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RESEARCH ARTICLE

Establishing an online resource to facilitate global collaboration and inclusion of underrepresented populations: Experience from the MJFF Global Genetic Parkinson's Disease Project



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Abstract

Parkinson's disease (PD) is the fastest-growing neurodegenerative disorder, currently affecting ~7 million people worldwide. PD is clinically and genetically heterogeneous, with at least 10% of all cases explained by a monogenic cause or strong genetic risk factor. However, the vast majority of our present data on monogenic PD is based on the investigation of patients of European White ancestry, leaving a large knowledge gap on monogenic PD in underrepresented populations. Gene-targeted therapies are being developed at a fast pace and have started entering clinical trials. In light of these developments, building a global network of centers working on monogenic PD, fostering collaborative research, and establishing a clinical trial-ready cohort is imperative. Based on a systematic review of the English literature on monogenic PD and a successful team science approach, we have built up a network of 59 sites worldwide and have collected information on the availability of data, bio-materials, and facilities. To enable access to this resource and to foster collaboration across centers, as well as between academia and industry, we have developed an interactive map and online tool allowing for a quick overview of available resources, along with an option to filter for specific items of interest. This initiative is currently being merged with the Global Parkinson's Genetics Program (GP2), which will attract additional centers with a focus on underrepresented sites. This growing resource and tool will facilitate collaborative research and impact the development and testing of new therapies for monogenic and potentially for idiopathic PD patients.

Introduction

As technologies for genetic testing are rapidly developing and are becoming more cost-effective, rare disorders and also rare subtypes of common disorders can increasingly be characterized genetically and thus stratified into genetically defined subgroups. This provides the basis not only to investigate disease mechanisms further but also to develop and test gene-targeted therapies. Parkinson's disease (PD), the most rapidly growing neurodegenerative disorder [1] can serve as a model disease for this approach, as PD is a common disorder affecting about 7 million people worldwide in 2022, including an estimated 700,000–840,000 (10–12%) hereditary cases with pathogenic genetic variants (monogenic PD and PD due to strong genetic risk factors). In light of the development of gene-targeted therapies for 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 [2–5]. Most study centers publishing in the English language are located in Europe and North America [6]. There is evidence for variable

penetrance and expressivity of the disease across populations and ethnicities in monogenic forms of PD [2]. However, the majority of published cases are reported to be White and originate from Europe or North America, whereas most African, Asian, and South American populations, especially indigenous people, are highly underrepresented. Little is known about the actual worldwide epidemiology, frequency of population-specific variants, and possible local factors influencing the manifestation and course of the disease. Notably, even for published cases, the availability of detailed genetic and clinical data is limited, and genetically stratified clinical trial-ready cohorts are highly sought after.

Global collaboration both within academic research and with the pharmaceutical industry is paramount to expanding our knowledge of disease mechanisms, developing gene-targeted medications, and testing them in clinical trials. Building an international network of researchers from academia and industry will facilitate including more underrepresented populations in investigations and trials, both by enhancing the visibility of existing study centers and by providing genetic testing facilities. To open this network to new members and specifically allow researchers or clinicians from currently underrepresented countries to engage in these collaborative efforts, we established an online resource that provides an overview of centers worldwide working on monogenic PD and their facilities. While this effort sprung from the MJFF Global Genetic Parkinson's Disease Project [6], it has recently been integrated into the Global Parkinson's Genetics Program (GP2, <https://gp2.org/>), which will build global will and capacity while addressing emerging research questions in PD genetics [7].

Methods

How to find eligible centers?

Performing a systematic literature review on monogenic PD in the English literature [3, 4], our group identified the need for a new, systematic, and global approach to obtain more detailed clinical and genetic data from individuals with monogenic PD. Starting in March 2018, we contacted by email all corresponding authors from articles that we had included in the review and ran an online survey to collect information on the number of subjects with monogenic PD they follow, along with available clinical and genetic data. In a second step, we invited all researchers to provide individual case-level data and offered a small per-case fee to reimburse them for their effort to retrieve and enter the data in another online survey. The vast majority of participating centers expressed enthusiasm about our project, their strong interest in being part of the emerging study group, and support for further collaborative efforts.

To establish the online resource, we contacted all participating researchers, including their collaborators ($n = 112$). We received responses from 59 centers (53%) in 36 countries on all inhabited continents (Europe ($n = 33$), North ($n = 4$) and South America ($n = 8$), Asia ($n = 10$), Australia ($n = 1$), Africa ($n = 3$)). All centers have agreed to be contacted by researchers and the pharmaceutical industry, while the majority of centers ($n = 41$, 69%) would prefer not to be contacted directly but to have requests filtered first. The Monogenic Network of GP2 will handle collaboration requests. All participants provided written informed consent to the publication of the provided data. The ethics committee of the University of Lübeck confirmed that no ethical approval was required for this study.

How to obtain the data of interest?

An essential part of this project was communication and information. Having identified eligible researchers, we sent out information emails about our project and kept all participants updated in regular progress emails. To further improve the retention rate, we ensured a quick

Table 1. Items assessed in the online survey.

Site details	Name of site
	Principal investigator
	City/ Country
	Active in other PD projects
	New PD patients/year
	Genetic testing available
	How are genetic testing costs covered?
	Qualified genetic counseling available?
Availability of clinical data	Already performing clinical trials?
	Sex
	Age
	Age at onset
	UPDRS
	Hoehn and Yahr scale
	Nonmotor scales
Data sharing	Olfactory testing
	IRB consent
Availability of biomaterials	Shipment outside the country
	DNA/RNA/Serum/Plasma/whole blood/CSF/fibroblasts/iPSCs/brain tissue (storage?)
Availability of Omics	Genomics/ Transcriptomics/ Proteomics/ Metabolomics
Laboratory facilities	CSF handling
	Serum Plasma handling
	Culturing of fibroblasts
	Isolation of cells from whole blood
	Generation of iPSCs
	Neuropathology
	MRI
SPECT/PET	
TCS	

PD: Parkinson's disease; UPDRS: Unified Parkinson's Disease Rating Scale; IRB: institutional review board; DNA: Deoxyribonucleic acid; RNA: Ribonucleic acid; CSF: cerebrospinal fluid; iPSCs: induced pluripotent stem cells; MRI: magnetic resonance imaging, SPECT/PET: Single-photon emission computed tomography/positron emission tomography, TCS: transcranial sonography

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response in case of any queries and consistently named a specific contact person. When designing the survey, we aimed at providing an accessible online format, allowing different browser types and devices (again, our team was available and provided help in case of any technical difficulties), kept it brief, and phrased questions in a concise and explicit way (Table 1). Whenever possible, questions were designed to allow single-choice answers only, and free text fields were limited to maximize comparison between centers. For convenience, already available information (such as the name and location of the study center) was prefilled by our team. Participants received an invitation email including a link to their individual survey. Once complete, the survey was submitted by the participant. We sent out two rounds of reminder emails, personally addressing each participant, to improve the response rate and make sure all invitees received their email and got the opportunity to present their study center.

After completing the survey, we reviewed the data and double-checked for any inaccurate entries. In case of ambiguity, we reached out to the respective researcher for approval of the

correction. After this first round of quality checks, we programmed the online tool and uploaded the provided data. In a second round of quality checks and to allow for possible updates, we invited all participants to review and verify the provided data and obtained permission to publish the presented resource. Regular updates of the resource and map will be provided biannually, and ongoing projects and trials using the network will be listed on the website to facilitate further collaboration while avoiding duplication of efforts.

Results

Our two-part online tool is now available at <https://gp2networkdev.wpengine.com/monogenic-resource-map/>. Firstly, it includes a searchable online table that allows for filtering for specific characteristics of interest (e.g., location of the center, available facilities, Table 1). Second, a map displays the locations of all research centers and provides individual profiles with information on each center (Fig 1).

The average number of new PD patients per year reported by the participants until May 2022 is 196. Genetic testing is regularly performed by 37 (63%) of the centers, and the costs are predominantly covered by in-house or external funding sources (39%), followed by coverage by health insurance and the patients themselves (10% each). The availability of biomaterials varies depending on how difficult they are to obtain, ranging from 53 centers (90%) reporting the availability of DNA for at least a subset of cases to 8 centers (14%) reporting the availability of brain tissue (Fig 2). Laboratory facilities that are part of the standard clinical workup like serum and plasma handling, are more frequently available (at 53 centers, 90%) than more specific ones that are more costly or require special training, such as the generation of induced pluripotent stem cells (at 24 centers, 41%; Fig 3).

Discussion and conclusions

Using a powerful team science approach, we have established a global network of academic centers involved in the clinical care of patients with monogenic PD and with a high interest in collaboration, research, and gene-targeted therapies for PD. Based on a systematic search of



Fig 1. The monogenic resource map. This world map displays the distribution of all participating centers worldwide. The pins mark the location of the study centers. Clicking on a pin opens the respective study center profile. The profiles summarize information on the site and the availability of demographic and clinical data, biomaterials, methods, and facilities and provide information on other collaborative projects that the study center is part of.

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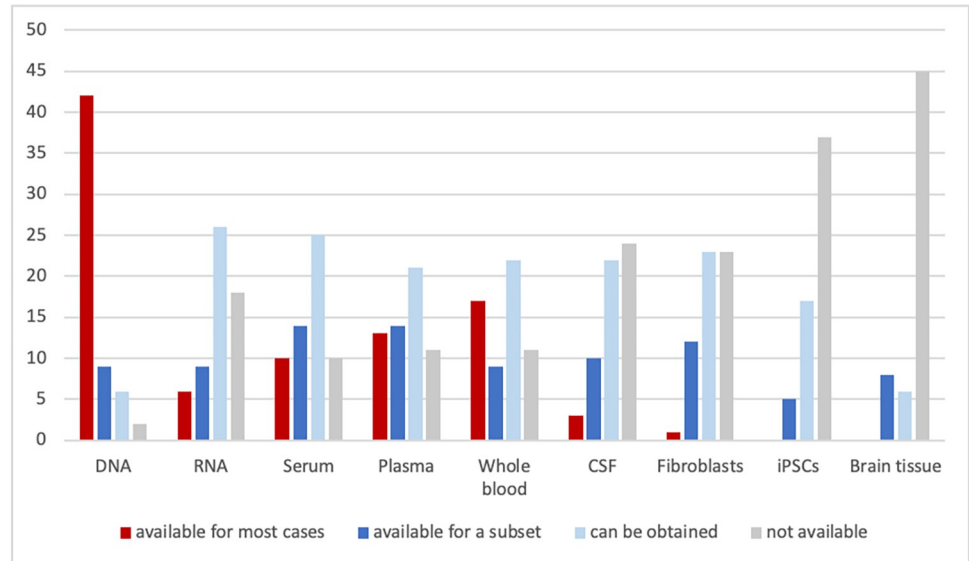


Fig 2. Availability of biomaterials. Number of centers reporting availability of the listed biomaterials. DNA: Deoxyribonucleic acid, RNA: Ribonucleic acid, CSF: cerebrospinal fluid, iPSCs: induced pluripotent stem cells.

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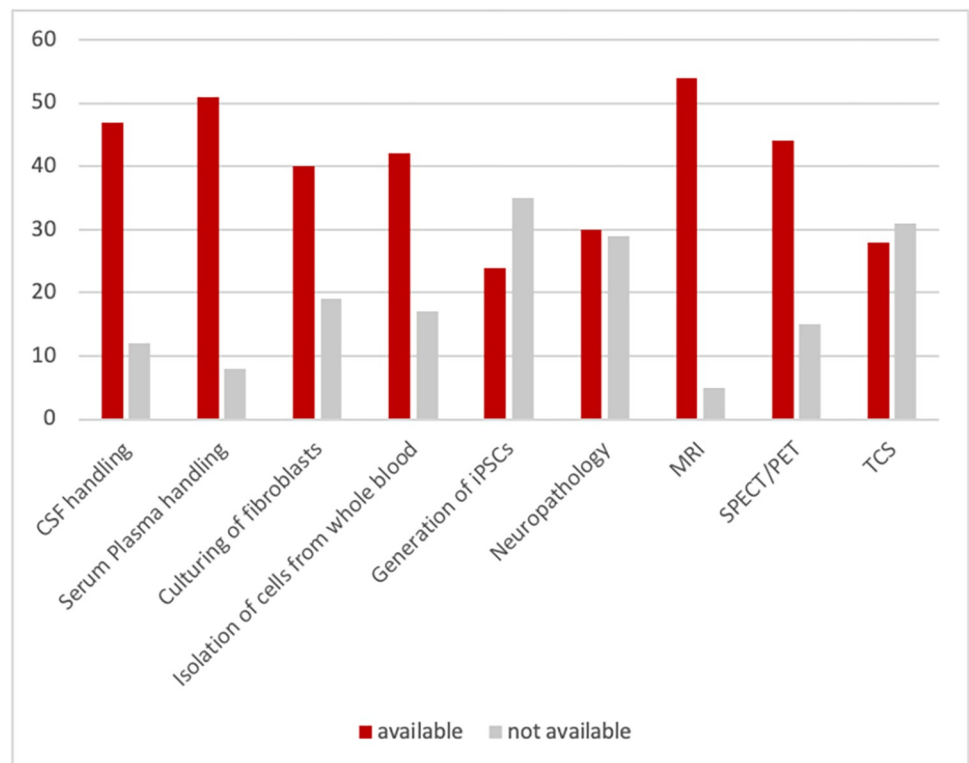


Fig 3. Availability of methods and facilities. Number of centers reporting availability of the listed methods and facilities. CSF: cerebrospinal fluid, iPSCs: induced pluripotent stem cells, MRI: magnetic resonance imaging, SPECT/PET: Single-photon emission computed tomography/positron emission tomography, TCS: transcranial sonography.

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the world literature on monogenic PD published in the English language, we have tried to be as inclusive as possible. We have set up the project to serve as a growing resource open to all interested participants. Having focused our initial approach on articles published in English is a limitation, as we certainly missed centers engaged in the care of patients with monogenic PD who did not publish on this topic or in a language other than English. This includes predominantly centers from regions with high percentages of underrepresented populations. In order to actively broaden this network and to reach out to active centers that have not yet published on monogenic PD (in English), the MJFF Global Genetic Parkinson's Disease Project is currently being merged within GP2, which presently includes 119 centers that will be approached to join this effort if not yet part of the network. Information on GP2 is already available in several languages (<https://gp2networkdev.wpengine.com/monogenic-resource-map/>), including Arabic, Mandarin, French, German, Japanese, and Spanish. Through this merger, we expect the resource to proliferate and, most importantly, to include an increasing number of previously underrepresented populations and centers.

To facilitate access to this resource and to foster collaboration across centers, as well as between academia and industry, we have developed an interactive map and online tool allowing for a quick overview and descriptive statistics on available data, materials, and facilities, as well as for filtering for specific items of interest, for example, centers who have induced pluripotent stem cell (iPSC) lines of *PRKN* mutation carriers.

We will exploit and expand existing networks through this project and resource to make more clinical and research centers visible and study subjects available to the clinical and basic PD research community. Furthermore, such studies will spur collaborations across global clinical sites and between academia and industry, thus facilitating and expediting the testing of new therapies in relevant PD genetic subtypes. Given the emerging knowledge about disease mechanisms contributing to PD pathogenesis, our hope is that different subpopulations of idiopathic PD subjects would also benefit from these large genetic cohort-based efforts.

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