Genetic screening of South African families with Parkinson's disease

Parkinson's disease (PD) appears to be increasing exponentially throughout the world, including in populations in sub-Saharan Africa.[1] The largest known risk factor for PD is increased age. Other risk factors include exposure to environmental factors (such as pesticides), male sex, a positive family history and genetic factors.[2,3] Over the past three decades, the discoveries of pathogenic variants in a large number of genes have highlighted a genetic component in about one in five people living with PD.[4] These discoveries have led to important insights into the cellular mechanisms that lead to the death of dopaminergic neurons.

Global genetics consortium to screen families with Parkinson's disease

The Global Parkinson's Genetics Program (GP2, http://gp2.org/) is a collaborative effort that has recently been established to improve the understanding on the genetic architecture of PD globally.[5,6] Their emphasis is on families from underrepresented populations.

GP2 is interested in recruiting large families with PD (≥3 affected family members) and families with early-onset disease (i.e. age at onset (AAO) of <50 years). They are also interested in obtaining DNA samples from both parents of an affected individual, as well as of other affected family members.

Acknowledging the rarity of large PD families and the significant efforts to recruit and obtain blood samples from family members for genetic studies, incentives will be provided (https://monogenic.gp2.org/LargeFamilyIncentive.html). Requirements to participate in GP2 include a GP2-approved consenting process, a blood sample from each participant and relevant clinical information (as summarised in Fig. 1). South African (SA) medical professionals with suitable families in collaboration with the researchers at Stellenbosch University will be able to send DNA and relevant patient information to GP2.

Benefits to study participants include:

- genetically-confirmed PD diagnosis and improved clinical management
- patient-centred treatment based on the specific pathogenic variant[7,8]
- if a monogenic cause is identified, presymptomatic testing of family members who could benefit from disease-modifying treatment, when available
- once a causal variant is identified, the proband can possibly enlist in clinical trials targeted at their specific disease-causing gene e.g. inase inhibitors of *LRRK2*, should they become available[9]
- ultimately, these genetic findings may aid in the development of novel and more effective drug treatments for PD.

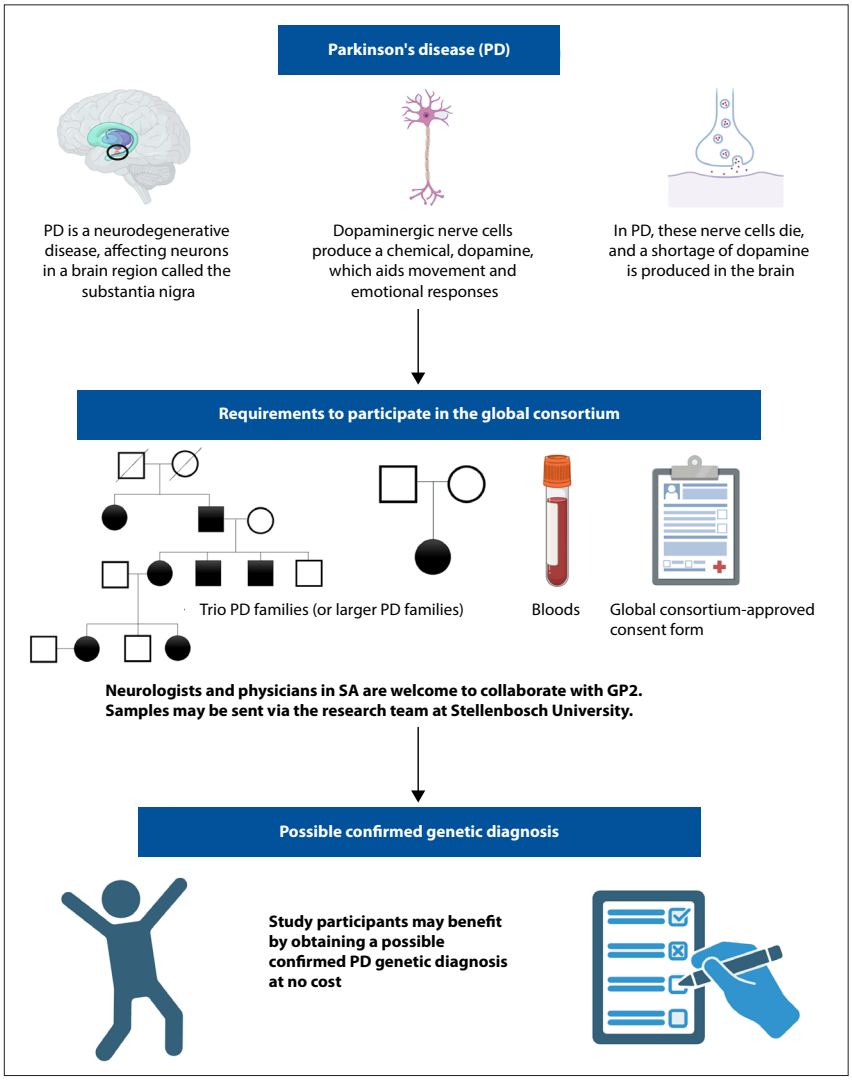

Fig. 1. Flowchart illustrating the South African (SA) Parkinson's Disease Research Group's collaboration with the Global Parkinson's Genetics Program (GP2) to unravel the genetic aetiology of the disorder in SA families.

Notably, individuals of African ancestry are distinguished by the greatest levels of genetic diversity worldwide, owing to them being some of the oldest populations, and adaptation of their genomes to changing climates, varying diets and exposure to transmissible diseases over thousands of years.[10] This genetic diversity may lead to novel genetic discoveries for PD.

In summary, this collaboration with the GP2 consortium aims to raise awareness that PD has a genetic component. Through GP2, SA families with PD can be genetically screened at no cost to the study participants or researchers, and the knowledge gained may be of great benefit to people with PD throughout the world.

Ethics. The research referred to in this editorial was approved by the Human Research Ethics Committee at Stellenbosch University (ref. no. 2002C/059).
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