

Embracing Monogenic Parkinson's Disease: The MJFF Global Genetic PD Cohort

Eva-Juliane Vollstedt, MD,¹  Susen Schaake, BSc,¹ Katja Lohmann, PhD,¹  Shalini Padmanabhan, PhD,² Alexis Brice, MD,³ Suzanne Lesage, PhD,⁴ Christelle Tesson, PhD,⁴ Marie Vidailhet, MD,³ Isabel Wurster, MD,⁵ Faycel Hentati, MD,⁶ Anat Mirelman, PhD,⁷  Nir Giladi, MD,⁸ Karen Marder, MD, MPH,⁹ Cheryl Waters, MD,¹⁰ Stanley Fahn, MD,¹⁰ Meike Kasten, MD,¹¹ Norbert Brüggemann, MD,¹²  Max Borsche, MD,¹²  Tatiana Foroud, PhD,¹³ Eduardo Tolosa, MD, PhD,¹⁴  Alicia Garrido, MD,¹⁴ Grazia Annesi, PhD,¹⁵ Monica Gagliardi, PhD,¹⁵ Maria Bozi, MD, PhD,¹⁶ Leonidas Stefanis, MD, PhD,¹⁷ Joaquim J. Ferreira, MD, PhD,¹⁸  Leonor Correia Guedes, MD, PhD,¹⁹ Micol Avenali, MD,²⁰ Simona Petrucci, MD, PhD,²¹ Lorraine Clark, PhD,²² Ekaterina Y. Fedotova, MD,²³ Natalya Y. Abramychева, PhD,²³ Victoria Alvarez, MD, PhD,²⁴ 

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*Correspondence to: Dr. Christine Klein, Institute of Neurogenetics, University of Lübeck, Ratzeburger Allee, 160 23538 Lübeck, Germany; E-mail: christine.klein@neuro.uni-luebeck.de

Members of the MJFF Global Genetic Parkinson's Disease Study Group are listed in the Appendix.

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Manuel Menéndez-González, MD, PhD,²⁵ Silvia Jesús Maestre, MD, PhD,²⁶ Pilar Gómez-Garre, PhD,²⁶ Pablo Mir, MD, PhD,²⁶  Andrea Carmine Belin, PhD,²⁷ Caroline Ran, PhD,²⁷ Chin-Hsien Lin, MD, PhD,²⁸ Ming-Che Kuo, MD,²⁸  David Crosiers, MD, PhD,²⁹ Zbigniew K. Wszolek, MD,³⁰ Owen A. Ross, PhD,³¹  Joseph Jankovic, MD,³² Kenya Nishioka, MD, PhD,³³  Manabu Funayama, PhD,³⁴ Jordi Clarimon, PhD,³⁵ Caroline H. Williams-Gray, BMBCCh, MRCP, PhD,³⁶  Marta Camacho, MSc,³⁶  Mario Cornejo-Olivas, MD,³⁷  Luis Torres-Ramirez, MD,³⁸ Yih-Ru Wu, MD,³⁹  Guey-Jen Lee-Chen, PhD,⁴⁰ Ana Morgadinho, MD,⁴¹ Teeratom Pulkes, MD, FRCP, PhD,⁴²  Pichet Termsarasab, MD,⁴²  Daniela Berg, MD,⁴³ Gregor Kuhlenbäumer, MD,⁴³ Andrea A. Kühn, MD,⁴⁴ Friederike Borngräber, MD,⁴⁴  Giuseppe de Michele, MD,⁴⁵ Anna De Rosa, MD,⁴⁵ Alexander Zimprich, MD,⁴⁶  Andreas Puschmann, MD, PhD,⁴⁷ George D. Mellick, MD,⁴⁸ Jolanta Dorszewska, MD, PhD,⁴⁹ Jonathan Carr, MD,⁵⁰ Rosangela Ferese, PhD,⁵¹ Stefano Gambardella, PhD,⁵¹  Bruce Chase, PhD,⁵²  Katerina Markopoulou, MD, PhD,⁵³ Wataru Satake, MD, PhD,⁵⁴ Tatsushi Toda, MD, PhD,⁵⁵ Malco Rossi, MD, PhD,⁵⁴ Marcelo Merello, MD, PhD,⁵⁶ Timothy Lynch, FRCPI, FRCP,⁵⁷ Diana A. Olszewska, MD, PhD,⁵⁷  Shen-Yang Lim, MD, FRACP,⁵⁸ Azlina Ahmad-Annuar, PhD,⁵⁹ Ai Huey Tan, MD, PhD, FRCP,⁵⁸  Bashayer Al-Mubarak, PhD,⁶⁰ Hasmet Hanagasi, MD,⁶¹ Dariusz Koziorowski, MD, PhD,⁶² Sibel Ertan, MD,⁶³ Gençer Genç, MD,⁶⁴ Patricia de Carvalho Aguiar, MD, PhD,⁶⁵ Melinda Barkhuizen, PhD,⁶⁶  Marcia M.G. Pimentel, PhD,⁶⁷ Rachel Saunders-Pullman, MD,⁶⁸ Bart van de Warrenburg, MD, PhD,⁶⁹ Susan Bressman, MD,⁷⁰ Mathias Toft, MD, PhD,⁷¹ Silke Appel-Cresswell, MD,⁷²  Anthony E. Lang, MD,⁷³ Matej Skorvaneck, MD, PhD,⁷⁴  Agnita J.W. Boon, MD, PhD,⁷⁵ Rejko Krüger, MD,⁷⁶ Esther M. Sammler, MD, PhD,⁷⁷  Vitor Tumas, MD,⁷⁸ Bao-rong Zhang, MD,⁷⁹  Gaetan Garraux, MD, PhD,⁸⁰ Sun Ju Chung, MD, PhD,⁸¹  Yun Joong Kim, MD, PhD,⁸² Juliane Winkelmann, MD,⁸³ Carolyn M. Sue, MD,⁸⁴ Eng-King Tan, MD,⁸⁵ Joana Damásio, MD,⁸⁶ Péter Klivényi, MD,⁸⁷ Vladimir S. Kostic, MD,⁸⁸ David Arkadir, MD, PhD,⁸⁹ Mika Martikainen, MD, PhD,⁹⁰ Vanderci Borges, MD, PhD,⁹¹ Jens Michael Hertz, MD,⁹² Laura Brighina, MD, PhD,⁹³ Mariana Spitz, MD, PhD,⁹⁴ Oksana Suchowesky, MD,⁹⁵ Olaf Riess, MD,⁹⁶ Parimal Das, PhD,⁹⁷ Brit Mollenhauer, MD,⁹⁸ Emilia M. Gatto, MD,⁹⁹ Maria Skaalum Petersen, PhD,¹⁰⁰ Nobutaka Hattori, MD, PhD,³⁴ Ruey-Meei Wu, MD, PhD,²⁸ Sergey N. Illarioshkin, MD, PhD,²³ Enza Maria Valente, MD, PhD,¹⁰¹ Jan O. Aasly,^{102,103} Anna Aasly, MSc,¹⁰⁴ Roy N. Alcalay, MD, MS,¹⁰ Avner Thaler, MD, PhD,¹⁰⁵ Matthew J. Farrer, PhD,¹⁰⁶ Kathrin Brockmann, MD,⁵ Jean-Christophe Corvol, MD,¹⁰⁷ Christine Klein, MD,^{1*} and on behalf of the MJFF Global Genetic Parkinson's Disease Study Group

¹Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

²Research Programs, The Michael J. Fox Foundation for Parkinson's Research, New York, New York, USA

³Department of Neurology, Sorbonne University, Paris Brain Institute - ICM, Inserm, CNRS, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Paris, France

⁴Sorbonne University, Paris Brain Institute - ICM, Inserm, CNRS, Paris, France

⁵Department of Neurodegenerative Diseases, University of Tuebingen, Tuebingen, Baden Wuerttemberg, Germany, Hertie Institute for Clinical Brain Research and German Centre for Neurodegenerative Diseases, Tuebingen, Germany

⁶Mongi Ben Hmida National Institute of Neurology, Tunis, Tunisia

⁷Laboratory of Early Markers of Neurodegeneration, Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

⁸Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sackler School of Medicine, Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

⁹Department of Neurology, Taub Institute for Alzheimer's Disease and the Aging Brain, Columbia University, New York, New York, USA

¹⁰Department of Neurology, Columbia University, New York, New York, USA

¹¹Department of Psychiatry and Psychotherapy and Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

¹²Department of Neurology and Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

¹³Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, USA

¹⁴Parkinson Disease and Movement Disorders Unit, Neurology Service, Hospital Clinic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED:CB06/05/0018-ISCIII), Barcelona, Spain

¹⁵Institute of Biomedical Research and Innovation, National Research Council, Cosenza, Italy

¹⁶Parkinson's and Movement Disorders Unit, 2nd Department of Neurology of the University of Athens, Attikon Hospital, Haidari, Athens, Greece; Psychiatry Hospital of Attica "Dafni," Neurology Department, Haidari, Athens, Greece

¹⁷First Department of Neurology, Medical School of the National and Kapodistrian University of Athens, Eginition Hospital, Athens, Greece

¹⁸Laboratory of Clinical Pharmacology and Therapeutics, University of Lisbon, Lisbon, Portugal; Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

¹⁹Department of Neuroscience and Mental Health, Neurology Department, Hospital de Santa Maria, CHULN, Lisbon, Portugal; Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

²⁰Neurorehabilitation Unit, IRCCS Mondino Foundation, Pavia, Italy; Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy

²¹Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy; Sant' Andrea University Hospital, Rome, Italy

²²Department of Pathology and Cell Biology, Vagelos College of Physicians & Surgeons, Columbia University Irving Medical Center, New York, NY, USA

- York, New York, USA; Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Irving Medical Center, New York, New York, USA; Laboratory of Personalized Genomic Medicine, Vagelos College of Physicians & Surgeons, Columbia University Irving Medical Center, New York, New York, USA
- ²³Department of Neurogenetics, Research Center of Neurology, Moscow, Russia
- ²⁴Laboratório de Genética, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain; Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain
- ²⁵Servicio Neurología, Hospital Universitario Central de Asturias, Oviedo, Spain; Instituto de Investigación; Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain
- ²⁶Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain
- ²⁷Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden
- ²⁸Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan; Department of Neurology, National Taiwan University College of Medicine, Taipei, Taiwan
- ²⁹Department of Neurology, Antwerp University Hospital, Edegem, Belgium; Born Bunge Institute, Department of Neurology, University of Antwerp, Wilrijk, Belgium; Center for Molecular Neurology, VIB, Wilrijk, Belgium
- ³⁰Department of Neurology, Mayo Clinic, Jacksonville, Florida, USA
- ³¹Department of Neuroscience, Mayo Clinic, Jacksonville, Florida, USA
- ³²Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA
- ³³Department of Neurology, Juntendo University School of Medicine, Bunkyo, Tokyo, Japan
- ³⁴Research Institute for Diseases of Old Age, Graduate School of Medicine, Juntendo University, Bunkyo, Tokyo, Japan
- ³⁵Department of Neurology, Biomedical Research Institute IIB-Sant Pau, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain
- ³⁶Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
- ³⁷Neurogenetics Research Center, Instituto Nacional de Ciencias Neurológicas, Lima, Peru; Center for Global Health, Universidad Peruana Cayetano Heredia, Lima, Peru
- ³⁸Movement Disorders Unit, Instituto Nacional de Ciencias Neurológicas, Lima, Peru
- ³⁹Department of Neurology, Chang Gung University, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan
- ⁴⁰Department of Life Science, National Taiwan Normal University, Taipei, Taiwan
- ⁴¹Movement Disorders Clinic, Department of Neurology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
- ⁴²Division of Neurology, Department of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
- ⁴³Department of Neurology, Christian-Albrechts-Universität, Kiel, Germany
- ⁴⁴Movement Disorder and Neuromodulation Unit, Charité, Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany
- ⁴⁵Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
- ⁴⁶Department of Neurology, Medical University, Vienna, Austria
- ⁴⁷Department of Neurology, Clinical Sciences, Lund University, Lund, Sweden; Department of Neurology, Skåne University, Lund, Sweden
- ⁴⁸Griffith Institute for Drug Discovery (GRIDD), School of Environment and Science, Griffith University, Brisbane, Queensland, Australia
- ⁴⁹Laboratory of Neurobiology, Department of Neurology, Poznan University of Medical Sciences, Poznan, Poland
- ⁵⁰Division of Neurology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa
- ⁵¹IRCCS Neuromed, Località Camerelle, Pozzilli, Isernia, Italy; Department of Biomolecular Sciences, University of Urbino "Carlo Bo", Urbino, Italy
- ⁵²Department of Neurology, NorthShore University HealthSystem, Evanston, Illinois, USA
- ⁵³Department of Neurology, NorthShore University HealthSystem, Evanston Illinois and Department of Neurology, University of Chicago, Chicago, Illinois, USA
- ⁵⁴Sección Movimientos Anormales, Departamento de Neurociencias, Fleni, Buenos Aires, Argentina; Argentine National Scientific and Technological Research Council (CONICET), Buenos Aires, Argentina
- ⁵⁵Department of Neurology, The University of Tokyo, Tokyo, Japan
- ⁵⁶Sección Movimientos Anormales, Departamento de Neurociencias, Fleni, Buenos Aires, Argentina; Argentine National Scientific and Technological Research Council (CONICET), Argentina; Pontificia Universidad Católica Argentina (UCA), Buenos Aires, Argentina
- ⁵⁷Department of Neurology, The Dublin Neurological Institute at the Mater Misericordiae University Hospital, Dublin, Ireland; School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland
- ⁵⁸Division of Neurology and the Mah Pooi Soo & Tan Chin Nam Centre for Parkinson's & Related Disorders, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
- ⁵⁹Department of Biomedical Science, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
- ⁶⁰Behavioural Genetics Unit, Department of Genetics, Research Centre, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
- ⁶¹Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey
- ⁶²Department of Neurology, Medical University in Warsaw, Warsaw, Poland
- ⁶³Department of Neurology, School of Medicine, Koç University, Istanbul, Turkey
- ⁶⁴Department of Neurology, University of Health Sciences, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey
- ⁶⁵Hospital Israelita Albert Einstein, São Paulo, Brazil; Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil
- ⁶⁶DST/NWU Preclinical Drug Development Platform, North-West University, Potchefstroom, North-West, South Africa
- ⁶⁷Department of Genetics, Institute of Biology Roberto Alcantara Gomes, State University of Rio de Janeiro, Rio de Janeiro, Brazil

- ⁶⁸Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, USA
- ⁶⁹Department of Neurology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands
- ⁷⁰Department of Neurology, Beth Israel Medical Center, New York, New York, USA; Department of Neurology at Albert Einstein College of Medicine, New York, New York, USA
- ⁷¹Department of Neurology, Oslo University Hospital, Oslo, Norway; Institute of Clinical Medicine, University of Oslo, Oslo, Norway
- ⁷²Pacific Parkinson's Research Centre, Division of Neurology, Department of Medicine, Vancouver, British Columbia, Canada
- ⁷³Edmond J. Safra Program in Parkinson's Disease, Division of Neurology, Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada
- ⁷⁴Department of Neurology, Pavol Jozef Šafárik University in Košice, Košice, Slovakia; Department of Neurology, University Hospital L. Pasteur, Kosice, Slovakia
- ⁷⁵Department of Clinical Genetics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands
- ⁷⁶Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-sur-Alzette, Luxembourg; Transversal Translational Medicine, Luxembourg Institute of Health (LIH), Strassen, Luxembourg; Parkinson Research Clinic, Centre Hospitalier de Luxembourg (CHL), Luxembourg, Luxembourg
- ⁷⁷Neurology Department, Ninewells Hospital and Medical School, Dundee, United Kingdom; MRC Protein Phosphorylation and Ubiquitylation Unit, University of Dundee, Dundee, UK
- ⁷⁸Behavioral and Movement Disorders Section, Ribeirão Preto Medical School, University of São Paulo, Brazil
- ⁷⁹Department of Neurology, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China
- ⁸⁰Department of Neurology, Centre Hospitalier Universitaire (CHU) de Liège, Liège, Belgium; MoVeRe Group, GIGA-CRC In Vivo Imaging, University of Liege, Liège, Belgium
- ⁸¹Medical Genetic Center, Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
- ⁸²Department of Neurology, Yonsei University College of Medicine, Seoul, South Korea; Department of Neurology, Yongin Severance Hospital, Yonsei University Health System, Yongin, South Korea
- ⁸³Institute of Neurogenomics, Helmholtz Zentrum Muenchen, Neuherberg, Germany; Neurogenetics, Technische Universitaet Muenchen, Munich, Germany; Institute of Human Genetics, Klinikum rechts der Isar der TUM, Munich, Germany; Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
- ⁸⁴Department of Neurogenetics, Kolling Institute, University of Sydney, Sydney, New South Wales, Australia; Department of Neurology, Royal North Shore Hospital, St Leonards, New South Wales, Australia
- ⁸⁵Department of Neurology, National Neuroscience Institute, Duke NUS Medical School, Singapore General Hospital, Singapore, Singapore
- ⁸⁶Department of Neurology, Hospital de Santo António - Centro Hospitalar Universitário do Porto, Porto, Portugal; UniGENE, Instituto de Biologia Molecular e Celular (IBMC), Instituto de Investigação e Inovação em Saúde (i3S), Universidade do Porto, Portugal
- ⁸⁷Department of Neurology, University of Szeged, Szeged, Hungary
- ⁸⁸Department for Neurodegeneration, Clinic for Neurology CCS, Belgrade, Serbia
- ⁸⁹Department of Neurology, Hadassah Medical Center and the Hebrew University, Jerusalem, Israel
- ⁹⁰Neurocenter, Turku University Hospital, Turku, Finland; Clinical Neurosciences, Faculty of Medicine, University of Turku, Turku, Finland
- ⁹¹Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil
- ⁹²Department of Clinical Genetics, Odense University Hospital, Odense C, Denmark
- ⁹³Department of Neurology, Milan Center for Neuroscience, University of Milano-Bicocca/San Gerardo Hospital, Monza, Italy
- ⁹⁴Neurology Service, State University of Rio de Janeiro, Rio de Janeiro, Brazil
- ⁹⁵Department of Medicine, Medical Genetics and Pediatrics, University of Alberta, Edmonton, Alberta, Canada
- ⁹⁶Institute of Medical Genetics and Applied Genomics, University of Tuebingen, Tuebingen, Germany
- ⁹⁷Centre for Genetic Disorders, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India
- ⁹⁸Movement Disorder Paracelsus-Elena-Klinik, Kassel, Germany; Department of Neurology, University Medical Center Göttingen, Göttingen, Germany
- ⁹⁹Movement Disorders, Department of Neurology, Instituto de Neurociencias Buenos Aires, Buenos Aires, Argentina
- ¹⁰⁰Centre of Health Science, University of the Faroe Islands, Tórshavn, Faroe Islands; Department of Occupational Medicine and Public Health, The Faroese Hospital System, Tórshavn, Faroe Islands
- ¹⁰¹Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia; Department of Molecular Medicine, University of Pavia, Pavia, Italy
- ¹⁰²Department of Neurology, St. Olavs Hospital, Trondheim, Norway
- ¹⁰³Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway
- ¹⁰⁴Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway
- ¹⁰⁵Movement Disorders, Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
- ¹⁰⁶Fixel Institute, Department of Neurology, University of Florida, Gainesville, Florida, USA
- ¹⁰⁷Sorbonne University, Paris Brain Institute - ICM, Inserm, CNRS, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Department of Neurology, Paris, France

ABSTRACT: Background: As gene-targeted therapies are increasingly being developed for Parkinson's disease (PD), identifying and characterizing carriers of specific genetic pathogenic variants is imperative. Only a small fraction of the estimated number of subjects with monogenic PD worldwide are currently represented in the literature and availability of clinical data and clinical trial-ready cohorts is limited.

Objective: The objectives are to (1) establish an international cohort of affected and unaffected individuals with PD-linked variants; (2) provide harmonized and quality-controlled clinical characterization data for each included individual; and (3) further promote collaboration of researchers in the field of monogenic PD.

Methods: We conducted a worldwide, systematic online survey to collect individual-level data on individuals with PD-linked variants in *SNCA*, *LRRK2*, *VPS35*, *PRKN*, *PINK1*, *DJ-1*, as well as selected pathogenic and risk variants in *GBA* and corresponding demographic, clinical, and genetic data. All registered cases underwent thorough quality checks, and pathogenicity scoring of the variants and genotype-phenotype relationships were analyzed.

Results: We collected 3888 variant carriers for our analyses, reported by 92 centers (42 countries) worldwide. Of the included individuals, 3185 had a diagnosis of PD (ie, 1306 *LRRK2*, 115 *SNCA*, 23 *VPS35*, 429 *PRKN*, 75 *PINK1*, 13 *DJ-1*, and 1224 *GBA*) and 703 were unaffected (ie, 328 *LRRK2*, 32 *SNCA*, 3 *VPS35*, 1 *PRKN*, 1 *PINK1*, and 338 *GBA*). In total, we identified 269 different pathogenic variants; 1322 individuals in our cohort (34%) were indicated as not previously published.

Conclusions: Within the MJFF Global Genetic PD Study Group, we (1) established the largest international cohort of affected and unaffected individuals carrying PD-linked variants; (2) provide harmonized and quality-controlled clinical and genetic data for each included individual; (3) promote collaboration in the field of genetic PD with a view toward clinical and genetic stratification of patients for gene-targeted clinical trials. © 2023 The Authors. *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

Key Words: Parkinson's disease; monogenic PD

Rapidly advancing sequencing technologies offer new and cost-effective approaches to increasingly define genetic subtypes of common diseases. An illustrative example is Parkinson's disease (PD) that can be genetically stratified into subgroups of patients with well-established, albeit individually rare, genetic forms of PD. These are due to pathogenic variants in *LRRK2*, *SNCA*, *VPS35*, *PRKN*, *PINK1*, *DJ-1*, and *GBA*, the latter acting as the strongest known genetic risk factor of PD.¹

As a relatively common disease with only up to 10% accounting for genetic subtypes,² PD is not considered a hereditary disorder per se. As genetic testing is not a common or even standard element of the diagnostic workup due to the absence of gene-specific therapies, it is currently most often performed in a research setting. However, scientific interest in publications on clinical-genetic screening studies of well-established PD genes is continuously declining, whereas the advent of first gene-targeted therapies^{3,4} immediately calls for well-characterized clinical trial-ready cohorts of variant carriers.

To address the lack of systematic data resources on monogenic PD, our team established the Movement Disorder Society Genetic Mutation Database (MDSGene, www.mdsgene.org). Although the actual number of PD patients with a genetic cause is estimated at ~650,000, ie, ~10% of the ~0.65 million PD patients worldwide,^{2,5} only a small fraction (n = 2120) of monogenic PD patients with individual

patient information are contained in the international medical literature published in the English language. Availability of quantitative clinical data is limited, and there is a strong focus on motor symptoms and on select ethnicities in the literature.^{6,7} However, frequency, clinical expression, and penetrance of genetic variants may vary considerably across different populations and ethnicities.⁸ For example, a landmark study comparing patients with the same pathogenic variant in *LRRK2* in a Norwegian and a Tunisian sample revealed a much higher proportion of affected variant carriers among the Tunisians than the Norwegians at a 60-year age cut-off. Knowing, understanding, and considering these population-specific factors facilitate the composition of study samples tailored to specific research questions or clinical trials.

The MDSGene resource served to systematically identify researchers following monogenic PD patients, 98% of whom expressed interest to jointly build up the MJFF Global Monogenic PD Study Group⁸ to address the following aims: (1) establish an international cohort of individuals with PD-linked variants; (2) provide harmonized and quality-controlled clinical characterization data for each included individual; (3) further promote the collaboration of researchers in the field of monogenic PD with a view toward demographic, clinical, and genetic stratification of patients for gene-targeted clinical trials.

Patients and Methods

Data Collection Process

To collect individual-level data on the patients that had been reported to us in the first phase of the MJFF Global Genetic PD Project,⁹ we developed an online survey. We focused on carriers of variants in genes associated with monogenic PD (*LRRK2*, *SNCA*, *VPS35*, *PRKN*, *PINK1*, *DJ-1*), but also included variants in the strongest genetic risk factor for PD, ie, *GBA*. Variants in other PD-linked genes were not included in the analyses (Appendix S1: Table 1). We collected detailed genetic information alongside demographic data, disease status, pedigrees, motor scales, nonmotor scales, risk factors, and medication (31 items, Appendix S1: Table 2). All members of the MJFF Global Genetic PD Study Group were invited to participate, and new members were included upon recommendation or request. The survey was open from October 2018 to March 2019, including two rounds of reminders and additional customized extensions of the deadline upon request by several study centers. After 1 year, from September to October 2020, we reopened the survey for its first annual update and invited members of the study group to update their data and to add newly identified individuals with PD-linked variants. An important part of the data collection process was the communication with study centers to keep them informed about the project, to address any questions regarding the survey, and to ensure a high quality of the collected data.

Nomenclature

The nomenclature of the genes follows the recommendations of the HUGO Gene Nomenclature Committee (www.genenames.org) with the exception of *PARK7* that we refer to as *DJ-1*. Variants are annotated corresponding

to the following transcript IDs: *LRRK2*: NM_198578.3, *SNCA*: NM_000345.3, *VPS35*: NM_018206.5, *PRKN*: NM_004562.2, *PINK1*: NM_032409.2, *DJ-1*: NM_001123377.1, *GBA*: NM_000157.3.

Inclusion and Exclusion Criteria

All registered variant carriers underwent thorough quality checks regarding both clinical and genetic data (Fig. 1). The mandatory minimal data set for eligible samples comprised information on the genetic variant, sex, disease status, and age at onset. In case of any missing or contradictory information, we asked the submitting researcher for clarification. Duplicate submissions and samples with an unresolved clinical or genetic status were excluded from further analyses.

Variants in *LRRK2*, *SNCA*, *VPS35*, *PRKN*, *PINK1*, and *DJ-1* were excluded if they had a minor allele frequency (MAF) $\geq 1\%$ based on the ethnicity with the maximal MAF in the gnomAD Browser v.2.1.1 (<https://gnomad.broadinstitute.org>), dbSNP (<http://www.ncbi.nlm.nih.gov/snp/>). Individuals with pathogenic variants in more than one PD gene were excluded, but those harboring an additional known risk variant in *LRRK2* (p.R1628P) or *GBA* (p.R83C, p.E365K, p.T408M, p.N409S, p.L483P, p.V499L, p.R535H) were included in our analyses. For *GBA*, we only included the four most frequent variants (p.E365K, p.T408M, p.N409S, p.L483P). Although p.N409S and p.L483P are considered pathogenic variants due to their causal link to Gaucher's disease and are rare ($<0.5\%$ globally according to gnomAD), p.E365K and p.T408M are classified as PD risk variants with a global MAF of $>0.5\%$.¹⁰ Analyses for *GBA* exclude digenic variant carriers; that is, all included individuals have been reported to carry one variant in *GBA* only.

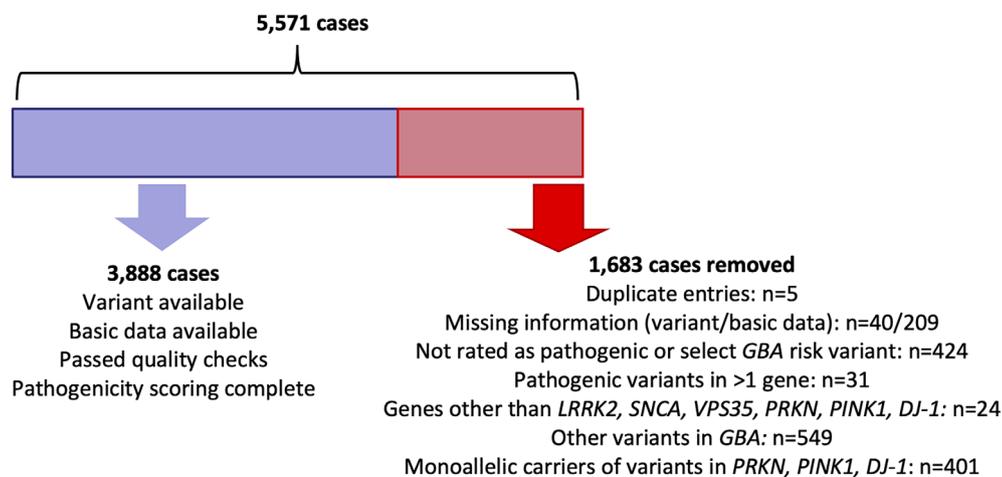


FIG. 1. Number of cases registered in the online survey and number of cases excluded after quality control and evaluating pathogenicity including reasons for exclusion.

Pathogenicity Scoring

Variants of eligible individuals underwent pathogenicity scoring. The presumed pathogenicity of a genetic variant was taken from MDSGene for previously scored variants or assessed using MDSGene criteria,⁶ (<https://mdsgene.org/methods>). The score is based on four items, including information on segregation, variant frequency in patients and controls, in-silico prediction using the Combined Annotation Dependent Depletion (CADD) score (<http://cadd.gs.washington.edu/>), and functional evidence extracted from published in-vitro and in-vivo studies. Based on these categories, a pathogenicity score was devised, and variants were classified as definitely pathogenic, probably pathogenic, possibly pathogenic, or benign.⁶ The MDSGene pathogenicity scoring was designed for causative, monogenic causes but is not applicable to variants with an MAF >1% such as risk variants in *GBA*.

Statistical Analyses

All statistical analyses were performed using *SPSS 26.0.0.0* (IBM, Armonk, NY). For median values, the interquartile range (IQR) is displayed in parentheses.

Results

The MJFF Global Genetic PD Cohort

To establish the cohort, we contacted researchers from 232 centers all over the world and obtained data from 92 centers in 42 countries. In total, 5571 cases were registered in our database, of whom 3888 were included in our analyses (1683 cases were excluded; for details, see Fig. 1).

Of these, 3175 had PD (ie, 1306 *LRRK2*, 115 *SNCA*, 23 *VPS35*, 429 *PRKN*, 75 *PINK1*, 3 *DJ-1*, and 1224 *GBA*) and 703 were unaffected individuals (ie, 328 *LRRK2*, 32 *SNCA*, 3 *VPS35*, 1 *PRKN*, 1 *PINK1*, and 338 *GBA*). These numbers exclude monoallelic carriers of variants in *PRKN* (PD: *n* = 217, unaffected: *n* = 89), *PINK1* (PD: *n* = 56, unaffected: *n* = 45), and *DJ-1* (PD: *n* = 4, unaffected: *n* = 3). Forty-four individuals carried pathogenic variants in other genes linked to forms of parkinsonism or related movement disorders (Appendix S1: Table 1). Individuals originated from 65 countries worldwide (Fig. 2A), and the predominant ethnicity was white (90%) (Fig. 2B).

The break-up of centers per continent is as follows: Europe: *n* = 48; Asia: *n* = 15; North America: *n* = 13; South America: *n* = 8; Australia: *n* = 3; Africa: *n* = 2 (Fig. 3A). About 75% of the world population (5.9 billion) inhabits the countries of origin included in our cohort, whereas the countries of 25% of the world population (~2 billion individuals) are not yet represented in the MJFF Global Genetic PD Cohort (Fig. 3B).

Data Completeness

Per inclusion criteria, basic data such as age at onset were complete for all participants. Availability of clinical data across the cohort ranged from more basic features (77% for disease duration) to more complex assessment of nonmotor symptoms (41% for cognition). Motor scales were available for 51% (MDS-UPDRS or UPDRS) and 47% (Hoehn and Yahr Stage) of the individuals with PD, respectively. Information on medication was reported for 60% of the sample, and risk factor data (smoking, caffeine) were available for a subset (20%) of individuals.

Gene-Specific Findings

The median age at onset of PD was younger in individuals with variants in recessively inherited genes than in those with variants in dominantly inherited genes and *GBA* (Fig. 4 and Appendix S1: Tables 4–6).

Gene-specific findings for dominantly (*LRRK2*, *SNCA*, *VPS35*) and recessively inherited genes (*PRKN*, *PINK1*, *DJ-1*) and *GBA* are summarized in the following paragraphs (Appendix S1: Tables 4–8; Supplementary Information 1–10; Figs. 7–49); For details on the genetic spectrum, see Appendix S1: Figures 1–6.

LRRK2

A total of 1308 individuals with PD (50% women) and 328 unaffected individuals (54% women) with variants in *LRRK2* were registered. Most participants were white (93%), including individuals who identify as Berber (20%) and Ashkenazi Jewish (17%). The most common countries of origin were Tunisia (20%), Spain (14%), and Israel (11%). The median age at onset of PD was 57 years (interquartile range [IQR]: 48–65 years) with a predominantly late onset (>40 years, *n* = 1167, 89%) and only a small fraction of patients with an early onset (20–40 years, *n* = 141, 11%). The median disease duration at the time of inclusion was 8 years (4–14, 9% missing data). Forty-eight percent of the individuals with PD and 89% of unaffected individuals reported a family history of PD.

SNCA

We obtained data on 147 individuals with variants in *SNCA* (115 with PD [52% women], 32 unaffected [56% women]). The majority were white (97%), and 45% originated from Greece. The median age at onset was 45 years (IQR: 38–52 years), and most patients had a late onset of PD (>40 years, *n* = 79, 69%), but early onset was also reported (20–40 years, *n* = 36, 31%). The median disease duration at the time of inclusion was 6 years (IQR: 3–9 years, 12% missing data). Eighty-nine percent of the PD cases and 100% of the unaffected individuals reported a family history of PD.

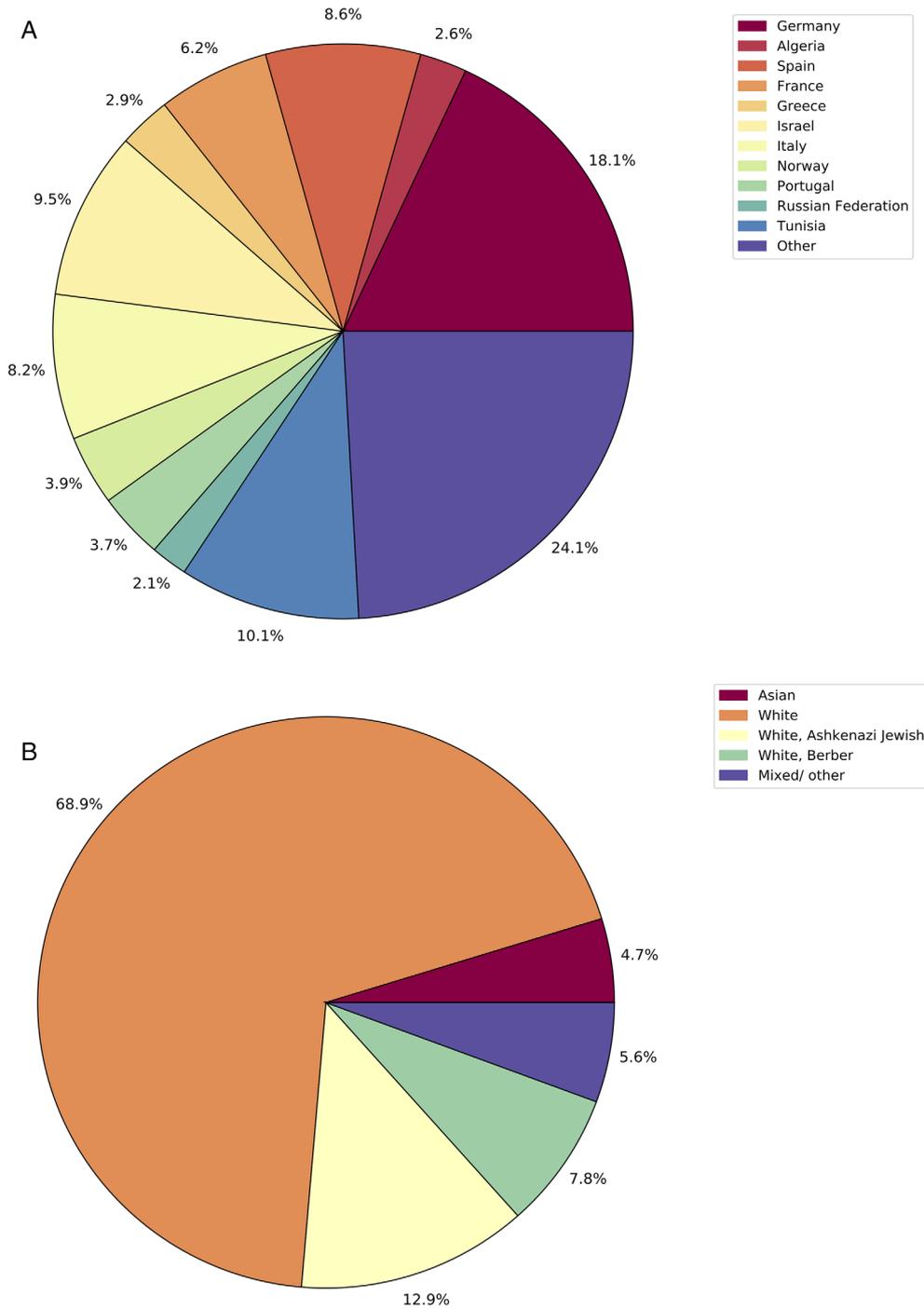


FIG. 2. (A) Reported country of origin of all samples (with and without Parkinson’s disease [PD]). Information missing for 941 individuals (22%). Other countries of origin included (all at <1%): Armenia, Argentina, Australia, Austria, Azerbaijan, Belgium, Bolivia, Canada, China, Czech Republic, Denmark, Ecuador, Estonia, Faroe Islands, Finland, Guadeloupe, Hungary, India, Indonesia, Jersey, Republic of Korea, Lebanon, Libya, Luxembourg, Malaysia, Mexico, Morocco, Netherlands, Peru, Philippines, Pakistan, Saudi Arabia, Serbia, Singapore, Slovakia, South Africa, Sudan, Switzerland, Thailand, Tonga, Ukraine, Venezuela, Vietnam. **(B)** Reported ethnicity of all samples (with and without PD). Other ethnicities/combinations reported in $\leq 2\%$ are summarized in “Mixed/other.”

VPS35

Twenty-six individuals had variants in *VPS35* (23 individuals with PD [61% women] and three unaffected individuals [33% women]). All individuals were

white, and the most common countries of origin were Germany (27%), France (19%), and Austria (15%). The median age at onset was 48 years (44–56 years), 21 individuals had a late onset (>40 years, 91%), and

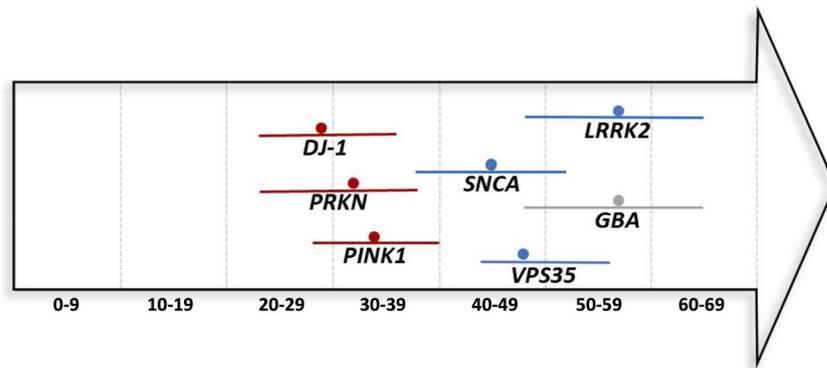


FIG. 4. Median age at onset of Parkinson's disease (PD) and interquartile ranges for subjects with variants in *LRRK2*, *SNCA*, *VPS35*, *PRKN*, *PINK1*, *DJ-1*, and *GBA*. Red: recessively inherited genes, blue: dominantly inherited genes, gray: *GBA*.

PINK1

For *PINK1*, we included 131 PD patients (49% women) and 46 unaffected individuals (33% women) in our cohort. Of these, 75 patients carried biallelic variants and were included in the following analyses. Sixty-three percent were white, and the most frequent countries of origin were Italy (25%), Malaysia (9%), and Germany (7%). The median age at onset of PD was 34 years (IQR: 28–40 years), and 54 patients had an early onset (20–40 years, 72%), 17 had a late onset (>40 years, 23%), and four patients had a juvenile onset (<20 years, 5%). The median disease duration was 17 years (7–29 years). Sixty-one percent reported a family history of PD (4% of missing data).

DJ-1

Our cohort includes 17 PD patients (41% women) and three unaffected individuals (67% women) with pathogenic variants in *DJ-1*. Of these, 13 patients carried biallelic variants and were included in the following analyses. Sixty-nine percent were white, and the largest portions originated from Malaysia (31%), Italy (15%), and France (15%). The median age at onset of PD was 29 years (IQR: 23–36 years), and the majority reported an early onset (20–40 years, $n = 11$, 85%). Two patients had a juvenile onset of PD (<20 years, 15%). The median disease duration was 14 years (7–16 years).

GBA

The most frequently reported variants in *GBA* were p.E365K, p.T408M, p.N409S, and p.L483P. We obtained data for 848 individuals carrying one of the two pathogenic variants, p.N409S or p.L483P (715 [84%] with PD [42% women] and 133 [16%] unaffected [28% women]). Eighty-eight percent were white and, of these, 34% identified as Ashkenazi Jewish. The median age at onset was 56 years (IQR 47–64). Of these, 648 patients had a late onset (>40 years, 90.6%), 66 had

an early onset (20–40 years, 9.2%), and one person had a juvenile onset (<20 years, 0.2%). The disease duration was 7 years (IQR 4–2 years).

A total of 714 persons harbored one of the two included *GBA* risk variants, p.E365K or p.T408M (510 [71%] with PD [42% women] and 204 [29%] unaffected [54% women]). Of these, 98% were white including 1% Ashkenazi Jewish. Affected individuals had a median age at onset of 63 years (IQR 54–69) including 467 with a late onset (>40 years, 91.6%), 42 an early onset (20–40 years, 8.2%) and 1 a juvenile onset (<20 years, 0.2%). The disease duration was 6 years (IQR 3–11 years).

Genetic Data and Pathogenicity Scoring

Across all cases (including monoallelic cases for *PRKN*, *PINK1*, and *DJ-1*), we found 266 different variants with 22% classified as definitely pathogenic, 48% as probably pathogenic, 30% as possibly pathogenic, and the four included *GBA* variants. Missense variants represent the most frequent variant type across all genes (84%) as well as for all genes individually, except for *PRKN*, in which structural variations were most common (51%). Candidate gene testing was the most frequently reported genetic test (42%), followed by PD gene panel (18%, Fig. 5).

Comparison With Published Data (MDSGene)

A total of 1275 individuals in our cohort (32%) were reported as not previously published. Comparing the numbers of individuals in our cohort with those of already published individuals curated in the MDSGene database, our cohort includes fewer individuals for most genes (79% for *SNCA*, 34% of *VPS35*, 65% for *PRKN*, 89% for *PINK1*, and 52% for *DJ-1*), but almost twice as many individuals with pathogenic variants in *LRRK2* (181%).

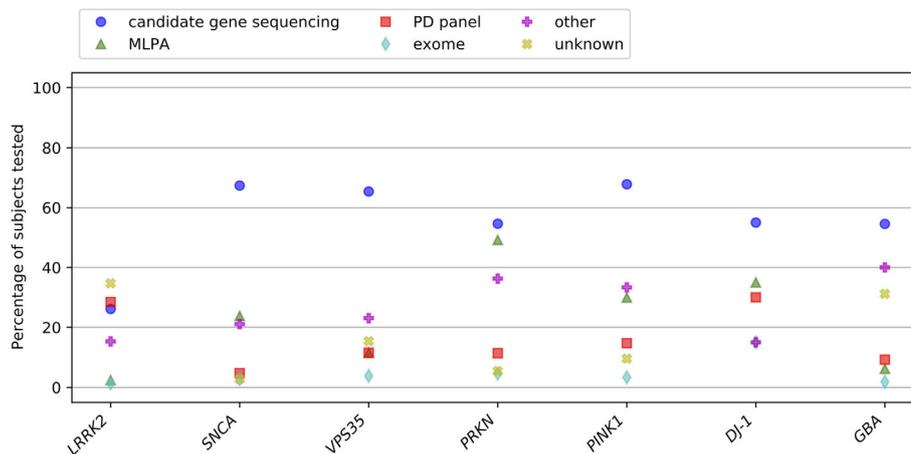


FIG. 5. Types of genetic testing performed per gene. MLPA: multiple ligation-dependent probe amplification.

MDSGene data are overall comparable to data on sex, age at onset, and variant spectrum from our cohort for the most commonly mutated dominant (*LRRK2*) and recessive (*PRKN*) genes (Appendix S1: Figs. 51 and 52).

The MJFF Global Genetic PD Study Group

The MJFF Global Genetic PD Study Group comprises 70 members initially identified through a search of corresponding authors of articles describing patients with monogenic PD included in the MDSGene database, 10 members additionally included from the Genetic Epidemiology of Parkinson's Disease (GEOPD) Consortium, and 90 (self-)referred members. All clinical and genetic information is being stored in a searchable database similar to the MDSGene database (www.mdsgene.org) that will be made available via the website of the Global Parkinson's Genetics Project (www.gp2.org) in the first quarter of 2023 upon completion of the ethical-legal framework for this database. A Steering Committee has been established and oversees the database as well as data use and access. Project suggestions from the study group or from external researchers will be reviewed by the Steering Committee for scientific and ethical content, as well as for potential overlap with ongoing analyses to avoid duplication of efforts and to promote collaboration among all interested researchers in the best possible way. The network welcomes new members on a rolling basis, and all current members are being contacted once a year for an update of potential new variant carriers to be included in the project. Communication is organized mainly via group or personal email by personnel at the coordinating site in Lübeck, currently having included ~15 personal emails per data contributor. Due to the SARS-CoV-2 pandemic, in-person meetings at international

conferences were currently possible only in 2018 and 2019 and are expected to be resumed in 2022.

Discussion

The MJFF Global Genetic PD Cohort is the first large-scale international collection of individuals with PD-linked variants. Although ~10% of the global PD population is expected to carry a pathogenic variant in *LRRK2*, *SNCA*, *VPS35*, *PRKN*, *PINK1*, *DJ-1* or variants in *GBA*, published clinical data are overall limited and non-systematic and no well-defined clinical trial-ready cohort is available to date. Lack of an overall genetic testing routine continuously identifying patients with genetic forms of a progressive degenerative disorder, as is the case in PD, does impact the availability of a clinical trial-ready cohort. For example, the recent antisense oligonucleotide trial in Huntington's disease,¹¹ currently affecting an estimated 390,000–780,000 patients worldwide, recruited four patients per day. In contrast, the MOVES-PD trial in PD patients with pathogenic *GBA* variants (NCT02906020) comprising ~8.5% of all PD patients, ie, an expected ~550,000 individuals, was able to include only one patient every 4 days. In contrast to PD, for Huntington's disease, as well as for other monogenic disorders, there are well-established networks, such as the European Huntington's Disease Network (EHDN; <http://www.ehdn.org>). The MJFF Global Genetic PD Cohort and Study Group aims to close this gap for hereditary PD, which represents a considerable fraction of all PD and where several promising therapeutic options targeting specific genes or pathways have been entering the clinical trial stage.

Although the need for clinical trial-ready cohorts is undisputed, the MJFF Global Genetic PD Cohort serves two additional important purposes: First, it provides carefully quality-controlled clinical and genetic data

with detailed phenotypic information, including scores for motor- and nonmotor assessments. Second, it includes all available variant carriers followed by the contributing centers, which specifically encompasses unpublished ones representing about one third of our cohort, and more detailed individual-level clinical information on those individuals who have already been included in publications. As a special feature of our cohort, we report whether a participant is still available for future research projects and, in addition to that, the majority of researchers are willing to collaborate and to identify study participants for future projects. Our approach thereby counteracts the increasing trend of decreasing reporting of variant carriers in the literature and the related problem of publication bias toward patients with atypical presentations, as genotype-phenotype studies of well-known genetic conditions are increasingly difficult to publish in traditional medical or genetic journals.

Our rigorous quality control, strongly supported by the high degree of responsivity and support of the contributing centers, resulted in the removal of about a third of all submitted variant carriers from the initially reported individuals. Reflecting global mobility and migration, we were able to include individuals originating from 65 countries, although our contributing centers were located in only 42 different countries. We tried to be as inclusive as possible by combining a systematic recruitment approach with “spreading-the-word” efforts and were able to cover a significant proportion of countries across the globe, which harbor about three quarters of the world population. Notably, however, in many particularly populous parts of the world, we could only include a relatively small number of centers so that our recruitment efforts resulted in overrepresentation of Europe, parts of Asia, and North America, as also reflected by “white” being by far the most common ethnicity (91%) in our data set.

The clinical and genetic findings in our cohort are well compatible with previous descriptions, which is at least partially driven by the fact that about two-thirds of our cohort constitute previously published patients represented in the MDSGene Database, albeit now with much more comprehensive clinical information available and information on availability for follow-up studies (eg, ~70% of the participants can be recontacted). As expected from Mendelian forms of PD, women account for about half of all of the described patients in our cohort. Median ages of onset range from 34 years (*DJ-1*) to 57 years (*LRRK2*). Interestingly, the majority (>40%) of variant carriers were identified by candidate gene sequencing, whereas panel sequencing was performed in only ~20% of the patients. With the exception of *PRKN*, where half of the described variants were gene dosage changes, point mutations were by far the most prevalent variant type.

Limitations of the current MJFF Global Genetic PD Cohort are its predominant inclusion of white individuals and its limited outreach to underrepresented populations including the lack of participants from the African continent, and overrepresentation of certain countries due to a higher frequency of specific pathogenic variants in select populations, resulting in easier and more frequent genetic testing for these variants. Furthermore, the data comprise a relatively small minimal data set with gaps for more detailed clinical information beyond the minimal data set and limited availability of structured information on ethnicity. Notably, additional bias will have been introduced due to a focus on tertiary referral centers and academic settings, as well as variable access to genetic testing resources in different countries. In keeping with the latter notion, there has been heterogeneous assessment of pathogenic variants across sites, ranging from single gene sequencing to panels and exomes, thereby impacting on detectable variants and, consequently, frequency and type of pathogenic variants identified. Lack of universally accepted PD genetic testing guidelines and methods promotes this heterogeneity further. Strengths include the large amount of carefully curated clinical and genetic data on ~4000 PD variant carriers, build-up of a strong and growing global network of doctors and researchers following PD variant carriers, a sustainable and user-friendly digital infrastructure for regular updates of the cohort, the timeliness of the effort while a number of clinical trials are already actively searching for eligible patients, inclusion of non-manifesting carriers enabling the study of possible modifying factors of penetrance, and establishment of a cohort for potential future neuroprotective trials.

Regarding future perspectives, we are completing the development of a searchable database that will be made publicly available to facilitate and democratize data access, while all communication with patients and unaffected variant carriers will rest with the local centers in a decentralized fashion to protect patient confidentiality and comply with cultural, ethical, and legal requirements at the respective local centers. Additional future aims and opportunities include (1) in-depth data mining and inclusion of all potentially pathogenic variants (eg, in *GBA*); (2) further expansion of the study group and cohort to better reflect underrepresented populations; these aims will be achieved in conjunction with *GEoPD* and the recently established Global Parkinson's Genetics Program (*GP2*)¹²; (3) performing regular annual updates to enable a sustainable and current resource; (4) creating a world map of genetic PD centers and facilities ranging from research facilities to information on clinical trial options to take international research and translational collaboration in PD genetics to a new level, which may also serve as a model for other rare disorders. ■

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Data Availability Statement

Data available on request from the authors.

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Appendix

MJFF Global Genetic Parkinson's Disease Study Group

Anna Aasly, Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway

Jan O. Aasly, Department of Neurology, St. Olavs Hospital, Trondheim, Norway; Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway

Natalya Y. Abramycheva, Department of Neurogenetics, Research Center of Neurology, Moscow, Russia

Azlina Ahmad-Annur, Department of Biomedical Science, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Alberto Albanese, Department of Neurology, IRCCS Istituto Clinico Humanitas, Rozzano, Milano, Italy; Department of Neurology, Catholic University, Milano, Italy

Roy N. Alcalay, Department of Neurology, Columbia University, New York, New York, USA

Amaal Aldakheel, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Thamer Alkhairallah, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Bashayer Al-Mubarak, Behavioural Genetics Unit, Department of Genetics, Research Centre, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Nada Al-tassan, Behavioural Genetics Unit, Department of Genetics, Research Centre, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Victoria Alvarez, Laboratorio de Genética, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain; Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain

Paolo Amami, Department of Neurology, IRCCS Istituto Clinico Humanitas, Rozzano, Milano, Italy

Grazia Annesi, Institute of Biomedical Research and Innovation, National Research Council, Cosenza, Italy

Silke Appel-Cresswell, Pacific Parkinson's Research Centre, Division of Neurology, Department of Medicine, Vancouver, British Columbia, Canada

Marco Antonio Araujo Leite, Division of Neurology, Movement Disorders Unit, Antônio Pedro University Hospital, Fluminense Federal University, Rio de Janeiro, Brazil

David Arkadir, Department of Neurology, Hadassah Medical Center and the Hebrew University, Jerusalem, Israel

Micol Avenali, Neurorehabilitation Unit, IRCCS Mondino Foundation, Pavia, Italy; Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy

Henrique Ballalai Ferraz, Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil

Soraya Bardien, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

Melinda Barkhuizen, DST/NWU Preclinical Drug Development Platform, North-West University, Potchefstroom, North-West, South Africa

Matthew J. Barrett, Department of Neurology, University of Virginia, Charlottesville, Virginia, USA

A. Nazlı Başak, Suna and Inan Kiraç Foundation, Neurodegeneration Research Laboratory, KUTTAM, School of Medicine, Koç University, Istanbul, Turkey

Daniela Berg, Department of Neurology, Christian-Albrechts-Universität, Kiel, Germany

Basar Bilgic, Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Bastiaan R. Bloem, Department of Neurology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands

Vincenzo Bonifati, Department of Clinical Genetics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

Agnita J. W. Boon, Department of Neurology, Erasmus MC, University Medical Center Rotterdam, The Netherlands

Vanderci Borges, Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil

Friederike Borngräber, Movement Disorder and Neuromodulation Unit, Charité, Universitätsmedizin Berlin, Department of Neurology, Campus Mitte, Berlin, Germany

Max Borsche, Department of Neurology and Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Maria Bozi, Parkinson's and Movement Disorders Unit, 2nd Dpt of Neurology of the University of Athens, Attikon Hospital, Haidari, Athens, Greece; Psychiatry Hospital of Attica "Dafni," Neurology Dpt, Haidari, Athens, Greece

Susan Bressman, Department of Neurology, Beth Israel Medical Center, New York, New York, USA; Department of Neurology at Albert Einstein College of Medicine, New York, New York, USA

Alexis Brice, Sorbonne University, Paris Brain Institute—ICM, Inserm, CNRS, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Department of Neurology, Paris, France

Laura Brighina, Department of Neurology, Milan Center for Neuroscience, University of Milano-Bicocca/San Gerardo Hospital, Monza, Monza Brianza, Italy

Kathrin Brockmann, Department of Neurodegenerative Diseases, University of Tuebingen, Tuebingen, Baden Wuerttemberg, Germany; Hertie Institute for Clinical Brain Research and German Centre for Neurodegenerative Diseases, Tuebingen, Baden Wuerttemberg, Germany

Norbert Brüggemann, Department of Neurology and Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Marta Camacho, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom

Andrea Carmine Belin, Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

Jonathan Carr, Division of Neurology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

Martin Emiliano Cesarini, Instituto de Neurociencias Buenos Aires (INEBA), Buenos Aires, Argentina

Mario Cornejo-Olivas, Neurogenetics Research Center, Instituto Nacional de Ciencias Neurológicas, Lima, Peru; Center for Global Health, Universidad Peruana Cayetano Heredia, Lima, Peru

Bruce Chase, Department of Neurology, NorthShore University HealthSystem, Evanston, Illinois, USA

Sun Ju Chung, Medical Genetic Center, Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Leonor Correia Guedes, Department of Neuroscience and Mental Health, Neurology Department, Hospital de Santa Maria, CHULN, Lisbon, Portugal; Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Jordi Clarimon, Department of Neurology, Biomedical Research Institute IIB-Sant Pau, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

Lorraine Clark, Department of Pathology and Cell Biology, Vagelos College of Physicians & Surgeons, Columbia University Irving Medical Center, New York, New York, USA; Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Irving Medical Center, New York, New York, USA; Laboratory of Personalized Genomic Medicine, Vagelos College of Physicians & Surgeons, Columbia University Irving Medical Center, New York, New York, USA

Jean-Christophe Corvol, Sorbonne University, Paris Brain Institute—ICM, Inserm, CNRS, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Department of Neurology, Paris, France

David Crosiers, Department of Neurology, Antwerp University Hospital, Edegem, Belgium; Born Bunge Institute, Department of Neurology, University of Antwerp, Wilrijk, Belgium; Center for Molecular Neurology, VIB, Wilrijk, Belgium

Parimal Das, Centre for Genetic Disorders, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Patricia de Carvalho Aguiar, Hospital Israelita Albert Einstein, São Paulo, Brazil; Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo, Brazil

Joana Damásio, Department of Neurology, Hospital de Santo António—Centro Hospitalar Universitário do Porto, Porto, Portugal; UnIGENe, Instituto de Biologia Molecular e Celular (IBMC), Instituto de Investigação e Inovação em Saúde (i3S), Universidade do Porto, Portugal

Giuseppe de Michele, Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy

Anna De Rosa, Department of Neurosciences and Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy

Elena Dieguez, Neurology Institute, Universidad de la Republica, Montevideo, Uruguay

Jolanta Dorszewska, Laboratory of Neurobiology, Department of Neurology, Poznan University of Medical Sciences, Poznan, Poland

Sibel Ertan, Department of Neurology, School of Medicine, Koç University, Istanbul, Turkey

Stanley Fahn, Department of Neurodegenerative Diseases, University of Tuebingen, Tuebingen, Baden Wuerttemberg, Germany; Hertie Institute for Clinical Brain Research and German Centre for Neurodegenerative Diseases, Tuebingen, Baden Wuerttemberg, Germany

Matthew J. Farrer, Fixel Institute, Department of Neurology, University of Florida, Gainesville, Florida, USA

Ekaterina Y. Fedotova, Department of Neurogenetics, Research Center of Neurology, Moscow, Russia

Rosangela Ferese, IRCCS Neuromed, Località Camerelle, Pozzilli, Isernia, Italy

Joaquim J. Ferreira, Laboratory of Clinical Pharmacology and Therapeutics, University of Lisbon, Lisbon, Portugal; Instituto de Medicina Molecular João Lobo Antunes, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Tatiana Foroud, Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, USA

Manabu Funayama, Research Institute for Diseases of Old Age, Graduate School of Medicine, Juntendo University, Bunkyo, Tokyo, Japan

Victor S. C. Fung, Movement Disorders Unit, Department of Neurology, Westmead Hospital, Sydney, Australia; Sydney Medical School, University of Sydney, Sydney, Australia

Monica Gagliardi, Department of Neurology, Columbia University, New York, New York, USA

Stefano Gambardella, IRCCS Neuromed, Località Camerelle, Pozzilli, Isernia, Italy

Gaetan Garraux, Department of Neurology, Centre Hospitalier Universitaire (CHU) de Liège, Liège, Belgium; MoVeRe group, GIGA-CRC In Vivo Imaging, University of Liege, Liège, Belgium

Alicia Garrido, Parkinson Disease and Movement Disorders Unit, Neurology Service, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED: CB06/05/0018-ISCI) Barcelona, Spain

Emilia M. Gatto, Movement Disorders, Department of Neurology, Instituto de Neurociencias Buenos Aires, Buenos Aires, Argentina

Gençer Genç, Department of Neurology, University of Health Sciences, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey

Nir Giladi, Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sackler School of Medicine, Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

Pilar Gómez-Garre, Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

Hasmet Hanagasi, Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Nobutaka Hattori, Department of Neurology, Juntendo University School of Medicine, Bunkyo, Tokyo, Japan

Faycel Hentati, Mongi Ben Hmida National Institute of Neurology, Tunis, Tunisia

Jens Michael Hertz, Department of Clinical Genetics, Odense University Hospital, Odense C, Denmark

Sergey N. Illarionkin, Department of Neurogenetics, Research Center of Neurology, Moscow, Russia

Joseph Jankovic, Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA

Cristina Januario, Movement Disorders Clinic, Department of Neurology, Universitário de Coimbra, Coimbra, Portugal

Silvia Jesús Maestre, Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

Valteri Kaasinen, Neurocenter, Turku University Hospital, Turku, Finland; Clinical Neurosciences, Faculty of Medicine, University of Turku, Turku, Finland

Meike Kasten, Department of Psychiatry and Psychotherapy and Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Hiroshi Kataoka, Department of Neurology, Nara Medical University, Kashihara, Nara, Japan

Anneke A. Kievit, Department of Clinical Genetics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

Yun Joong Kim, Department of Neurology, Yonsei University College of Medicine, Seoul, South Korea; Department of Neurology, Yongin Severance Hospital, Yonsei University Health System, Yongin, South Korea

Christine Klein, Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Péter Klivényi, Department of Neurology, University of Szeged, Szeged, Hungary

Vladimir S. Kostic, Department for Neurodegeneration, Clinic for Neurology CCS, Belgrade, Serbia

Dariusz Koziorowski, Department of Neurology, Medical University in Warsaw, Warsaw, Poland

Rejko Krüger, Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-sur-Alzette, Luxembourg; Transversal Translational Medicine, Luxembourg Institute of Health (LIH), Strassen, Luxembourg; Parkinson Research Clinic, Centre Hospitalier de Luxembourg (CHL), Luxembourg, Luxembourg

Andrea A. Kühn, Movement Disorder and Neuromodulation Unit, Charité, Universitätsmedizin Berlin, Department of Neurology, Campus Mitte, Berlin, Germany

Gregor Kuhlensäumer, Department of Neurology, Christian-Albrechts-Universität, Kiel, Germany

Ming-Che Kuo, Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan; Department of Neurology, National Taiwan University College of Medicine, Taipei, Taiwan

Anthony E. Lang, Edmond J. Safra Program in Parkinson's Disease, Division of Neurology, Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada

Guey-Jen Lee-Chen, Department of Life Science, National Taiwan Normal University, Taipei, Taiwan

Suzanne Lesage, Sorbonne University, Paris Brain Institute—ICM, Inserm, CNRS, Paris, France

Jia Lun Lim, Department of Biomedical Science, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Shen-Yang Lim, Division of Neurology and the Mah Pooi Soo & Tan Chin Nam Centre for Parkinson's & Related Disorders, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Chin-Hsien Lin, Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan; Department of Neurology, National Taiwan University College of Medicine, Taipei, Taiwan

Katja Lohmann, Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Timothy Lynch, Department of Neurology, The Dublin Neurological Institute at the Mater Misericordiae University Hospital, Dublin, Ireland; School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland

Karen Marder, Department of Neurology, Taub Institute for Alzheimer's Disease and the Aging Brain, Columbia University, New York, New York, USA

Katerina Markopoulou, Department of Neurology, NorthShore University HealthSystem, Evanston, Illinois, USA; Department of Neurology, University of Chicago, Chicago, Illinois, USA

Mika Martikainen, Neurocenter, Turku University Hospital, Turku, Finland; Clinical Neurosciences, Faculty of Medicine, University of Turku, Turku, Finland

Patrick May, Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-sur-Alzette, Luxembourg

Allan McCarthy, The Dublin Neurological Institute at the Mater Misericordiae University Hospital, Dublin, Ireland & Department of Neurology, The Adelaide and Meath Hospital, Dublin, Ireland

George D. Mellick, Griffith Institute for Drug Discovery (GRIDD), School of Environment and Science, Griffith University, Brisbane, Queensland, Australia

Manuel Menéndez-González, Servicio Neurología, Hospital Universitario Central de Asturias, Oviedo, Spain; Instituto de Investigación; Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain

Marcelo Merello, Sección Movimientos Anormales, Departamento de Neurociencias, Fleni, Buenos Aires, Argentina; Argentine National Scientific and Technological Research Council (CONICET), Argentina; Pontificia Universidad Católica Argentina (UCA), Argentina

Pablo Mir, Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

Anat Mirelman, Laboratory of Early Markers of Neurodegeneration, Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

Brit Mollenhauer, Movement Disorder Paracelsus-Elena-Klinik, Kassel, Germany; Department of Neurology, University Medical Center Göttingen, Göttingen, Germany

Hugo Morales Briceno, Movement Disorders Unit, Department of Neurology, Westmead Hospital, Sydney, Australia; Sydney Medical School, University of Sydney, Sydney, Australia

Ana Morgadinho, Movement Disorders Clinic, Department of Neurology, Universitário de Coimbra, Coimbra, Portugal

Huw Morris, Queen Square Brain Bank for Neurological Disorders, Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, University College London, London, United Kingdom

Alexandra Mosejova, Department of Neurology, Pavol Jozef Šafárik University in Košice, Košice, Slovakia

Kenya Nishioka, Department of Neurology, Juntendo University School of Medicine, Bunkyo, Tokyo, Japan

Özgür Öztop Çakmak, Department of Neurology, School of Medicine, Koç University, Istanbul, Turkey

Diana A. Olszewska, Department of Neurology, The Dublin Neurological Institute at the Mater Misericordiae University Hospital, Dublin, Ireland; School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland

Avi Orr-Urtreger, The Genomic Research Laboratory for Neurodegeneration, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Sinthuja Pachcek, Luxembourg Centre for Systems Biomedicine (LCsB), University of Luxembourg, Esch-sur-Alzette, Luxembourg

Shalini Padmanabhan, Research Programs, The Michael J. Fox Foundation for Parkinson's Research, New York, New York, USA

Maria Teresa Periñán, Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

Simona Petrucci, Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy; Sant' Andrea University Hospital, Rome, Italy

Marcia M. G. Pimentel, Department of Genetics, Institute of Biology Roberto Alcantara Gomes, State University of Rio de Janeiro, Rio de Janeiro, Brazil

Radha Procopio, Institute of Neurology, Department of Medical and Surgical Sciences, University Magna Graecia, Catanzaro, Italy

Teeratorn Pulkes, Division of Neurology, Department of Medicine, Ramathibodi Hospital, Mahidol University, Rajthevi, Bangkok, Thailand

Andreas Puschmann, Department of Neurology, Clinical Sciences, Lund University, Lund, Sweden; Department of Neurology, Skåne University, Lund, Sweden

Caroline Ran, Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

Olaf Riess, Institute of Medical Genetics and Applied Genomics, University of Tuebingen, Tuebingen, Germany

Owen A. Ross, Department of Neuroscience, Mayo Clinic, Jacksonville, Florida, USA

Malco Rossi, Sección Movimientos Anormales, Departamento de Neurociencias, Fleni, Buenos Aires, Argentina; Argentine; National Scientific and Technological Research Council (CONICET), Buenos Aires, Argentina

Javier Ruiz-Martinez, Neuroscience Area, Biodonostia Research Institute, San Sebastian, Gipuzkoa, Spain; Department of Neurology, University Hospital Donostia, San Sebastian, Gipuzkoa, Spain

Esther M. Sammler, Neurology Department, Ninewells Hospital and Medical School, Dundee, United Kingdom; MRC Protein Phosphorylation and Ubiquitylation Unit, University of Dundee, Dundee, United Kingdom

João Santos Pereira, Movement Disorders Section, Neurology Service, Pedro Ernesto University Hospital, State University of Rio de Janeiro, Rio de Janeiro, Brazil

Wataru Satake, Department of Neurology, The University of Tokyo, Tokyo, Japan

Rachel Saunders-Pullman, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Susen Schaake,

Maria Skaalum Petersen, Centre of Health Science, University of the Faroe Islands, Tórshavn, Faroe Islands; Department of Occupational Medicine and Public Health, The Faroese Hospital System, Faroe Islands

Matej Skorvanek, Department of Neurology, Pavol Jozef Šafárik University in Košice, Košice, Slovakia; Department of Neurology, University Hospital L. Pasteur, Kosice, Slovakia

Leonidas Stefanis, First Department of Neurology, Medical School of the National and Kapodistrian University of Athens, Eginition Hospital, Athens, Greece

Alexandra I. Soto-Beasley, Department of Neuroscience, Mayo Clinic, Jacksonville, Florida, USA

Mário Sousa, Movement Disorders Clinic, Department of Neurology, Universitário de Coimbra, Coimbra, Portugal

Mariana Spitz, Neurology Service, State University of Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil

Oksana Suchowersky, Department of Medicine, Medical Genetics and Pediatrics, University of Alberta, Edmonton, Alberta, Canada

Carolyn M. Sue, Department of Neurogenetics, Kolling Institute, University of Sydney, Sydney, New South Wales, Australia; Department of Neurology, Royal North Shore Hospital, St Leonards, New South Wales, Australia

Ai Huey Tan, Division of Neurology and the Mah Pooi Soo & Tan Chin Nam Centre for Parkinson's & Related Disorders, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Eng-King Tan, Department of Neurology, National Neuroscience Institute, Duke NUS Medical School, Singapore General Hospital, Singapore, Singapore

Avner Thaler, Movement Disorders, Neurological Institute, Tel-Aviv Medical Center, Tel-Aviv, Israel; Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Fatih Tepgeç, Department of Medical Genetics, Istanbul Faculty of Medicine, Istanbul, Turkey

Pichet Termsarasab, Division of Neurology, Department of Medicine, Ramathibodi Hospital, Mahidol University, Rajthevi, Bangkok, Thailand

Christelle Tesson, Sorbonne University, Paris Brain Institute—ICM, Inserm, CNRS, Paris, France

Tatsushi Toda, The University of Tokyo, Tokyo, Japan

Mathias Toft, Department of Neurology, Oslo University Hospital, Oslo, Norway; Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Eduardo Tolosa, Parkinson Disease and Movement Disorders Unit, Neurology Service, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED:CB06/05/0018-ISCI) Barcelona, Spain

Luis Torres-Ramirez, Movement Disorders Unit, Instituto Nacional de Ciencias Neurológicas, Lima, Peru

Vitor Tumas, Behavioral and Movement Disorders Section, Ribeirão Preto Medical School, University of São Paulo, Brazil

Oya Uyguner, Department of Medical Genetics, Istanbul Faculty of Medicine, Istanbul, Turkey

Enza Maria Valente, Neurogenetics Research Centre, IRCCS Mondino Foundation, Pavia; Department of Molecular Medicine, University of Pavia, Pavia, Italy

Bart van de Warrenburg, Department of Neurology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands

Marie Vidailhet, Sorbonne University, Paris Brain Institute—ICM, Inserm, CNRS, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Department of Neurology, Paris, France

Eva-Juliane Vollstedt, Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Ronald L. Walton, Department of Neuroscience, Mayo Clinic, Jacksonville, Florida, USA

Cheryl Waters, Department of Neurodegenerative Diseases, University of Tuebingen, Tuebingen, Baden Wuerttemberg, Germany; Hertie Institute for Clinical Brain Research and German Centre for

Neurodegenerative Diseases, Tuebingen, Baden Wuerttemberg, Germany

Caroline H. Williams-Gray, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom

Juliane Winkelmann, Institute of Neurogenomics, Helmholtz Zentrum Muenchen, Neuherberg, Germany; Neurogenetics, Technische Universitaet Muenchen, Munich, Germany; Institute of Human Genetics, Klinikum rechts der Isar der TUM, Munich, Germany; Munich Cluster for Systems Neurology (SyNergy), Munich, Germany

Yih-Ru Wu, Department of Neurology, Chang Gung University, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan

Isabel Wurster, Department of Neurodegenerative Diseases, University of Tuebingen, Tuebingen, Baden Wuerttemberg, Germany; Hertie Institute for Clinical Brain Research and German Centre for Neurodegenerative Diseases, Tuebingen, Baden Wuerttemberg, Germany

Zbigniew K. Wszolek, Department of Neurology, Mayo Clinic, Jacksonville, Florida, USA

Ruey-Meei Wu, Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan; Department of Neurology, National Taiwan University College of Medicine, Taipei, Taiwan

Bao-rong Zhang, Department of Neurology, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang, China

Alexander Zimprich, Department of Neurology, Medical University, Vienna, Austria

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