336582[34]
MTM1	Myotubularin	NM_000252	- Congenital myopathy (X-linked myotubular myopathy)	XLR	9285787[35] 9305655[36] 11793470[37] 15725586[38]	11275328[39]
DNM2	Dynamin 2	NM_001005360 NM_001005361 NM_001005362	- Centronuclear myopathy 1 / - Charcot-Marie-Tooth disease, axonal type 2M / - Charcot-Marie-Tooth disease, dominant intermediate B / - Lethal congenital contracture syndrome 5	AD / AD / AD / AR	23092955 [40]	20858595[41]
BIN1	Bridging integrator type 1 (Amphiphysin 2)	NM_139343	- Congenital myopathy (centronuclear myopathy 2)	AD (late onset), AR	25260562 [42] 29103045[43] 17676042[44] 20142620[45]	17676042[44]
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / AD/AR AR / AD	17444505[46] 28716623[47]	
KBTBD13	Kelch repeat and BTB (POZ) domain-containing protein 13	NM_001101362	- Nemaline myopathy 6	AD	21109227[48]	

SPEG	SPEG complex locus	NM_005876	- Congenital myopathy (centronuclear myopathy 5)	AR	25087613[49] 28624463[50] 29614691[51]	29474540[52]
MEGF10	Multiple EGF-like domains 10	NM_032446	- Congenital myopathy (early-onset myopathy with areflexia, respiratory distress and dysphagia)	AR	22101682[53] 29128256[54]	22371254[55]
MYH2	Myosin Heavy chain type 2, skeletal muscle, adult	NM_017534	- Congenital myopathy (proximal myopathy and ophthalmoplegia) / - Distal arthrogryposis	AD, AR / AD	24193343[56] 23489661[57]	11171584[58]
CACNA1S	Calcium channel, voltage-dependent, L type, alpha 1S subunit	NM_000069	- Congenital myopathy / - Hypokalemic periodic paralysis, type 1	AD, AR / AD	8004673[59] 28012042[60]	20033060[61]
HACD1 [PTPLA]	Protein tyrosine phosphatase-like (3- Hydroxyacyl-CoA dehydratase)	NM_014241	- Congenital myopathy	AR	23933735[62]	27939133[63]
TRIM32	Tripartite motif-containing 32	NM_012210	- LGMD2H	AR	11822024[64] 15886712[65]	19155210[66]
CNTN1	Contactin-1	NM_001843	- Congenital myopathy (Compton-North)	AR	19026398[67]	19026398[67]
MYBPC3	Cardiac myosin binding protein-C	NM_000256	- Congenital myopathy	AR	19858127[68]	
CCDC78	Coiled-coil domain-containing 78	NM_001031737	- Congenital myopathy (centronuclear myopathy 4)	AD	22818856[69]	22818856[69]
CASQ1	Calsequestrin type 1	NM_001231	- Tubular aggregate myopathy (vacuolar myopathy with CASQ1 aggregates)	AD	26136523[70] 25116801[71]	29039140[72]
STIM1	Stromal interaction molecule 1	NM_003156 NM_001277961	- Tubular aggregate myopathy 1	AD	24570283[73] 23332920[74]	23332920[74]
ORAI1	calcium release-activated calcium modulator 1	NM_032790	- Tubular aggregate myopathy 2	AD	25227914[75] 27882542[76]	24591628[77] 28058752[78]
PYROXD1	Pyridine Nucleotide-Disulphide Oxidoreductase Domain 1	NM_024854	- Early-Onset myopathy with internalized nuclei and myofibrillar disorganization	AR	27745833[79]	27745833[79]
KY	Kyphoscoliosis Peptidase	NM_178554	- Congenital myopathy with core targetoid	AR	27484770[80] 27485408[81]	15385448[82] 20206623[83]
TRIP4	Thyroid hormone receptor interactor 4	NM_016213	- Muscular dystrophy, congenital, davignon-chauveau type	AR	27008887[84] 26924529[85]	26924529[85]
SCN4A	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	26700687[86]	
SPTBN4	Spectrin, beta, nonerythrocytic, 4	NM_020971	- Myopathy, congenital, with neuropathy and deafness	AR	28540413[87]	
MAP3K20 [ZAK]	Mitogen-activated protein kinase kinase kinase 20	NM_016653 NM_133646	- Centronuclear myopathy 6 with fiber-type disproportion	AR	27816943[88]	
MYMK	Myomaker	NM_001080483	- Carey-Fineman-Ziter syndrome	AR	28681861[89]	
ASCC1	Activating Signal Cointegrator 1 Complex Subunit 1	NM_001198800	- Spinal muscular atrophy with congenital bone fractures 2	AR	26924529[85] 28218388[90]	26924529[85]

1 Fischer D, Herasse M, Ferreiro A *et al.* Muscle imaging in dominant core myopathies linked or unlinked to the ryanodine receptor 1 gene. *Neurology* 2006; **67**: 2217–2220.

2 Jungbluth H, Zhou H, Sewry CA *et al.* Centronuclear myopathy due to a de novo dominant mutation in the skeletal muscle ryanodine receptor (RYR1) gene. *Neuromuscul Disord NMD* 2007; **17**: 338–345.

3 Takeshima H, Iino M, Takekura H *et al.* Excitation-contraction uncoupling and muscular degeneration in mice lacking functional skeletal muscle ryanodine-receptor gene. *Nature* 1994; **369**: 556–559.

4 D'Arcy CE, Bjorksten A, Yiu EM *et al.* King-denborough syndrome caused by a novel mutation in the ryanodine receptor gene. *Neurology* 2008; **71**: 776–777.

5 Monnier N, Kozak-Ribbens G, Krivosic-Horber R *et al.* Correlations between genotype and pharmacological, histological, functional, and clinical phenotypes in malignant hyperthermia susceptibility. *Hum Mutat* 2005; **26**: 413–425.

6 Gillard EF, Otsu K, Fujii J *et al.* A substitution of cysteine for arginine 614 in the ryanodine receptor is potentially causative of human malignant hyperthermia. *Genomics* 1991; **11**: 751–755.

7 Monnier N, Marty I, Faure J *et al.* Null mutations causing depletion of the type 1 ryanodine receptor (RYR1) are commonly associated with recessive structural congenital myopathies with cores. *Hum Mutat* 2008; **29**: 670–678.

8 Zhou H, Rokach O, Feng L *et al.* RyR1 deficiency in congenital myopathies disrupts excitation-contraction coupling. *Hum Mutat* 2013; **34**: 986–996.

9 Jungbluth H, Lillis S, Zhou H *et al.* Late-onset axial myopathy with cores due to a novel heterozygous dominant mutation in the skeletal muscle ryanodine receptor (RYR1) gene. *Neuromuscul Disord NMD* 2009; **19**: 344–347.

10 Monnier N, Laquerrière A, Marret S *et al.* First genomic rearrangement of the RYR1 gene associated with an atypical presentation of lethal neonatal hypotonia. *Neuromuscul Disord NMD* 2009; **19**: 680–684.

11 Telegrafi A, Webb BD, Robbins SM *et al.* Identification of STAC3 variants in non-Native American families with overlapping features of Carey-Fineman-Ziter syndrome and Moebius syndrome. *Am J Med Genet A* 2017; **173**: 2763–2771.

12 Grzybowski M, Schänzer A, Pepler A, Heller C, Neubauer BA, Hahn A. Novel STAC3 Mutations in the First Non-Amerindian Patient with Native American Myopathy. *Neuropediatrics* 2017; **48**: 451–455.

13 Linsley JW, Hsu I-U, Groom L *et al.* Congenital myopathy results from misregulation of a muscle Ca2+ channel by mutant Stac3. *Proc Natl Acad Sci U S A* 2017; **114**: E228–E236.

14 Polster A, Nelson BR, Olson EN, Beam KG. Stac3 has a direct role in skeletal muscle-type excitation-contraction coupling that is disrupted by a myopathy-causing mutation. *Proc Natl Acad Sci U S A* 2016; **113**: 10986–10991.

15 Ravenscroft G, Jackaman C, Sewry CA *et al.* Actin nemaline myopathy mouse reproduces disease, suggests other actin disease phenotypes and provides cautionary note on muscle transgene expression. *PloS One* 2011; **6**: e28699.

16 Nowak KJ, Wattanasirichaigoon D, Goebel HH *et al.* Mutations in the skeletal muscle alpha-actin gene in patients with actin myopathy and nemaline myopathy. *Nat Genet* 1999; **23**: 208–212.

17 Laing NG, Dye DE, Wallgren-Pettersson C *et al.* Mutations and polymorphisms of the skeletal muscle alpha-actin gene (ACTA1). *Hum Mutat* 2009; **30**: 1267–1277.

18 Laing NG, Clarke NF, Dye DE *et al.* Actin mutations are one cause of congenital fibre type disproportion. *Ann Neurol* 2004; **56**: 689–694.

19 Clarke NF, Ilkovski B, Cooper S *et al.* The pathogenesis of ACTA1-related congenital fiber type disproportion. *Ann Neurol* 2007; **61**: 552–561.

20 Nowak KJ, Ravenscroft G, Laing NG. Skeletal muscle α-actin diseases (actinopathies): pathology and mechanisms. *Acta Neuropathol (Berl)* 2013; **125**: 19–32.

21 Clarke NF, Domazetovska A, Waddell L, Kornberg A, McLean C, North KN. Cap disease due to mutation of the beta-tropomyosin gene (TPM2). *Neuromuscul Disord NMD* 2009; **19**: 348–351.

22 Ohlsson M, Quijano-Roy S, Darin N *et al.* New morphologic and genetic findings in cap disease associated with beta-tropomyosin (TPM2) mutations. *Neurology* 2008; **71**: 1896–1901.

23 Marttila M, Lemola E, Wallefeld W *et al.* Abnormal actin binding of aberrant β-tropomyosins is a molecular cause of muscle weakness in TPM2-related nemaline and cap myopathy. *Biochem J* 2012; **442**: 231–239.

24 Marttila M, Lehtokari V-L, Marston S *et al.* Mutation update and genotype-phenotype correlations of novel and previously described mutations in TPM2 and TPM3 causing congenital myopathies. *Hum Mutat* 2014; **35**: 779–790.

25 Clarke NF, Kolski H, Dye DE *et al.* Mutations in TPM3 are a common cause of congenital fiber type disproportion. *Ann Neurol* 2008; **63**: 329–337.

26 Yuen M, Cooper ST, Marston SB *et al.* Muscle weakness in TPM3-myopathy is due to reduced Ca2+-sensitivity and impaired acto-myosin cross-bridge cycling in slow fibres. *Hum Mol Genet* 2015; **24**: 6278–6292.

27 Schreckenbach T, Schröder JM, Voit T *et al.* Novel TPM3 mutation in a family with cap myopathy and review of the literature. *Neuromuscul Disord NMD* 2014; **24**: 117–124.

28 Malfatti E, Schaeffer U, Chapon F *et al.* Combined cap disease and nemaline myopathy in the same patient caused by an autosomal dominant mutation in the TPM3 gene. *Neuromuscul Disord NMD* 2013; **23**: 992–997.

29 Moghadaszadeh B, Petit N, Jaillard C *et al.* Mutations in SEPN1 cause congenital muscular dystrophy with spinal rigidity and restrictive respiratory syndrome. *Nat Genet* 2001; **29**: 17–18.

30 Scoto M, Cirak S, Mein R *et al.* SEPN1-related myopathies: clinical course in a large cohort of patients. *Neurology* 2011; **76**: 2073–2078.

31 Arbogast S, Beuvin M, Fraysse B, Zhou H, Muntoni F, Ferreiro A. Oxidative stress in SEPN1-related myopathy: from pathophysiology to treatment. *Ann Neurol* 2009; **65**: 677–686.

32 Marino M, Stoilova T, Giorgi C *et al.* SEPN1, an endoplasmic reticulum-localized selenoprotein linked to skeletal muscle pathology, counteracts hyperoxidation by means of redox-regulating SERCA2 pump activity. *Hum Mol Genet* 2015; **24**: 1843–1855.

33 Lamont PJ, Wallefeld W, Hilton-Jones D *et al.* Novel mutations widen the phenotypic spectrum of slow skeletal/β-cardiac myosin (MYH7) distal myopathy. *Hum Mutat* 2014; **35**: 868–879.

34 Armel TZ, Leinwand LA. Mutations in the beta-myosin rod cause myosin storage myopathy via multiple mechanisms. *Proc Natl Acad Sci U S A* 2009; **106**: 6291–6296.

35 de Gouyon BM, Zhao W, Laporte J, Mandel JL, Metzenberg A, Herman GE. Characterization of mutations in the myotubularin gene in twenty six patients with X-linked myotubular myopathy. *Hum Mol Genet* 1997; **6**: 1499–1504.

36 Laporte J, Guiraud-Chaumeil C, Vincent MC *et al.* Mutations in the MTM1 gene implicated in X-linked myotubular myopathy. ENMC International Consortium on Myotubular Myopathy. European Neuro-Muscular Center. *Hum Mol Genet* 1997; **6**: 1505–1511.

37 Herman GE, Kopacz K, Zhao W, Mills PL, Metzenberg A, Das S. Characterization of mutations in fifty North American patients with X-linked myotubular myopathy. *Hum Mutat* 2002; **19**: 114–121.

38 Tsai T-C, Horinouchi H, Noguchi S *et al.* Characterization of MTM1 mutations in 31 Japanese families with myotubular myopathy, including a patient carrying 240 kb deletion in Xq28 without male hypogenitalism. *Neuromuscul Disord NMD* 2005; **15**: 245–252.

39 Laporte J, Blondeau F, Buj-Bello A, Mandel JL. The myotubularin family: from genetic disease to phosphoinositide metabolism. *Trends Genet TIG* 2001; **17**: 221–228.

40 Koutsopoulos OS, Kretz C, Weller CM *et al.* Dynamin 2 homozygous mutation in humans with a lethal congenital syndrome. *Eur J Hum Genet EJHG* 2013; **21**: 637–642.

41 Durieux A-C, Vignaud A, Prudhon B *et al.* A centronuclear myopathy-dynamin 2 mutation impairs skeletal muscle structure and function in mice. *Hum Mol*

Genet 2010; **19**: 4820–4836.
42 Böhm J, Biancalana V, Malfatti E *et al.* Adult-onset autosomal dominant centronuclear myopathy due to BIN1 mutations. *Brain J Neurol* 2014; **137**: 3160–3170.
43 Kouwenberg C, Bohm J, Erasmus C *et al.* Dominant Centronuclear Myopathy with Early Childhood Onset due to a Novel Mutation in BIN1. *J Neuromuscul Dis* 2017; **4**: 349–355.
44 Nicot A-S, Toussaint A, Tosch V *et al.* Mutations in amphiphysin 2 (BIN1) disrupt interaction with dynamin 2 and cause autosomal recessive centronuclear myopathy. *Nat Genet* 2007; **39**: 1134–1139.
45 Claeys KG, Maisonobe T, Böhm J *et al.* Phenotype of a patient with recessive centronuclear myopathy and a novel BIN1 mutation. *Neurology* 2010; **74**: 519–521.
46 Carmignac V, Salih MAM, Quijano-Roy S *et al.* C-terminal titin deletions cause a novel early-onset myopathy with fatal cardiomyopathy. *Ann Neurol* 2007; **61**: 340–351.
47 Harris E, Töpf A, Vihola A *et al.* A 'second truncation' in TTN causes early onset recessive muscular dystrophy. *Neuromuscul Disord NMD* 2017; **27**: 1009–1017.
48 Sambuughin N, Yau KS, Olivé M *et al.* Dominant mutations in KBTBD13, a member of the BTB/Kelch family, cause nemaline myopathy with cores. *Am J Hum Genet* 2010; **87**: 842–847.
49 Agrawal PB, Pierson CR, Joshi M *et al.* SPEG interacts with myotubularin, and its deficiency causes centronuclear myopathy with dilated cardiomyopathy. *Am J Hum Genet* 2014; **95**: 218–226.
50 Wang H, Castiglioni C, Kaçar Bayram A *et al.* Insights from genotype-phenotype correlations by novel SPEG mutations causing centronuclear myopathy. *Neuromuscul Disord NMD* 2017; **27**: 836–842.
51 Lornage X, Sabouraud P, Lannes B *et al.* Novel SPEG Mutations in Congenital Myopathy without Centralized Nuclei. *J Neuromuscul Dis* 2018; **5**: 257–260.
52 Huntoon V, Widrick JJ, Sanchez C *et al.* SPEG-deficient skeletal muscles exhibit abnormal triad and defective calcium handling. *Hum Mol Genet* 2018; **27**: 1608–1617.
53 Logan CV, Lucke B, Pottinger C *et al.* Mutations in MEGF10, a regulator of satellite cell myogenesis, cause early onset myopathy, areflexia, respiratory distress and dysphagia (EMARDD). *Nat Genet* 2011; **43**: 1189–1192.
54 Harris E, Marini-Bettolo C, Töpf A *et al.* MEGF10 related myopathies: A new case with adult onset disease with prominent respiratory failure and review of reported phenotypes. *Neuromuscul Disord NMD* 2018; **28**: 48–53.
55 Boyden SE, Mahoney LJ, Kawahara G *et al.* Mutations in the satellite cell gene MEGF10 cause a recessive congenital myopathy with minicores. *Neurogenetics* 2012; **13**: 115–124.
56 Tajsharghi H, Hammans S, Lindberg C *et al.* Recessive myosin myopathy with external ophthalmoplegia associated with MYH2 mutations. *Eur J Hum Genet EJHG* 2014; **22**: 801–808.
57 D'Amico A, Fattori F, Bellacchio E, Catteruccia M, Servidei S, Bertini E. A new de novo missense mutation in MYH2 expands clinical and genetic findings in hereditary myosin myopathies. *Neuromuscul Disord NMD* 2013; **23**: 437–440.
58 Allen DL, Harrison BC, Sartorius C, Byrnes WC, Leinwand LA. Mutation of the IIB myosin heavy chain gene results in muscle fiber loss and compensatory hypertrophy. *Am J Physiol Cell Physiol* 2001; **280**: C637-645.
59 Ptácek LJ, Tawil R, Griggs RC *et al.* Dihydropyridine receptor mutations cause hypokalemic periodic paralysis. *Cell* 1994; **77**: 863–868.
60 Schartner V, Romero NB, Donkervoort S *et al.* Dihydropyridine receptor (DHPR, CACNA1S) congenital myopathy. *Acta Neuropathol (Berl)* 2017; **133**: 517–533.
61 Piétri-Rouxel F, Gentil C, Vassilopoulos S *et al.* DHPR alpha1S subunit controls skeletal muscle mass and morphogenesis. *EMBO J* 2010; **29**: 643–654.
62 Muhammad E, Reish O, Ohno Y *et al.* Congenital myopathy is caused by mutation of HACD1. *Hum Mol Genet* 2013; **22**: 5229–5236.
63 Walmsley GL, Blot S, Venner K *et al.* Progressive Structural Defects in Canine Centronuclear Myopathy Indicate a Role for HACD1 in Maintaining Skeletal Muscle Membrane Systems. *Am J Pathol* 2017; **187**: 441–456.
64 Frosk P, Weiler T, Nylen E *et al.* Limb-girdle muscular dystrophy type 2H associated with mutation in TRIM32, a putative E3-ubiquitin-ligase gene. *Am J Hum Genet* 2002; **70**: 663–672.
65 Frosk P, Del Bigio MR, Wrogemann K, Greenberg CR. Hutterite brothers both affected with two forms of limb girdle muscular dystrophy: LGMD2H and LGMD2I. *Eur J Hum Genet EJHG* 2005; **13**: 978–982.
66 Kudryashova E, Wu J, Havton LA, Spencer MJ. Deficiency of the E3 ubiquitin ligase TRIM32 in mice leads to a myopathy with a neurogenic component. *Hum Mol Genet* 2009; **18**: 1353–1367.
67 Compton AG, Albrecht DE, Seto JT *et al.* Mutations in contactin-1, a neural adhesion and neuromuscular junction protein, cause a familial form of lethal congenital myopathy. *Am J Hum Genet* 2008; **83**: 714–724.
68 Tajsharghi H, Leren TP, Abdul-Hussein S *et al.* Unexpected myopathy associated with a mutation in MYBPC3 and misplacement of the cardiac myosin binding protein C. *J Med Genet* 2010; **47**: 575–577.
69 Majczenko K, Davidson AE, Camelo-Piragua S *et al.* Dominant mutation of CCDC78 in a unique congenital myopathy with prominent internal nuclei and atypical cores. *Am J Hum Genet* 2012; **91**: 365–371.
70 Di Blasi C, Sansanelli S, Ruggieri A *et al.* A CASQ1 founder mutation in three Italian families with protein aggregate myopathy and hyperCKaemia. *J Med Genet* 2015; **52**: 617–626.
71 Rossi D, Vezzani B, Galli L *et al.* A mutation in the CASQ1 gene causes a vacuolar myopathy with accumulation of sarcoplasmic reticulum protein aggregates. *Hum Mutat* 2014; **35**: 1163–1170.
72 Böhm J, Lornage X, Chevessier F *et al.* CASQ1 mutations impair calsequestrin polymerization and cause tubular aggregate myopathy. *Acta Neuropathol (Berl)* 2018; **135**: 149–151.
73 Hedberg C, Niceta M, Fattori F *et al.* Childhood onset tubular aggregate myopathy associated with de novo STIM1 mutations. *J Neurol* 2014; **261**: 870–876.
74 Böhm J, Chevessier F, Maues De Paula A *et al.* Constitutive activation of the calcium sensor STIM1 causes tubular-aggregate myopathy. *Am J Hum Genet* 2013; **92**: 271–278.
75 Endo Y, Noguchi S, Hara Y *et al.* Dominant mutations in ORAI1 cause tubular aggregate myopathy with hypocalcemia via constitutive activation of store-operated Ca^{2+} channels. *Hum Mol Genet* 2015; **24**: 637–648.
76 Garibaldi M, Fattori F, Riva B *et al.* A novel gain-of-function mutation in ORAI1 causes late-onset tubular aggregate myopathy and congenital miosis. *Clin Genet* 2017; **91**: 780–786.
77 Nesin V, Wiley G, Kousi M *et al.* Activating mutations in STIM1 and ORAI1 cause overlapping syndromes of tubular myopathy and congenital miosis. *Proc Natl Acad Sci U S A* 2014; **111**: 4197–4202.
78 Böhm J, Bulla M, Urquhart JE *et al.* ORAI1 Mutations with Distinct Channel Gating Defects in Tubular Aggregate Myopathy. *Hum Mutat* 2017; **38**: 426–438.
79 O'Grady GL, Best HA, Sztal TE *et al.* Variants in the Oxidoreductase PYROXD1 Cause Early-Onset Myopathy with Internalized Nuclei and Myofibrillar Disorganization. *Am J Hum Genet* 2016; **99**: 1086–1105.
80 Straussberg R, Schottmann G, Sadeh M *et al.* Kyphoscoliosis peptidase (KY) mutation causes a novel congenital myopathy with core targetoid defects. *Acta Neuropathol (Berl)* 2016; **132**: 475–478.
81 Hedberg-Oldfors C, Darin N, Olsson Engman M *et al.* A new early-onset neuromuscular disorder associated with kyphoscoliosis peptidase (KY) deficiency. *Eur J Hum Genet EJHG* 2016; **24**: 1771–1777.
82 Beatham J, Romero R, Townsend SKM, Hacker T, van der Ven PFM, Blanco G. Filamin C interacts with the muscular dystrophy KY protein and is abnormally distributed in mouse KY deficient muscle fibres. *Hum Mol Genet* 2004; **13**: 2863–2874.
83 Baker J, Riley G, Romero MR *et al.* Identification of a Z-band associated protein complex involving KY, FLNC and IGFN1. *Exp Cell Res* 2010; **316**: 1856–1870.

84 Davignon L, Chauveau C, Julien C *et al.* The transcription coactivator ASC-1 is a regulator of skeletal myogenesis, and its deficiency causes a novel form of congenital muscle disease. *Hum Mol Genet* 2016; **25**: 1559–1573.
85 Knierim E, Hirata H, Wolf NI *et al.* Mutations in Subunits of the Activating Signal Cointegrator 1 Complex Are Associated with Prenatal Spinal Muscular Atrophy and Congenital Bone Fractures. *Am J Hum Genet* 2016; **98**: 473–489.
86 Zaharieva IT, Thor MG, Oates EC *et al.* Loss-of-function mutations in SCN4A cause severe foetal hypokinesia or 'classical' congenital myopathy. *Brain J Neurol* 2016; **139**: 674–691.
87 Knierim E, Gill E, Seifert F *et al.* A recessive mutation in beta-IV-spectrin (SPTBN4) associates with congenital myopathy, neuropathy, and central deafness. *Hum Genet* 2017; **136**: 903–910.
88 Vasli N, Harris E, Karamchandani J *et al.* Recessive mutations in the kinase ZAK cause a congenital myopathy with fibre type disproportion. *Brain J Neurol* 2017; **140**: 37–48.
89 Di Gioia SA, Connors S, Matsunami N *et al.* A defect in myoblast fusion underlies Carey-Fineman-Ziter syndrome. *Nat Commun* 2017; **8**: 16077.
90 Oliveira J, Martins M, Pinto Leite R, Sousa M, Santos R. The new neuromuscular disease related with defects in the ASC-1 complex: report of a second case confirms ASCC1 involvement. *Clin Genet* 2017; **92**: 434–439.

Arthrogryposes foetales et néonatales - Liste de gènes unique exhaustive (37 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
ADCY6	Adenylate cyclase 6	NM_015270 NM_020983	- Lethal congenital contracture syndrome 8	AR	24319099[1]	
CHAT	Choline acetyltransferase	NM_020549 NM_001142933	- Congenital myasthenic syndrome 6 (presynaptic)	AR	26080897[2] 20301347[4]	17586598[3]
CHRNA1	Cholinergic receptor, nicotinic, alpha polypeptide 1	NM_000079 NM_001039523	- Congenital myasthenic syndrome 1A / - Congenital myasthenic syndrome 1B / - Multiple pterygium syndrome, lethal type	AD / AD, AR / AR	18252226[6] 18179903[7]	27626380[5]
CHRNB1	Cholinergic receptor, nicotinic, beta polypeptide 1	NM_000747	- Congenital myasthenic syndrome 2C, associated with acetylcholine receptor deficiency / - Congenital myasthenic syndrome 2A + Fetal akinesia deformation sequence	AR / AD	27364156[8]	
CHRND	Cholinergic receptor, nicotinic, delta polypeptide	NM_000751	- Congenital myasthenic syndrome 3A/ - Congenital myasthenic syndrome 3B/ - Congenital myasthenic syndrome 3C / - Multiple pterygium syndrome, lethal type	AD / AR / AR / AR	18252226[6] 18179903[7]	18398509[9]
CHRNG	Cholinergic receptor, nicotinic, gamma polypeptide	NM_005199	- Multiple pterygium syndrome, lethal type / - Non lethal multiple pterygium syndrome (Escobar syndrome)	AR / AR	16826531[10] 18252226[6] 18179903[7]	16826520 [11]
CNTNAP1	Contactin-associated protein-1	NM_003632	Lethal congenital contracture syndrome 7	AR	24319099[1]	
DNM2	Dynamin 2	NM_001005360 NM_001005361 NM_001005362	- Centronuclear myopathy 1 / - Charcot-Marie-Tooth disease, axonal type 2M / - Charcot-Marie-Tooth disease, dominant intermediate B / - Lethal congenital contracture syndrome 5	AD / AD / AD / AR	23092955[12]	
DOK7	Downstream of tyrosine kinase 7	NM_173660	- Congenital myasthenic syndrome 10 / - Fetal akinesia deformation sequence	AR / AR	25537362[13] 19261599[15]	20147321[14]
ERBB3	V-ERB-B2 avian erythroblastic leukemia viral oncogene homolog 3	NM_001982 NM_001005915	- Lethal congenital contractural syndrome 2	AR	17701904[16]	
GLE1	GLE1, RNA export mediator	NM_001003722	- Lethal congenital contracture syndrome 1	AR	18204449[17] 27684565[18]	22357925[19] 24243016[20]
ADGRG6	Adhesion G protein-coupled receptor G6	NM_020455 NM_001032394	- Lethal congenital contracture syndrome 9	AR	26004201[21]	21613327[22]
MAGEL2	MAGE-like 2	NM_019066	- Schaaf-Yang syndrome	AD	26365340[23] 28281571[24] 29359444 [25]	17728320[26]

MUSK	Muscle, skeletal, receptor tyrosine kinase	NM_005592	- Congenital myasthenic syndrome 9, associated with acetylcholine receptor deficiency / - Fetal akinesia deformation sequence	AR / AR	25537362[13] 25612909[27]	25537362[13]
MYBPC1	Myosin-binding protein C (slow type)	NM_002465 NM_001254719	- Distal arthrogryposis type 1B / - Lethal congenital contracture syndrome 4	AD / AR	22610851[28]	23873045[29]
MYH3	Myosin, Heavy chain 3, skeletal muscle, embryonic	NM_002470	- Distal arthrogryposis, type 2A / type 2B / type 8 - Multiple pterygium syndrom	AD / AD / AD AD	16642020[30] 25256237[31] 25957469[32]	
MYOD1	Myogenic differentiation antigen 1	NM_002478	- Fetal akinesia deformation sequence	AR	26733463[33]	20544915[34]
NEB	Nebulin	NM_001271208 NM_001164507	- Nemaline Myopathy 2	AR	12207937[35] 25205138[36]	10051637[37]
PIP5K1C	Phosphatidylinositol 4-phosphate 5-kinase, type I, Gamma	NM_012398 NM_001300849	- Lethal congenital contractural syndrome 3	AR	17701898[38]	
RAPSN	Receptor-associated protein of the synapse (Rapsyn)	NM_005055	- Congenital myasthenic syndrome 11, associated with acetylcholine receptor deficiency / - Fetal akinesia deformation sequence	AR / AR	15328566[39] 12730725[40] 12796535[41] 18252226[6] 18179903[7]	16945936[42] 11323662[43]
RYR1	Ryanodin receptor type 1	NM_000540	- Central core disease / - King-Denborough syndrome / - Minicore myopathy with external ophthalmoplegia / - Congenital neuromuscular disease with uniform type 1 fiber (RYR1-related congenital myopathy with fatigable weakness, responding to pyridostigimine)	AD, AR / AD / AR / AD, AR	25476234[44]	
SCN4A	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	26700687[45]	
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / ? / AR / AD	29575618[46]	
ZBTB42	Zinc finger- and BTB domain-containing protein 42	NM_001137601	- Lethal congenital contracture syndrome 6	AR	25055871[47]	
BICD2	Bicaudal D, drosophila, homolog of, 2	NM_015250 NM_001003800	- Spinal muscular atrophy, lower extremity-predominant, 2	AD	23664116[48] 23664119[49] 23664120[50]	29528393[51] 28883039[52]
DYNC1H1	Dynein, cytoplasmic 1, heavy chain 1	NM_001376	- Spinal muscular atrophy, lower extremity-predominant 1	AD	22459677[53] 25609763[54]	28196890[55]
ECEL1	Endothelin-converting enzyme-like 1	NM_004826	- Distal arthrogryposis type 5D	AR	23236030[56] 23261301[57]	29132416[58]

		NM_001290787				
FBN2	Fibrillin 2	NM_001999	- Congenital contractural arachnodactyly	AD	7493032 [59] 11754102[60] 18767143[61] 19006240 [62]	
MYH2	Myosin Heavy chain type 2, skeletal muscle, adult	NM_017534	- Congenital myopathy (proximal myopathy and ophthalmoplegia) / - Distal arthrogryposis	AD, AR / AD	20418530[63] 23388406 [64]	
MYH8	Myosin, heavy chain 8, skeletal muscle, perinatal	NM_002472	- Trismus-pseudocamptodactyly syndrome	AD	15282353[65] 17041932[66]	
NALCN	Sodium Leak Channel, non selective	NM_052867	- Congenital contractures of the limbs and face, hypotonia, and developmental delay / - Infantile hypotonia, with psychomotor retardation and characteristic facies 1	AD / AR	25683120[67] 27214504 [68] 25864427[69] 24075186 [70]	
PIEZO2	PIEZO-type mechanosensitive ion channel component 2	NM_022068	- Distal arthrogryposis type 3 / - Arthrogryposis, muscle weakness and scoliosis / - Distal arthrogryposis type 5	AD / AR / AD	23487782[71] 27843126[72] 27974811[73] 24726473[74] 25712306 [75]	
TNNI2	Troponin I (fast-twitch skeletal muscle isoform)	NM_003282 NM_001145829	- Distal arthrogryposis multiplex congenita type 2B	AD	12592607[76] 16802141 [77]	
TNNT3	Troponin T3 (fast skeletal)	NM_001042782 NM_006757	- Distal arthyrgryposis type 2B	AD	12865991[78] 25337069[79] 21402185[80]	
TPM2	Tropomyosin type 2	NM_003289	- Nemaline Myopathy 4 / - CAP myopathy 2 / - Distal arthrogryposis multiplex congenita type 1 / - Distal arthrogryposis type 2B	AD / AD / AD / AD	23401156[81] 23401156[81] 12592607[76] 23401156 [81]	17430991[82] 29097206[83]
TRPV4	Transient receptor potential cation channel, subfamily V, member 4	NM_021625 NM_001177431	- Congenital distal spinal muscular atrophy, non progressive	AD	25900305[84] 24789864[85]	
ZC4H2	Zinc Finger C4H2 domain-containing protein	NM_018684	- Wieacker-Wolff syndrome	XLR / (XLD)	23623388[86] 26056227[87] 28345801 [89]	26056227[87] 29803542 [88]

1 Laquérriere A, Maluenda J, Camus A *et al.* Mutations in CNTNAP1 and ADCY6 are responsible for severe arthrogryposis multiplex congenita with axoglial defects. *Hum Mol Genet* 2014; **23**: 2279–2289.

2 Arredondo J, Lara M, Gospe SM *et al.* Choline Acetyltransferase Mutations Causing Congenital Myasthenic Syndrome: Molecular Findings and Genotype-Phenotype Correlations. *Hum Mutat* 2015; **36**: 881–893.

3 Proschowsky HF, Flagstad A, Cirera S, Joergensen CB, Fredholm M. Identification of a mutation in the CHAT gene of Old Danish Pointing Dogs affected with congenital myasthenic syndrome. *J Hered* 2007; **98**: 539–543.

4 Abicht A, Müller J, Lochmüller H. Congenital Myasthenic Syndromes. In: Adam MP, Ardinger HH, Pagon RA *et al.* (eds). *GeneReviews®*. University of Washington, Seattle: Seattle (WA), 1993http://www.ncbi.nlm.nih.gov/books/NBK1168/ (accessed 13 Jun2018).

5 Dickinson ME, Flenniken AM, Ji X *et al.* High-throughput discovery of novel developmental phenotypes. *Nature* 2016; **537**: 508–514.

6 Michalk A, Stricker S, Becker J *et al.* Acetylcholine receptor pathway mutations explain various fetal akinesia deformation sequence disorders. *Am J Hum Genet* 2008; **82**: 464–476.

7 Vogt J, Harrison BJ, Spearman H *et al.* Mutation analysis of CHRNA1, CHRNB1, CHRND, and RAPSN genes in multiple pterygium syndrome/fetal akinesia patients. *Am J Hum Genet* 2008; **82**: 222–227.

8 Agerholm JS, McEvoy FJ, Menzi F, Jagannathan V, Drögemüller C. A CHRNB1 frameshift mutation is associated with familial arthrogryposis multiplex congenita in Red dairy cattle. *BMC Genomics* 2016; **17**: 479.

9 Shen X-M, Fukuda T, Ohno K, Sine SM, Engel AG. Congenital myasthenia-related AChR delta subunit mutation interferes with intersubunit communication essential for channel gating. *J Clin Invest* 2008; **118**: 1867–1876.

10 Morgan NV, Brueton LA, Cox P *et al.* Mutations in the embryonal subunit of the acetylcholine receptor (CHRNG) cause lethal and Escobar variants of multiple pterygium syndrome. *Am J Hum Genet* 2006; **79**: 390–395.

11 Hoffmann K, Muller JS, Stricker S *et al.* Escobar syndrome is a prenatal myasthenia caused by disruption of the acetylcholine receptor fetal gamma subunit.

Am J Hum Genet 2006; **79**: 303–312.
12 Koutsopoulos OS, Kretz C, Weller CM *et al.* Dynamin 2 homozygous mutation in humans with a lethal congenital syndrome. *Eur J Hum Genet EJHG* 2013; **21**: 637–642.
13 Tan-Sindhunata MB, Mathijssen IB, Smit M *et al.* Identification of a Dutch founder mutation in MUSK causing fetal akinesia deformation sequence. *Eur J Hum Genet EJHG* 2015; **23**: 1151–1157.
14 Müller JS, Jepson CD, Laval SH, Bushby K, Straub V, Lochmüller H. Dok-7 promotes slow muscle integrity as well as neuromuscular junction formation in a zebrafish model of congenital myasthenic syndromes. *Hum Mol Genet* 2010; **19**: 1726–1740.
15 Vogt J, Morgan NV, Marton T *et al.* Germline mutation in DOK7 associated with fetal akinesia deformation sequence. *J Med Genet* 2009; **46**: 338–340.
16 Narkis G, Ofir R, Manor E, Landau D, Elbedour K, Birk OS. Lethal congenital contractural syndrome type 2 (LCCS2) is caused by a mutation in ERBB3 (Her3), a modulator of the phosphatidylinositol-3-kinase/Akt pathway. *Am J Hum Genet* 2007; **81**: 589–595.
17 Nousiainen HO, Kestilä M, Pakkasjärvi N *et al.* Mutations in mRNA export mediator GLE1 result in a fetal motoneuron disease. *Nat Genet* 2008; **40**: 155–157.
18 Smith C, Parboosingh JS, Boycott KM *et al.* Expansion of the GLE1-associated arthrogryposis multiplex congenita clinical spectrum. *Clin Genet* 2017; **91**: 426–430.
19 Jao L-E, Appel B, Wente SR. A zebrafish model of lethal congenital contracture syndrome 1 reveals Gle1 function in spinal neural precursor survival and motor axon arborization. *Dev Camb Engl* 2012; **139**: 1316–1326.
20 Folkmann AW, Collier SE, Zhan X, Aditi null, Ohi MD, Wente SR. Gle1 functions during mRNA export in an oligomeric complex that is altered in human disease. *Cell* 2013; **155**: 582–593.
21 Ravenscroft G, Nolent F, Rajagopalan S *et al.* Mutations of GPR126 are responsible for severe arthrogryposis multiplex congenita. *Am J Hum Genet* 2015; **96**: 955–961.
22 Monk KR, Oshima K, Jörs S, Heller S, Talbot WS. Gpr126 is essential for peripheral nerve development and myelination in mammals. *Dev Camb Engl* 2011; **138**: 2673–2680.
23 Mejlachowicz D, Nolent F, Maluenda J *et al.* Truncating Mutations of MAGEL2, a Gene within the Prader-Willi Locus, Are Responsible for Severe Arthrogryposis. *Am J Hum Genet* 2015; **97**: 616–620.
24 Urreizti R, Cueto-Gonzalez AM, Franco-Valls H *et al.* A De Novo Nonsense Mutation in MAGEL2 in a Patient Initially Diagnosed as Opitz-C: Similarities Between Schaaf-Yang and Opitz-C Syndromes. *Sci Rep* 2017; **7**: 44138.
25 Enya T, Okamoto N, Iba Y *et al.* Three patients with Schaaf-Yang syndrome exhibiting arthrogryposis and endocrinological abnormalities. *Am J Med Genet A* 2018; **176**: 707–711.
26 Bischof JM, Stewart CL, Wevrick R. Inactivation of the mouse Magel2 gene results in growth abnormalities similar to Prader-Willi syndrome. *Hum Mol Genet* 2007; **16**: 2713–2719.
27 Wilbe M, Ekvall S, Eurenius K *et al.* MuSK: a new target for lethal fetal akinesia deformation sequence (FADS). *J Med Genet* 2015; **52**: 195–202.
28 Markus B, Narkis G, Landau D, Birk RZ, Cohen I, Birk OS. Autosomal recessive lethal congenital contractural syndrome type 4 (LCCS4) caused by a mutation in MYBPC1. *Hum Mutat* 2012; **33**: 1435–1438.
29 Ha K, Buchan JG, Alvarado DM *et al.* MYBPC1 mutations impair skeletal muscle function in zebrafish models of arthrogryposis. *Hum Mol Genet* 2013; **22**: 4967–4977.
30 Toydemir RM, Rutherford A, Whitby FG, Jorde LB, Carey JC, Bamshad MJ. Mutations in embryonic myosin heavy chain (MYH3) cause Freeman-Sheldon syndrome and Sheldon-Hall syndrome. *Nat Genet* 2006; **38**: 561–565.
31 Beck AE, McMillin MJ, Gildersleeve HIS, Shively KMB, Tang A, Bamshad MJ. Genotype-phenotype relationships in Freeman-Sheldon syndrome. *Am J Med Genet A* 2014; **164A**: 2808–2813.
32 Chong JX, Burrage LC, Beck AE *et al.* Autosomal-Dominant Multiple Pterygium Syndrome Is Caused by Mutations in MYH3. *Am J Hum Genet* 2015; **96**: 841–849.
33 Watson CM, Crinnion LA, Murphy H *et al.* Deficiency of the myogenic factor MyoD causes a perinatally lethal fetal akinesia. *J Med Genet* 2016; **53**: 264–269.
34 Macharia R, Otto A, Valasek P, Patel K. Neuromuscular junction morphology, fiber-type proportions, and satellite-cell proliferation rates are altered in MyoD(-/-) mice. *Muscle Nerve* 2010; **42**: 38–52.
35 Wallgren-Pettersson C, Donner K, Sewry C *et al.* Mutations in the nebulin gene can cause severe congenital nemaline myopathy. *Neuromuscul Disord NMD* 2002; **12**: 674–679.
36 Lehtokari V-L, Kiiski K, Sandaradura SA *et al.* Mutation update: the spectra of nebulin variants and associated myopathies. *Hum Mutat* 2014; **35**: 1418–1426.
37 Pelin K, Hilpelä P, Donner K *et al.* Mutations in the nebulin gene associated with autosomal recessive nemaline myopathy. *Proc Natl Acad Sci U S A* 1999; **96**: 2305–2310.
38 Narkis G, Ofir R, Landau D *et al.* Lethal contractural syndrome type 3 (LCCS3) is caused by a mutation in PIP5K1C, which encodes PIPKI gamma of the phophatidylinsitol pathway. *Am J Hum Genet* 2007; **81**: 530–539.
39 Ioos C, Barois A, Richard P, Eymard B, Hantaï D, Estournet-Mathiaud B. Congenital myasthenic syndrome due to rapsyn deficiency: three cases with arthrogryposis and bulbar symptoms. *Neuropediatrics* 2004; **35**: 246–249.
40 Dunne V, Maselli RA. Identification of pathogenic mutations in the human rapsyn gene. *J Hum Genet* 2003; **48**: 204–207.
41 Müller JS, Mildner G, Müller-Felber W *et al.* Rapsyn N88K is a frequent cause of congenital myasthenic syndromes in European patients. *Neurology* 2003; **60**: 1805–1810.
42 Cossins J, Burke G, Maxwell S *et al.* Diverse molecular mechanisms involved in AChR deficiency due to rapsyn mutations. *Brain J Neurol* 2006; **129**: 2773–2783.
43 Lin W, Burgess RW, Dominguez B, Pfaff SL, Sanes JR, Lee KF. Distinct roles of nerve and muscle in postsynaptic differentiation of the neuromuscular synapse. *Nature* 2001; **410**: 1057–1064.
44 McKie AB, Alsaedi A, Vogt J *et al.* Germline mutations in RYR1 are associated with foetal akinesia deformation sequence/lethal multiple pterygium syndrome. *Acta Neuropathol Commun* 2014; **2**: 148.
45 Zaharieva IT, Thor MG, Oates EC *et al.* Loss-of-function mutations in SCN4A cause severe foetal hypokinesia or 'classical' congenital myopathy. *Brain J Neurol* 2016; **139**: 674–691.
46 Chervinsky E, Khayat M, Soltsman S, Habiballa H, Elpeleg O, Shalev S. A homozygous TTN gene variant associated with lethal congenital contracture syndrome. *Am J Med Genet A* 2018; **176**: 1001–1005.
47 Patel N, Smith LL, Faqeih E, Mohamed J, Gupta VA, Alkuraya FS. ZBTB42 mutation defines a novel lethal congenital contracture syndrome (LCCS6). *Hum Mol Genet* 2014; **23**: 6584–6593.
48 Neveling K, Martinez-Carrera LA, Hölker I *et al.* Mutations in BICD2, which encodes a golgin and important motor adaptor, cause congenital autosomal-dominant spinal muscular atrophy. *Am J Hum Genet* 2013; **92**: 946–954.
49 Peeters K, Litvinenko I, Asselbergh B *et al.* Molecular defects in the motor adaptor BICD2 cause proximal spinal muscular atrophy with autosomal-dominant inheritance. *Am J Hum Genet* 2013; **92**: 955–964.
50 Oates EC, Rossor AM, Hafezparast M *et al.* Mutations in BICD2 cause dominant congenital spinal muscular atrophy and hereditary spastic paraplegia. *Am J Hum Genet* 2013; **92**: 965–973.
51 Martinez Carrera LA, Gabriel E, Donohoe CD *et al.* Novel insights into SMALED2: BICD2 mutations increase microtubule stability and cause defects in axonal and NMJ development. *Hum Mol Genet* 2018; **27**: 1772–1784.

52 Huynh W, Vale RD. Disease-associated mutations in human BICD2 hyperactivate motility of dynein-dynactin. *J Cell Biol* 2017; **216**: 3051–3060.
53 Harms MB, Ori-McKenney KM, Scoto M *et al.* Mutations in the tail domain of DYNC1H1 cause dominant spinal muscular atrophy. *Neurology* 2012; **78**: 1714–1720.
54 Scoto M, Rossor AM, Harms MB *et al.* Novel mutations expand the clinical spectrum of DYNC1H1-associated spinal muscular atrophy. *Neurology* 2015; **84**: 668–679.
55 Hoang HT, Schlager MA, Carter AP, Bullock SL. DYNC1H1 mutations associated with neurological diseases compromise processivity of dynein-dynactin-cargo adaptor complexes. *Proc Natl Acad Sci U S A* 2017; **114**: E1597–E1606.
56 Dieterich K, Quijano-Roy S, Monnier N *et al.* The neuronal endopeptidase ECEL1 is associated with a distinct form of recessive distal arthrogryposis. *Hum Mol Genet* 2013; **22**: 1483–1492.
57 McMillin MJ, Below JE, Shively KM *et al.* Mutations in ECEL1 cause distal arthrogryposis type 5D. *Am J Hum Genet* 2013; **92**: 150–156.
58 Nagata K, Takahashi M, Kiryu-Seo S, Kiyama H, Saido TC. Distinct functional consequences of ECEL1/DINE missense mutations in the pathogenesis of congenital contracture disorders. *Acta Neuropathol Commun* 2017; **5**: 83.
59 Putnam EA, Zhang H, Ramirez F, Milewicz DM. Fibrillin-2 (FBN2) mutations result in the Marfan-like disorder, congenital contractural arachnodactyly. *Nat Genet* 1995; **11**: 456–458.
60 Gupta PA, Putnam EA, Carmical SG *et al.* Ten novel FBN2 mutations in congenital contractural arachnodactyly: delineation of the molecular pathogenesis and clinical phenotype. *Hum Mutat* 2002; **19**: 39–48.
61 Frédéric MY, Monino C, Marschall C *et al.* The FBN2 gene: new mutations, locus-specific database (Universal Mutation Database FBN2), and genotype-phenotype correlations. *Hum Mutat* 2009; **30**: 181–190.
62 Callewaert BL, Loeys BL, Ficcadenti A *et al.* Comprehensive clinical and molecular assessment of 32 probands with congenital contractural arachnodactyly: report of 14 novel mutations and review of the literature. *Hum Mutat* 2009; **30**: 334–341.
63 Tajsharghi H, Hilton-Jones D, Raheem O, Saukkonen AM, Oldfors A, Udd B. Human disease caused by loss of fast IIa myosin heavy chain due to recessive MYH2 mutations. *Brain J Neurol* 2010; **133**: 1451–1459.
64 Lossos A, Oldfors A, Fellig Y, Meiner V, Argov Z, Tajsharghi H. MYH2 mutation in recessive myopathy with external ophthalmoplegia linked to chromosome 17p13.1-p12. *Brain J Neurol* 2013; **136**: e238.
65 Veugelers M, Bressan M, McDermott DA *et al.* Mutation of perinatal myosin heavy chain associated with a Carney complex variant. *N Engl J Med* 2004; **351**: 460–469.
66 Toydemir RM, Chen H, Proud VK *et al.* Trismus-pseudocamptodactyly syndrome is caused by recurrent mutation of MYH8. *Am J Med Genet A* 2006; **140**: 2387–2393.
67 Chong JX, McMillin MJ, Shively KM *et al.* De novo mutations in NALCN cause a syndrome characterized by congenital contractures of the limbs and face, hypotonia, and developmental delay. *Am J Hum Genet* 2015; **96**: 462–473.
68 Karakaya M, Heller R, Kunde V *et al.* Novel Mutations in the Nonselective Sodium Leak Channel (NALCN) Lead to Distal Arthrogryposis with Increased Muscle Tone. *Neuropediatrics* 2016; **47**: 273–277.
69 Aoyagi K, Rossignol E, Hamdan FF *et al.* A Gain-of-Function Mutation in NALCN in a Child with Intellectual Disability, Ataxia, and Arthrogryposis. *Hum Mutat* 2015; **36**: 753–757.
70 Al-Sayed MD, Al-Zaidan H, Albakheet A *et al.* Mutations in NALCN cause an autosomal-recessive syndrome with severe hypotonia, speech impairment, and cognitive delay. *Am J Hum Genet* 2013; **93**: 721–726.
71 Coste B, Houge G, Murray MF *et al.* Gain-of-function mutations in the mechanically activated ion channel PIEZO2 cause a subtype of Distal Arthrogryposis. *Proc Natl Acad Sci U S A* 2013; **110**: 4667–4672.
72 Delle Vedove A, Storbeck M, Heller R *et al.* Biallelic Loss of Proprioception-Related PIEZO2 Causes Muscular Atrophy with Perinatal Respiratory Distress, Arthrogryposis, and Scoliosis. *Am J Hum Genet* 2016; **99**: 1206–1216.
73 Haliloglu G, Becker K, Temucin C *et al.* Recessive PIEZO2 stop mutation causes distal arthrogryposis with distal muscle weakness, scoliosis and proprioception defects. *J Hum Genet* 2017; **62**: 497–501.
74 McMillin MJ, Beck AE, Chong JX *et al.* Mutations in PIEZO2 cause Gordon syndrome, Marden-Walker syndrome, and distal arthrogryposis type 5. *Am J Hum Genet* 2014; **94**: 734–744.
75 Okubo M, Fujita A, Saito Y *et al.* A family of distal arthrogryposis type 5 due to a novel PIEZO2 mutation. *Am J Med Genet A* 2015; **167A**: 1100–1106.
76 Sung SS, Brassington A-ME, Grannatt K *et al.* Mutations in genes encoding fast-twitch contractile proteins cause distal arthrogryposis syndromes. *Am J Hum Genet* 2003; **72**: 681–690.
77 Jiang M, Zhao X, Han W *et al.* A novel deletion in TNNI2 causes distal arthrogryposis in a large Chinese family with marked variability of expression. *Hum Genet* 2006; **120**: 238–242.
78 Sung SS, Brassington A-ME, Krakowiak PA, Carey JC, Jorde LB, Bamshad M. Mutations in TNNT3 cause multiple congenital contractures: a second locus for distal arthrogryposis type 2B. *Am J Hum Genet* 2003; **73**: 212–214.
79 Daly SB, Shah H, O'Sullivan J *et al.* Exome Sequencing Identifies a Dominant TNNT3 Mutation in a Large Family with Distal Arthrogryposis. *Mol Syndromol* 2014; **5**: 218–228.
80 Zhao N, Jiang M, Han W *et al.* A novel mutation in TNNT3 associated with Sheldon-Hall syndrome in a Chinese family with vertical talus. *Eur J Med Genet* 2011; **54**: 351–353.
81 Beck AE, McMillin MJ, Gildersleeve HIS *et al.* Spectrum of mutations that cause distal arthrogryposis types 1 and 2B. *Am J Med Genet A* 2013; **161A**: 550–555.
82 Ochala J, Li M, Tajsharghi H *et al.* Effects of a R133W beta-tropomyosin mutation on regulation of muscle contraction in single human muscle fibres. *J Physiol* 2007; **581**: 1283–1292.
83 Borovikov YS, Simonyan AO, Karpicheva OE *et al.* The reason for a high Ca2+-sensitivity associated with Arg91Gly substitution in TPM2 gene is the abnormal behavior and high flexibility of tropomyosin during the ATPase cycle. *Biochem Biophys Res Commun* 2017; **494**: 681–686.
84 Evangelista T, Bansagi B, Pyle A *et al.* Phenotypic variability of TRPV4 related neuropathies. *Neuromuscul Disord NMD* 2015; **25**: 516–521.
85 Echaniz-Laguna A, Dubourg O, Carlier P *et al.* Phenotypic spectrum and incidence of TRPV4 mutations in patients with inherited axonal neuropathy. *Neurology* 2014; **82**: 1919–1926.
86 Hirata H, Nanda I, van Riesen A *et al.* ZC4H2 mutations are associated with arthrogryposis multiplex congenita and intellectual disability through impairment of central and peripheral synaptic plasticity. *Am J Hum Genet* 2013; **92**: 681–695.
87 May M, Hwang K-S, Miles J *et al.* ZC4H2, an XLID gene, is required for the generation of a specific subset of CNS interneurons. *Hum Mol Genet* 2015; **24**: 4848–4861.
88 Kondo D, Noguchi A, Takahashi I *et al.* A novel ZC4H2 gene mutation, K209N, in Japanese siblings with arthrogryposis multiplex congenita and intellectual disability: characterization of the K209N mutation and clinical findings. *Brain Dev* 2018. doi:10.1016/j.braindev.2018.05.003.
89 Zanzottera C, Milani D, Alfei E *et al.* ZC4H2 deletions can cause severe phenotype in female carriers. *Am J Med Genet A* 2017; **173**: 1358–1363.

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Dystrophies musculaires congénitales hors alpha-dystroglycanopathies - Liste de gènes principale (8 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
LAMA2	Laminin alpha 2 (merosin, included)	NM_000426	- Muscular dystrophy, congenital merosin-deficient - MDC1A	AR	18700894[1] 16216942[2]	7874173[3]
COL6A1	Collagen, type VI, alpha-1	NM_001848	- Bethlem myopathy/ - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	15955946[4] 1193296[5] 24038877[7] 19564581[8]	9817932[6] 20338942[9]
COL6A2	Collagen, type VI, alpha-2	NM_001849	- Bethlem myopathy / - Ullrich congenital muscular dystrophy -UCMD / - Congenital myosclerosis	AD, AR/ AD, AR / AR	18852439[10] 25533456[11] 24038877[7] 20106987[13] 18852439[10]	28650483[12]
COL6A3	Collagen, type VI, alpha-3	NM_004369	- Bethlem myopathy/ - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	10399756[14] 24038877[7] 11992252[16]	24563484[15] 24563484[15]
SELENON [SEPN1]	Selenoprotein N (1)	NM_020451	- Rigid spine muscular dystrophy 1 / - Congenital myopathy with fiber-type disproportion	AR / AD, AR	11528383[17] 12192640[18] 16365872[20]	19557870[19] 19557870[19]
FHL1	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset - Emery-Dreifuss muscular dystrophy 6, X-linked - Myopathy, X-linked,with postural atrophy - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	18274675[21] 19181672[22] 18952429[23] 16919903[24]	29735270[25]
LMNA	Lamin A/C	NM_170707	- LGMD1B / - Emery-Dreifuss muscular dystrophy 2 / - Emery-Dreifuss muscular dystrophy 3 / - Congenital muscular dystrophy due to LMNA defect (L-CMD)	AD / AD / AR / AD	10814726[26] 15668447[27] 17377071[29] 15691357[30] 10739764[31] 22431096[32] 15148145[33] 15961312[34]	20848652[28] 20848652[28] 20848652[28] 20848652[28]
ACTA1	Actin, alpha, skeletal muscle 1	NM_001100	- Actin congenital myopathy with cores / - Actin congenital myopathy with excess of thin myofilaments / - Congenital myopathy with fiber-type disproportion 1 - Nemaline Myopathy 3	AD, AR / AD, AR / AD, AR / AD, AR	11333380[35] 255310[36] 10508519[38] 19562689[39] 19562689[39] 15468086[40] 11333380[35] 19562689[39]	22174871[37] 22174871[37] 17387733[41] 22825594[42]

Dystrophies musculaires congénitales hors alpha-dystroglycanopathies - Liste de gènes exhaustive (17 gènes):

(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
(LAMA2)	Laminin alpha 2 (merosin, included)	NM_000426	- Muscular dystrophy, congenital merosin-deficient - MDC1A	AR	18700894[1] 16216942[2]	7874173[3]
(COL6A1)	Collagen, type VI, alpha-1	NM_001848	- Bethlem myopathy/ - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	15955946[4] 1193296[5] 24038877[7] 19564581[8]	9817932[6] 20338942[9]
(COL6A2)	Collagen, type VI, alpha-2	NM_001849	- Bethlem myopathy / - Ullrich congenital muscular dystrophy -UCMD / - Congenital myosclerosis	AD, AR/ AD, AR / AR	24038877[7] 20106987[13] 18852439[10]	28650483[12]
(COL6A3)	Collagen, type VI, alpha-3	NM_004369	- Bethlem myopathy/ - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	24038877[7] 11992252[16]	24563484[15]
(SELENON [SEPN1])	Selenoprotein N (1)	NM_020451	- Rigid spine muscular dystrophy 1 / - Congenital myopathy with fiber-type disproportion	AR / AD, AR	11528383[17] 12192640[18] 16365872[20]	19557870[19] 19557870[19]
(FHL1)	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset - Emery-Dreifuss muscular dystrophy 6, X-linked - Myopathy, X-linked,with postural atrophy - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	18274675[21] 19181672[22] 18952429[23] 16919903[24]	29735270[25]
(LMNA)	Lamin A/C	NM_170707	- LGMD1B / - Emery-Dreifuss muscular dystrophy 2 / - Emery-Dreifuss muscular dystrophy 3 / - Congenital muscular dystrophy due to LMNA defect (L-CMD)	AD / AD / AR / AD	15148145[33] 15961312[34]	20848652[28]
(ACTA1)	Actin, alpha, skeletal muscle 1	NM_001100	- Actin congenital myopathy with cores / - Actin congenital myopathy with excess of thin myofilaments / - Congenital myopathy with fiber-type disproportion 1 - Nemaline Myopathy 3	AD, AR / AD, AR / AD, AR / AD, AR	11333380[35] 255310[36] 10508519[38] 19562689[39] 19562689[39] 15468086[40] 11333380[35] 19562689[39]	22174871[37] 22174871[37] 17387733[41] 22825594[42]
ITGA7	Integrin alpha 7	NM_002206 NM_001144997	Congenital muscular dystrophy due to ITGA7 deficiency	AR	9590299[43]	9354797[44]
DNM2	Dynamin 2	NM_001005360 NM_001005361 NM_001005362	- Centronuclear myopathy 1 / - Charcot-Marie-Tooth disease, axonal type 2M / - Charcot-Marie-Tooth disease, dominant intermediate B - Lethal congenital contracture syndrome 5	AD / AD / AD / AR	23092955[45]	20858595[46]
TCAP	Titin-CAP (Telethonin)	NM_003673	- LGMD2G	AR	25055047[47] 27618135[48]	19679566[49]
CHKB	Choline kinase, beta	NM_005198	- Congenital muscular dystrophy, megaconial type	AR	21665002[50] 24997086[51]	16371353[52]
TRAPPC11	Trafficking protein particle complex, subunit 11	NM_021942	- LGMD2S	AR	28827486[53] 23830518[54]	23830518[54]

COL12A1	Collagen type XII alpha 1 chain	NM_004370	- Bethlem myopathy / - Ullrich congenital muscular dystrophy – UCMD	AD, AR / AD, AR	24334769 [55] 24334604[56] 24334604[56]	21670218[57] 21670218[57]
GOLGA2	Golgin A2	NM_004486	- Developmental delay, seizures, progressive microcephaly, and muscular dystrophy - Mucopolysaccharidosis type 3	?/ AR	26742501[58]	26742501[58]
INPP5K	Inositol polyphosphate-5-phosphatase k	NM_001135642	Muscular dystrophy, congenital, with cataracts and intellectual disability	AR	28190456[59] 28190459[60]	28190456[59]
TRIP4	Thyroid hormone receptor interactor 4	NM_016213	- Muscular dystrophy, congenital, davignon-chauveau type	AR	27008887[61] 26924529[62]	26924529[62]

1 Oliveira J, Santos R, Soares-Silva I *et al.* LAMA2 gene analysis in a cohort of 26 congenital muscular dystrophy patients. *Clin Genet* 2008; **74**: 502–512.

2 Di Blasi C, Piga D, Brioschi P *et al.* LAMA2 gene analysis in congenital muscular dystrophy: new mutations, prenatal diagnosis, and founder effect. *Arch Neurol* 2005; **62**: 1582–1586.

3 Xu H, Wu XR, Wewer UM, Engvall E. Murine muscular dystrophy caused by a mutation in the laminin alpha 2 (Lama2) gene. *Nat Genet* 1994; **8**: 297–302.

4 Lucioli S, Giusti B, Mercuri E *et al.* Detection of common and private mutations in the COL6A1 gene of patients with Bethlem myopathy. *Neurology* 2005; **64**: 1931–1937.

5 Ducibella T, Albertini DF, Anderson E, Biggers JD. The preimplantation mammalian embryo: characterization of intercellular junctions and their appearance during development. *Dev Biol* 1975; **45**: 231–250.

6 Bonaldo P, Braghetta P, Zanetti M, Piccolo S, Volpin D, Bressan GM. Collagen VI deficiency induces early onset myopathy in the mouse: an animal model for Bethlem myopathy. *Hum Mol Genet* 1998; **7**: 2135–2140.

7 Butterfield RJ, Foley AR, Dastgir J *et al.* Position of glycine substitutions in the triple helix of COL6A1, COL6A2, and COL6A3 is correlated with severity and mode of inheritance in collagen VI myopathies. *Hum Mutat* 2013; **34**: 1558–1567.

8 Nadeau A, Kinali M, Main M *et al.* Natural history of Ullrich congenital muscular dystrophy. *Neurology* 2009; **73**: 25–31.

9 Telfer WR, Busta AS, Bonnemann CG, Feldman EL, Dowling JJ. Zebrafish models of collagen VI-related myopathies. *Hum Mol Genet* 2010; **19**: 2433–2444.

10 Merlini L, Martoni E, Grumati P *et al.* Autosomal recessive myosclerosis myopathy is a collagen VI disorder. *Neurology* 2008; **71**: 1245–1253.

11 Zamurs LK, Idoate MA, Hanssen E, Gomez-Ibañez A, Pastor P, Lamandé SR. Aberrant mitochondria in a Bethlem myopathy patient with a homozygous amino acid substitution that destabilizes the collagen VI α2(VI) chain. *J Biol Chem* 2015; **290**: 4272–4281.

12 Meehan TF, Conte N, West DB *et al.* Disease model discovery from 3,328 gene knockouts by The International Mouse Phenotyping Consortium. *Nat Genet* 2017; **49**: 1231–1238.

13 Zhang R-Z, Zou Y, Pan T-C *et al.* Recessive COL6A2 C-globular missense mutations in Ullrich congenital muscular dystrophy: role of the C2a splice variant. *J Biol Chem* 2010; **285**: 10005–10015.

14 Pepe G, Bertini E, Giusti B *et al.* A novel de novo mutation in the triple helix of the COL6A3 gene in a two-generation Italian family affected by Bethlem myopathy. A diagnostic approach in the mutations' screening of type VI collagen. *Neuromuscul Disord NMD* 1999; **9**: 264–271.

15 Pan T-C, Zhang R-Z, Arita M *et al.* A mouse model for dominant collagen VI disorders: heterozygous deletion of Col6a3 Exon 16. *J Biol Chem* 2014; **289**: 10293–10307.

16 Demir E, Sabatelli P, Allamand V *et al.* Mutations in COL6A3 cause severe and mild phenotypes of Ullrich congenital muscular dystrophy. *Am J Hum Genet* 2002; **70**: 1446–1458.

17 Moghadaszadeh B, Petit N, Jaillard C *et al.* Mutations in SEPN1 cause congenital muscular dystrophy with spinal rigidity and restrictive respiratory syndrome. *Nat Genet* 2001; **29**: 17–18.

18 Ferreiro A, Quijano-Roy S, Pichereau C *et al.* Mutations of the selenoprotein N gene, which is implicated in rigid spine muscular dystrophy, cause the classical phenotype of multiminicore disease: reassessing the nosology of early-onset myopathies. *Am J Hum Genet* 2002; **71**: 739–749.

19 Arbogast S, Beuvin M, Fraysse B, Zhou H, Muntoni F, Ferreiro A. Oxidative stress in SEPN1-related myopathy: from pathophysiology to treatment. *Ann Neurol* 2009; **65**: 677–686.

20 Clarke NF, Kidson W, Quijano-Roy S *et al.* SEPN1: associated with congenital fiber-type disproportion and insulin resistance. *Ann Neurol* 2006; **59**: 546–552.

21 Schessl J, Zou Y, McGrath MJ *et al.* Proteomic identification of FHL1 as the protein mutated in human reducing body myopathy. *J Clin Invest* 2008; **118**: 904–912.

22 Schessl J, Taratuto AL, Sewry C *et al.* Clinical, histological and genetic characterization of reducing body myopathy caused by mutations in FHL1. *Brain J Neurol* 2009; **132**: 452–464.

23 Shalaby S, Hayashi YK, Goto K *et al.* Rigid spine syndrome caused by a novel mutation in four-and-a-half LIM domain 1 gene (FHL1). *Neuromuscul Disord NMD* 2008; **18**: 959–961.

24 Ohsawa M, Liewluck T, Ogata K *et al.* Familial reducing body myopathy. *Brain Dev* 2007; **29**: 112–116.

25 Keßler M, Kieltsch A, Kayvanpour E *et al.* A zebrafish model for FHL1-opathy reveals loss-of-function effects of human FHL1 mutations. *Neuromuscul Disord NMD* 2018. doi:10.1016/j.nmd.2018.03.001.

26 Muchir A, Bonne G, van der Kooi AJ *et al.* Identification of mutations in the gene encoding lamins A/C in autosomal dominant limb girdle muscular dystrophy with atrioventricular conduction disturbances (LGMD1B). *Hum Mol Genet* 2000; **9**: 1453–1459.

27 van Engelen BGM, Muchir A, Hutchison CJ, van der Kooi AJ, Bonne G, Lammens M. The lethal phenotype of a homozygous nonsense mutation in the lamin A/C gene. *Neurology* 2005; **64**: 374–376.

28 Scharner J, Brown CA, Bower M *et al.* Novel LMNA mutations in patients with Emery-Dreifuss muscular dystrophy and functional characterization of four LMNA mutations. *Hum Mutat* 2011; **32**: 152–167.

29 Benedetti S, Menditto I, Degano M *et al.* Phenotypic clustering of lamin A/C mutations in neuromuscular patients. *Neurology* 2007; **69**: 1285–1292.

30 Wessely R, Seidl S, Schömig A. Cardiac involvement in Emery-Dreifuss muscular dystrophy. *Clin Genet* 2005; **67**: 220–223.

31 Raffaele Di Barletta M, Ricci E, Galluzzi G *et al.* Different mutations in the LMNA gene cause autosomal dominant and autosomal recessive Emery-Dreifuss muscular dystrophy. *Am J Hum Genet* 2000; **66**: 1407–1412.

32 Jimenez-Escrig A, Gobernado I, Garcia-Villanueva M, Sanchez-Herranz A. Autosomal recessive Emery-Dreifuss muscular dystrophy caused by a novel mutation (R225Q) in the lamin A/C gene identified by exome sequencing. *Muscle Nerve* 2012; **45**: 605–610.

33 Mercuri E, Poppe M, Quinlivan R *et al.* Extreme variability of phenotype in patients with an identical missense mutation in the lamin A/C gene: from congenital onset with severe phenotype to milder classic Emery-Dreifuss variant. *Arch Neurol* 2004; **61**: 690–694.

34 D'Amico A, Haliloglu G, Richard P *et al.* Two patients with 'Dropped head syndrome' due to mutations in LMNA or SEPN1 genes. *Neuromuscul Disord NMD* 2005; **15**: 521–524.

35 Ilkovski B, Cooper ST, Nowak K *et al.* Nemaline myopathy caused by mutations in the muscle alpha-skeletal-actin gene. *Am J Hum Genet* 2001; **68**: 1333–1343.

36 Van Duyn RL, Folkerts TM. Concentrations of tylosin in blood and lung tissue from calves given single and repeated daily intramuscular doses. *Vet Med Small Anim Clin VM SAC* 1979; **74**: 375–377.
37 Ravenscroft G, Jackaman C, Sewry CA *et al.* Actin nemaline myopathy mouse reproduces disease, suggests other actin disease phenotypes and provides cautionary note on muscle transgene expression. *PloS One* 2011; **6**: e28699.
38 Nowak KJ, Wattanasirichaigoon D, Goebel HH *et al.* Mutations in the skeletal muscle alpha-actin gene in patients with actin myopathy and nemaline myopathy. *Nat Genet* 1999; **23**: 208–212.
39 Laing NG, Dye DE, Wallgren-Pettersson C *et al.* Mutations and polymorphisms of the skeletal muscle alpha-actin gene (ACTA1). *Hum Mutat* 2009; **30**: 1267–1277.
40 Laing NG, Clarke NF, Dye DE *et al.* Actin mutations are one cause of congenital fibre type disproportion. *Ann Neurol* 2004; **56**: 689–694.
41 Clarke NF, Ilkovski B, Cooper S *et al.* The pathogenesis of ACTA1-related congenital fiber type disproportion. *Ann Neurol* 2007; **61**: 552–561.
42 Nowak KJ, Ravenscroft G, Laing NG. Skeletal muscle α-actin diseases (actinopathies): pathology and mechanisms. *Acta Neuropathol (Berl)* 2013; **125**: 19–32.
43 Hayashi YK, Chou FL, Engvall E *et al.* Mutations in the integrin alpha7 gene cause congenital myopathy. *Nat Genet* 1998; **19**: 94–97.
44 Mayer U, Saher G, Fässler R *et al.* Absence of integrin alpha 7 causes a novel form of muscular dystrophy. *Nat Genet* 1997; **17**: 318–323.
45 Koutsopoulos OS, Kretz C, Weller CM *et al.* Dynamin 2 homozygous mutation in humans with a lethal congenital syndrome. *Eur J Hum Genet EJHG* 2013; **21**: 637–642.
46 Durieux A-C, Vignaud A, Prudhon B *et al.* A centronuclear myopathy-dynamin 2 mutation impairs skeletal muscle structure and function in mice. *Hum Mol Genet* 2010; **19**: 4820–4836.
47 Francis A, Sunitha B, Vinodh K *et al.* Novel TCAP mutation c.32C>A causing limb girdle muscular dystrophy 2G. *PloS One* 2014; **9**: e102763.
48 de Fuenmayor-Fernández de la Hoz CP, Hernández-Laín A, Olivé M, Fernández-Marmiesse A, Domínguez-González C. Novel mutation in TCAP manifesting with asymmetric calves and early-onset joint retractions. *Neuromuscul Disord NMD* 2016; **26**: 749–753.
49 Zhang R, Yang J, Zhu J, Xu X. Depletion of zebrafish Tcap leads to muscular dystrophy via disrupting sarcomere-membrane interaction, not sarcomere assembly. *Hum Mol Genet* 2009; **18**: 4130–4140.
50 Mitsuhashi S, Ohkuma A, Talim B *et al.* A congenital muscular dystrophy with mitochondrial structural abnormalities caused by defective de novo phosphatidylcholine biosynthesis. *Am J Hum Genet* 2011; **88**: 845–851.
51 Castro-Gago M, Dacruz-Alvarez D, Pintos-Martínez E *et al.* Exome sequencing identifies a CHKB mutation in Spanish patient with megaconial congenital muscular dystrophy and mtDNA depletion. *Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc* 2014; **18**: 796–800.
52 Sher RB, Aoyama C, Huebsch KA *et al.* A rostrocaudal muscular dystrophy caused by a defect in choline kinase beta, the first enzyme in phosphatidylcholine biosynthesis. *J Biol Chem* 2006; **281**: 4938–4948.
53 Fee DB, Harmelink M, Monrad P, Pyzik E. Siblings With Mutations in TRAPPC11 Presenting With Limb-Girdle Muscular Dystrophy 2S. *J Clin Neuromuscul Dis* 2017; **19**: 27–30.
54 Bögershausen N, Shahrzad N, Chong JX *et al.* Recessive TRAPPC11 mutations cause a disease spectrum of limb girdle muscular dystrophy and myopathy with movement disorder and intellectual disability. *Am J Hum Genet* 2013; **93**: 181–190.
55 Hicks D, Farsani GT, Laval S *et al.* Mutations in the collagen XII gene define a new form of extracellular matrix-related myopathy. *Hum Mol Genet* 2014; **23**: 2353–2363.
56 Zou Y, Zwolanek D, Izu Y *et al.* Recessive and dominant mutations in COL12A1 cause a novel EDS/myopathy overlap syndrome in humans and mice. *Hum Mol Genet* 2014; **23**: 2339–2352.
57 Izu Y, Sun M, Zwolanek D *et al.* Type XII collagen regulates osteoblast polarity and communication during bone formation. *J Cell Biol* 2011; **193**: 1115–1130.
58 Shamseldin HE, Bennett AH, Alfadhel M, Gupta V, Alkuraya FS. GOLGA2, encoding a master regulator of golgi apparatus, is mutated in a patient with a neuromuscular disorder. *Hum Genet* 2016; **135**: 245–251.
59 Wiessner M, Roos A, Munn CJ *et al.* Mutations in INPP5K, Encoding a Phosphoinositide 5-Phosphatase, Cause Congenital Muscular Dystrophy with Cataracts and Mild Cognitive Impairment. *Am J Hum Genet* 2017; **100**: 523–536.
60 Osborn DPS, Pond HL, Mazaheri N *et al.* Mutations in INPP5K Cause a Form of Congenital Muscular Dystrophy Overlapping Marinesco-Sjögren Syndrome and Dystroglycanopathy. *Am J Hum Genet* 2017; **100**: 537–545.
61 Davignon L, Chauveau C, Julien C *et al.* The transcription coactivator ASC-1 is a regulator of skeletal myogenesis, and its deficiency causes a novel form of congenital muscle disease. *Hum Mol Genet* 2016; **25**: 1559–1573.
62 Knierim E, Hirata H, Wolf NI *et al.* Mutations in Subunits of the Activating Signal Cointegrator 1 Complex Are Associated with Prenatal Spinal Muscular Atrophy and Congenital Bone Fractures. *Am J Hum Genet* 2016; **98**: 473–489.

Version actualisée du 21.01.2019

Alpha-Dystroglycanopathies - Liste de gènes principale (13 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
FKTN	Fukutin	NM_001079802	- LGMD2M / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 4 / - Muscular dystrophy-dystroglycanopathy (congenital without mental retardation), type B, 4	AR / AR / AR	17878207[1] 19179078[2]	27194101[3]
FKRP	Fukutin-related protein	NM_024301	- LGMD2I / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 5 / - Muscular dystrophy-dystroglycanopathy (congenital with or without mental retardation), type B, 5	AR / AR/ AR	11592034[4] 15883334[5]	27194101 [3]
ISPD	Isoprenoid synthase domain-containing protein	NM_001101426	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 7 / - LGMD2U (Limb-Girdle, Muscular dystrophy related to ISPD)	AR / AR	23217329[6] 22522421[7]	27194101[3]
POMT1	Protein O-mannosyltransferase 1	NM_007171	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 1 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 1 / - LGMD2K	AR / AR / AR	12369018[8] 17878207[1]	21782786[9]
POMT2	Protein O-mannosyltransferase 2	NM_013382	- LGMD2N / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 2 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 2	AR / AR / AR	17878207[1] 19138766[10]	21782786[9]
POMGNT1	Protein O-mannose Beta-1,2-N-acetyl glucosaminyltransferase	NM_001243766	- LGMD2O / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 3 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 3	AR / AR / AR	19067344[11] 15236414[12]	11709191[13]
GMPPB	GDP-mannose pyrophosphorylase, beta subunit	NM_013334	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 14 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 14 / - LGMD2T	AR / AR / AR	23768512[14] 26133662[15]	23768512[14]
B3GALNT2	Beta-1,3-N-acetylgalactosaminyl transferase 2	NM_152490	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 11	AR	23453667[16] 24084573[17]	23929950[18]
POMK	Protein-O-mannose kinase	NM_032237	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 12 / - Muscular dystrophy-dystroglycanopathy (limb-girdle), type C, 12	AR / AR	24556084[19] 24925318[20]	23929950[18]

TMEM5	Transmembrane protein 5	NM_014254	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 10	AR	23217329[6] 23519211[21]	27733679[22]
LARGE1 [LARGE]	Acetylglucosaminyltransferase-like protein	NM_004737	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 6 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 6	AR / AR	19067344[11] 17436019[23]	22223806[24]
POMGNT2	Protein O-mannose beta-1,4- N-acetylglucosaminyltransferase 2	NM_032806	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 8	AR	19067344[11] 15236414[12]	11709191[13]
B4GAT1 [B3GNT1]	Beta-1,4-glucuronyltransferase 1	NM_006876	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 13	AR	23359570[25] 23877401[26]	23359570[25]

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Alpha-Dystroglycanopathies - Liste de gènes exhaustive (18 gènes):

(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
(FKTN)	Fukutin	NM_001079802	- LGMD2M / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 4 / - Muscular dystrophy-dystroglycanopathy (congenital without mental retardation), type B, 4	AR / AR / AR	17878207[1] 19179078[2]	27194101[3]
(FKRP)	Fukutin-related protein	NM_024301	- LGMD2I / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 5 / - Muscular dystrophy-dystroglycanopathy (congenital with or without mental retardation), type B, 5	AR / AR / AR	11592034[4] 15883334[5]	27194101[3]
(ISPD)	Isoprenoid synthase domain-containing protein	NM_001101426	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 7 / - LGMD2U (Limb-Girdle, Muscular dystrophy related to ISPD)	AR / AR	23217329[6] 22522421[7]	27194101[3]
(POMT1)	Protein O-mannosyltransferase 1	NM_007171	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 1 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 1 / - LGMD2K	AR / AR / AR	12369018[8] 17878207[1]	21782786[9]
(POMT2)	Protein O-mannosyltransferase 2	NM_013382	- LGMD2N / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 2 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 2	AR / AR / AR	17878207[1] 19138766[10]	21782786[9]
(POMGNT1)	Protein O-mannose Beta-1,2-N-acetylglucosaminyltransferase	NM_001243766	- LGMD2O / - Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 3 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 3	AR / AR / AR	19067344[11] 15236414[12]	11709191[13]
(GMPPB)	GDP-mannose pyrophosphorylase, beta subunit	NM_013334	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 14 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 14 / - LGMD2T	AR / AR / AR	23768512[14] 26133662[15]	23768512[14]
(B3GALNT2)	Beta-1,3-N-acetylgalactosaminyl transferase 2	NM_152490	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 11	AR	23453667[16] 24084573[17]	23929950[18]
(POMK)	Protein-O-mannose kinase	NM_032237	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 12 / - Muscular dystrophy-dystroglycanopathy (limb-girdle), type C, 12	AR / AR	24556084[19] 24925318[20]	23929950[18]

(TMEM5)	Transmembrane protein 5	NM_014254	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 10	AR	23217329[6] 23519211[21]	27733679[22]
(LARGE1 [LARGE])	Acetylglucosaminyltransferase-like protein	NM_004737	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 6 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 6	AR / AR	19067344[11] 17436019[23]	22223806[24]
(POMGNT2)	Protein O-mannose beta-1,4- N-acetylglucosaminyl transferase 2	NM_032806	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 8	AR	19067344[11] 15236414[12]	11709191[13]
(B4GAT1 [B3GNT1])	Beta-1,4-glucuronyltransferase 1	NM_006876	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 13	AR	23359570[25] 23877401[26]	23359570[25]
DPM1	Dolichyl-phosphate mannosyltransferase 1, catalytic subunit	NM_003859	- DPM1-CDG (Congenital Disorder of Glycosylation)	AR	10642602[27] 10642597[28] 23856421[29]	10835346[30]
DPM2	Dolichyl-phosphate mannosyltransferase 2, regulatory subunit	NM_003863	- DPM2-CDG (Congenital Disorder of Glycosylation)	AR	19901254[31] 23109149[32]	9724629[33]
DPM3	Dolichyl-phosphate mannosyltransferase 3	NM_153741	- DPM3-CDG (Congenital Disorder of Glycosylation)	AR	19576565[34] 28803818[35]	10835346[30]
DOLK	Dolichol kinase	NM_014908	- DOLK-CDG (Congenital Disorder of Glycosylation)	AR	22242004[36] 17273964[37]	16923818[38]
DAG1	Dystrophin-associated glycoprotein 1	NM_001165928	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 9 / - LGMD2P (Recessive LGMD with primary alphaDG defect)	AR / AR	14678799[39] 25503980[40]	21388311[41]

1 Godfrey C, Clement E, Mein R *et al.* Refining genotype phenotype correlations in muscular dystrophies with defective glycosylation of dystroglycan. *Brain J Neurol* 2007; **130**: 2725–2735.

2 Vuillaumier-Barrot S, Quijano-Roy S, Bouchet-Seraphin C *et al.* Four Caucasian patients with mutations in the fukutin gene and variable clinical phenotype. *Neuromuscul Disord NMD* 2009; **19**: 182–188.

3 Gerin I, Ury B, Breloy I *et al.* ISPD produces CDP-ribitol used by FKTN and FKRP to transfer ribitol phosphate onto α-dystroglycan. *Nat Commun* 2016; **7**: 11534.

4 Brockington M, Blake DJ, Prandini P *et al.* Mutations in the fukutin-related protein gene (FKRP) cause a form of congenital muscular dystrophy with secondary laminin alpha2 deficiency and abnormal glycosylation of alpha-dystroglycan. *Am J Hum Genet* 2001; **69**: 1198–1209.

5 Schwartz M, Hertz JM, Sveen ML, Vissing J. LGMD2I presenting with a characteristic Duchenne or Becker muscular dystrophy phenotype. *Neurology* 2005; **64**: 1635–1637.

6 Vuillaumier-Barrot S, Bouchet-Séraphin C, Chelbi M *et al.* Identification of mutations in TMEM5 and ISPD as a cause of severe cobblestone lissencephaly. *Am J Hum Genet* 2012; **91**: 1135–1143.

7 Roscioli T, Kamsteeg E-J, Buysse K *et al.* Mutations in ISPD cause Walker-Warburg syndrome and defective glycosylation of α-dystroglycan. *Nat Genet* 2012; **44**: 581–585.

8 Beltrán-Valero de Bernabé D, Currier S, Steinbrecher A *et al.* Mutations in the O-mannosyltransferase gene POMT1 give rise to the severe neuronal migration disorder Walker-Warburg syndrome. *Am J Hum Genet* 2002; **71**: 1033–1043.

9 Akasaka-Manya K, Manya H, Hayashi M, Endo T. Different roles of the two components of human protein O-mannosyltransferase, POMT1 and POMT2. *Biochem Biophys Res Commun* 2011; **411**: 721–725.

10 Yanagisawa A, Bouchet C, Quijano-Roy S *et al.* POMT2 intragenic deletions and splicing abnormalities causing congenital muscular dystrophy with mental retardation. *Eur J Med Genet* 2009; **52**: 201–206.

11 Clement E, Mercuri E, Godfrey C *et al.* Brain involvement in muscular dystrophies with defective dystroglycan glycosylation. *Ann Neurol* 2008; **64**: 573–582.

12 Vervoort VS, Holden KR, Ukadike KC, Collins JS, Saul RA, Srivastava AK. POMGnT1 gene alterations in a family with neurological abnormalities. *Ann Neurol* 2004; **56**: 143–148.

13 Yoshida A, Kobayashi K, Manya H *et al.* Muscular dystrophy and neuronal migration disorder caused by mutations in a glycosyltransferase, POMGnT1. *Dev Cell* 2001; **1**: 717–724.

14 Carss KJ, Stevens E, Foley AR *et al.* Mutations in GDP-mannose pyrophosphorylase B cause congenital and limb-girdle muscular dystrophies associated with hypoglycosylation of α-dystroglycan. *Am J Hum Genet* 2013; **93**: 29–41.

15 Belaya K, Rodríguez Cruz PM, Liu WW *et al.* Mutations in GMPPB cause congenital myasthenic syndrome and bridge myasthenic disorders with dystroglycanopathies. *Brain J Neurol* 2015; **138**: 2493–2504.

16 Stevens E, Carss KJ, Cirak S *et al.* Mutations in B3GALNT2 cause congenital muscular dystrophy and hypoglycosylation of α-dystroglycan. *Am J Hum Genet* 2013; **92**: 354–365.

17 Hedberg C, Oldfors A, Darin N. B3GALNT2 is a gene associated with congenital muscular dystrophy with brain malformations. *Eur J Hum Genet EJHG* 2014; **22**: 707–710.

18 Yoshida-Moriguchi T, Willer T, Anderson ME *et al.* SGK196 is a glycosylation-specific O-mannose kinase required for dystroglycan function. *Science* 2013; **341**: 896–899.
19 von Renesse A, Petkova MV, Lützkendorf S *et al.* POMK mutation in a family with congenital muscular dystrophy with merosin deficiency, hypomyelination, mild hearing deficit and intellectual disability. *J Med Genet* 2014; **51**: 275–282.
20 Di Costanzo S, Balasubramanian A, Pond HL *et al.* POMK mutations disrupt muscle development leading to a spectrum of neuromuscular presentations. *Hum Mol Genet* 2014; **23**: 5781–5792.
21 Jae LT, Raaben M, Riemersma M *et al.* Deciphering the glycosylome of dystroglycanopathies using haploid screens for lassa virus entry. *Science* 2013; **340**: 479–483.
22 Manya H, Yamaguchi Y, Kanagawa M *et al.* The Muscular Dystrophy Gene TMEM5 Encodes a Ribitol β1,4-Xylosyltransferase Required for the Functional Glycosylation of Dystroglycan. *J Biol Chem* 2016; **291**: 24618–24627.
23 van Reeuwijk J, Grewal PK, Salih MAM *et al.* Intragenic deletion in the LARGE gene causes Walker-Warburg syndrome. *Hum Genet* 2007; **121**: 685–690.
24 Inamori K, Yoshida-Moriguchi T, Hara Y, Anderson ME, Yu L, Campbell KP. Dystroglycan function requires xylosyl- and glucuronyltransferase activities of LARGE. *Science* 2012; **335**: 93–96.
25 Buysse K, Riemersma M, Powell G *et al.* Missense mutations in β-1,3-N-acetylglucosaminyltransferase 1 (B3GNT1) cause Walker-Warburg syndrome. *Hum Mol Genet* 2013; **22**: 1746–1754.
26 Shaheen R, Faqeih E, Ansari S, Alkuraya FS. A truncating mutation in B3GNT1 causes severe Walker-Warburg syndrome. *Neurogenetics* 2013; **14**: 243–245.
27 Imbach T, Schenk B, Schollen E *et al.* Deficiency of dolichol-phosphate-mannose synthase-1 causes congenital disorder of glycosylation type Ie. *J Clin Invest* 2000; **105**: 233–239.
28 Kim S, Westphal V, Srikrishna G *et al.* Dolichol phosphate mannose synthase (DPM1) mutations define congenital disorder of glycosylation Ie (CDG-Ie). *J Clin Invest* 2000; **105**: 191–198.
29 Yang AC, Ng BG, Moore SA *et al.* Congenital disorder of glycosylation due to DPM1 mutations presenting with dystroglycanopathy-type congenital muscular dystrophy. *Mol Genet Metab* 2013; **110**: 345–351.
30 Maeda Y, Tanaka S, Hino J, Kangawa K, Kinoshita T. Human dolichol-phosphate-mannose synthase consists of three subunits, DPM1, DPM2 and DPM3. *EMBO J* 2000; **19**: 2475–2482.
31 Messina S, Tortorella G, Concolino D *et al.* Congenital muscular dystrophy with defective alpha-dystroglycan, cerebellar hypoplasia, and epilepsy. *Neurology* 2009; **73**: 1599–1601.
32 Barone R, Aiello C, Race V *et al.* DPM2-CDG: a muscular dystrophy-dystroglycanopathy syndrome with severe epilepsy. *Ann Neurol* 2012; **72**: 550–558.
33 Maeda Y, Tomita S, Watanabe R, Ohishi K, Kinoshita T. DPM2 regulates biosynthesis of dolichol phosphate-mannose in mammalian cells: correct subcellular localization and stabilization of DPM1, and binding of dolichol phosphate. *EMBO J* 1998; **17**: 4920–4929.
34 Lefeber DJ, Schönberger J, Morava E *et al.* Deficiency of Dol-P-Man synthase subunit DPM3 bridges the congenital disorders of glycosylation with the dystroglycanopathies. *Am J Hum Genet* 2009; **85**: 76–86.
35 Van den Bergh PYK, Sznajer Y, Van Parys V *et al.* A homozygous DPM3 mutation in a patient with alpha-dystroglycan-related limb girdle muscular dystrophy. *Neuromuscul Disord NMD* 2017; **27**: 1043–1046.
36 Lefeber DJ, de Brouwer APM, Morava E *et al.* Autosomal recessive dilated cardiomyopathy due to DOLK mutations results from abnormal dystroglycan O-mannosylation. *PLoS Genet* 2011; **7**: e1002427.
37 Kranz C, Jungeblut C, Denecke J *et al.* A defect in dolichol phosphate biosynthesis causes a new inherited disorder with death in early infancy. *Am J Hum Genet* 2007; **80**: 433–440.
38 Shridas P, Waechter CJ. Human dolichol kinase, a polytopic endoplasmic reticulum membrane protein with a cytoplasmically oriented CTP-binding site. *J Biol Chem* 2006; **281**: 31696–31704.
39 Dinçer P, Balci B, Yuva Y *et al.* A novel form of recessive limb girdle muscular dystrophy with mental retardation and abnormal expression of alpha-dystroglycan. *Neuromuscul Disord NMD* 2003; **13**: 771–778.
40 Dong M, Noguchi S, Endo Y *et al.* DAG1 mutations associated with asymptomatic hyperCKemia and hypoglycosylation of α-dystroglycan. *Neurology* 2015; **84**: 273–279.
41 Hara Y, Balci-Hayta B, Yoshida-Moriguchi T *et al.* A dystroglycan mutation associated with limb-girdle muscular dystrophy. *N Engl J Med* 2011; **364**: 939–946.

Version actualisée du 21.01.2019

Myopathies distales et scapulopéronières - Liste de gènes unique exhaustive (24 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
DYSF	Dysferlin	NM_003494	- LGMD2B / - Miyoshi muscular dystrophy 1 / - Distal myopathy with anterior tibial onset	AR / AR / AR	9731526[1] 12796534[2] 21301039[3]	21522182[4]
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / AR/ AD AR / AD	29435569[5] 12145747[6]	20634290[7]
GNE	UDP-N-acetylglucosamine-2- epimerase/N-acetylmannosamine kinase	NM_001128227	- Distal myopathy with rimmed vacuoles (Nonaka) and Hereditary inclusion body myopathy	AR	11528398 [8] 12473753[9] 2500214[10] 6737002[11]	17704511[12]
MYH7	Myosin, heavy polypeptide 7, cardiac muscle, beta	NM_000257	- Laing distal myopathy / - Congenital myopathy (myosin storage myopathy) / - Scapuloperoneal syndrome, myopathic type	AD / AD, AR / AD	14520662[13] 23478172[14] 15322983[16] 27387980[17]	19336582[15]
MATR3	Matrin 3	NM_199189	- Amyotrophic lateral sclerosis 21 / - Vocal cord and pharyngeal distal myopathy	AD / AD	25154462[18] 23842731[19] 19344878 [20]	28977530[21]
TIA1	TIA1 cytotoxic granule-associated RNA-binding protein	NM_022173	- Welander distal myopathy	AD, AR	23401021[22] 23348830[23]	
MYOT	Myotilin	NM_006790	- LGMD1A / - Myopathy, myofibrillar, 3 / - Myopathy, spheroid body	AD / AD / AD	15111675[24] 17698502[25]	16801328[26]
NEB	Nebulin	NM_001271208 NM_001164507	- Nemaline myopathy 2	AR	17525139[27] 21724397[28]	23715096[29]
CAV3	Caveolin 3	NM_033337	- LGMD1C / - Distal myopathy, Tateyama type / - Rippling muscle disease	AD / AD / AD	11805270[30] 18930476[31] 12557291[33]	11115849[32]
LDB3 [ZASP]	LIM domain binding 3	NM_001080114 NM_001171610 NM_007078	- Late onset distal myopathy (Markesbery-Griggs) / - Myopathy, myofibrillar, 4	AD / AD	26342832[34] 27389816[35] 15668942[36] 27546599[38] 23263837[39]	12499364[37]

ANO5	Anoctamin 5	NM_213599	- LGMD2L / - Miyoshi muscular dystrophy 3 (Early onset calf distal myopathy)	AR / AR	20096397[40] 22402862[42]	29789544[41]
DNM2	Dynamin 2	NM_001005360 NM_001005361 NM_001005362	- Centronuclear myopathy 1 / - Charcot-Marie-Tooth disease, axonal type 2M / - Charcot-Marie-Tooth disease, dominant intermediate B / - Lethal congenital contracture syndrome 5	AD / AD / AD / AR	18560793[43] 17134899[45]	20858595[44]
FLNC	Filamin C	NM_001458	- Myopathy, distal, 4 / - Myopathy, myofibrillar, 5	AD / AD	15824355[46] 21620354[48]	26472074[47]
VCP	Valosin-containing protein	NM_007126	- Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia 1 / - Charcot-Marie-Tooth disease, type 2Y	AD / AD	18260132[49] 18845250[50] 21684747[51] 26853221[53] 26105173[54]	20147319[52]
TCAP	Titin-CAP (Telethonin)	NM_003673	- LGMD2G	AR	27618135[55]	
PNPLA2	Patatin-like phospholipase domain-containing protein 2	NM_020376	- Neutral lipid storage disease with myopathy without ichthyosis	AR	21544567[56] 18657972[57] 24836204[58]	21857651[59]
DES	Desmin	NM_001927	- LGMD1E / - LGMD2R / - Myopathy, myofibrillar, 1 / - Scapuloperoneal syndrome, neurogenic, Kaeser type	AD / AR / AD, AR / AD	11061256[60] 12620971[61] 11668632[63]	16217025[62]
CRYAB	Crystallin, Alpha-B	NM_001885	- Myopathy, myofibrillar, fatal infantile hypertrophy, alpha-B crystallin-related	AD, AR	20171888[64] 27389816[35]	27904835 [65]
FHL1	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset / - Emery-Dreifuss muscular dystrophy 6, X-linked / - Myopathy, X-linked,with postural atrophy / - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	25246303[66] 24613424[67]	29735270[68]
LMNA	Lamin A/C	NM_170707	- LGMD1B / - Emery-Dreifuss muscular dystrophy 2 / - Emery-Dreifuss muscular dystrophy 3 / - Congenital muscular dystrophy due to LMNA defect (L-CMD)	AD / AD / AR / AD	18551513[69]	15548545[70]
SQSTM1	Sequestosome 1	NM_003900 NM_001142298	- Distal myopathy with rimmed vacuoles	AD	26208961[71]	
KLHL9	Kelch-like 9	NM_018847	- Distal myopathy	AD	20554658[72]	
ADSSL1	Adenylosuccinate synthase-like 1	NM_152328	- Myopathy, distal, 5	AR	26506222[73]	
DNAJB6	DNAJ/HSP40 homolog, subfamily B, member 6	NM_058246	- LGMD1D	AD	29437287[74] 22334415[75] 26205529[76]	26362252[77]

1 Liu J, Aoki M, Illa I *et al.* Dysferlin, a novel skeletal muscle gene, is mutated in Miyoshi myopathy and limb girdle muscular dystrophy. *Nat Genet* 1998; **20**: 31–36.

2 Takahashi T, Aoki M, Tateyama M *et al.* Dysferlin mutations in Japanese Miyoshi myopathy: relationship to phenotype. *Neurology* 2003; **60**: 1799–1804.

3 Kawai H. [Miyoshi distal muscular dystrophy (Miyoshi myopathy)]. *Brain Nerve Shinkei Kenkyu No Shinpo* 2011; **63**: 147–156.

4 Cacciottolo M, Numitone G, Aurino S *et al.* Muscular dystrophy with marked Dysferlin deficiency is consistently caused by primary dysferlin gene mutations. *Eur J Hum Genet EJHG* 2011; **19**: 974–980.
5 Savarese M, Maggi L, Vihola A *et al.* Interpreting Genetic Variants in Titin in Patients With Muscle Disorders. *JAMA Neurol* 2018; **75**: 557–565.
6 Hackman P, Vihola A, Haravuori H *et al.* Tibial muscular dystrophy is a titinopathy caused by mutations in TTN, the gene encoding the giant skeletal-muscle protein titin. *Am J Hum Genet* 2002; **71**: 492–500.
7 Sarparanta J, Blandin G, Charton K *et al.* Interactions with M-band titin and calpain 3 link myospryn (CMYA5) to tibial and limb-girdle muscular dystrophies. *J Biol Chem* 2010; **285**: 30304–30315.
8 Eisenberg I, Avidan N, Potikha T *et al.* The UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase gene is mutated in recessive hereditary inclusion body myopathy. *Nat Genet* 2001; **29**: 83–87.
9 Nishino I, Noguchi S, Murayama K *et al.* Distal myopathy with rimmed vacuoles is allelic to hereditary inclusion body myopathy. *Neurology* 2002; **59**: 1689–1693.
10 Cade J, Margetts B. Cigarette smoking and serum lipid and lipoprotein concentrations. *BMJ* 1989; **298**: 1312.
11 Argov Z, Yarom R. 'Rimmed vacuole myopathy' sparing the quadriceps. A unique disorder in Iranian Jews. *J Neurol Sci* 1984; **64**: 33–43.
12 Malicdan MCV, Noguchi S, Nonaka I, Hayashi YK, Nishino I. A Gne knockout mouse expressing human GNE D176V mutation develops features similar to distal myopathy with rimmed vacuoles or hereditary inclusion body myopathy. *Hum Mol Genet* 2007; **16**: 2669–2682.
13 Tajsharghi H, Thornell L-E, Lindberg C, Lindvall B, Henriksson K-G, Oldfors A. Myosin storage myopathy associated with a heterozygous missense mutation in MYH7. *Ann Neurol* 2003; **54**: 494–500.
14 Clarke NF, Amburgey K, Teener J *et al.* A novel mutation expands the genetic and clinical spectrum of MYH7-related myopathies. *Neuromuscul Disord NMD* 2013; **23**: 432–436.
15 Armel TZ, Leinwand LA. Mutations in the beta-myosin rod cause myosin storage myopathy via multiple mechanisms. *Proc Natl Acad Sci U S A* 2009; **106**: 6291–6296.
16 Meredith C, Herrmann R, Parry C *et al.* Mutations in the slow skeletal muscle fiber myosin heavy chain gene (MYH7) cause laing early-onset distal myopathy (MPD1). *Am J Hum Genet* 2004; **75**: 703–708.
17 Fiorillo C, Astrea G, Savarese M *et al.* MYH7-related myopathies: clinical, histopathological and imaging findings in a cohort of Italian patients. *Orphanet J Rare Dis* 2016; **11**: 91.
18 Müller TJ, Kraya T, Stoltenburg-Didinger G *et al.* Phenotype of matrin-3-related distal myopathy in 16 German patients. *Ann Neurol* 2014; **76**: 669–680.
19 Kraya T, Zierz S. Distal myopathies: from clinical classification to molecular understanding. *J Neural Transm Vienna Austria 1996* 2013; **120 Suppl 1**: S3-7.
20 Senderek J, Garvey SM, Krieger M *et al.* Autosomal-dominant distal myopathy associated with a recurrent missense mutation in the gene encoding the nuclear matrix protein, matrin 3. *Am J Hum Genet* 2009; **84**: 511–518.
21 Banerjee A, Vest KE, Pavlath GK, Corbett AH. Nuclear poly(A) binding protein 1 (PABPN1) and Matrin3 interact in muscle cells and regulate RNA processing. *Nucleic Acids Res* 2017; **45**: 10706–10725.
22 Hackman P, Sarparanta J, Lehtinen S *et al.* Welander distal myopathy is caused by a mutation in the RNA-binding protein TIA1. *Ann Neurol* 2013; **73**: 500–509.
23 Klar J, Sobol M, Melberg A *et al.* Welander distal myopathy caused by an ancient founder mutation in TIA1 associated with perturbed splicing. *Hum Mutat* 2013; **34**: 572–577.
24 Selcen D, Engel AG. Mutations in myotilin cause myofibrillar myopathy. *Neurology* 2004; **62**: 1363–1371.
25 Berciano J, Gallardo E, Domínguez-Perles R *et al.* Autosomal-dominant distal myopathy with a myotilin S55F mutation: sorting out the phenotype. *J Neurol Neurosurg Psychiatry* 2008; **79**: 205–208.
26 Garvey SM, Miller SE, Claflin DR, Faulkner JA, Hauser MA. Transgenic mice expressing the myotilin T57I mutation unite the pathology associated with LGMD1A and MFM. *Hum Mol Genet* 2006; **15**: 2348–2362.
27 Wallgren-Pettersson C, Lehtokari V-L, Kalimo H *et al.* Distal myopathy caused by homozygous missense mutations in the nebulin gene. *Brain J Neurol* 2007; **130**: 1465–1476.
28 Lehtokari V-L, Pelin K, Herczegfalvi A *et al.* Nemaline myopathy caused by mutations in the nebulin gene may present as a distal myopathy. *Neuromuscul Disord NMD* 2011; **21**: 556–562.
29 Ottenheijm CAC, Buck D, de Winter JM *et al.* Deleting exon 55 from the nebulin gene induces severe muscle weakness in a mouse model for nemaline myopathy. *Brain J Neurol* 2013; **136**: 1718–1731.
30 Tateyama M, Aoki M, Nishino I *et al.* Mutation in the caveolin-3 gene causes a peculiar form of distal myopathy. *Neurology* 2002; **58**: 323–325.
31 González-Pérez P, Gallano P, González-Quereda L *et al.* Phenotypic variability in a Spanish family with a Caveolin-3 mutation. *J Neurol Sci* 2009; **276**: 95–98.
32 Hagiwara Y, Sasaoka T, Araishi K *et al.* Caveolin-3 deficiency causes muscle degeneration in mice. *Hum Mol Genet* 2000; **9**: 3047–3054.
33 Fischer D, Schroers A, Blümcke I *et al.* Consequences of a novel caveolin-3 mutation in a large German family. *Ann Neurol* 2003; **53**: 233–241.
34 Béhin A, Salort-Campana E, Wahbi K *et al.* Myofibrillar myopathies: State of the art, present and future challenges. *Rev Neurol (Paris)* 2015; **171**: 715–729.
35 Kley RA, Olivé M, Schröder R. New aspects of myofibrillar myopathies. *Curr Opin Neurol* 2016; **29**: 628–634.
36 Selcen D, Engel AG. Mutations in ZASP define a novel form of muscular dystrophy in humans. *Ann Neurol* 2005; **57**: 269–276.
37 Huang C, Zhou Q, Liang P *et al.* Characterization and in vivo functional analysis of splice variants of cypher. *J Biol Chem* 2003; **278**: 7360–7365.
38 Zheng J, Chen S, Chen Y, Zhu M, Hong D. A novel mutation in the PDZ-like motif of ZASP causes distal ZASP-related myofibrillar myopathy. *Neuropathol Off J Jpn Soc Neuropathol* 2017; **37**: 45–51.
39 Kraya T, Kress W, Stoevesant D, Deschauer M, Zierz S. [Myofibrillary myopathy due to the ZASP mutation Ala147Thr : two cases with exclusively distal leg involvement]. *Nervenarzt* 2013; **84**: 209–213.
40 Bolduc V, Marlow G, Boycott KM *et al.* Recessive mutations in the putative calcium-activated chloride channel Anoctamin 5 cause proximal LGMD2L and distal MMD3 muscular dystrophies. *Am J Hum Genet* 2010; **86**: 213–221.
41 Sui T, Xu L, Lau YS *et al.* Development of muscular dystrophy in a CRISPR-engineered mutant rabbit model with frame-disrupting ANO5 mutations. *Cell Death Dis* 2018; **9**: 609.
42 Penttilä S, Palmio J, Suominen T *et al.* Eight new mutations and the expanding phenotype variability in muscular dystrophy caused by ANO5. *Neurology* 2012; **78**: 897–903.
43 Gallardo E, Claeys KG, Nelis E *et al.* Magnetic resonance imaging findings of leg musculature in Charcot-Marie-Tooth disease type 2 due to dynamin 2 mutation. *J Neurol* 2008; **255**: 986–992.
44 Durieux A-C, Vignaud A, Prudhon B *et al.* A centronuclear myopathy-dynamin 2 mutation impairs skeletal muscle structure and function in mice. *Hum Mol Genet* 2010; **19**: 4820–4836.
45 Schessl J, Medne L, Hu Y *et al.* MRI in DNM2-related centronuclear myopathy: evidence for highly selective muscle involvement. *Neuromuscul Disord NMD* 2007; **17**: 28–32.
46 Williams DR, Reardon K, Roberts L *et al.* A new dominant distal myopathy affecting posterior leg and anterior upper limb muscles. *Neurology* 2005; **64**: 1245–1254.
47 Chevessier F, Schuld J, Orfanos Z *et al.* Myofibrillar instability exacerbated by acute exercise in filaminopathy. *Hum Mol Genet* 2015; **24**: 7207–7220.
48 Duff RM, Tay V, Hackman P *et al.* Mutations in the N-terminal actin-binding domain of filamin C cause a distal myopathy. *Am J Hum Genet* 2011; **88**: 729–740.
49 Kimonis VE, Mehta SG, Fulchiero EC *et al.* Clinical studies in familial VCP myopathy associated with Paget disease of bone and frontotemporal dementia. *Am J Med Genet A* 2008; **146A**: 745–757.
50 Kimonis VE, Fulchiero E, Vesa J, Watts G. VCP disease associated with myopathy, Paget disease of bone and frontotemporal dementia: review of a unique

disorder. *Biochim Biophys Acta* 2008; **1782**: 744–748.
51 Palmio J, Sandell S, Suominen T *et al.* Distinct distal myopathy phenotype caused by VCP gene mutation in a Finnish family. *Neuromuscul Disord NMD* 2011; **21**: 551–555.
52 Custer SK, Neumann M, Lu H, Wright AC, Taylor JP. Transgenic mice expressing mutant forms VCP/p97 recapitulate the full spectrum of IBMPFD including degeneration in muscle, brain and bone. *Hum Mol Genet* 2010; **19**: 1741–1755.
53 Boland-Freitas R, Graham J, Davis M, Geevasinga N, Vucic S, Ng K. Late-onset distal myopathy of the upper limbs due to P.Ile151Val mutation in the valosin-containing protein. *Muscle Nerve* 2016; **54**: 165–166.
54 Figueroa-Bonaparte S, Hudson J, Barresi R *et al.* Mutational spectrum and phenotypic variability of VCP-related neurological disease in the UK. *J Neurol Neurosurg Psychiatry* 2016; **87**: 680–681.
55 de Fuenmayor-Fernández de la Hoz CP, Hernández-Laín A, Olivé M, Fernández-Marmiesse A, Domínguez-González C. Novel mutation in TCAP manifesting with asymmetric calves and early-onset joint retractions. *Neuromuscul Disord NMD* 2016; **26**: 749–753.
56 Reilich P, Horvath R, Krause S *et al.* The phenotypic spectrum of neutral lipid storage myopathy due to mutations in the PNPLA2 gene. *J Neurol* 2011; **258**: 1987–1997.
57 Ohkuma A, Nonaka I, Malicdan MCV *et al.* Distal lipid storage myopathy due to PNPLA2 mutation. *Neuromuscul Disord NMD* 2008; **18**: 671–674.
58 Kaneko K, Kuroda H, Izumi R *et al.* A novel mutation in PNPLA2 causes neutral lipid storage disease with myopathy and triglyceride deposit cardiomyovasculopathy: a case report and literature review. *Neuromuscul Disord NMD* 2014; **24**: 634–641.
59 Haemmerle G, Moustafa T, Woelkart G *et al.* ATGL-mediated fat catabolism regulates cardiac mitochondrial function via PPAR-α and PGC-1. *Nat Med* 2011; **17**: 1076–1085.
60 Sugawara M, Kato K, Komatsu M *et al.* A novel de novo mutation in the desmin gene causes desmin myopathy with toxic aggregates. *Neurology* 2000; **55**: 986–990.
61 Schröder R, Goudeau B, Simon MC *et al.* On noxious desmin: functional effects of a novel heterozygous desmin insertion mutation on the extrasarcomeric desmin cytoskeleton and mitochondria. *Hum Mol Genet* 2003; **12**: 657–669.
62 Bär H, Mücke N, Kostareva A, Sjöberg G, Aebi U, Herrmann H. Severe muscle disease-causing desmin mutations interfere with in vitro filament assembly at distinct stages. *Proc Natl Acad Sci U S A* 2005; **102**: 15099–15104.
63 Goudeau B, Dagvadorj A, Rodrigues-Lima F *et al.* Structural and functional analysis of a new desmin variant causing desmin-related myopathy. *Hum Mutat* 2001; **18**: 388–396.
64 Reilich P, Schoser B, Schramm N *et al.* The p.G154S mutation of the alpha-B crystallin gene (CRYAB) causes late-onset distal myopathy. *Neuromuscul Disord NMD* 2010; **20**: 255–259.
65 Fichna JP, Potulska-Chromik A, Miszta P *et al.* A novel dominant D109A CRYAB mutation in a family with myofibrillar myopathy affects αB-crystallin structure. *BBA Clin* 2017; **7**: 1–7.
66 D'Arcy C, Kanellakis V, Forbes R *et al.* X-linked Recessive Distal Myopathy With Hypertrophic Cardiomyopathy Caused by a Novel Mutation in the FHL1 Gene. *J Child Neurol* 2015; **30**: 1211–1217.
67 Bertrand AT, Bönnemann CG, Bonne G, FHL1 myopathy consortium. 199th ENMC international workshop: FHL1 related myopathies, June 7-9, 2013, Naarden, The Netherlands. *Neuromuscul Disord NMD* 2014; **24**: 453–462.
68 Keßler M, Kieltsch A, Kayvanpour E *et al.* A zebrafish model for FHL1-opathy reveals loss-of-function effects of human FHL1 mutations. *Neuromuscul Disord NMD* 2018. doi:10.1016/j.nmd.2018.03.001.
69 Quijano-Roy S, Mbieleu B, Bönnemann CG *et al.* De novo LMNA mutations cause a new form of congenital muscular dystrophy. *Ann Neurol* 2008; **64**: 177–186.
70 Arimura T, Helbling-Leclerc A, Massart C *et al.* Mouse model carrying H222P-Lmna mutation develops muscular dystrophy and dilated cardiomyopathy similar to human striated muscle laminopathies. *Hum Mol Genet* 2005; **14**: 155–169.
71 Bucelli RC, Arhzaouy K, Pestronk A *et al.* SQSTM1 splice site mutation in distal myopathy with rimmed vacuoles. *Neurology* 2015; **85**: 665–674.
72 Cirak S, von Deimling F, Sachdev S *et al.* Kelch-like homologue 9 mutation is associated with an early onset autosomal dominant distal myopathy. *Brain J Neurol* 2010; **133**: 2123–2135.
73 Park HJ, Hong YB, Choi Y-C *et al.* ADSSL1 mutation relevant to autosomal recessive adolescent onset distal myopathy. *Ann Neurol* 2016; **79**: 231–243.
74 Jonson PH, Palmio J, Johari M *et al.* Novel mutations in DNAJB6 cause LGMD1D and distal myopathy in French families. *Eur J Neurol* 2018; **25**: 790–794.
75 Harms MB, Sommerville RB, Allred P *et al.* Exome sequencing reveals DNAJB6 mutations in dominantly-inherited myopathy. *Ann Neurol* 2012; **71**: 407–416.
76 Ruggieri A, Brancati F, Zanotti S *et al.* Complete loss of the DNAJB6 G/F domain and novel missense mutations cause distal-onset DNAJB6 myopathy. *Acta Neuropathol Commun* 2015; **3**: 44.
77 Bengoechea R, Pittman SK, Tuck EP, True HL, Weihl CC. Myofibrillar disruption and RNA-binding protein aggregation in a mouse model of limb-girdle muscular dystrophy 1D. *Hum Mol Genet* 2015; **24**: 6588–6602.

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Myopathies rétractiles - Liste de gènes unique exhaustive (29 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
COL1A1	collagen, type I, alpha-1	NM_000088	- Ehlers-Danlos syndrome, classic / - Ehlers-Danlos syndrome arthrochalasique	AD / AD	28192633[1] 27011056[2] 2679961[3]	24443344[4]
COL1A2	collagen, type I, alpha-2	NM_000089	- Ehlers-Danlos syndrome arthrochalasique,	AD	1681602[5] 28192633[1]	
COL3A1	Collagen type III alpha-1	NM_000090	- Ehlers-Danlos syndrome, hypermobile	AD	28192633[1]	
COL5A1	collagen, type V, alpha-1	NM_001278074	- Ehlers-Danlos syndrome, classic	AD	28192633[1] 23587214[6] 27011056[2]	15580559[7]
COL5A2	collagen, type V, alpha-2	NM_000393	- Ehlers-Danlos syndrome classic	AD	28192633[1] 23587214[6] 27011056[2]	15580559[7]
COL5A3	collagen, type V, alpha-3	NM_015719	- COL5A- / COL5A2-like phenotype	AD ?	10722718[8] 26910848[9]	
COL6A1	Collagen, type VI, alpha-1	NM_001848	- Bethlem myopathy / - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	25535305[10] 21943391[11]	26948708[12]
COL6A2	Collagen, type VI, alpha-2	NM_001849	- Bethlem myopathy / - Ullrich congenital muscular dystrophy -UCMD / - Congenital myosclerosis	AD, AR/ AD, AR / AR	25535305[10] 21943391[11]	26948708[12]
COL6A3	Collagen, type VI, alpha-3	NM_004369	- Bethlem myopathy / - Ullrich congenital muscular dystrophy - UCMD	AD, AR / AD, AR	25535305[10] 21943391[11]	26948708[12]
COL6A6	Collagen, type VI, alpha-6	NM_001102608	- COL6-like phenotype	AR ?	20882040[13]	24907562[14]
COL12A1	collagen, type XII, alpha-1	NM_004370	- Bethlem myopathy / - Ullrich congenital muscular dystrophy – UCMD	AD, AR / AD, AR	27348394[15] 29342313[16]	24334604[17]
TNXB	Tenascin XB	NM_019105	- Ehlers-Danlos syndrome due to tenascin X deficiency	AR	27582382[18] 23768946[19]	11925569[20]
SELENON [SEPN1]	Selenoprotein N (1)	NM_020451	- Rigid spine muscular dystrophy 1 / - Congenital myopathy with fiber-type disproportion	AR / AD, AR	20937510[21] 11528383[22]	19067361[23]
RYR1	Ryanodin receptor type 1	NM_000540	- Central core disease / - King-Denborough syndrome / - Minicore myopathy with external ophthalmoplegia / - Congenital neuromuscular disease with uniform type 1 fiber (RYR1-related congenital myopathy with fatigable weakness, responding to pyridostigimine)	AD, AR / AD / AR / AD, AR	28818389[24]	

LMNA	Lamin A/C	NM_170707	- LGMD1B / - Emery-Dreifuss muscular dystrophy 2 / - Emery-Dreifuss muscular dystrophy 3 / - Congenital muscular dystrophy due to LMNA defect (L-CMD)	AD / AD / AR / AD	18551513[25]	15548545[26]
EMD	Emerin	NM_000117	- Emery-Dreifuss muscular dystrophy 1, X-linked	XLR	20301609[27] 23622360[28]	
FHL1	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset / - Emery-Dreifuss muscular dystrophy 6, X-linked / - Myopathy, X-linked,with postural atrophy / - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	24613424[29]	29735270[30]
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / ? / AR / AD	29435569[31]	20634290[32]
PLOD1	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase	NM_000302	- Ehlers-Danlos syndrome cyphoscoliotic	AR	28306229[33]	
ADAMTS2	A disintegrin-like and metalloproteinase with thrombospondin type 1 motif, 2	NM_014244	- Ehlers-Danlos syndrome dermatosparaxis	AR	28306229[33]	
ITGA7	Integrin alpha 7	NM_002206 NM_001144997	- Congenital muscular dystrophy due to ITGA7 deficiency	AR		12588796[34]
TRIM32	Tripartite motif-containing 32	NM_012210	- LGMD2H	AR	17994549[35]	17994549[35]
BAG3	BCL2-associated athanogene 3	NM_004281	- Myofibrillar myopathy 6	AD	26342832[36]	
LAMA2	Laminin alpha 2 (merosin, included)	NM_000426	- Muscular dystrophy, congenital merosin-deficient - MDC1A	AR	27858741[37]	
HSPG2	Heparan sulfate proteoglycan of basement membrane (perlecan)	NM_005529 NM_001291860	- Dyssegmental dysplasia, Silverman-Handmaker type / - Schwartz-Jampel syndrome, type 1	AR / AR	26031903[38]	

FBLN5	Fibuline 5	NM_006329	- Cutis laxa, autosomal dominant 2 / - Cutis laxa, autosomal recessive, type IA/ - Neuropathy, hereditary, with or without age-related macular degeneration	AD / AR / AD	28383366[39]	26469761[40]
FKBP14	FK506-binding protein 14	NM_017946	- Ehlers-Danlos syndrome with progressive kyphoscoliosis, myopathy, and hearing loss	AR	28306229[33]	
STIM1	Stromal interaction molecule 1	NM_003156 NM_001277961	- Tubular aggregate myopathy 1	AD	23332920[41] 27876257[42]	
GAA	Glucosidase, Alpha, Acid	NM_000152 NM_001079803	- Glycogen storage disease Type II (Pompe disease) - GSDII / - LGMD2V (Adult onset LGMD2 related to GAA deficiency)	AR / AR	**Not applicable**	

1 Bowen JM, Sobey GJ, Burrows NP *et al.* Ehlers-Danlos syndrome, classical type. *Am J Med Genet C Semin Med Genet* 2017; **175**: 27–39.
2 Weerakkody RA, Vandrovcova J, Kanonidou C *et al.* Targeted next-generation sequencing makes new molecular diagnoses and expands genotype-phenotype relationship in Ehlers-Danlos syndrome. *Genet Med Off J Am Coll Med Genet* 2016; **18**: 1119–1127.
3 Doble A, Thomas BJ, Furr PM *et al.* A search for infectious agents in chronic abacterial prostatitis using ultrasound guided biopsy. *Br J Urol* 1989; **64**: 297–301.
4 Chen F, Guo R, Itoh S *et al.* First mouse model for combined osteogenesis imperfecta and Ehlers-Danlos syndrome. *J Bone Miner Res Off J Am Soc Bone Miner Res* 2014; **29**: 1412–1423.
5 Mahnir VM, Kozlovskaya EP. Structure-toxicity relationships of neurotoxin RTX-III from the sea anemone Radianthus macrodactylus: modification of amino groups. *Toxicon Off J Int Soc Toxinology* 1991; **29**: 819–826.
6 Ritelli M, Dordoni C, Venturini M *et al.* Clinical and molecular characterization of 40 patients with classic Ehlers-Danlos syndrome: identification of 18 COL5A1 and 2 COL5A2 novel mutations. *Orphanet J Rare Dis* 2013; **8**: 58.
7 Malfait F, Coucke P, Symoens S, Loeys B, Nuytinck L, De Paepe A. The molecular basis of classic Ehlers-Danlos syndrome: a comprehensive study of biochemical and molecular findings in 48 unrelated patients. *Hum Mutat* 2005; **25**: 28–37.
8 Imamura Y, Scott IC, Greenspan DS. The pro-alpha3(V) collagen chain. Complete primary structure, expression domains in adult and developing tissues, and comparison to the structures and expression domains of the other types V and XI procollagen chains. *J Biol Chem* 2000; **275**: 8749–8759.
9 Mak KM, Png CYM, Lee DJ. Type V Collagen in Health, Disease, and Fibrosis. *Anat Rec Hoboken NJ 2007* 2016; **299**: 613–629.
10 Deconinck N, Richard P, Allamand V *et al.* Bethlem myopathy: long-term follow-up identifies COL6 mutations predicting severe clinical evolution. *J Neurol Neurosurg Psychiatry* 2015; **86**: 1337–1346.
11 Allamand V, Briñas L, Richard P, Stojkovic T, Quijano-Roy S, Bonne G. ColVI myopathies: where do we stand, where do we go? *Skelet Muscle* 2011; **1**: 30.
12 Saunier M, Bönnemann CG, Durbeej M, Allamand V, CMD Animal Model Consortium. 212th ENMC International Workshop: Animal models of congenital muscular dystrophies, Naarden, The Netherlands, 29-31 May 2015. *Neuromuscul Disord NMD* 2016; **26**: 252–259.
13 Sabatelli P, Gara SK, Grumati P *et al.* Expression of the collagen VI α5 and α6 chains in normal human skin and in skin of patients with collagen VI-related myopathies. *J Invest Dermatol* 2011; **131**: 99–107.
14 Tagliavini F, Pellegrini C, Sardone F *et al.* Defective collagen VI α6 chain expression in the skeletal muscle of patients with collagen VI-related myopathies. *Biochim Biophys Acta* 2014; **1842**: 1604–1612.
15 Punetha J, Kesari A, Hoffman EP *et al.* Novel Col12A1 variant expands the clinical picture of congenital myopathies with extracellular matrix defects. *Muscle Nerve* 2017; **55**: 277–281.
16 Witting N, Krag T, Werlauff U *et al.* Collagen XII myopathy with rectus femoris atrophy and collagen XII retention in fibroblasts. *Muscle Nerve* 2018; **57**: 1026–1030.
17 Zou Y, Zwolanek D, Izu Y *et al.* Recessive and dominant mutations in COL12A1 cause a novel EDS/myopathy overlap syndrome in humans and mice. *Hum Mol Genet* 2014; **23**: 2339–2352.
18 Demirdas S, Dulfer E, Robert L *et al.* Recognizing the tenascin-X deficient type of Ehlers-Danlos syndrome: a cross-sectional study in 17 patients. *Clin Genet* 2017; **91**: 411–425.
19 Pénisson-Besnier I, Allamand V, Beurrier P *et al.* Compound heterozygous mutations of the TNXB gene cause primary myopathy. *Neuromuscul Disord NMD* 2013; **23**: 664–669.
20 Mao JR, Taylor G, Dean WB *et al.* Tenascin-X deficiency mimics Ehlers-Danlos syndrome in mice through alteration of collagen deposition. *Nat Genet* 2002; **30**: 421–425.
21 Cagliani R, Fruguglietti ME, Berardinelli A *et al.* New molecular findings in congenital myopathies due to selenoprotein N gene mutations. *J Neurol Sci* 2011; **300**: 107–113.
22 Moghadaszadeh B, Petit N, Jaillard C *et al.* Mutations in SEPN1 cause congenital muscular dystrophy with spinal rigidity and restrictive respiratory syndrome. *Nat Genet* 2001; **29**: 17–18.
23 Maiti B, Arbogast S, Allamand V *et al.* A mutation in the SEPN1 selenocysteine redefinition element (SRE) reduces selenocysteine incorporation and leads to SEPN1-related myopathy. *Hum Mutat* 2009; **30**: 411–416.
24 Abath Neto O, Moreno C de AM, Malfatti E *et al.* Common and variable clinical, histological, and imaging findings of recessive RYR1-related centronuclear myopathy patients. *Neuromuscul Disord NMD* 2017; **27**: 975–985.
25 Quijano-Roy S, Mbieleu B, Bönnemann CG *et al.* De novo LMNA mutations cause a new form of congenital muscular dystrophy. *Ann Neurol* 2008; **64**: 177–186.
26 Arimura T, Helbling-Leclerc A, Massart C *et al.* Mouse model carrying H222P-Lmna mutation develops muscular dystrophy and dilated cardiomyopathy similar to human striated muscle laminopathies. *Hum Mol Genet* 2005; **14**: 155–169.
27 Bonne G, Leturcq F, Ben Yaou R. Emery-Dreifuss Muscular Dystrophy. In: Adam MP, Ardinger HH, Pagon RA *et al.* (eds). *GeneReviews®*. University of Washington, Seattle: Seattle (WA), 1993http://www.ncbi.nlm.nih.gov/books/NBK1436/ (accessed 7 Jun2018).
28 Bonne G, Quijano-Roy S. Emery-Dreifuss muscular dystrophy, laminopathies, and other nuclear envelopathies. *Handb Clin Neurol* 2013; **113**: 1367–1376.

29 Bertrand AT, Bönnemann CG, Bonne G, FHL1 myopathy consortium. 199th ENMC international workshop: FHL1 related myopathies, June 7-9, 2013, Naarden, The Netherlands. *Neuromuscul Disord NMD* 2014; **24**: 453–462.
30 Keßler M, Kieltsch A, Kayvanpour E *et al.* A zebrafish model for FHL1-opathy reveals loss-of-function effects of human FHL1 mutations. *Neuromuscul Disord NMD* 2018. doi:10.1016/j.nmd.2018.03.001.
31 Savarese M, Maggi L, Vihola A *et al.* Interpreting Genetic Variants in Titin in Patients With Muscle Disorders. *JAMA Neurol* 2018; **75**: 557–565.
32 Sarparanta J, Blandin G, Charton K *et al.* Interactions with M-band titin and calpain 3 link myospryn (CMYA5) to tibial and limb-girdle muscular dystrophies. *J Biol Chem* 2010; **285**: 30304–30315.
33 Malfait F, Francomano C, Byers P *et al.* The 2017 international classification of the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet* 2017; **175**: 8–26.
34 Nawrotzki R, Willem M, Miosge N, Brinkmeier H, Mayer U. Defective integrin switch and matrix composition at alpha 7-deficient myotendinous junctions precede the onset of muscular dystrophy in mice. *Hum Mol Genet* 2003; **12**: 483–495.
35 Saccone V, Palmieri M, Passamano L *et al.* Mutations that impair interaction properties of TRIM32 associated with limb-girdle muscular dystrophy 2H. *Hum Mutat* 2008; **29**: 240–247.
36 Béhin A, Salort-Campana E, Wahbi K *et al.* Myofibrillar myopathies: State of the art, present and future challenges. *Rev Neurol (Paris)* 2015; **171**: 715–729.
37 Nelson I, Stojkovic T, Allamand V *et al.* Laminin α2 Deficiency-Related Muscular Dystrophy Mimicking Emery-Dreifuss and Collagen VI related Diseases. *J Neuromuscul Dis* 2015; **2**: 229–240.
38 Iwata S, Ito M, Nakata T *et al.* A missense mutation in domain III in HSPG2 in Schwartz-Jampel syndrome compromises secretion of perlecan into the extracellular space. *Neuromuscul Disord NMD* 2015; **25**: 667–671.
39 Duz MB, Kirat E, Coucke PJ *et al.* A novel case of autosomal dominant cutis laxa in a consanguineous family: report and literature review. *Clin Dysmorphol* 2017; **26**: 142–147.
40 Nakasaki M, Hwang Y, Xie Y *et al.* The matrix protein Fibulin-5 is at the interface of tissue stiffness and inflammation in fibrosis. *Nat Commun* 2015; **6**: 8574.
41 Böhm J, Chevessier F, Maues De Paula A *et al.* Constitutive activation of the calcium sensor STIM1 causes tubular-aggregate myopathy. *Am J Hum Genet* 2013; **92**: 271–278.
42 Noury J-B, Böhm J, Peche GA *et al.* Tubular aggregate myopathy with features of Stormorken disease due to a new STIM1 mutation. *Neuromuscul Disord NMD* 2017; **27**: 78–82.

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Myopathies myofibrillaires et Myopathies à inclusions - Liste de gènes unique exhaustive (15 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
CRYAB	Crystallin, Alpha-B	NM_001885	- Myopathy, myofibrillar, fatal infantile hypertrophy, alpha-B crystallin-related	AD, AR	9731540[1] 14681890[2]	27904835[3]
DES	Desmin	NM_001927	- LGMD1E / - LGMD2R / - Myopathy, myofibrillar, 1 / - Scapuloperoneal syndrome, neurogenic, Kaeser type	AD / AR / AD, AR / AD	9697706[4] 10545598[5]	16217025[6]
LDB3 [ZASP]	LIM domain binding 3	NM_001080114 NM_001171610 NM_007078	- Late onset distal myopathy (Markesbery-Griggs) / - Myopathy, myofibrillar, 4	AD / AD	15668942[7] 26342832[8]	12499364[9]
MYOT	Myotilin	NM_006790	- LGMD1A / - Myopathy, myofibrillar, 3 / - Myopathy, spheroid body	AD / AD / AD	15111675[10] 26342832[8]	12499399[11]
FLNC	Filamin C	NM_001458	- Myopathy, distal, 4 / - Myopathy, myofibrillar, 5	AD / AD	15929027[12] 19050726 [13]	26969713[14]
BAG3	BCL2-associated athanogene 3	NM_004281	- Myopathy, myofibrillar, 6	AD	19085932[15] 20605452[16]	16936253[17]
ACTA1	Actin, alpha, skeletal muscle 1	NM_001100	- Actin congenital myopathy with cores / - Actin congenital myopathy with excess of thin myofilaments / - Congenital myopathy with fiber-type disproportion 1 / - Nemaline Myopathy 3	AD,AR / AD, AR / AD, AR / AD, AR	11333380[18] 15198992[19]	22825594[20]
FHL1	Four-and-a-half LIM domains 1	NM_001159702	- Reducing body myopathy, X-linked 1a, severe, infantile or early childhood onset / - Reducing body myopathy, X-linked 1b, with late childhood or adult onset / - Emery-Dreifuss muscular dystrophy 6, X-linked / - Myopathy, X-linked,with postural atrophy / - Scapuloperoneal myopathy, X-linked	XLD / XL? / XLR / XLR / XLD	18274675[21] 19181672[22]	29735270[23]
TTN	Titin	NM_001267550 NM_133379	- LGMD2J / - Myopathy, proximal, with early respiratory muscle involvement / - Salih myopathy / - Tibial muscular dystrophy, late onset (Udd myopathy)	AR / ? / AR / AD	29435569[24] 22577215[25]	20634290[26]
VCP	Valosin-containing protein	NM_007126	- Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia 1 / - Charcot-Marie-Tooth disease, type 2Y	AD / AD	18260132[27] 18845250[28]	20147319[29]
GNE	UDP-N-acetylglucosamine-2- epimerase/N-acetylmannosamine kinase	NM_001128227	- Distal myopathy with rimmed vacuoles (Nonaka) and Hereditary inclusion body myopathy	AR	11528398[30] 12473753[31]	17704511[32]

MYH2	Myosin Heavy chain type 2, skeletal muscle, adult	NM_017534	- Congenital myopathy (proximal myopathy and ophthalmoplegia) / - Distal arthrogryposis	AD, AR / AD	23388406[33] 23489661[34]	11171584[35]
SQSTM1	Sequestosome 1	NM_003900 NM_001142298	- Distal myopathy with rimmed vacuoles	AD	26208961[36]	
HNRNPA1	Heterogeneous nuclear ribonucleoprotein a1	NM_031157	- Inclusion body myopathy with early-onset Paget disease without frontotemporal dementia 3	AD	23455423[37] 27066560[38]	
DNAJB6	DNAJ/HSP40 homolog, subfamily B, member 6	NM_058246	- LGMD1D	AD	29437287[39] 23394708[40]	22366786[41]

1 Vicart P, Caron A, Guicheney P *et al.* A missense mutation in the alphaB-crystallin chaperone gene causes a desmin-related myopathy. *Nat Genet* 1998; **20**: 92–95.

2 Selcen D, Engel AG. Myofibrillar myopathy caused by novel dominant negative alpha B-crystallin mutations. *Ann Neurol* 2003; **54**: 804–810.

3 Fichna JP, Potulska-Chromik A, Miszta P *et al.* A novel dominant D109A CRYAB mutation in a family with myofibrillar myopathy affects αB-crystallin structure. *BBA Clin* 2017; **7**: 1–7.

4 Goldfarb LG, Park KY, Cervenáková L *et al.* Missense mutations in desmin associated with familial cardiac and skeletal myopathy. *Nat Genet* 1998; **19**: 402–403.

5 Sjöberg G, Saavedra-Matiz CA, Rosen DR *et al.* A missense mutation in the desmin rod domain is associated with autosomal dominant distal myopathy, and exerts a dominant negative effect on filament formation. *Hum Mol Genet* 1999; **8**: 2191–2198.

6 Bär H, Mücke N, Kostareva A, Sjöberg G, Aebi U, Herrmann H. Severe muscle disease-causing desmin mutations interfere with in vitro filament assembly at distinct stages. *Proc Natl Acad Sci U S A* 2005; **102**: 15099–15104.

7 Selcen D, Engel AG. Mutations in ZASP define a novel form of muscular dystrophy in humans. *Ann Neurol* 2005; **57**: 269–276.

8 Béhin A, Salort-Campana E, Wahbi K *et al.* Myofibrillar myopathies: State of the art, present and future challenges. *Rev Neurol (Paris)* 2015; **171**: 715–729.

9 Huang C, Zhou Q, Liang P *et al.* Characterization and in vivo functional analysis of splice variants of cypher. *J Biol Chem* 2003; **278**: 7360–7365.

10 Selcen D, Engel AG. Mutations in myotilin cause myofibrillar myopathy. *Neurology* 2004; **62**: 1363–1371.

11 Salmikangas P, van der Ven PFM, Lalowski M *et al.* Myotilin, the limb-girdle muscular dystrophy 1A (LGMD1A) protein, cross-links actin filaments and controls sarcomere assembly. *Hum Mol Genet* 2003; **12**: 189–203.

12 Vorgerd M, van der Ven PFM, Bruchertseifer V *et al.* A mutation in the dimerization domain of filamin c causes a novel type of autosomal dominant myofibrillar myopathy. *Am J Hum Genet* 2005; **77**: 297–304.

13 Shatunov A, Olivé M, Odgerel Z *et al.* In-frame deletion in the seventh immunoglobulin-like repeat of filamin C in a family with myofibrillar myopathy. *Eur J Hum Genet EJHG* 2009; **17**: 656–663.

14 Ruparelia AA, Oorschot V, Ramm G, Bryson-Richardson RJ. FLNC myofibrillar myopathy results from impaired autophagy and protein insufficiency. *Hum Mol Genet* 2016; **25**: 2131–2142.

15 Selcen D, Muntoni F, Burton BK *et al.* Mutation in BAG3 causes severe dominant childhood muscular dystrophy. *Ann Neurol* 2009; **65**: 83–89.

16 Odgerel Z, Sarkozy A, Lee H-S *et al.* Inheritance patterns and phenotypic features of myofibrillar myopathy associated with a BAG3 mutation. *Neuromuscul Disord NMD* 2010; **20**: 438–442.

17 Homma S, Iwasaki M, Shelton GD, Engvall E, Reed JC, Takayama S. BAG3 deficiency results in fulminant myopathy and early lethality. *Am J Pathol* 2006; **169**: 761–773.

18 Ilkovski B, Cooper ST, Nowak K *et al.* Nemaline myopathy caused by mutations in the muscle alpha-skeletal-actin gene. *Am J Hum Genet* 2001; **68**: 1333–1343.

19 Ilkovski B, Nowak KJ, Domazetovska A *et al.* Evidence for a dominant-negative effect in ACTA1 nemaline myopathy caused by abnormal folding, aggregation and altered polymerization of mutant actin isoforms. *Hum Mol Genet* 2004; **13**: 1727–1743.

20 Nowak KJ, Ravenscroft G, Laing NG. Skeletal muscle α-actin diseases (actinopathies): pathology and mechanisms. *Acta Neuropathol (Berl)* 2013; **125**: 19–32.

21 Schessl J, Zou Y, McGrath MJ *et al.* Proteomic identification of FHL1 as the protein mutated in human reducing body myopathy. *J Clin Invest* 2008; **118**: 904–912.

22 Schessl J, Taratuto AL, Sewry C *et al.* Clinical, histological and genetic characterization of reducing body myopathy caused by mutations in FHL1. *Brain J Neurol* 2009; **132**: 452–464.

23 Keßler M, Kieltsch A, Kayvanpour E *et al.* A zebrafish model for FHL1-opathy reveals loss-of-function effects of human FHL1 mutations. *Neuromuscul Disord NMD* 2018. doi:10.1016/j.nmd.2018.03.001.

24 Savarese M, Maggi L, Vihola A *et al.* Interpreting Genetic Variants in Titin in Patients With Muscle Disorders. *JAMA Neurol* 2018; **75**: 557–565.

25 Pfeffer G, Elliott HR, Griffin H *et al.* Titin mutation segregates with hereditary myopathy with early respiratory failure. *Brain J Neurol* 2012; **135**: 1695–1713.

26 Sarparanta J, Blandin G, Charton K *et al.* Interactions with M-band titin and calpain 3 link myospryn (CMYA5) to tibial and limb-girdle muscular dystrophies. *J Biol Chem* 2010; **285**: 30304–30315.

27 Kimonis VE, Mehta SG, Fulchiero EC *et al.* Clinical studies in familial VCP myopathy associated with Paget disease of bone and frontotemporal dementia. *Am J Med Genet A* 2008; **146A**: 745–757.

28 Kimonis VE, Fulchiero E, Vesa J, Watts G. VCP disease associated with myopathy, Paget disease of bone and frontotemporal dementia: review of a unique disorder. *Biochim Biophys Acta* 2008; **1782**: 744–748.

29 Custer SK, Neumann M, Lu H, Wright AC, Taylor JP. Transgenic mice expressing mutant forms VCP/p97 recapitulate the full spectrum of IBMPFD including degeneration in muscle, brain and bone. *Hum Mol Genet* 2010; **19**: 1741–1755.

30 Eisenberg I, Avidan N, Potikha T *et al.* The UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase gene is mutated in recessive hereditary inclusion body myopathy. *Nat Genet* 2001; **29**: 83–87.

31 Nishino I, Noguchi S, Murayama K *et al.* Distal myopathy with rimmed vacuoles is allelic to hereditary inclusion body myopathy. *Neurology* 2002; **59**: 1689–1693.

32 Malicdan MCV, Noguchi S, Nonaka I, Hayashi YK, Nishino I. A Gne knockout mouse expressing human GNE D176V mutation develops features similar to distal myopathy with rimmed vacuoles or hereditary inclusion body myopathy. *Hum Mol Genet* 2007; **16**: 2669–2682.

33 Lossos A, Oldfors A, Fellig Y, Meiner V, Argov Z, Tajsharghi H. MYH2 mutation in recessive myopathy with external ophthalmoplegia linked to chromosome 17p13.1-p12. *Brain J Neurol* 2013; **136**: e238.

34 D'Amico A, Fattori F, Bellacchio E, Catteruccia M, Servidei S, Bertini E. A new de novo missense mutation in MYH2 expands clinical and genetic findings in hereditary myosin myopathies. *Neuromuscul Disord NMD* 2013; **23**: 437–440.

35 Allen DL, Harrison BC, Sartorius C, Byrnes WC, Leinwand LA. Mutation of the IIB myosin heavy chain gene results in muscle fiber loss and compensatory hypertrophy. *Am J Physiol Cell Physiol* 2001; **280**: C637-645.
36 Bucelli RC, Arhzaouy K, Pestronk A *et al.* SQSTM1 splice site mutation in distal myopathy with rimmed vacuoles. *Neurology* 2015; **85**: 665–674.
37 Kim HJ, Kim NC, Wang Y-D *et al.* Mutations in prion-like domains in hnRNPA2B1 and hnRNPA1 cause multisystem proteinopathy and ALS. *Nature* 2013; **495**: 467–473.
38 Izumi R, Warita H, Niihori T *et al.* Isolated inclusion body myopathy caused by a multisystem proteinopathy-linked hnRNPA1 mutation. *Neurol Genet* 2015; **1**: e23.
39 Jonson PH, Palmio J, Johari M *et al.* Novel mutations in DNAJB6 cause LGMD1D and distal myopathy in French families. *Eur J Neurol* 2018; **25**: 790–794.
40 Sato T, Hayashi YK, Oya Y *et al.* DNAJB6 myopathy in an Asian cohort and cytoplasmic/nuclear inclusions. *Neuromuscul Disord NMD* 2013; **23**: 269–276.
41 Sarparanta J, Jonson PH, Golzio C *et al.* Mutations affecting the cytoplasmic functions of the co-chaperone DNAJB6 cause limb-girdle muscular dystrophy. *Nat Genet* 2012; **44**: 450–455, S1-2.

Myasthenies congénitales - Liste de gènes principale (9 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
CHRNE	Cholinergic receptor, nicotinic, epsilon polypeptide	NM_000080	- Congenital myasthenic syndrome 4A, slow-channel / - Congenital myasthenic syndrome 4B, fast-channel / - Congenital myasthenic syndrome 4C, associated with acetylcholine receptor deficiency	AD, AR / AR/ AR	8357190[1] 7531341[2] 8957026[3]	8957026[3]
RAPSN	Receptor-associated protein of the synapse (Rapsyn)	NM_005055	- Congenital myasthenic syndrome 11, associated with acetylcholine receptor deficiency / - Fetal akinesia deformation sequence	AR / AR	11791205[4] 20930056[5]	11791205[4]
DOK7	Downstream of tyrosine kinase 7	NM_173660	- Congenital myasthenic syndrome 10 / - Fetal akinesia deformation sequence	AR / AR	16917026[6] 17439981[7]	18165682[8]
COLQ	Collagenic tail of endplate acetylcholinesterase	NM_005677	- Congenital myasthenic syndrome 5	AR	9758617[9] 9689136[10] 10665486[11]	14702351[12]
CHAT	Choline acetyltransferase	NM_020549 NM_001142933	- Congenital myasthenic syndrome 6 (presynaptic)	AR	11172068[13] 12756141[14]	26080897[15]
CHRNA1	Cholinergic receptor, nicotinic, alpha polypeptide 1	NM_000079 NM_001039523	- Congenital myasthenic syndrome 1A / - Congenital myasthenic syndrome 1B / - Multiple pterygium syndrome, lethal type	AD/ AD,AR / AR	8872460 [16] 7619526[17] 15079006[18]	8872460 [16]
CHRNB1	Cholinergic receptor, nicotinic, beta polypeptide 1	NM_000747	- Congenital myasthenic syndrome 2C, associated with acetylcholine receptor deficiency / - Congenital myasthenic syndrome 2A + Fetal akinesia deformation sequence	AR / AD	8872460 [16] 10562302[19] 8651643[20]	8872460 [16]
CHRND	Cholinergic receptor, nicotinic, delta polypeptide	NM_000751	- Congenital myasthenic syndrome 3A/ - Congenital myasthenic syndrome 3B/ - Congenital myasthenic syndrome 3C / - Multiple pterygium syndrome, lethal type	AD / AR / AR / AR	12499478[21] 11782989[22] 11435464[23]	12499478[21]
GFPT1	Glutamine:Fructose-6-Phosphate amido Transaminase 1	NM_002056 NM_001244710	- Congenital myasthenia 12, with tubular aggregates	AR	21310273[24] 21975507[25]	21310273 [24]

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Myasthenies congénitales - Liste de gènes exhaustive (32 gènes):

(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
(CHRNE)	Cholinergic receptor, nicotinic, epsilon polypeptide	NM_000080	- Congenital myasthenic syndrome 4A, slow-channel / - Congenital myasthenic syndrome 4B, fast-channel / - Congenital myasthenic syndrome 4C, associated with acetylcholine receptor deficiency	AD, AR / AR/ AR	8357190[1] 7531341[2] 8957026[3]	8957026[3]
(RAPSN)	Receptor-associated protein of the synapse (Rapsyn)	NM_005055	- Congenital myasthenic syndrome 11, associated with acetylcholine receptor deficiency / - Fetal akinesia deformation sequence	AR / AR	11791205[4] 20930056[5]	11791205[4]
(DOK7)	Downstream of tyrosine kinase 7	NM_173660	- Congenital myasthenic syndrome 10 / - Fetal akinesia deformation sequence	AR / AR	16917026[6] 17439981[7]	18165682[8]
(COLQ)	Collagenic tail of endplate acetylcholinesterase	NM_005677	- Congenital myasthenic syndrome 5	AR	9758617[9] 9689136[10] 10665486[11]	14702351[12]
(CHAT)	Choline acetyltransferase	NM_020549 NM_001142933	- Congenital myasthenic syndrome 6 (presynaptic)	AR	11172068[13] 12756141[14]	26080897[15]
(CHRNA1)	Cholinergic receptor, nicotinic, alpha polypeptide 1	NM_000079 NM_001039523	- Congenital myasthenic syndrome 1A / - Congenital myasthenic syndrome 1B / - Multiple pterygium syndrome, lethal type	AD/ AD, AR / AR	8872460 [16] 7619526[17] 15079006[18]	8872460 [16] 15079006[18]
(CHRNB1)	Cholinergic receptor, nicotinic, beta polypeptide 1	NM_000747	- Congenital myasthenic syndrome 2C, associated with acetylcholine receptor deficiency / - Congenital myasthenic syndrome 2A + Fetal akinesia deformation sequence	AR / AD	8872460 [16] 10562302[19] 8651643[20]	8872460 [16]
(CHRND)	Cholinergic receptor, nicotinic, delta polypeptide	NM_000751	- Congenital myasthenic syndrome 3A/ - Congenital myasthenic syndrome 3B/ - Congenital myasthenic syndrome 3C / - Multiple pterygium syndrome, lethal type	AD / AR / AR / AR	12499478[21] 11782989[22] 11435464[23]	12499478[21]
(GFPT1)	Glutamine:Fructose-6-Phosphate amido Transaminase 1	NM_002056 NM_001244710	- Congenital myasthenia 12, with tubular aggregates	AR	21310273[24] 21975507[25]	21310273 [24]
AGRN	Agrin	NM_198576	- Congenital myasthenic syndrome 8, with pre- and postsynaptic defects	AR	19631309[26] 22205389[27]	19631309[26]
ALG14	Asparagine-Linked Glycosylation 14, S. cerevisiae, homolog of	NM_144988	- Congenital myasthenic syndrome 15, without tubular aggregates	AR ?	23404334[28]	

ALG2	Asparagine-Linked Glycosylation 2, S. cerevisiae, homolog of	NM_033087	- Congenital myasthenic syndrome 14, with tubular aggregates	AR	23404334[28]	
BIN1	Bridging integrator type 1 (Amphiphysin 2)	NM_139343	- Congenital myopathy (centronuclear myopathy)	AD (late onset) AR	21482111 [29]	
COL13A1	Collagen Type XIII, Alpha-1	NM_001130103	- Congenital myasthenic syndrome 19	AR	26626625[30]	26626625[30]
DNM2	Dynamin 2	NM_001005360 NM_001005361 NM_001005362	- Centronuclear myopathy 1 / - Charcot-Marie-Tooth disease, axonal type 2M / - Charcot-Marie-Tooth disease, dominant intermediate B / - Lethal congenital contracture syndrome 5	AD / AD / AD / AR	25127990[31]	
DPAGT1	Dolichyl-Phosphate N-Acetylglucosaminephosphotransferase	NM_001382	- Congenital myasthenic syndrome 13, with tubular aggregates / - DPAGT1-CDG/ALG7-CDG	AR / AR	22742743[32] 23447650[33]	
GMPPB	GDP-mannose pyrophosphorylase, beta subunit	NM_013334	- Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 14 / - Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 14 / - LGMD2T	AR / AR / AR	26133662[34]	
LAMB2	Laminin Beta-2	NM_002292	- Pierson syndrome	AR	19251977[35]	
LRP4	Low Density Lipoprotein Receptor-Related Protein 4	NM_002334	- Congenital myasthenic syndrome 17	AR	24234652[36]	24234652[36]
MTM1	Myotubularin	NM_000252	- Congenital myopathy (myotubular myopathy, X-linked)	XLR	25127990[31]	
MUSK	Muscle, skeletal, receptor tyrosine kinase	NM_005592	- Congenital myasthenic syndrome 9, associated with acetylcholine receptor deficiency / - Fetal akinesia deformation sequence	AR / AR	15496425[37] 19949040[38]	15496425[37] 18718936[39]
MYO9A	Myosin IXA	NM_006901	- Congenital myasthenic syndrome, type not numbered yet - Presynaptic congenital myasthenic syndrome	AR / AR	27259756[40]	
PLEC	Plectin	NM_000445	- Congenital myasthenic syndrome with epidermolysis bullosa / - Epidermolysis bullosa simplex with muscular dystrophy / - LGMD2Q	AR / AR / AR	10446808[41] 20624679[42]	25318670[43]
PREPL	Prolyl Endopeptidase-Like	NM_006036	- Congenital myasthenic syndrome 22	AR	24610330[44]	
RYR1	Ryanodin receptor type 1	NM_000540	- Central core disease / - King-Denborough syndrome / - Minicore myopathy with external ophthalmoplegia /	AD, AR / AD / AR /	25127990[31]	

			- Congenital neuromuscular disease with uniform type 1 fiber (RYR1-related congenital myopathy with fatigable weakness, responding to pyridostigimine)	AD, AR		
SCN4A	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	12766226[45] 25707578[46]	
SLC25A1	Solute Carrier Family 25 (Mitochondrial Carrier; Citrate Transporter), Member 1	NM_005984	- Combined D-2- and L-2-hydroxyglutaric aciduria (Impaired neuromuscular transmission due to mitochondrial citrate carrier mutations)	AR	26870663[47]	26870663[47]
SLC5A7	Solute Carrier Family 5 (Choline transporter), Member 7	NM_021815	- Congenital myasthenic syndrome 20, presynaptic / - Distal hereditary motor neuronopathy type VIIA	AR / AD	27569547[48] 29088354[49]	27569547[48] 29088354[49]
SNAP25	Synaptosomal-associated Protein 25kDa	NM_003081 NM_130811	- Congenital myasthenic syndrome 18	AD	25792100[50]	
SYT2	Synaptotagmin 2	NM_177402	- Congenital myasthenic syndrome 7, presynaptic (Lambert-Eaton myasthenic syndrome and nonprogressive motor neuropathy)	AD	25192047[51] 29874875[52]	25192047[51]
TPM3	Tropomyosin type 3	NM_152263	- Nemaline Myopathy 1 / - Congenital myopathy with fiber-type disproportion / - CAP myopathy 1	AD, AR / AD, AR / AD, AR	25127990[31]	
CHRNG	Cholinergic receptor, nicotinic, gamma polypeptide	NM_005199	- Multiple pterygium syndrome, lethal type / - Non lethal multiple pterygium syndrome (Escobar syndrome)	AR / AR	16826520[53] 16826531[54]	16826520 [53]

1 Engel AG, Hutchinson DO, Nakano S *et al.* Myasthenic syndromes attributed to mutations affecting the epsilon subunit of the acetylcholine receptor. *Ann N Y Acad Sci* 1993; **681**: 496–508.

2 Ohno K, Hutchinson DO, Milone M *et al.* Congenital myasthenic syndrome caused by prolonged acetylcholine receptor channel openings due to a mutation in the M2 domain of the epsilon subunit. *Proc Natl Acad Sci U S A* 1995; **92**: 758–762.

3 Engel AG, Ohno K, Bouzat C, Sine SM, Griggs RC. End-plate acetylcholine receptor deficiency due to nonsense mutations in the epsilon subunit. *Ann Neurol* 1996; **40**: 810–817.

4 Ohno K, Engel AG, Shen X-M *et al.* Rapsyn mutations in humans cause endplate acetylcholine-receptor deficiency and myasthenic syndrome. *Am J Hum Genet* 2002; **70**: 875–885.

5 Gaudon K, Pénisson-Besnier I, Chabrol B *et al.* Multiexon deletions account for 15% of congenital myasthenic syndromes with RAPSN mutations after negative DNA sequencing. *J Med Genet* 2010; **47**: 795–796.

6 Beeson D, Higuchi O, Palace J *et al.* Dok-7 mutations underlie a neuromuscular junction synaptopathy. *Science* 2006; **313**: 1975–1978.

7 Müller JS, Herczegfalvi A, Vilchez JJ *et al.* Phenotypical spectrum of DOK7 mutations in congenital myasthenic syndromes. *Brain J Neurol* 2007; **130**: 1497–1506.

8 Hamuro J, Higuchi O, Okada K *et al.* Mutations causing DOK7 congenital myasthenia ablate functional motifs in Dok-7. *J Biol Chem* 2008; **283**: 5518–5524.

9 Donger C, Krejci E, Serradell AP *et al.* Mutation in the human acetylcholinesterase-associated collagen gene, COLQ, is responsible for congenital myasthenic syndrome with end-plate acetylcholinesterase deficiency (Type Ic). *Am J Hum Genet* 1998; **63**: 967–975.

10 Ohno K, Brengman J, Tsujino A, Engel AG. Human endplate acetylcholinesterase deficiency caused by mutations in the collagen-like tail subunit (ColQ) of the asymmetric enzyme. *Proc Natl Acad Sci U S A* 1998; **95**: 9654–9659.

11 Ohno K, Engel AG, Brengman JM *et al.* The spectrum of mutations causing end-plate acetylcholinesterase deficiency. *Ann Neurol* 2000; **47**: 162–170.

12 Kimbell LM, Ohno K, Engel AG, Rotundo RL. C-terminal and heparin-binding domains of collagenic tail subunit are both essential for anchoring

acetylcholinesterase at the synapse. *J Biol Chem* 2004; **279**: 10997–11005.
13 Ohno K, Tsujino A, Brengman JM *et al.* Choline acetyltransferase mutations cause myasthenic syndrome associated with episodic apnea in humans. *Proc Natl Acad Sci U S A* 2001; **98**: 2017–2022.
14 Kraner S, Laufenberg I, Strassburg HM, Sieb JP, Steinlein OK. Congenital myasthenic syndrome with episodic apnea in patients homozygous for a CHAT missense mutation. *Arch Neurol* 2003; **60**: 761–763.
15 Arredondo J, Lara M, Gospe SM *et al.* Choline Acetyltransferase Mutations Causing Congenital Myasthenic Syndrome: Molecular Findings and Genotype-Phenotype Correlations. *Hum Mutat* 2015; **36**: 881–893.
16 Engel AG, Ohno K, Milone M *et al.* New mutations in acetylcholine receptor subunit genes reveal heterogeneity in the slow-channel congenital myasthenic syndrome. *Hum Mol Genet* 1996; **5**: 1217–1227.
17 Sine SM, Ohno K, Bouzat C *et al.* Mutation of the acetylcholine receptor alpha subunit causes a slow-channel myasthenic syndrome by enhancing agonist binding affinity. *Neuron* 1995; **15**: 229–239.
18 Webster R, Brydson M, Croxen R, Newsom-Davis J, Vincent A, Beeson D. Mutation in the AChR ion channel gate underlies a fast channel congenital myasthenic syndrome. *Neurology* 2004; **62**: 1090–1096.
19 Quiram PA, Ohno K, Milone M *et al.* Mutation causing congenital myasthenia reveals acetylcholine receptor beta/delta subunit interaction essential for assembly. *J Clin Invest* 1999; **104**: 1403–1410.
20 Gomez CM, Maselli R, Gammack J *et al.* A beta-subunit mutation in the acetylcholine receptor channel gate causes severe slow-channel syndrome. *Ann Neurol* 1996; **39**: 712–723.
21 Shen X-M, Ohno K, Fukudome T *et al.* Congenital myasthenic syndrome caused by low-expressor fast-channel AChR delta subunit mutation. *Neurology* 2002; **59**: 1881–1888.
22 Gomez CM, Maselli RA, Vohra BPS *et al.* Novel delta subunit mutation in slow-channel syndrome causes severe weakness by novel mechanisms. *Ann Neurol* 2002; **51**: 102–112.
23 Brownlow S, Webster R, Croxen R *et al.* Acetylcholine receptor delta subunit mutations underlie a fast-channel myasthenic syndrome and arthrogryposis multiplex congenita. *J Clin Invest* 2001; **108**: 125–130.
24 Senderek J, Müller JS, Dusl M *et al.* Hexosamine biosynthetic pathway mutations cause neuromuscular transmission defect. *Am J Hum Genet* 2011; **88**: 162–172.
25 Guergueltcheva V, Müller JS, Dusl M *et al.* Congenital myasthenic syndrome with tubular aggregates caused by GFPT1 mutations. *J Neurol* 2012; **259**: 838–850.
26 Huzé C, Bauché S, Richard P *et al.* Identification of an agrin mutation that causes congenital myasthenia and affects synapse function. *Am J Hum Genet* 2009; **85**: 155–167.
27 Maselli RA, Fernandez JM, Arredondo J *et al.* LG2 agrin mutation causing severe congenital myasthenic syndrome mimics functional characteristics of non-neural (z-) agrin. *Hum Genet* 2012; **131**: 1123–1135.
28 Cossins J, Belaya K, Hicks D *et al.* Congenital myasthenic syndromes due to mutations in ALG2 and ALG14. *Brain J Neurol* 2013; **136**: 944–956.
29 Liewluck T, Shen X-M, Milone M, Engel AG. Endplate structure and parameters of neuromuscular transmission in sporadic centronuclear myopathy associated with myasthenia. *Neuromuscul Disord NMD* 2011; **21**: 387–395.
30 Logan CV, Cossins J, Rodríguez Cruz PM *et al.* Congenital Myasthenic Syndrome Type 19 Is Caused by Mutations in COL13A1, Encoding the Atypical Non-fibrillar Collagen Type XIII α1 Chain. *Am J Hum Genet* 2015; **97**: 878–885.
31 Rodríguez Cruz PM, Sewry C, Beeson D *et al.* Congenital myopathies with secondary neuromuscular transmission defects; a case report and review of the literature. *Neuromuscul Disord NMD* 2014; **24**: 1103–1110.
32 Belaya K, Finlayson S, Slater CR *et al.* Mutations in DPAGT1 cause a limb-girdle congenital myasthenic syndrome with tubular aggregates. *Am J Hum Genet* 2012; **91**: 193–201.
33 Finlayson S, Palace J, Belaya K *et al.* Clinical features of congenital myasthenic syndrome due to mutations in DPAGT1. *J Neurol Neurosurg Psychiatry* 2013; **84**: 1119–1125.
34 Belaya K, Rodríguez Cruz PM, Liu WW *et al.* Mutations in GMPPB cause congenital myasthenic syndrome and bridge myasthenic disorders with dystroglycanopathies. *Brain J Neurol* 2015; **138**: 2493–2504.
35 Maselli RA, Ng JJ, Anderson JA *et al.* Mutations in LAMB2 causing a severe form of synaptic congenital myasthenic syndrome. *J Med Genet* 2009; **46**: 203–208.
36 Ohkawara B, Cabrera-Serrano M, Nakata T *et al.* LRP4 third β-propeller domain mutations cause novel congenital myasthenia by compromising agrin-mediated MuSK signaling in a position-specific manner. *Hum Mol Genet* 2014; **23**: 1856–1868.
37 Chevessier F, Faraut B, Ravel-Chapuis A *et al.* MUSK, a new target for mutations causing congenital myasthenic syndrome. *Hum Mol Genet* 2004; **13**: 3229–3240.
38 Mihaylova V, Salih M a. M, Mukhtar MM *et al.* Refinement of the clinical phenotype in musk-related congenital myasthenic syndromes. *Neurology* 2009; **73**: 1926–1928.
39 Chevessier F, Girard E, Molgó J *et al.* A mouse model for congenital myasthenic syndrome due to MuSK mutations reveals defects in structure and function of neuromuscular junctions. *Hum Mol Genet* 2008; **17**: 3577–3595.
40 O'Connor E, Töpf A, Müller JS *et al.* Identification of mutations in the MYO9A gene in patients with congenital myasthenic syndrome. *Brain J Neurol* 2016; **139**: 2143–2153.
41 Banwell BL, Russel J, Fukudome T, Shen XM, Stilling G, Engel AG. Myopathy, myasthenic syndrome, and epidermolysis bullosa simplex due to plectin deficiency. *J Neuropathol Exp Neurol* 1999; **58**: 832–846.
42 Forrest K, Mellerio JE, Robb S *et al.* Congenital muscular dystrophy, myasthenic symptoms and epidermolysis bullosa simplex (EBS) associated with mutations in the PLEC1 gene encoding plectin. *Neuromuscul Disord NMD* 2010; **20**: 709–711.
43 Mihailovska E, Raith M, Valencia RG *et al.* Neuromuscular synapse integrity requires linkage of acetylcholine receptors to postsynaptic intermediate filament networks via rapsyn-plectin 1f complexes. *Mol Biol Cell* 2014; **25**: 4130–4149.
44 Régal L, Shen X-M, Selcen D *et al.* PREPL deficiency with or without cystinuria causes a novel myasthenic syndrome. *Neurology* 2014; **82**: 1254–1260.
45 Tsujino A, Maertens C, Ohno K *et al.* Myasthenic syndrome caused by mutation of the SCN4A sodium channel. *Proc Natl Acad Sci U S A* 2003; **100**: 7377–7382.
46 Arnold WD, Feldman DH, Ramirez S *et al.* Defective fast inactivation recovery of Nav 1.4 in congenital myasthenic syndrome. *Ann Neurol* 2015; **77**: 840–850.
47 Chaouch A, Porcelli V, Cox D *et al.* Mutations in the Mitochondrial Citrate Carrier SLC25A1 are Associated with Impaired Neuromuscular Transmission. *J Neuromuscul Dis* 2014; **1**: 75–90.
48 Bauché S, O'Regan S, Azuma Y *et al.* Impaired Presynaptic High-Affinity Choline Transporter Causes a Congenital Myasthenic Syndrome with Episodic Apnea. *Am J Hum Genet* 2016; **99**: 753–761.
49 Wang H, Salter CG, Refai O *et al.* Choline transporter mutations in severe congenital myasthenic syndrome disrupt transporter localization. *Brain J Neurol* 2017; **140**: 2838–2850.
50 Engel AG, Shen X-M, Selcen D, Sine SM. Congenital myasthenic syndromes: pathogenesis, diagnosis, and treatment. *Lancet Neurol* 2015; **14**: 420–434.
51 Herrmann DN, Horvath R, Sowden JE *et al.* Synaptotagmin 2 mutations cause an autosomal-dominant form of lambert-eaton myasthenic syndrome and nonprogressive motor neuropathy. *Am J Hum Genet* 2014; **95**: 332–339.
52 Rodríguez Cruz PM, Palace J, Beeson D. The Neuromuscular Junction and Wide Heterogeneity of Congenital Myasthenic Syndromes. *Int J Mol Sci* 2018; **19**. doi:10.3390/ijms19061677.

53 Hoffmann K, Muller JS, Stricker S *et al.* Escobar syndrome is a prenatal myasthenia caused by disruption of the acetylcholine receptor fetal gamma subunit. *Am J Hum Genet* 2006; **79**: 303–312.
54 Morgan NV, Brueton LA, Cox P *et al.* Mutations in the embryonal subunit of the acetylcholine receptor (CHRNG) cause lethal and Escobar variants of multiple pterygium syndrome. *Am J Hum Genet* 2006; **79**: 390–395.

Paralysies périodiques - Liste de gènes unique exhaustive (3 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
CACNA1S (mutational hotspots in exons 4, 11, 21 and 30)	Calcium Channel, Voltage-Dependent, L Type, Alpha-1S Subunit	NM_000069	- Congenital myopathy / - Hypokalemic periodic paralysis, type 1	AD, AR / AD	8004673[1] 7987325[2]	23187123[3]
KCNJ2	Potassium channel, Inwardly Rectifying, Subfamily J, Member 2	NM_000891	- Andersen-Tawil syndrome	AD	12148092[4] 17324964[5]	12163457[6]
SCN4A (mutational hotspots in exons 5, 12 13, 18, 19, 23, 24)	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	1686388[7] 10944223[8] 11353725[9] 15596759[10]	9886942[11] 10227633[12] 17591984[13]

1 Ptácek LJ, Tawil R, Griggs RC *et al.* Dihydropyridine receptor mutations cause hypokalemic periodic paralysis. *Cell* 1994; **77**: 863–868.
2 Jurkat-Rott K, Lehmann-Horn F, Elbaz A *et al.* A calcium channel mutation causing hypokalemic periodic paralysis. *Hum Mol Genet* 1994; **3**: 1415–1419.
3 Wu F, Mi W, Hernández-Ochoa EO *et al.* A calcium channel mutant mouse model of hypokalemic periodic paralysis. *J Clin Invest* 2012; **122**: 4580–4591.
4 Andelfinger G, Tapper AR, Welch RC, Vanoye CG, George AL, Benson DW. KCNJ2 mutation results in Andersen syndrome with sex-specific cardiac and skeletal muscle phenotypes. *Am J Hum Genet* 2002; **71**: 663–668.
5 Bendahhou S, Fournier E, Gallet S, Ménard D, Larroque M-M, Barhanin J. Corticosteroid-exacerbated symptoms in an Andersen's syndrome kindred. *Hum Mol Genet* 2007; **16**: 900–906.
6 Tristani-Firouzi M, Jensen JL, Donaldson MR *et al.* Functional and clinical characterization of KCNJ2 mutations associated with LQT7 (Andersen syndrome). *J Clin Invest* 2002; **110**: 381–388.
7 Ebers GC, George AL, Barchi RL *et al.* Paramyotonia congenita and hyperkalemic periodic paralysis are linked to the adult muscle sodium channel gene. *Ann Neurol* 1991; **30**: 810–816.
8 Jurkat-Rott K, Mitrovic N, Hang C *et al.* Voltage-sensor sodium channel mutations cause hypokalemic periodic paralysis type 2 by enhanced inactivation and reduced current. *Proc Natl Acad Sci U S A* 2000; **97**: 9549–9554.
9 Sternberg D, Maisonobe T, Jurkat-Rott K *et al.* Hypokalaemic periodic paralysis type 2 caused by mutations at codon 672 in the muscle sodium channel gene SCN4A. *Brain J Neurol* 2001; **124**: 1091–1099.
10 Vicart S, Sternberg D, Fournier E *et al.* New mutations of SCN4A cause a potassium-sensitive normokalemic periodic paralysis. *Neurology* 2004; **63**: 2120–2127.
11 Rojas CV, Neely A, Velasco-Loyden G, Palma V, Kukuljan M. Hyperkalemic periodic paralysis M1592V mutation modifies activation in human skeletal muscle Na+ channel. *Am J Physiol* 1999; **276**: C259-266.
12 Hayward LJ, Sandoval GM, Cannon SC. Defective slow inactivation of sodium channels contributes to familial periodic paralysis. *Neurology* 1999; **52**: 1447–1453.
13 Struyk AF, Cannon SC. A Na+ channel mutation linked to hypokalemic periodic paralysis exposes a proton-selective gating pore. *J Gen Physiol* 2007; **130**: 11–20.

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Myotonies non-dystrophiques - Liste de gènes principale (2 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
CLCN1	Chloride Channel 1, skeletal muscle (CLC-1)	NM_000083	- Thomsen Myotonia congenita / - Becker congenita myotonia	AD / AR	1379744[1] 7981750[2]	8382498[532] 8112288[4]
SCN4A	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	1310898[5] 16832098[6]	8308722[7]

Myotonies non-dystrophiques - Liste de gènes exhaustive (7 gènes):
(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
(CLCN1)	Chloride Channel 1, skeletal muscle (CLC-1)	NM_000083	- Thomsen Myotonia congenita / - Becker congenita myotonia	AD / AR	1379744[1] 7981750[2]	8382498[3] 8112288[4]
(SCN4A)	Sodium Channel , voltage-gated, type 4, alpha subunit	NM_000334	- Paramyotonia congenital (von Eulenburg disease) / - Sodium channel myotonia (also called potassium aggravated myotonia, including myotonia fluctuans, myotonia permanens and acetazolamide responsive myotonia) / - Congenital myasthenic syndrome 16 / - Hyperkalemic periodic paralysis, type 2 / - Hypokalemic periodic paralysis, type 2 + Fetal akinesia deformation sequence	AD / AD / AR / AD / AD	1310898[5] 16832098[6]	8308722[7]
ATP2A1	ATPase, Ca(2+) Transporting, Fast-twitch 1 (SERCA1)	NM_004320	- Brody myopathy	AR	8841193[8] 26248958[9]	10914677[10]
CAV3	Caveolin 3	NM_033337	- LGMD1C / - Distal myopathy, Tateyama type / - Rippling muscle disease	AD / AD / AD	11431690[11] 22581547[12]	21294223[13]
KCNA1	Potassium Voltage-Gated Channel, Shaker-Related Subfamily, Member 1	NM_000217	- Myokymia with or without episodic ataxia type 1	AD	7842011[14] 19307729[15]	17136396[16]
HSPG2	Heparan sulfate proteoglycan of basement membrane (perlecan)	NM_005529 NM_001291860	- Dyssegmental dysplasia, Silverman-Handmaker type / - Schwartz-Jampel syndrome, type 1	AR / AR	11101850[17] 1194153[18]	16927315[19] 17213231[20]
KCNQ2	Potassium Voltage-Gated Channel, KGT-like Subfamily Member 2	NM_172107 NM_004518	- Epileptic encephalopathy, early infantile, 7 / - Myokymia	AD / AD	17872363[21] 11572947[22]	

1 Koch MC, Steinmeyer K, Lorenz C *et al.* The skeletal muscle chloride channel in dominant and recessive human myotonia. *Science* 1992; **257**: 797–800.
2 George AL, Crackower MA, Abdalla JA, Hudson AJ, Ebers GC. Molecular basis of Thomsen's disease (autosomal dominant myotonia congenita). *Nat Genet* 1993; **3**: 305–310.
3 Fahlke C, Zachar E, Rüdel R. Chloride channels with reduced single-channel conductance in recessive myotonia congenita. *Neuron* 1993; **10**: 225–232.
4 Steinmeyer K, Lorenz C, Pusch M, Koch MC, Jentsch TJ. Multimeric structure of ClC-1 chloride channel revealed by mutations in dominant myotonia congenita (Thomsen). *EMBO J* 1994; **13**: 737–743.
5 McClatchey AI, Van den Bergh P, Pericak-Vance MA *et al.* Temperature-sensitive mutations in the III-IV cytoplasmic loop region of the skeletal muscle sodium channel gene in paramyotonia congenita. *Cell* 1992; **68**: 769–774.
6 Colding-Jørgensen E, Duno M, Vissing J. Autosomal dominant monosymptomatic myotonia permanens. *Neurology* 2006; **67**: 153–155.
7 Lerche H, Heine R, Pika U *et al.* Human sodium channel myotonia: slowed channel inactivation due to substitutions for a glycine within the III-IV linker. *J Physiol* 1993; **470**: 13–22.
8 Odermatt A, Taschner PE, Khanna VK *et al.* Mutations in the gene-encoding SERCA1, the fast-twitch skeletal muscle sarcoplasmic reticulum Ca2+ ATPase, are associated with Brody disease. *Nat Genet* 1996; **14**: 191–194.
9 Mussini J-M, Magot A, Hantaï D, Sternberg D, Chevessier F, Péréon Y. Atypical nuclear abnormalities in a patient with Brody disease. *Neuromuscul Disord*

NMD 2015; **25**: 773–779.
10 Odermatt A, Barton K, Khanna VK *et al.* The mutation of Pro789 to Leu reduces the activity of the fast-twitch skeletal muscle sarco(endo)plasmic reticulum Ca2+ ATPase (SERCA1) and is associated with Brody disease. *Hum Genet* 2000; **106**: 482–491.
11 Betz RC, Schoser BG, Kasper D *et al.* Mutations in CAV3 cause mechanical hyperirritability of skeletal muscle in rippling muscle disease. *Nat Genet* 2001; **28**: 218–219.
12 Milone M, McEvoy KM, Sorenson EJ, Daube JR. Myotonia associated with caveolin-3 mutation. *Muscle Nerve* 2012; **45**: 897–900.
13 Ullrich ND, Fischer D, Kornblum C *et al.* Alterations of excitation-contraction coupling and excitation coupled Ca(2+) entry in human myotubes carrying CAV3 mutations linked to rippling muscle. *Hum Mutat* 2011; **32**: 309–317.
14 Browne DL, Gancher ST, Nutt JG *et al.* Episodic ataxia/myokymia syndrome is associated with point mutations in the human potassium channel gene, KCNA1. *Nat Genet* 1994; **8**: 136–140.
15 Glaudemans B, van der Wijst J, Scola RH *et al.* A missense mutation in the Kv1.1 voltage-gated potassium channel-encoding gene KCNA1 is linked to human autosomal dominant hypomagnesemia. *J Clin Invest* 2009; **119**: 936–942.
16 Chen H, von Hehn C, Kaczmarek LK, Ment LR, Pober BR, Hisama FM. Functional analysis of a novel potassium channel (KCNA1) mutation in hereditary myokymia. *Neurogenetics* 2007; **8**: 131–135.
17 Nicole S, Davoine CS, Topaloglu H *et al.* Perlecan, the major proteoglycan of basement membranes, is altered in patients with Schwartz-Jampel syndrome (chondrodystrophic myotonia). *Nat Genet* 2000; **26**: 480–483.
18 McMahon TA. Using body size to understand the structural design of animals: quadrupedal locomotion. *J Appl Physiol* 1975; **39**: 619–627.
19 Stum M, Davoine C-S, Vicart S *et al.* Spectrum of HSPG2 (Perlecan) mutations in patients with Schwartz-Jampel syndrome. *Hum Mutat* 2006; **27**: 1082–1091.
20 Rodgers KD, Sasaki T, Aszodi A, Jacenko O. Reduced perlecan in mice results in chondrodysplasia resembling Schwartz-Jampel syndrome. *Hum Mol Genet* 2007; **16**: 515–528.
21 Wuttke TV, Jurkat-Rott K, Paulus W, Garncarek M, Lehmann-Horn F, Lerche H. Peripheral nerve hyperexcitability due to dominant-negative KCNQ2 mutations. *Neurology* 2007; **69**: 2045–2053.
22 Dedek K, Kunath B, Kananura C, Reuner U, Jentsch TJ, Steinlein OK. Myokymia and neonatal epilepsy caused by a mutation in the voltage sensor of the KCNQ2 K+ channel. *Proc Natl Acad Sci U S A* 2001; **98**: 12272–12277.

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Myopathies métaboliques - Liste de gènes principale (5 gènes):

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
GAA	Glucosidase, Alpha, Acid	NM_000152 NM_001079803	- Glycogen storage disease Type II (Pompe disease) - GSDII / - LGMD2V (Adult onset LGMD2 related to GAA deficiency)	AR / AR	29149851[1] 29880332[2]	29422078[3]
AGL	Amylo-1,6-glucosidase, 4-alpha-glucanotransferase	NM_000642	- Glycogen storage disease type IIIa - GSD IIIa / - Glycogen storage disease type IIIb - GSD IIIb / - Glycogen storage disease type IIIc - GSD IIIc / - Glycogen storage disease type IIId - GSD IIId	AR / AR / AR / AR	27106217[4] 28888851[5]	5240360[6]
PYGM	Glycogen phosphorylase, muscle	NM_005609	- Glycogen storage disease Type V (McArdle disease)	AR	21802952[7] 29143597[8]	22347505[9]
PFKM	Phosphofructokinase, muscle type	NM_000289 NM_001166686	- Glycogen storage disease Type VII (Tarui)	AR	7479776[10] 24427140[11]	24306210[12]
CPT2	Carnitine palmitoyltransferase II	NM_000098	- CPT II deficiency, infantile / - CPT II deficiency, lethal neonatal / - CPT II deficiency, myopathic, stress-induced	AR / AR / (AD), AR	10607472 [13] 20691590[14] 18769256[15]	9600456[16]

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Myopathies métaboliques - Liste de gènes exhaustive (35 gènes):

(Entre parenthèses: gènes également inclus dans la liste principale correspondante)

SYMBOLE DU GENE (GENE SYMBOL, version anglaise)	NOM DU GENE (GENE NAME, version anglaise)	RefSeq NM_DIAG	PATHOLOGIES* (dénominations OMIM, versions anglaises)	MODE(S) DE TRANSMISSION	Publications princeps associées (PMIDs; cliniques: colonne de gauche; fonctionnelles: colonne de droite)	
(GAA)	Glucosidase, Alpha, Acid	NM_000152 NM_001079803	- Glycogen storage disease Type II (Pompe disease) - GSDII - LGMD2V (Adult onset LGMD2 related to GAA deficiency)	AR / AR	29149851[1] 29880332[2]	29422078[3]
(AGL)	Amylo-1,6-glucosidase, 4-alpha-glucanotransferase	NM_000642	- Glycogen storage disease type IIIa - GSD IIIa - Glycogen storage disease type IIIb - GSD IIIb - Glycogen storage disease type IIIc - GSD IIIc - Glycogen storage disease type IIId - GSD IIId	AR / AR / AR / AR	27106217[4] 28888851[5]	5240360[6]
(PYGM)	Glycogen phosphorylase, muscle	NM_005609	- Glycogen storage disease Type V (McArdle disease)	AR	21802952[7] 29143597[8]	22347505[9]
(PFKM)	Phosphofructokinase, muscle type	NM_000289 NM_001166686	- Glycogen storage disease Type VII (Tarui)	AR	7479776[10] 24427140[11]	24306210[12]
(CPT2)	Carnitine palmitoyltransferase II	NM_000098	- CPT II deficiency, infantile / - CPT II deficiency, lethal neonatal / - CPT II deficiency, myopathic, stress-induced	AR / AR / (AD), AR	10607472 [13] 20691590[14] 18769256[15]	9600456[16]
GBE1	Glycogen branching enzyme	NM_000158	- Glycogen storage disease type IV / - Polyglucosan body disease, adult form	AR / AR	25728520[17] 27546458[18]	17994551[19]
PHKA1	Phosphorylase kinase, muscle, alpha-1 subunit	NM_002637	Glycogen storage disease type IXd (ex type VIII) or X-linked muscle phosphorylase kinase deficiency	XLR	15637709[20] 12825073[21]	18401027[22]
PHKB	Phosphorylase kinase, beta subunit	NM_000293	Glycogen storage disease type IXb	AR	9215682[23]	25266922[24]
PGM1	Phosphoglucomutase 1	NM_002633	- PGM1-CDG (Congenital Disorder of Glycosylation) / - Glycogen storage disease type XIV	AR/ AR	19625727[25] 24499211[26]	23780368[27]
GYG1	Glycogenin 1	NM_004130	- Glycogen storage disease type XV / - Polyglucosan body myopathy 2	AR / AR	20357282[28] 29264399[29]	29143313[30]
GYS1	Glycogen synthase 1	NM_001161587 NM_002103	- Glycogen storage disease, type 0	AR	18358695[31] 19699667[32]	18358695[31]
PRKAG2	Protein kinase, AMP-activated, non-catalytic, gamma 2	NM_016203	- Glycogen storage disease of heart, lethal congenital - Cardiomyopathy, familial hypertrophic, with Wolff-Parkinson-white syndrome - CMH6	AD / AD	28431061[33] 27841901[34]	28009297[35]
RBCK1	RanBP-type and C3HC4-type zinc finger-containing 1	NM_031229	- Polyglucosan body myopathy 1 with or without immunodeficiency	AR	23798481[36] 23889995[37] 25041762[38]	
PGK1	Phosphoglycerate kinase 1	NM_000291	- Phosphoglycerate kinase 1 deficiency	XLR	16740138[39] 19157875[40] 26883264[41]	17661373[42]

PGAM2	Phosphoglycerate mutase 2 (muscle)	NM_000290	- Glycogen storage disease X - GSD10	AR	23169535[43] 28779239[44]	19273759[45]
LDHA	Lactate dehydrogenase A	NM_005566	- Glycogen storage disease XI - GSD11	AR	29198466[46] 7603529[47]	9457676[48]
ENO3	Enolase 3	NM_001193503 NM_001976	- Glycogen storage disease XIII GSD13	AR	25267339[49] 11506403[50]	
LAMP2	Lysosome-Associated Membrane Protein 2	NM_002294 NM_001122606 NM_013995	- Danon disease	XLD	26748608[51] 29753918[52]	
AMPD1	adenosine monophosphate deaminase 1	NM_000036	- Myopathy due to myoadenylate deaminase deficiency	AR	28751290[53] 12117480[54]	6724999[55]
SLC22A5	Solute carrier family 22 (organic cation transporter), member 5	NM_003060	- Primary systemic carnitine deficiency	AR	10051646[56] 11058897[57]	9916797[58]
SLC25A20	Solute carrier family 25 (carnitine/acylcarnitine translocase), member 20	NM_000387	- Carnitine-acylcarnitine translocase deficiency	AR	15363639[59] 15365988[60]	15515015[61]
ETFA	Electron transfer flavoprotein, alpha polypeptide	NM_000126	- Multiple acyl-CoA dehydrogenase deficiency (MADD; Glutaric aciduria type IIA)	AR	12815589[62]	
ETFB	Electron transfer flavoprotein, beta polypeptide	NM_001985	- Multiple acyl-CoA dehydrogenase deficiency (MADD; Glutaric aciduria type IIB)	AR		
ETFDH	Electron transfer flavoprotein dehydrogenase	NM_004453	- Multiple acyl-CoA dehydrogenase deficiency (MADD; Glutaric aciduria type IIC)	AR		
RYR1	Ryanodin receptor type 1	NM_000540	- Central core disease / - King-Denborough syndrome - Minicore myopathy with external ophthalmoplegia / - Congenital neuromuscular disease with uniform type 1 fiber (RYR1-related congenital myopathy with fatigable weakness, responding to pyridostigimine)	AD, AR / AD / AR / AD, AR	29635721[63] 23628358[64]	
ACADVL	Acyl-CoA dehydrogenase, very long chain	NM_000018	Acyl-CoA dehydrogenase (very long chain) deficiency (VLCAD deficiency)	AR	9973285[65] 10077518[66]	23480858[67]
ABHD5	Abhydrolase domain-containing 5	NM_016006	- Triglyceride storage disease with impaired long-chain fatty acid oxidation (Chanarin-Dorfman syndrome)	AR	20691590[14] 18769256[15]	
PNPLA2	Patatin-like phospholipase domain-containing protein 2 (desnutrin)	NM_020376	- Neutral lipid storage disease with myopathy without ichthyosis	AR	20691590[14] 21544567[68]	17187067[69]
LPIN1	Lipin 1	NM_145693	- Acute recurrent myoglobinuria	AR	20583302[70]	23928362[71]

PNPLA8	Patatin-like phospholipase domain-containing protein 8	NM_015723	- Mitochondrial myopathy with lactic acidosis (MMLA)	AR	25512002[72]	17923475[73]
SLC25A32	Solute carrier family 25 (mitochondrial carrier, folate), member 32	NM_030780	- Riboflavin-responsive exercise intolerance (RREI)	AR	26933868[74] 28443623[75]	29666258[76]
FLAD1	Flavin adenine dinucleotide synthetase, S. cerevisiae, homolog of	NM_025207	- Lipid storage myopathy due to flavin adenine dinucleotide synthetase deficiency	AR	27259049[77] 28433476[78]	27259049[77]
ISCU	Iron-sulfur cluster scaffold, e. Coli, homolog of	NM_014301	- Myopathy with lactic acidosis, hereditary	AR	18304497[79] 18296749[80]	
YARS2	TYROSYL-trna SYNTHETASE 2	NM_001040436	- Myopathy, lactic acidosis, and sideroblastic anemia 2	AR	20598274[81] 24430573[82]	24344687[83]
ACAD9	Acyl-CoA Dehydrogenase 9	NM_014049	- Mitochondrial complex I deficiency due to ACAD9 deficiency	AR	22499348[84]	25721401[85]

1 Johnson K, Töpf A, Bertoli M *et al.* Identification of GAA variants through whole exome sequencing targeted to a cohort of 606 patients with unexplained limb-girdle muscle weakness. *Orphanet J Rare Dis* 2017; **12**: 173.

2 Savarese M, Torella A, Musumeci O *et al.* Targeted gene panel screening is an effective tool to identify undiagnosed late onset Pompe disease. *Neuromuscul Disord NMD* 2018. doi:10.1016/j.nmd.2018.03.011.

3 Parini R, De Lorenzo P, Dardis A *et al.* Long term clinical history of an Italian cohort of infantile onset Pompe disease treated with enzyme replacement therapy. *Orphanet J Rare Dis* 2018; **13**: 32.

4 Sentner CP, Hoogeveen IJ, Weinstein DA *et al.* Glycogen storage disease type III: diagnosis, genotype, management, clinical course and outcome. *J Inherit Metab Dis* 2016; **39**: 697–704.

5 Decostre V, Laforêt P, De Antonio M *et al.* Long term longitudinal study of muscle function in patients with glycogen storage disease type IIIa. *Mol Genet Metab* 2017; **122**: 108–116.

6 Moses SW, Chayoth R, Levin S, Lazarovitz E, Rubinstein D. Glucose and glycogen metabolism in erythrocytes from normal and glycogen storage disease type III subjects. *J Clin Invest* 1968; **47**: 1343–1348.

7 Vieitez I, Teijeira S, Fernandez JM *et al.* Molecular and clinical study of McArdle's disease in a cohort of 123 European patients. Identification of 20 novel mutations. *Neuromuscul Disord NMD* 2011; **21**: 817–823.

8 Santalla A, Nogales-Gadea G, Encinar AB *et al.* Genotypic and phenotypic features of all Spanish patients with McArdle disease: a 2016 update. *BMC Genomics* 2017; **18**: 819.

9 Nogales-Gadea G, Consuegra-García I, Rubio JC *et al.* A transcriptomic approach to search for novel phenotypic regulators in McArdle disease. *PloS One* 2012; **7**: e31718.

10 Vasconcelos O, Sivakumar K, Dalakas MC *et al.* Nonsense mutation in the phosphofructokinase muscle subunit gene associated with retention of intron 10 in one of the isolated transcripts in Ashkenazi Jewish patients with Tarui disease. *Proc Natl Acad Sci U S A* 1995; **92**: 10322–10326.

11 Vives-Corrons J-L, Koralkova P, Grau JM, Mañú Pereira MDM, Van Wijk R. First description of phosphofructokinase deficiency in spain: identification of a novel homozygous missense mutation in the PFKM gene. *Front Physiol* 2013; **4**: 393.

12 Keildson S, Fadista J, Ladenvall C *et al.* Expression of phosphofructokinase in skeletal muscle is influenced by genetic variation and associated with insulin sensitivity. *Diabetes* 2014; **63**: 1154–1165.

13 Bonnefont JP, Demaugre F, Prip-Buus C *et al.* Carnitine palmitoyltransferase deficiencies. *Mol Genet Metab* 1999; **68**: 424–440.

14 Laforêt P, Vianey-Saban C. Disorders of muscle lipid metabolism: diagnostic and therapeutic challenges. *Neuromuscul Disord NMD* 2010; **20**: 693–700.

15 Bruno C, Dimauro S. Lipid storage myopathies. *Curr Opin Neurol* 2008; **21**: 601–606.

16 Wataya K, Akanuma J, Cavadini P *et al.* Two CPT2 mutations in three Japanese patients with carnitine palmitoyltransferase II deficiency: functional analysis and association with polymorphic haplotypes and two clinical phenotypes. *Hum Mutat* 1998; **11**: 377–386.

17 Colombo I, Pagliarani S, Testolin S *et al.* Adult polyglucosan body disease: clinical and histological heterogeneity of a large Italian family. *Neuromuscul Disord NMD* 2015; **25**: 423–428.

18 Malfatti E, Barnerias C, Hedberg-Oldfors C *et al.* A novel neuromuscular form of glycogen storage disease type IV with arthrogryposis, spinal stiffness and rare polyglucosan bodies in muscle. *Neuromuscul Disord NMD* 2016; **26**: 681–687.

19 Massa R, Bruno C, Martorana A, de Stefano N, van Diggelen OP, Federico A. Adult polyglucosan body disease: proton magnetic resonance spectroscopy of the brain and novel mutation in the GBE1 gene. *Muscle Nerve* 2008; **37**: 530–536.

20 Wuyts W, Reyniers E, Ceuterick C, Storm K, de Barsy T, Martin J-J. Myopathy and phosphorylase kinase deficiency caused by a mutation in the PHKA1 gene. *Am J Med Genet A* 2005; **133A**: 82–84.

21 Burwinkel B, Hu B, Schroers A *et al.* Muscle glycogenosis with low phosphorylase kinase activity: mutations in PHKA1, PHKG1 or six other candidate genes explain only a minority of cases. *Eur J Hum Genet EJHG* 2003; **11**: 516–526.

22 Ørngreen MC, Schelhaas HJ, Jeppesen TD *et al.* Is muscle glycogenolysis impaired in X-linked phosphorylase b kinase deficiency? *Neurology* 2008; **70**: 1876–1882.

23 Burwinkel B, Maichele AJ, Aagenaes O *et al.* Autosomal glycogenosis of liver and muscle due to phosphorylase kinase deficiency is caused by mutations in the phosphorylase kinase beta subunit (PHKB). *Hum Mol Genet* 1997; **6**: 1109–1115.

24 Roscher A, Patel J, Hewson S *et al.* The natural history of glycogen storage disease types VI and IX: Long-term outcome from the largest metabolic center in Canada. *Mol Genet Metab* 2014; **113**: 171–176.

25 Stojkovic T, Vissing J, Petit F *et al.* Muscle glycogenosis due to phosphoglucomutase 1 deficiency. *N Engl J Med* 2009; **361**: 425–427.

26 Tegtmeyer LC, Rust S, van Scherpenzeel M *et al.* Multiple phenotypes in phosphoglucomutase 1 deficiency. *N Engl J Med* 2014; **370**: 533–542.

27 Preisler N, Laforêt P, Echaniz-Laguna A *et al.* Fat and carbohydrate metabolism during exercise in phosphoglucomutase type 1 deficiency. *J Clin Endocrinol Metab* 2013; **98**: E1235-1240.

28 Moslemi A-R, Lindberg C, Nilsson J, Tajsharghi H, Andersson B, Oldfors A. Glycogenin-1 deficiency and inactivated priming of glycogen synthesis. *N Engl J Med* 2010; **362**: 1203–1210.

29 Ben Yaou R, Hubert A, Nelson I *et al.* Clinical heterogeneity and phenotype/genotype findings in 5 families with GYG1 deficiency. *Neurol Genet* 2017; **3**:

e208.
30 Hedberg-Oldfors C, Mensch A, Visuttijai K *et al.* Polyglucosan myopathy and functional characterization of a novel GYG1 mutation. *Acta Neurol Scand* 2018; **137**: 308–315.
31 McCue ME, Valberg SJ, Miller MB *et al.* Glycogen synthase (GYS1) mutation causes a novel skeletal muscle glycogenosis. *Genomics* 2008; **91**: 458–466.
32 Cameron JM, Levandovskiy V, MacKay N *et al.* Identification of a novel mutation in GYS1 (muscle-specific glycogen synthase) resulting in sudden cardiac death, that is diagnosable from skin fibroblasts. *Mol Genet Metab* 2009; **98**: 378–382.
33 Thevenon J, Laurent G, Ader F *et al.* High prevalence of arrhythmic and myocardial complications in patients with cardiac glycogenosis due to PRKAG2 mutations. *Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol* 2017; **19**: 651–659.
34 Ntusi NA, Shaboodien G, Badri M, Gumedze F, Mayosi BM. Clinical features, spectrum of causal genetic mutations and outcome of hypertrophic cardiomyopathy in South Africans. *Cardiovasc J Afr* 2016; **27**: 152–158.
35 Hinson JT, Chopra A, Lowe A *et al.* Integrative Analysis of PRKAG2 Cardiomyopathy iPS and Microtissue Models Identifies AMPK as a Regulator of Metabolism, Survival, and Fibrosis. *Cell Rep* 2016; **17**: 3292–3304.
36 Nilsson J, Schoser B, Laforet P *et al.* Polyglucosan body myopathy caused by defective ubiquitin ligase RBCK1. *Ann Neurol* 2013; **74**: 914–919.
37 Wang K, Kim C, Bradfield J *et al.* Whole-genome DNA/RNA sequencing identifies truncating mutations in RBCK1 in a novel Mendelian disease with neuromuscular and cardiac involvement. *Genome Med* 2013; **5**: 67.
38 Fanin M, Nascimbeni AC, Savarese M *et al.* Familial polyglucosan body myopathy with unusual phenotype. *Neuropathol Appl Neurobiol* 2015; **41**: 385–390.
39 Flanagan JM, Rhodes M, Wilson M, Beutler E. The identification of a recurrent phosphoglycerate kinase mutation associated with chronic haemolytic anaemia and neurological dysfunction in a family from USA. *Br J Haematol* 2006; **134**: 233–237.
40 Spiegel R, Gomez EA, Akman HO, Krishna S, Horovitz Y, DiMauro S. Myopathic form of phosphoglycerate kinase (PGK) deficiency: a new case and pathogenic considerations. *Neuromuscul Disord NMD* 2009; **19**: 207–211.
41 Coppens S, Koralkova P, Aeby A *et al.* Recurrent episodes of myoglobinuria, mental retardation and seizures but no hemolysis in two brothers with phosphoglycerate kinase deficiency. *Neuromuscul Disord NMD* 2016; **26**: 207–210.
42 Svaasand EK, Aasly J, Landsem VM, Klungland H. Altered expression of PGK1 in a family with phosphoglycerate kinase deficiency. *Muscle Nerve* 2007; **36**: 679–684.
43 Salameh J, Goyal N, Choudry R, Camelo-Piragua S, Chong PST. Phosphoglycerate mutase deficiency with tubular aggregates in a patient from Panama. *Muscle Nerve* 2013; **47**: 138–140.
44 Vivante A, Ityel H, Pode-Shakked B *et al.* Exome sequencing in Jewish and Arab patients with rhabdomyolysis reveals single-gene etiology in 43% of cases. *Pediatr Nephrol Berl Ger* 2017; **32**: 2273–2282.
45 Naini A, Toscano A, Musumeci O, Vissing J, Akman HO, DiMauro S. Muscle phosphoglycerate mutase deficiency revisited. *Arch Neurol* 2009; **66**: 394–398.
46 Yue D, Zhu W, Zhao C. Exertional myalgia, contractures and annular erythema in a patient with muscle lactate dehydrogenase (LDH) deficiency. *Neuromuscul Disord NMD* 2018; **28**: 59.
47 Kanno T, Maekawa M. Lactate dehydrogenase M-subunit deficiencies: clinical features, metabolic background, and genetic heterogeneities. *Muscle Nerve Suppl* 1995; **3**: S54-60.
48 Pretsch W, Chatterjee B, Favor J, Merkle S, Sandulache R. Molecular, genetic and biochemical characterization of lactate dehydrogenase-A enzyme activity mutations in Mus musculus. *Mamm Genome Off J Int Mamm Genome Soc* 1998; **9**: 144–149.
49 Musumeci O, Brady S, Rodolico C *et al.* Recurrent rhabdomyolysis due to muscle β-enolase deficiency: very rare or underestimated? *J Neurol* 2014; **261**: 2424–2428.
50 Comi GP, Fortunato F, Lucchiari S *et al.* Beta-enolase deficiency, a new metabolic myopathy of distal glycolysis. *Ann Neurol* 2001; **50**: 202–207.
51 Cetin H, Wöhrer A, Rittelmeyer I *et al.* The c.65-2A>G splice site mutation is associated with a mild phenotype in Danon disease due to the transcription of normal LAMP2 mRNA. *Clin Genet* 2016; **90**: 366–371.
52 Gourzi P, Pantou MP, Gkouziouta A *et al.* A new phenotype of severe dilated cardiomyopathy associated with a mutation in the LAMP2 gene previously known to cause hypertrophic cardiomyopathy in the context of Danon disease. *Eur J Med Genet* 2018. doi:10.1016/j.ejmg.2018.05.015.
53 Lim L, Palayer M, Bruneau A *et al.* Myoadenylate deaminase deficiency: a frequent cause of muscle pain A case detected by exercise testing. *Ann Biol Clin (Paris)* 2017; **75**: 445–449.
54 Gross M, Rötzer E, Kölle P *et al.* A G468-T AMPD1 mutant allele contributes to the high incidence of myoadenylate deaminase deficiency in the Caucasian population. *Neuromuscul Disord NMD* 2002; **12**: 558–565.
55 Rossi LN, Cornelio F, Dworzak F, Morandi L, Rossi G, Di Mauro S. Myoadenylate deaminase deficiency in a 5-year-old boy with intermittent muscle pain. *Helv Paediatr Acta* 1984; **39**: 89–93.
56 Wang Y, Ye J, Ganapathy V, Longo N. Mutations in the organic cation/carnitine transporter OCTN2 in primary carnitine deficiency. *Proc Natl Acad Sci U S A* 1999; **96**: 2356–2360.
57 Wang Y, Taroni F, Garavaglia B, Longo N. Functional analysis of mutations in the OCTN2 transporter causing primary carnitine deficiency: lack of genotype-phenotype correlation. *Hum Mutat* 2000; **16**: 401–407.
58 Nezu J, Tamai I, Oku A *et al.* Primary systemic carnitine deficiency is caused by mutations in a gene encoding sodium ion-dependent carnitine transporter. *Nat Genet* 1999; **21**: 91–94.
59 Rubio-Gozalbo ME, Bakker JA, Waterham HR, Wanders RJA. Carnitine-acylcarnitine translocase deficiency, clinical, biochemical and genetic aspects. *Mol Aspects Med* 2004; **25**: 521–532.
60 Iacobazzi V, Invernizzi F, Baratta S *et al.* Molecular and functional analysis of SLC25A20 mutations causing carnitine-acylcarnitine translocase deficiency. *Hum Mutat* 2004; **24**: 312–320.
61 Peluso G, Petillo O, Margarucci S *et al.* Differential carnitine/acylcarnitine translocase expression defines distinct metabolic signatures in skeletal muscle cells. *J Cell Physiol* 2005; **203**: 439–446.
62 Olsen RKJ, Andresen BS, Christensen E, Bross P, Skovby F, Gregersen N. Clear relationship between ETF/ETFDH genotype and phenotype in patients with multiple acyl-CoA dehydrogenation deficiency. *Hum Mutat* 2003; **22**: 12–23.
63 Witting N, Laforêt P, Voermans NC *et al.* Phenotype and genotype of muscle ryanodine receptor rhabdomyolysis-myalgia syndrome. *Acta Neurol Scand* 2018; **137**: 452–461.
64 Dlamini N, Voermans NC, Lillis S *et al.* Mutations in RYR1 are a common cause of exertional myalgia and rhabdomyolysis. *Neuromuscul Disord NMD* 2013; **23**: 540–548.
65 Andresen BS, Olpin S, Poorthuis BJ *et al.* Clear correlation of genotype with disease phenotype in very-long-chain acyl-CoA dehydrogenase deficiency. *Am J Hum Genet* 1999; **64**: 479–494.
66 Mathur A, Sims HF, Gopalakrishnan D *et al.* Molecular heterogeneity in very-long-chain acyl-CoA dehydrogenase deficiency causing pediatric cardiomyopathy and sudden death. *Circulation* 1999; **99**: 1337–1343.
67 Schiff M, Mohsen A-W, Karunanidhi A, McCracken E, Yeasted R, Vockley J. Molecular and cellular pathology of very-long-chain acyl-CoA dehydrogenase deficiency. *Mol Genet Metab* 2013; **109**: 21–27.
68 Reilich P, Horvath R, Krause S *et al.* The phenotypic spectrum of neutral lipid storage myopathy due to mutations in the PNPLA2 gene. *J Neurol* 2011; **258**: 1987–1997.
69 Fischer J, Lefèvre C, Morava E *et al.* The gene encoding adipose triglyceride lipase (PNPLA2) is mutated in neutral lipid storage disease with myopathy. *Nat Genet* 2007; **39**: 28–30.
70 Michot C, Hubert L, Brivet M *et al.* LPIN1 gene mutations: a major cause of severe rhabdomyolysis in early childhood. *Hum Mutat* 2010; **31**: E1564-1573.
71 Michot C, Mamoune A, Vamecq J *et al.* Combination of lipid metabolism alterations and their sensitivity to inflammatory cytokines in human lipin-1-

deficient myoblasts. *Biochim Biophys Acta* 2013; **1832**: 2103–2114.
72 Saunders CJ, Moon SH, Liu X *et al.* Loss of function variants in human PNPLA8 encoding calcium-independent phospholipase A2 γ recapitulate the mitochondriopathy of the homologous null mouse. *Hum Mutat* 2015; **36**: 301–306.
73 Mancuso DJ, Sims HF, Han X *et al.* Genetic ablation of calcium-independent phospholipase A2gamma leads to alterations in mitochondrial lipid metabolism and function resulting in a deficient mitochondrial bioenergetic phenotype. *J Biol Chem* 2007; **282**: 34611–34622.
74 Schiff M, Veauville-Merllié A, Su CH *et al.* SLC25A32 Mutations and Riboflavin-Responsive Exercise Intolerance. *N Engl J Med* 2016; **374**: 795–797.
75 Hellebrekers DMEI, Sallevelt SCEH, Theunissen TEJ *et al.* Novel SLC25A32 mutation in a patient with a severe neuromuscular phenotype. *Eur J Hum Genet EJHG* 2017; **25**: 886–888.
76 Kim J, Lei Y, Guo J *et al.* Formate rescues neural tube defects caused by mutations in Slc25a32. *Proc Natl Acad Sci U S A* 2018; **115**: 4690–4695.
77 Olsen RKJ, Koňaříková E, Giancaspero TA *et al.* Riboflavin-Responsive and -Non-responsive Mutations in FAD Synthase Cause Multiple Acyl-CoA Dehydrogenase and Combined Respiratory-Chain Deficiency. *Am J Hum Genet* 2016; **98**: 1130–1145.
78 Auranen M, Paetau A, Piirilä P *et al.* Patient with multiple acyl-CoA dehydrogenation deficiency disease and FLAD1 mutations benefits from riboflavin therapy. *Neuromuscul Disord NMD* 2017; **27**: 581–584.
79 Mochel F, Knight MA, Tong W-H *et al.* Splice mutation in the iron-sulfur cluster scaffold protein ISCU causes myopathy with exercise intolerance. *Am J Hum Genet* 2008; **82**: 652–660.
80 Olsson A, Lind L, Thornell L-E, Holmberg M. Myopathy with lactic acidosis is linked to chromosome 12q23.3-24.11 and caused by an intron mutation in the ISCU gene resulting in a splicing defect. *Hum Mol Genet* 2008; **17**: 1666–1672.
81 Riley LG, Cooper S, Hickey P *et al.* Mutation of the mitochondrial tyrosyl-tRNA synthetase gene, YARS2, causes myopathy, lactic acidosis, and sideroblastic anemia--MLASA syndrome. *Am J Hum Genet* 2010; **87**: 52–59.
82 Nakajima J, Eminoglu TF, Vatansever G *et al.* A novel homozygous YARS2 mutation causes severe myopathy, lactic acidosis, and sideroblastic anemia 2. *J Hum Genet* 2014; **59**: 229–232.
83 Riley LG, Menezes MJ, Rudinger-Thirion J *et al.* Phenotypic variability and identification of novel YARS2 mutations in YARS2 mitochondrial myopathy, lactic acidosis and sideroblastic anaemia. *Orphanet J Rare Dis* 2013; **8**: 193.
84 Haack TB, Haberberger B, Frisch E-M *et al.* Molecular diagnosis in mitochondrial complex I deficiency using exome sequencing. *J Med Genet* 2012; **49**: 277–283.
85 Schiff M, Haberberger B, Xia C *et al.* Complex I assembly function and fatty acid oxidation enzyme activity of ACAD9 both contribute to disease severity in ACAD9 deficiency. *Hum Mol Genet* 2015; **24**: 3238–3247.