EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Curriculum Vitae

PERSONAL INFORMATION

Leonard van den Berg

WORK EXPERIENCE

2014- 2018 **Director of the Netherlands Neuromuscular Centre**
Spierziekten Centrum Nederland (Netherlands)

2011- 2019 **Director Section Neuromuscular Diseases, Brain Centre Rudolf Magnus**
University Medical Centre Utrecht (Netherlands)

2002- Present **Director Laboratory for Experimental Neurology**
UMC Utrecht (Netherlands)

2002- Present **Director Netherlands ALS Centre**
UMC Utrecht (Netherlands)

1997- Present **Neurologist, Subspecialty in Neuromuscular and Motor Neuron Diseases**
UMC Utrecht (Netherlands)

EDUCATION AND TRAINING

2018- Present **Certificate of re-registration BROK**
University Medical Center Utrecht (Netherlands)

2011- Present **Certificate BROK Exam (GCP)**
University Medical Center Utrecht (Netherlands)

1991- 1997 **Neurologist in training**
University Medical Centre Utrecht (Netherlands)
Neurologist in training. The program was sponsored by a personal grant from the Netherlands Organisation for Scientific Research (Prioriteitsprogramma Klinisch Wetenschappelijk Onderzoek; combination of Residency and PhD program).

1991- 1995 **PhD thesis The Immune Response to Glycoconjugates in Peripheral Neuropathy.**
University Medical Centre Utrecht (Netherlands)

1989- 1992 **Research Fellow**
Neurological Institute, Columbia University, New York, USA (United States)

1983- 1991 **Medical School**
University of Groningen (Netherlands)

ADDITIONAL INFORMATION

Expertise

Neuromuscular Diseases

Publications

Selection of publications

1. Hardiman O, van den Berg LH. The Beginning of Genomic Therapies for ALS. N Engl J Med 2020;383:180-181.

2. Van Eijk RPA, Jones AR, Sproviero W, Shatunov A, Shaw PJ, Leigh PN, Young CA, Shaw CE, Mora G, Mandrioli J, Borghero G, Volanti P, Diekstra FP, van Rheenen W, Verstraete E, Eijkemans MJC, Veldink JH, Chio A, Al-Chalabi A, van den Berg LH*, van Es MA*,; For UKMND-LiCALS and LITALS Study Group. Meta-analysis of pharmacogenetic interactions in ALS clinical trials. Neurology 2017;89:1915-1922.

3. Westeneng HJ, van Veenhuijzen K, van der Spek RA, Peters S, Visser AE, van Rheenen W, Veldink JH, van den Berg LH. Associations between lifestyle and amyotrophic lateral sclerosis stratified by C9orf72 genotype: a longitudinal, population-based, case-control study. Lancet Neurol. 2021;20:373-384.

4. Van Es MA, Hardiman O, Chio A, Al-Chalabi A, Pasterkamp RJ, Veldink JH, van den Berg LH. Amyotrophic lateral sclerosis. Lancet 2017;264:1413-1420.

5. Al-Chalabi A, van den Berg LH, Veldink J. Gene discovery in ALS: implications for clinical management. Nat Rev Neurol 2017;13:96-104.

6. Al-Chalabi A, Hardiman O, Kiernan MC, Chio A, Rix-Brooks B, van den Berg LH. ALS: moving towards a new classification system. Lancet Neurol 2016;15:1182-94.

7. Van Es MA, Veldink JH, Saris CGJ, Blauw HM, van Vught PWJ, Birve A, Lemmens R, Schelhaas HJ, Groen EJN, Huisman MHB, van der Kooi AJ, de Visser M, Dahlberg C, Estrada K, Rivadeneira F, Hofman A, Zwarts MJ, van Doormaal PTC, Rujescu D, Strengman E, Giegling I, Muglia P, Tomik B, Slowik A, Uitterlinden AG, Hendrich C, Waibel S, Meyer T, Ludolph AC, Glass JD, Purcell S, Cichon S, Nothen MM, Wichman HE, Schreiber S, Vermeulen SHHM, Kiemeney LA, Wokke JH, Cronin S, Mc Laughlin RL, Hardiman O, Fumoto K, Pasterkamp RJ, Meininger V, Melki J, Leigh PN, Shaw CE, Landers JE, Al-Chalabi A, Brown RH, Robberecht W, Andersen PM, Ophoff RA, van den Berg LH. Genome-wide association study identifies 19p 13.3 (UNC13A) and 9p 21.2 as susceptibility loci for sporadic ALS. Nature Genet 2009;41:1083-1087.

8. Blauw HM, Veldink JH, van Es MA, van Vught PW, Saris CGJ, van der Zwaag B, Franke L, Burbach JPH, Wokke JHJ, Ophoff RA, van den Berg LH. Genome-wide copy number variation in ALS. Lancet Neurol 2008;7:319-326.

9. Van Es MA, van Vught PW, Blauw H, Franke LW, Saris CGJ, van den Bosch L, de Jong SW, de Jong V, Baas F, Van 't lot R, Lemmers R, Schelhaas JH, Birve A, Sleegers K, van Broeckhoven C, Schmyck JC, Traynr BJ, Wokke JH, Wijmenga C, Robberecht W, Andersen PM, Veldink JH, Ophoff RA*, van den Berg LH*. Genetic variation in DPP6 is associated with susceptibility to ALS. Nature Genet 2008;40:29-31.

10. Tan H, Westeneng H, van der Burgh H, van Es M, Bakker L; van Veenhuijzen K, van Eijk K, van Eijk R, Veldink J, van den Berg LH. The distinct traits of the UNC13A polymorphism in ALS. Ann Neurol 2020 Jul Online Ahead of Print.

11. Peters S, Visser AE, D'Ovidio F, Vlaanderen J, Portengen L, Beghi E, Chio A, Logroscino G, Hardiman O, Pupillo E, Veldink JH, Vermeulen R, van den Berg LH; Euro-MOTOR consortium. Effect modification of the association between total cigarette smoking and ALS risk by intensity, duration and time-since-quitting: Euro-MOTOR. J Neurol Neurosurg Psych 2020;91:33-39.

12. Visser AE, D'Ovidio F, Peters S, Vermeulen RC, Beghi E, Chio A, Veldink JH, Logroscino G, Hardiman O, van den Berg LH; Euro-MOTOR consortium. Multicentre, population-based, case-control study of particulates, combustion products and ALS risk. J Neurol Neurosurg Psychiatry 2019;90:854-860.

13. Peters S, Visser AE, D'Ovidio F, Beghi E, Chio A, Logroscino G, Hardiman O, Kromhout H, Huss A, Veldink J, Vermeulen R, van den Berg LH; Euro-MOTOR consortium. Associations of Electric Shock and Extremely Low-Frequency Magnetic Field Exposure and the Risk of ALS: Euro-MOTOR. Am J Epidemiol 2019;188:796-805.

14. Visser AE, Rooney JPK, D'Ovidio F, Westeneng HJ, Vermeulen RCH, Beghi E, Chio A, Logroscino G, Hardiman O, Veldink JH, van den Berg LH; Euro-MOTOR consortium. Multicentre, cross-cultural, population-based, case-control study of physical activity as risk factor for ALS. J Neurol Neurosurg Psychiatry 2018;8:797-803.

15. Van Rheenen W, van der Spek R, Bakker MK, van Vugt J, Hop PJ, Zwamborn RAJ, de Klein N, Westra HJ, Bakker OB, Deelen P, Shireby G, Hannon E, Moisse M, Baird D, Byrne RP, Doherty M, Iacoangeli A, Shatunov A, Ticozzi N, Cooper-Knock J, Gromicho M, Chandran S, Pal S, Morrison KE, Shaw PJ, Hardy J, Orrell RW, Sendtner M, Meyer T, Basak N, van der Kooi AJ, Ratti A, Fogh I Corti S, Chio A, Calvo A, Grassano M, Beghi E, Logroscino G, Gotkine M, Baloh RH, Vourc'h P,

Corcia P, Couratier P, Millecamps S, Salachas F, Ludolph AC, Weishaupt JH, Freischmidt A, Brice A, Wood N, Topp S, Rademakers R, Tittmann L, Lieb W, Andre Franke A, Ripke S, Braun A, Kraft J, Whiteman DC, Olsen CM, Uitterlinden AG, Albert Hofman A, Rietschel M, Cichon S, Nothen MM, Amouyel P, SLALOM Consortium, PARALS Consortium, SLAGEN Consortium, SLAP Consortium, Traynor BJ, Singleton AB, Mitne Neto M, Cauchi RJ, Ophoff RA, Wiedau-Pazos M, Lomen-Hoerth C, van Deerlin VM, Grosskreutz J, Rodiger A, Gaur N, Jork A, Barthel T, Theele E, Ilse B, Stubendorff B, Witte OW, Steinbach R, Hubner CA, Graff C, Brylev L, Ataulina A, Rogelj B, Koritnik B, Zidar J, Ravnik-Glavac M, Glavac D, Stevic Z, Drory V, Povedano M, Blair IP, Kiernan MC, Benyamin B, Henderson RD, Furlong S, Mathers S, McCombe PA, Needham M, Ngo ST, Nicholson GA, Roger Pamphlett R, Rowe DB, Steyn FJ, Williams KL, Mather KA, Sachdev PS, Henders AK, Wallace L, Carvalho M, Petri S, Rouleau G, Silani V, Curtis C, Breen G, Glass J, Brown RH, Landers JE, Shaw CE, Andersen PM, Pasterkamp RJ, Fan D, Garton FC, McRae AF, Smith, GD, Gaunt TR Eberle MA, Mill J, McLaughlin RL, Hardiman O, Kenna KP, Wray NR, Tsai E, Runz H, Lude Franke L, Ammar Al-Chalabi AA, Van Damme P, van den Berg LH*, Veldink JH* (shared last authors). Common and rare variant association analyses in Amyotrophic Lateral Sclerosis identify 15 risk loci with distinct genetic architectures and neuron-specific biology. Nature Gen 2021, in press.

16. Project MinE ALS Sequencing Consortium. Project MinE: study design and pilot analyses of a large-scale whole-genome sequencing study in ALS. Eur J Hum Genet 2018;26:1537-1546.

17. McLaughlin RL, Schijven D, van Rheenen W, van Eijk KR, O'Brien M, Kahn RS, Ophoff RA, Goris A, Bradley DG, Al-Chalabi A, van den Berg LH, Luykx JJ, Hardiman O, Veldink JH; Project MinE GWAS Consortium; Schizophrenia Working Group of the Psychiatric Genomics Consortium. Genetic correlation between ALS and schizophrenia. Nat Commun 2017;8:14774.

18. Van Rheenen W, Shatunov A, Dekker AM, McLaughlin RL, Diekstra FP, Pulit SL, van der Spek RA, Vosa U, de Jong S, Robinson MR, Yang J, Fogh I, van Doormaal PT, Tazelaar GH, Koppers M, Blokhuis AM, Sproviero W, Jones AR, Kenna KP, van Eijk KR, Harschnitz O, Schellevis RD, Brands WJ, Medic J, Menelaou A, Vajda A, Ticozzi N, Lin K, Rogelj B, Vrabec K, Ravnik-Glavac M, Koritnik B, Zidar J, Leonardis L, Groselj LD, Millecamps S, Salachas F, Meininger V, de Carvalho M, Pinto S, Mora JS, Rojas-Garcia R, Polak M, Chandran S, Colville S, Swingler R, Morrison KE, Shaw PJ, Hardy J, Orrell RW, Pittman A, Sidle K, Fratta P, Malaspina A, Topp S, Petri S, Abdulla S, Drepper C, Sendtner M, Meyer T, Ophoff RA, Staats KA, Wiedau-Pazos M, Lomen-Hoerth C, Van Deerlin VM, Trojanowski JQ, Elman L, McCluskey L, Basak AN, Tunca C, Hamzeiy H, Parman Y, Meitinger T, Lichtner P, Radivojkov-Blagojevic M, Andres CR, Maurel C, Bensimon G, Landwehrmeyer B, Brice A, Payan CA, Saker-Delye S, Durr A, Wood NW, Tittmann L, Lieb W, Franke A, Rietschel M, Cichon S, Nothen MM, Amouyel P, Tzourio C, Dartigues JF, Uitterlinden AG, Rivadeneira F, Estrada K, Hofman A, Curtis C, Blauw HM, van der Kooi AJ, de Visser M, Goris A, Weber M, Shaw CE, Smith BN, Pansarasa O, Cereda C, Del Bo R, Comi GP, D'Alfonso S, Bertolin C, Soraru G, Mazzini L, Pensato V, Gellera C, Tiloca C, Ratti A, Calvo A, Moglia C, Brunetti M, Arcuti S, Capozzo R, Zecca C, Lunetta C, Penco S, Riva N, Padovani A, Filosto M, Muller B, Stuit RJ; PARALS Registry; SLALOM Group; SLAP Registry; FALS Sequencing Consortium; SLAGEN Consortium; NNIPPS Study Group, Blair I, Zhang K, McCann EP, Fifita JA, Nicholson GA, Rowe DB, Pamphlett R, Kiernan MC, Grosskreutz J, Witte OW, Ringer T, Prell T, Stubendorff B, Kurth I, Hubner CA, Leigh PN, Casale F, Chio A, Beghi E, Pupillo E, Tortelli R, Logroscino G, Powell J, Ludolph AC, Weishaupt JH, Robberecht W, Van Damme P, Franke L, Pers TH, Brown RH, Glass JD, Landers JE, Hardiman O, Andersen PM, Corcia P, Vourc'h P, Silani V, Wray NR, Visscher PM, de Bakker PI, van Es MA, Pasterkamp RJ, Lewis CM, Breen G, Al-Chalabi A*, Veldink JH*, van den Berg LH*. Genome-wide association analyses identify new risk variants 2 and the genetic architecture of ALS. Nature Gen 2016;48:1043-8.

19. Kenna KP, van Doormaal PT, Dekker AM, Ticozzi N, Kenna BJ, Diekstra FP, van Rheenen W, van Eijk KR, Jones AR, Keagle P, Shatunov A, Sproviero W, Smith BN, van Es MA, Topp SD, Kenna A, Miller JW, Fallini C, Tiloca C, McLaughlin RL, Vance C, Troakes C, Colombrita C, Mora G, Calvo A, Verde F, Al-Sarraj S, King A, Calini D, de Belleroche J, Baas F, van der Kooi AJ, de Visser M, Ten Asbroek AL, Sapp PC, McKenna-Yasek D, Polak M, Asress S, Munoz-Blanco JL, Strom TM, Meitinger T, Morrison KE; SLAGEN Consortium, Lauria G, Williams KL, Leigh PN, Nicholson GA, Blair IP, Leblond CS, Dion PA, Rouleau GA, Pall H, Shaw PJ, Turner MR, Talbot K, Taroni F, Boylan KB, Van Blitterswijk M, Rademakers R, Esteban-Perez J, Garcia- Redondo A, Van Damme P, Robberecht W, Chio A, Gellera C, Drepper C, Sendtner M, Ratti A, Glass JD, Mora JS, Basak NA, Hardiman O, Ludolph AC, Andersen PM, Weishaupt JH, Brown RH Jr, Al-Chalabi A, Silani V*, Shaw CE*, van den Berg LH*, Veldink JH*, Landers JE*. NEK1 variants confer susceptibility to ALS. Nature Gen 2016;48:1037-42.

20. Meier JM, van der Burgh HK, Nitert AD, Bede P, de Lange SC, Hardiman O, van den Heuvel MP*, van den Berg LH*. Connectome-Based Propagation Model in ALS. Ann Neurol

2020;33:220-229.

21. Van der Burgh HK, Westeneng HJ, Walhout R, van Veenhuijzen K, Tan HHG, Meier JM, Bakker LA, Hendrikse J, van Es MA, Veldink JH, van den Heuvel MP, van den Berg LH. Multimodal Longitudinal Study of Structural Brain Involvement in ALS. Neurology 2020;94:e2592-e2604

22. Ormel PR, Vieira de Sa R, van Bodegraven EJ, Karst H, Harschnitz O, Sneeboer MAM, Johansen LE, van Dijk RE, Scheefhals N, Berdenis van Berlekom A, Ribes Martinez E, Kling S, MacGillavry HD, van den Berg LH, Kahn RS, Hol EM, de Witte LD, Pasterkamp RJ. Microglia innately develop within cerebral organoids. Nat Commun 2018;9:4167.

23. Shi Y, Lin S, Staats KA, Li Y, Chang WH, Hung ST, Hendricks E, Linares GR, Wang Y, Son EY, Wen X, Kisler K, Wilkinson B, Menendez L, Sugawara T, Woolwine P, Huang M, Cowan MJ, Ge B, Koutsodendris N, Sandor KP, Komberg J, Vangoor VR, Senthilkumar K, Hennes V, Seah C, Nelson AR, Cheng TY, Lee SJ, August PR, Chen JA, Wisniewski N, Hanson-Smith V, Belgard TG, Zhang A, Coba M, Grunseich C, Ward ME, van den Berg LH, Pasterkamp RJ, Trotti D, Zlokovic BV, Ichida JK. Haploinsufficiency leads to neurodegeneration in C9ORF72 ALS/FTD human induced motor neurons. Nat Med 2018;24:313-325.

24. Harschnitz O, van den Berg LH, Johansen LE, Jansen MD, Kling S, Vieira De Sa R, Vlam L, van Rheenen W, Karst H, Wierenga CJ, Pasterkamp RJ, van der Pol WL. Autoantibody pathogenicity in a multifocal motor neuropathy iPSC-derived model. Ann Neurol 2016;80:71-88.

25. Westeneng HJ, Debray TPA, Visser AE, van Eijk RPA, Rooney JPK, Calvo A, Martin S, McDermott CJ, Thompson AG, Pinto S, Kobeleva X, Rosenbohm A, Stubendorff B, Sommer H, Middelkoop BM, Dekker AM, van Vugt JJFA, van Rheenen W, Vajda A, Heverin M, Kazoka M, Hollinger H, Gromicho M, Korner S, Ringer TM, Rodiger A, Gunkel A, Shaw CE, Bredenoord AL, van Es MA, Corcia P, Couratier P, Weber M, Grosskreutz J, Ludolph AC, Petri S, de Carvalho M, Van Damme P, Talbot K, Turner MR, Shaw PJ, Al-Chalabi A, Chio A, Hardiman O, Moons KGM, Veldink JH, van den Berg LH. Prognosis for patients with ALS: development and validation of a personalised prediction model. Lancet Neurol 2018;17:423-433.

26. van Eijk RPA, Nikolakopoulos S, Roes KCB, Middelkoop BM, Ferguson TA, Shaw PJ, Leigh PN, Al-Chalabi A, Eijkemans MJC, van den Berg LH. Critical design considerations for time-to-event endpoints in ALS clinical trials. J Neurol Neurosurg Psych 2019;90:1331-1337.

27. van Eijk RPA, Westeneng HJ, Nikolakopoulos S, Verhagen IE, van Es MA, Eijkemans MJC, van den Berg LH. Refining eligibility criteria for ALS clinical trials. Neurology 2019;92:e451-e460.

28. Van Eijk RPA, Nikolapoulos S, Roes KCB, Kendall L, Han SS, Lavros A, Epstein N, Kliest T, de Jongh AS, Westeneng HJ, Al-Chalabi A, Van Damme P, Hardiman O, Shaw PJ, McDermott CJ, Eijkemans MJC, van den Berg LH. Challenging the established Order: innovating clinical trials for ALS. Neurology 2021 online ahead of print.

LvdB is author of over 650 peer reviewed publications in Neurology, Neuroscience, Genetics, Bioinformatics, Trial Innovation and Epidemiology.

His datasets contributed to >75 papers in other disease areas, such as cancer, auto-immune disease, cardiovascular disease, psychiatric disease.

Projects

Netherlands ALS Centre/ Prospective ALS study in the Netherlands: www.ALS-Centrum.nl. Founder and Director of the Netherlands ALS Centre Netherlands (from 2003): (1) a specialized ALS outpatient clinic and national multidisciplinary care network has been established for patients suspected of ALS or other motor neuron diseases (>600 referrals/year), and (2) in close collaboration with the Netherlands ALS Foundation and patients, ALS has been turned from a completely unknown disease in 2003 to one of the best-known diseases through effective awareness campaigns. These efforts strongly support our research activities to find a cure for this devastating disease: a large, nation-wide prospective population-based study was created aiming at a complete ascertainment of incident ALS patients in The Netherlands. Validated, up-to-date questionnaires are being used to collect data on environmental/lifestyle risk factors and DNA/RNA/plasma from all patients and matched controls through the patients' general practitioners to provide class I level of evidence of both exogenous and genetic factors that determine risk and outcome of ALS: a detailed MND database and biobank of >5,000 patients and > 7,500 matched controls are now available. This is presently the largest dataset in the world that contains the combination of extensive genetic and environment/lifestyle data enabling studies on gene-environment interaction. As part of an EU project, the database has been extended with data collected in Ireland, Italy, Belgium and the UK using the same questionnaires and protocols.

European Network to Cure ALS: www.ENCALS.eu. Founder and Chair (since 2010, re-elected 4 times) of a network of ALS Care and Research Centres. ENCALS fosters high standards of care and research collaborations, and holds a European ALS Symposium annually (>400 attendees).

Project MinE: www.ProjectMinE.com. Founder of an international project (22 countries) to sequence the genomes of 22,500 people, 17,000 with ALS, 5,500 without, to understand the genetic basis of ALS, discovering several ALS genes and loci (e.g. van Rheenen et al. Nature Genetics 2016 and 2021) as well as showing that there is a major contribution from rare genetic variations to ALS risk, that gene burden lowers age of onset, and that there is a 14% overlap in genetic risk between ALS and schizophrenia. (http://databrowser.projectmine.com)

Treatment Research Initiative to Cure ALS: www.TRICALS.org. Founder (from 2017) of an international Platform to accelerate finding treatments for ALS patients by incorporating innovation (genetics, validated algorithm for personalised prediction of survival, joint model analyses, digital health technology) into clinical trial design to make them more efficient and effective.

Served as an expert advisor and member of over 30 steering and scientific advisory boards.

Member External Scientific Advisory Boards: NIHR Sheffield Biomedical Research Centre, UK; FutureNeuro - the SFI Centre for chronic and rare neurological disease, Royal College of Surgeons in Ireland; INSERM U1253, "iBrain", Universite Francois-Rabelais de Tours, France.

Co-Chair (2007-2017) Belgium-Netherlands Neuromuscular Research Study Group.

Memberships

Appointed as life member of The Royal Netherlands Academy of Arts and Sciences.

Other Relevant Information

(Inter)national Awards

The Sean M. Healey International Prize for Innovation in ALS Research recognizes an individual or a team of investigators who catalyze exceptional discoveries leading to a transformative advance in therapy development in ALS.

2019 Appointed as life member of The Royal Netherlands Academy of Arts and Sciences. Awarded on the basis of scientific and scholarly achievement.

2015 'Winkler Medal' from The Netherlands Neurological Association awarded for the most significant scientific contribution to neuroscience to one scientist every 5 years (2000-2015).

2013 'Forbes Norris Award' from the International Alliance of ALS/MND Associations. Award presented to researchers who combine outstanding patient care with excellent research, which leads to a significant contribution to science.

2010 'Sheila Essey Award' from the American Academy of Neurology recognizing significant research contributions in the search for the cause, prevention of, and cure for ALS.