

CLNE0020: Motoneurons, Neuromuscular Junctions and Associated Disease

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[1]

J. A. Morren and N. Galvez-Jimenez, 'Current and prospective disease-modifying therapies for amyotrophic lateral sclerosis', *Expert Opinion on Investigational Drugs*, vol. 21, no. 3, pp. 297–320, Mar. 2012, doi: 10.1517/13543784.2012.657303.

[2]

H. Mitsumoto, B. R. Brooks, and V. Silani, 'Clinical trials in amyotrophic lateral sclerosis: why so many negative trials and how can trials be improved?', *The Lancet Neurology*, vol. 13, no. 11, pp. 1127–1138, Nov. 2014, doi: 10.1016/S1474-4422(14)70129-2.

[3]

N. J. Maragakis, 'What can we learn from the edaravone development program for ALS?', *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, vol. 18, no. sup1, pp. 98–103, Oct. 2017, doi: 10.1080/21678421.2017.1361446.

[4]

J. Hughes, S. Rees, S. Kalindjian, and K. Philpott, 'Principles of early drug discovery', *British Journal of Pharmacology*, vol. 162, no. 6, pp. 1239–1249, Mar. 2011, doi: 10.1111/j.1476-5381.2010.01127.x.

[5]

D. J. Birnkrant et al., 'Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management', *The Lancet Neurology*, vol. 17, no. 3, pp. 251–267, Mar. 2018, doi: 10.1016/S1474-4422(18)30024-3.

[6]

D. J. Birnkrant et al., 'Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management', *The Lancet Neurology*, vol. 17, no. 4, pp. 347–361, Apr. 2018, doi: 10.1016/S1474-4422(18)30025-5.

[7]

D. J. Birnkrant et al., 'Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan', *The Lancet Neurology*, vol. 17, no. 5, pp. 445–455, May 2018, doi: 10.1016/S1474-4422(18)30026-7.

[8]

E. Mercuri et al., 'Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care', *Neuromuscular Disorders*, vol. 28, no. 2, pp. 103–115, Feb. 2018, doi: 10.1016/j.nmd.2017.11.005.

[9]

R. S. Finkel et al., 'Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics', *Neuromuscular Disorders*, vol. 28, no. 3, pp. 197–207, Mar. 2018, doi: 10.1016/j.nmd.2017.11.004.

[10]

M. Scoto, R. S. Finkel, E. Mercuri, and F. Muntoni, 'Therapeutic approaches for spinal muscular atrophy (SMA)', *Gene Therapy*, vol. 24, no. 9, pp. 514–519, Sep. 2017, doi: 10.1038/gt.2017.45.

[11]

D. Ramsey et al., 'Revised Hammersmith Scale for spinal muscular atrophy: A SMA specific clinical outcome assessment tool', *PLOS ONE*, vol. 12, no. 2, Feb. 2017, doi: 10.1371/journal.pone.0172346.

[12]

E. S. Mazzone et al., 'Revised upper limb module for spinal muscular atrophy: Development of a new module', *Muscle & Nerve*, vol. 55, no. 6, pp. 869–874, Jun. 2017, doi: 10.1002/mus.25430.

[13]

E. Westerberg, C. J. Molin, S. Spörndly Nees, J. Widenfalk, and A. R. Punga, 'The impact of physical exercise on neuromuscular function in Myasthenia gravis patients', *Medicine*, vol. 97, no. 31, Aug. 2018, doi: 10.1097/MD.00000000000011510.

[14]

J. H. Peragallo, 'Pediatric Myasthenia Gravis', *Seminars in Pediatric Neurology*, vol. 24, no. 2, pp. 116–121, May 2017, doi: 10.1016/j.spen.2017.04.003.

[15]

M. Laurá et al., 'Prevalence and orthopedic management of foot and ankle deformities in Charcot-Marie-Tooth disease', *Muscle & Nerve*, vol. 57, no. 2, pp. 255–259, Feb. 2018, doi: 10.1002/mus.25724.

[16]

M. M. Reilly et al., '221st ENMC International Workshop':, *Neuromuscular Disorders*, vol. 27, no. 12, pp. 1138–1142, Dec. 2017, doi: 10.1016/j.nmd.2017.09.005.

[17]

G. M. Ramdharry et al., 'A pilot study of proximal strength training in Charcot-Marie-Tooth disease', *Journal of the Peripheral Nervous System*, vol. 19, no. 4, pp. 328–332, Dec. 2014, doi: 10.1111/jns.12100.

[18]

S. Gibson and V. Haringer, 'Amyotrophic lateral sclerosis: clinical perspectives', *Orphan*

Drugs: Research and Reviews, Apr. 2015, doi: 10.2147/ODRR.S63585.

[19]

D. J. Berlowitz et al., 'Identifying who will benefit from non-invasive ventilation in amyotrophic lateral sclerosis/motor neurone disease in a clinical cohort', *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 87, no. 3, pp. 280–286, Mar. 2016, doi: 10.1136/jnnp-2014-310055.

[20]

C. A. Harwood, C. J. McDermott, and P. J. Shaw, 'Clinical aspects of motor neurone disease', *Medicine*, vol. 40, no. 10, pp. 540–545, Oct. 2012, doi: 10.1016/j.mpmed.2012.07.003.

[21]

V. E. Drory, E. Goltsman, J. Goldman Reznik, A. Mosek, and A. D. Korczyn, 'The value of muscle exercise in patients with amyotrophic lateral sclerosis', *Journal of the Neurological Sciences*, vol. 191, no. 1–2, pp. 133–137, Oct. 2001, doi: 10.1016/S0022-510X(01)00610-4.

[22]

A. Al-Chalabi, L. H. van den Berg, and J. Veldink, 'Gene discovery in amyotrophic lateral sclerosis: implications for clinical management', *Nature Reviews Neurology*, vol. 13, no. 2, pp. 96–104, Feb. 2017, doi: 10.1038/nrneurol.2016.182.

[23]

M. T. Carrì, N. D'Ambrosi, and M. Cozzolino, 'Pathways to mitochondrial dysfunction in ALS pathogenesis', *Biochemical and Biophysical Research Communications*, vol. 483, no. 4, pp. 1187–1193, Feb. 2017, doi: 10.1016/j.bbrc.2016.07.055.

[24]

G. Lin, D. Mao, and H. J. Bellen, 'Amyotrophic Lateral Sclerosis Pathogenesis Converges on Defects in Protein Homeostasis Associated with TDP-43 Mislocalization and Proteasome-Mediated Degradation Overload', in *Fly Models of Human Diseases*, vol. 121, Elsevier, 2017, pp. 111–171. doi: 10.1016/bs.ctdb.2016.07.004.

[25]

Z. Monahan, F. Shewmaker, and U. B. Pandey, 'Stress granules at the intersection of autophagy and ALS', *Brain Research*, vol. 1649, pp. 189–200, Oct. 2016, doi: 10.1016/j.brainres.2016.05.022.

[26]

C. Ruegsegger and S. Saxena, 'Proteostasis impairment in ALS', *Brain Research*, vol. 1648, pp. 571–579, Oct. 2016, doi: 10.1016/j.brainres.2016.03.032.

[27]

A. E. Renton, A. Chiò, and B. J. Traynor, 'State of play in amyotrophic lateral sclerosis genetics', *Nature Neuroscience*, vol. 17, no. 1, pp. 17–23, Jan. 2014, doi: 10.1038/nn.3584.

[28]

T. M. Jessell, 'Neuronal specification in the spinal cord: inductive signals and transcriptional codes', *Nature Reviews Genetics*, vol. 1, no. 1, pp. 20–29, Oct. 2000, doi: 10.1038/35049541.

[29]

R. Harland, 'Neural induction', *Current Opinion in Genetics & Development*, vol. 10, no. 4, pp. 357–362, Aug. 2000, doi: 10.1016/S0959-437X(00)00096-4.

[30]

J. S. Dasen and T. M. Jessell, 'Chapter Six Hox Networks and the Origins of Motor Neuron Diversity', in *Hox Genes*, vol. 88, Elsevier, 2009, pp. 169–200. doi: 10.1016/S0070-2153(09)88006-X.

[31]

D. Bonanomi and S. L. Pfaff, 'Motor Axon Pathfinding', *Cold Spring Harbor Perspectives in*

Biology, vol. 2, no. 3, pp. a001735–a001735, Mar. 2010, doi: 10.1101/cshperspect.a001735.

[32]

H. Darabid, A. P. Perez-Gonzalez, and R. Robitaille, 'Neuromuscular synaptogenesis: coordinating partners with multiple functions', *Nature Reviews Neuroscience*, vol. 15, no. 11, pp. 703–718, Nov. 2014, doi: 10.1038/nrn3821.

[33]

K. C. Kanning, A. Kaplan, and C. E. Henderson, 'Motor Neuron Diversity in Development and Disease', *Annual Review of Neuroscience*, vol. 33, no. 1, pp. 409–440, Jun. 2010, doi: 10.1146/annurev.neuro.051508.135722.

[34]

D. R. Ladle, E. Pecho-Vrieseling, and S. Arber, 'Assembly of Motor Circuits in the Spinal Cord: Driven to Function by Genetic and Experience-Dependent Mechanisms', *Neuron*, vol. 56, no. 2, pp. 270–283, Oct. 2007, doi: 10.1016/j.neuron.2007.09.026.

[35]

R. M. Brownstone and T. V. Bui, 'Spinal interneurons providing input to the final common path during locomotion', in *Breathe, Walk and Chew: The Neural Challenge: Part I*, vol. 187, Elsevier, 2010, pp. 81–95. doi: 10.1016/B978-0-444-53613-6.00006-X.

[36]

L. Li, W.-C. Xiong, and L. Mei, 'Neuromuscular Junction Formation, Aging, and Disorders', *Annual Review of Physiology*, vol. 80, no. 1, pp. 159–188, Feb. 2018, doi: 10.1146/annurev-physiol-022516-034255.

[37]

N. Singhal and P. T. Martin, 'Role of extracellular matrix proteins and their receptors in the development of the vertebrate neuromuscular junction', *Developmental Neurobiology*, vol. 71, no. 11, pp. 982–1005, Nov. 2011, doi: 10.1002/dneu.20953.

[38]

H. Nishimune et al., 'Laminins promote postsynaptic maturation by an autocrine mechanism at the neuromuscular junction', *The Journal of Cell Biology*, vol. 182, no. 6, pp. 1201–1215, Sep. 2008, doi: 10.1083/jcb.200805095.

[39]

R. Rudolf, M. M. Khan, S. Labeit, and M. R. Deschenes, 'Degeneration of Neuromuscular Junction in Age and Dystrophy', *Frontiers in Aging Neuroscience*, vol. 6, May 2014, doi: 10.3389/fnagi.2014.00099.

[40]

R. A. Jones et al., 'Cellular and Molecular Anatomy of the Human Neuromuscular Junction', *Cell Reports*, vol. 21, no. 9, pp. 2348–2356, Nov. 2017, doi: 10.1016/j.celrep.2017.11.008.

[41]

E. O'Connor et al., 'Clinical and research strategies for limb-girdle congenital myasthenic syndromes', *Annals of the New York Academy of Sciences*, vol. 1412, no. 1, pp. 102–112, Jan. 2018, doi: 10.1111/nyas.13520.

[42]

A. G. Engel, X.-M. Shen, D. Selcen, and S. M. Sine, 'Congenital myasthenic syndromes: pathogenesis, diagnosis, and treatment', *The Lancet Neurology*, vol. 14, no. 4, pp. 420–434, Apr. 2015, doi: 10.1016/S1474-4422(14)70201-7.

[43]

P. M. R. Cruz, J. Palace, and D. Beeson, 'Congenital myasthenic syndromes and the neuromuscular junction', *Current Opinion in Neurology*, vol. 27, no. 5, pp. 566–575, Oct. 2014, doi: 10.1097/WCO.0000000000000134.

[44]

P. M. Rodríguez Cruz, J. Palace, and D. Beeson, 'Inherited disorders of the neuromuscular junction: an update', *Journal of Neurology*, vol. 261, no. 11, pp. 2234–2243, Nov. 2014, doi: 10.1007/s00415-014-7520-7.

[45]

K. Belaya et al., 'Mutations in *SGCG* cause congenital myasthenic syndrome and bridge myasthenic disorders with dystroglycanopathies', *Brain*, vol. 138, no. 9, pp. 2493–2504, Sep. 2015, doi: 10.1093/brain/awv185.

[46]

P. M. Rodríguez Cruz et al., 'Congenital myopathies with secondary neuromuscular transmission defects; A case report and review of the literature', *Neuromuscular Disorders*, vol. 24, no. 12, pp. 1103–1110, Dec. 2014, doi: 10.1016/j.nmd.2014.07.005.

[47]

S. J. Crisp, D. M. Kullmann, and A. Vincent, 'Autoimmune synaptopathies', *Nature Reviews Neuroscience*, vol. 17, no. 2, pp. 103–117, Feb. 2016, doi: 10.1038/nrn.2015.27.

[48]

N. E. Gilhus, 'Myasthenia Gravis', *New England Journal of Medicine*, vol. 375, no. 26, pp. 2570–2581, Dec. 2016, doi: 10.1056/NEJMra1602678.

[49]

L. L. Kusner and H. J. Kaminski, 'Myasthenia Gravis', in *Neurobiology of Brain Disorders*, Elsevier, 2015, pp. 135–150. doi: 10.1016/B978-0-12-398270-4.00010-0.

[50]

D. G. Leung, *Other Proven and Putative Autoimmune Disorders of the Peripheral Nervous System*, vol. 1. Oxford University Press, 2017. doi: 10.1093/med/9780199937837.003.0098.

[51]

J. Spillane, D. J. Beeson, and D. M. Kullmann, 'Myasthenia and related disorders of the neuromuscular junction', *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 81, no. 8, pp. 850–857, Aug. 2010, doi: 10.1136/jnnp.2008.169367.

[52]

M. N. Meriggioli and D. B. Sanders, 'Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity', *The Lancet Neurology*, vol. 8, no. 5, pp. 475–490, May 2009, doi: 10.1016/S1474-4422(09)70063-8.

[53]

J. Spillane et al., 'Lambert-Eaton syndrome IgG inhibits transmitter release via P/Q Ca^{2+} channels', *Neurology*, vol. 84, no. 6, pp. 575–579, Feb. 2015, doi: 10.1212/WNL.0000000000001225.

[54]

G. I. Wolfe et al., 'Randomized Trial of Thymectomy in Myasthenia Gravis', *New England Journal of Medicine*, vol. 375, no. 6, pp. 511–522, Aug. 2016, doi: 10.1056/NEJMoa1602489.

[55]

Orrell, Richard WBarclay, Chris, 'Diagnosis and management of motor neurone disease', *Practitioner*, vol. 260, pp. 17–21, [Online]. Available: <https://search.proquest.com/docview/1844334383/64C39DCAF3D346C0PQ/1?accountid=14511>

[56]

S. Morgan and R. W. Orrell, 'Pathogenesis of amyotrophic lateral sclerosis', *British Medical Bulletin*, vol. 119, no. 1, pp. 87–98, Sep. 2016, doi: 10.1093/bmb/ldw026.

[57]

G. Fuller and M. Manford, *Neurology: an illustrated colour text*, 3rd ed. Edinburgh: Churchill

Livingstone Elsevier, 2010. [Electronic resource]. Available:
http://ucl.alma.exlibrisgroup.com/view/action/uresolver.do?operation=resolveService&package_service_id=3669595080004761&institutionId=4761&customerId=4760

[58]

'Motor neurone disease: assessment and management | Guidance and guidelines | NICE', [Online]. Available: <https://www.nice.org.uk/guidance/ng42>

[59]

P. Couratier, P. Corcia, G. Lautrette, M. Nicol, P.-M. Preux, and B. Marin, 'Epidemiology of amyotrophic lateral sclerosis: A review of literature', *Revue Neurologique*, vol. 172, no. 1, pp. 37–45, Jan. 2016, doi: 10.1016/j.neurol.2015.11.002.

[60]

M. Otto et al., 'Roadmap and standard operating procedures for biobanking and discovery of neurochemical markers in ALS', *Amyotrophic Lateral Sclerosis*, vol. 13, no. 1, pp. 1–10, Jan. 2012, doi: 10.3109/17482968.2011.627589.

[61]

C.-H. Lu et al., 'Neurofilament light chain: A prognostic biomarker in amyotrophic lateral sclerosis', *Neurology*, vol. 84, no. 22, pp. 2247–2257, Jun. 2015, doi: 10.1212/WNL.0000000000001642.

[62]

M. Benatar et al., 'ALS biomarkers for therapy development: State of the field and future directions', *Muscle & Nerve*, vol. 53, no. 2, pp. 169–182, Feb. 2016, doi: 10.1002/mus.24979.

[63]

U. Andreasson, K. Blennow, and H. Zetterberg, 'Update on ultrasensitive technologies to facilitate research on blood biomarkers for central nervous system disorders', *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, vol. 3, pp. 98–102, 2016, doi: 10.1016/j.dadm.2016.05.005.

[64]

T. F. Gendron et al., 'Poly(GP) proteins are a useful pharmacodynamic marker for -associated amyotrophic lateral sclerosis', *Science Translational Medicine*, vol. 9, no. 383, Mar. 2017, doi: 10.1126/scitranslmed.aai7866.

[65]

A. Vincent, 'Unravelling the pathogenesis of myasthenia gravis', *Nature Reviews Immunology*, vol. 2, no. 10, pp. 797–804, Oct. 2002, doi: 10.1038/nri916.

[66]

L. Jacobson, A. Polizzi, G. Morriss-Kay, and A. Vincent, 'Plasma from human mothers of fetuses with severe arthrogryposis multiplex congenita causes deformities in mice', *Journal of Clinical Investigation*, vol. 103, no. 7, pp. 1031–1038, Apr. 1999, doi: 10.1172/JCI5943.

[67]

S. Viegas et al., 'Passive and active immunization models of MuSK-Ab positive myasthenia: Electrophysiological evidence for pre and postsynaptic defects', *Experimental Neurology*, vol. 234, no. 2, pp. 506–512, Apr. 2012, doi: 10.1016/j.expneurol.2012.01.025.

[68]

I. Koneczny, J. Cossins, and A. Vincent, 'The role of muscle-specific tyrosine kinase (MuSK) and mystery of MuSK myasthenia gravis', *Journal of Anatomy*, vol. 224, no. 1, pp. 29–35, Jan. 2014, doi: 10.1111/joa.12034.

[69]

I. Koneczny, J. Cossins, P. Waters, D. Beeson, and A. Vincent, 'MuSK Myasthenia Gravis IgG4 Disrupts the Interaction of LRP4 with MuSK but Both IgG4 and IgG1-3 Can Disperse Preformed Agrin-Independent AChR Clusters', *PLoS ONE*, vol. 8, no. 11, Nov. 2013, doi: 10.1371/journal.pone.0080695.

[70]

S. J. Crisp, D. M. Kullmann, and A. Vincent, 'Autoimmune synaptopathies', *Nature Reviews Neuroscience*, vol. 17, no. 2, pp. 103–117, Feb. 2016, doi: 10.1038/nrn.2015.27.

[71]

I. O. C. Woollacott and J. D. Rohrer, 'The clinical spectrum of sporadic and familial forms of frontotemporal dementia', *Journal of Neurochemistry*, vol. 138, pp. 6–31, Aug. 2016, doi: 10.1111/jnc.13654.

[72]

E. Gordon, J. D. Rohrer, and N. C. Fox, 'Advances in neuroimaging in frontotemporal dementia', *Journal of Neurochemistry*, vol. 138, pp. 193–210, Aug. 2016, doi: 10.1111/jnc.13656.

[73]

'Volume 58, Issue 3, March 2016', Volume 58, Issue 3, March 2016, [Online]. Available: <https://link.springer.com/journal/12031/58/3>

[74]

N. M. Badders et al., 'Selective modulation of the androgen receptor AF2 domain rescues degeneration in spinal bulbar muscular atrophy', *Nature Medicine*, vol. 24, no. 4, pp. 427–437, Mar. 2018, doi: 10.1038/nm.4500.

[75]

L. K. Beitel, C. Alvarado, S. Mokhtar, M. Paliouras, and M. Trifiro, 'Mechanisms Mediating Spinal and Bulbar Muscular Atrophy: Investigations into Polyglutamine-Expanded Androgen Receptor Function and Dysfunction', *Frontiers in Neurology*, vol. 4, 2013, doi: 10.3389/fneur.2013.00053.

[76]

C. J. Cortes et al., 'Muscle Expression of Mutant Androgen Receptor Accounts for Systemic and Motor Neuron Disease Phenotypes in Spinal and Bulbar Muscular Atrophy', *Neuron*,

vol. 82, no. 2, pp. 295–307, Apr. 2014, doi: 10.1016/j.neuron.2014.03.001.

[77]

P. Fratta et al., 'Correlation of clinical and molecular features in spinal bulbar muscular atrophy', *Neurology*, vol. 82, no. 23, pp. 2077–2084, Jun. 2014, doi: 10.1212/WNL.0000000000000507.

[78]

A. P. Lieberman et al., 'Peripheral Androgen Receptor Gene Suppression Rescues Disease in Mouse Models of Spinal and Bulbar Muscular Atrophy', *Cell Reports*, vol. 7, no. 3, pp. 774–784, May 2014, doi: 10.1016/j.celrep.2014.02.008.

[79]

B. Malik et al., 'Absence of disturbed axonal transport in spinal and bulbar muscular atrophy', *Human Molecular Genetics*, vol. 20, no. 9, pp. 1776–1786, May 2011, doi: 10.1093/hmg/ddr061.

[80]

B. Malik, N. Nirmalananthan, A. L. Gray, A. R. La Spada, M. G. Hanna, and L. Greensmith, 'Co-induction of the heat shock response ameliorates disease progression in a mouse model of human spinal and bulbar muscular atrophy: implications for therapy', *Brain*, vol. 136, no. 3, pp. 926–943, Mar. 2013, doi: 10.1093/brain/aws343.

[81]

R. Manzano et al., 'Beyond motor neurons: expanding the clinical spectrum in Kennedy's disease', *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 89, no. 8, pp. 808–812, Aug. 2018, doi: 10.1136/jnnp-2017-316961.

[82]

C. Milioto et al., 'Beta-agonist stimulation ameliorates the phenotype of spinal and bulbar muscular atrophy mice and patient-derived myotubes', *Scientific Reports*, vol. 7, no. 1, Dec. 2017, doi: 10.1038/srep41046.