

SUMMARY

[0005] In one aspect, there is provided a method of identifying whether a subject is at risk of developing PD, whether a subject is suffering from PD, or whether a subject is in need of early therapeutic intervention for PD, the method comprising: a. obtaining a DNA sample from the subject; and b. detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in the sample; wherein the presence of one or more genetic variants identifies that the subject is at risk of developing PD, the subject is suffering from PD, or the subject is in need of early therapeutic intervention for PD.

[0006] In one aspect, there is provided a method of determining the prognosis of a subject with PD or a subject at risk of developing PD, the method comprising: a. obtaining a DNA sample from the subject; and b. detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in the sample; wherein the presence of one or more genetic variants indicates that the subject has a poor prognosis.

[0007] In another aspect, there is provided a method of calculating a polygenic risk score (PRS) of a subject of developing PD, the method comprising the steps of: a. obtaining a DNA sample from the subject; b. detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in the sample; and running genotyping analysis of DNA; and c. measuring the total number of the genetic variants detected in step b to calculate a PRS of a subject of developing PD.

[0007a] In another aspect, there is provided a method of identifying whether a subject is at risk of developing Parkinson's disease (PD), whether a subject is suffering from PD, or whether a subject is in need of early therapeutic intervention for PD, the method comprising detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject, wherein the presence of one or more genetic variants identifies that the subject is at risk of developing PD, the subject is suffering from PD, or the subject is in need of early therapeutic intervention for PD.

[0007b] In another aspect, there is provided a method of determining the prognosis of a subject with PD or a subject at risk of developing PD, the method comprising detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*,
5 *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject, wherein the presence of one or more genetic variants indicates that the subject has a poor prognosis.

[0007c] In another aspect, there is provided a method of calculating a polygenic risk score (PRS) of a subject of developing PD, the method comprising the steps of: a. detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting
10 of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject; and b. measuring the total number of the genetic variants detected in step b to calculate a PRS of a subject of developing PD.

[0008] In another aspect, there is provided a kit comprising one or more reagents to detect
15 the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a sample, together with instructions for use.

[0009] In yet another aspect, there is provided a PD biomarker, wherein the biomarker is a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*,
20 *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of identifying whether a subject is at risk of developing Parkinson's disease (PD), whether a subject is suffering from PD, or whether a subject is in need of early therapeutic intervention for PD, the method comprising detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject, wherein the presence of one or more genetic variants identifies that the subject is at risk of developing PD, the subject is suffering from PD, or the subject is in need of early therapeutic intervention for PD.
2. A method of determining the prognosis of a subject with PD or a subject at risk of developing PD, the method comprising detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject, wherein the presence of one or more genetic variants indicates that the subject has a poor prognosis.
3. The method of claims 1 or 2, wherein the method further comprises detecting the presence of a genetic variant at the loci of one or more genes selected from *ILIR2*, *SCN3A*, *SATB1*, *NCKIPSD*, *CDC71*, *ALAS1*, *TLR9*, *DNAH1*, *BAP1*, *PHF7*, *NISCH*, *STAB1*, *ITIH3*, *ITIH4*, *ANK2*, *CAMK2D*, *ELOVL7*, *ZNF184*, *CTSB*, *SORBS3*, *PDLIM2*, *C8orf58*, *BIN3*, *SH3GL2*, *FAM171A1*, *GALC*, *COQ7*, *TOX3*, *ATP6V0A1*, *PSMC3I*, *TUBG2*, *GBA-SYT11*, *RAB7L1-NUCKS1*, *SIPAIL2*, *ACMSD-TMEM163*, *STK39*, *KRT8P25-APOOP2*, *NMD3*, *TMEM175-GAK-DGKQ*, *BST1*, *HLA-DQB1*, *GPNMB*, *FGF20*, *MMP16*, *ITGA8*, *INPP5F*, *MIR4697*, *LRRK2*, *CCDC62*, *GCH1*, *TMEM229B*, *VPS13C*, *BCKDK-STX1B*, *SREBF1-RAII*, *MAPT*, *SPPL2B*, *DDRGK1*, *USP25*, *FCGR2A*, *VAMP4*, *KCNS3*, *KCNIP3*, *LINC00693*, *KPNA1*, *MED12L*, *SPTSSB*, *LCORL*, *CLCN3*, *PAM*, *C5orf24*, *TRIM40*, *RIMS1*, *RPS12*, *GS1-124K5.11*, *FAM49B*, *UBAP2*, *GBF1*, *RNF141*, *SCAF11*, *FBRSL1*, *CAB39L*, *MBNL2*, *MIPOL1*, *RPS6KL1*, *CD19*, *NOD2*, *CNOT1*, *CHRNA1*, *UBTF*, *FAM171A2*, *BRIPI*, *DNAH17*, *ASXL3*, *MEX3C*, *CRLS1*, *DYRK1A* and combinations thereof.

4. A method of calculating a polygenic risk score (PRS) of a subject of developing PD, the method comprising the steps of:
 - a. detecting the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCC1*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a DNA sample obtained from the subject; and
 - b. measuring the total number of the genetic variants detected in step b to calculate a PRS of a subject of developing PD.
5. The method of claim 4, further comprising detecting the presence of a genetic variant and measuring the total number of genetic variants at the loci of one or more genes selected from the group consisting of *ILIR2*, *SCN3A*, *SATB1*, *NCKIPSD*, *CDC71*, *ALAS1*, *TLR9*, *DNAH1*, *BAP1*, *PHF7*, *NISCH*, *STAB1*, *ITIH3*, *ITIH4*, *ANK2*, *CAMK2D*, *ELOVL7*, *ZNF184*, *CTSB*, *SORBS3*, *PDLIM2*, *C8orf58*, *BIN3*, *SH3GL2*, *FAM171A1*, *GALC*, *COQ7*, *TOX3*, *ATP6V0A1*, *PSMC3L*, *TUBG2*, *GBA-SYT11*, *RAB7L1-NUCKS1*, *SIPA1L2*, *ACMSD-TMEM163*, *STK39*, *KRT8P25-APOOP2*, *NMD3*, *TMEM175-GAK-DGKQ*, *BST1*, *HLA-DQB1*, *GPNMB*, *FGF20*, *MMP16*, *ITGA8*, *INPP5F*, *MIR4697*, *LRRK2*, *CCDC62*, *GCH1*, *TMEM229B*, *VPS13C*, *BCKDK-STX1B*, *SREBF1-RAI1*, *MAPT*, *SPPL2B*, *DDRKG1*, *USP25*, *FCGR2A*, *VAMP4*, *KCNS3*, *KCNIP3*, *LINC00693*, *KPNA1*, *MED12L*, *SPTSSB*, *LCORL*, *CLCN3*, *PAM*, *C5orf24*, *TRIM40*, *RIMS1*, *RPS12*, *GS1-124K5.11*, *FAM49B*, *UBAP2*, *GBF1*, *RNF141*, *SCAF11*, *FBRSL1*, *CAB39L*, *MBNL2*, *MIPOL1*, *RPS6KL1*, *CD19*, *NOD2*, *CNOT1*, *CHRNBI*, *UBTF*, *FAM171A2*, *BRIP1*, *DNAH17*, *ASXL3*, *MEX3C*, *CRLS1*, *DYRK1A* and combinations thereof.
6. The method of claims 4 or 5, wherein the total number of genetic variants is weighted by the effect size of each variant.
7. The method of any one of claims 4-6, wherein the PRS of the subject is compared with PRSs in a reference population to determine the percentile risk of the subject's risk of developing PD.

8. The method of claim 7, wherein a subject with a higher percentile PRS has a higher risk of developing PD compared to a subject with lower percentile PRS.
9. The method of any one of claims 1-8, wherein the one or more genetic variants is a polymorphism, optionally wherein the polymorphism is a SNP or SNV.
10. The method of claim 9, wherein the genetic variant is an effect allele or risk allele of the SNP or SNV.
11. The method of any one of claims 1-10, wherein the genetic variant is a SNP selected from the group consisting of rs6826785, rs141336855, rs6679073, rs2292056, rs16846351, rs3816248, rs12278023, rs9638616, rs1887316, rs246814, rs31244, rs4130047 and combinations thereof.
12. The method of claim 11, wherein the effect allele of rs6826785 is cytosine (C), the effect allele of rs141336855 is thymine (T), the effect allele of rs6679073 is adenine (A), the effect allele of rs2292056 is guanine (G), the effect allele of rs16846351 is guanine (G), the effect allele of rs3816248 is cytosine (C), the effect allele of rs12278023 is cytosine (C), the effect allele of rs9638616 is thymine (T), the effect allele of rs1887316 is adenine (A), the effect allele of rs246814 is thymine (T), the effect allele of rs31244 is guanine (G), and the effect allele of rs4130047 is cytosine (C).
13. The method of claims 3 or 5, wherein the genetic variant is a SNP selected from the group consisting of rs34043159, GSA-rs353116, rs4073221, rs12497850, rs143918452, rs78738012, rs2694528, rs9468199, rs2740594, rs2280104, rs13294100, rs10906923, rs8005172, rs11343, rs4784227, rs601999, rs35749011, rs10797576, rs6430538, rs1474055, rs115185635, rs34016896, rs34311866, rs11724635, rs9275326, rs199347, rs591323, rs60298754, rs7077361, rs117896735, rs329648, rs11060180, rs11158026, rs1555399, rs2414739, rs14235, rs11868035, rs17649553, rs113579895, rs62120679, rs8118008, rs2823357, rs6658353, rs11578699, rs76116224, rs2042477, rs6808178, rs55961674, rs11707416, rs1450522, rs34025766, rs62333164, rs26431, rs11950533, rs9261484, rs12528068, rs75859381, rs76949143,

rs2086641, rs6476434, rs10748818, rs7938782, rs7134559, GSA-rs11610045, rs9568188, rs4771268, rs12147950, rs3742785, rs2904880, rs6500328, rs200564078, rs12600861, rs2269906, rs850738, rs61169879, rs666463, rs1941685, rs8087969, rs77351827, rs2248244, rs4613239, rs1474055 and combinations thereof.

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14. The method of any one of the preceding claims, wherein the subject is of Asian ethnicity or ancestry.

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15. The method of claim 14, wherein the subject is of Han Chinese ancestry or Chinese ethnicity or ancestry with no mixed ancestry, or a South Korean ethnicity or ancestry.

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16. A kit comprising one or more reagents to detect the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCC1*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof in a sample, together with instructions for use.

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17. The kit of claim 16, further comprising reagents to detect the presence of a genetic variant at the loci of one or more genes selected from the group consisting of *ILIR2*, *SCN3A*, *SATB1*, *NCKIPSD*, *CDC71*, *ALAS1*, *TLR9*, *DNAH1*, *BAP1*, *PHF7*, *NISCH*, *STAB1*, *ITIH3*, *ITIH4*, *ANK2*, *CAMK2D*, *ELOVL7*, *ZNF184*, *CTSB*, *SORBS3*, *PDLIM2*, *C8orf58*, *BIN3*, *SH3GL2*, *FAM171A1*, *GALC*, *COQ7*, *TOX3*, *ATP6V0A1*, *PSMC3I*, *TUBG2*, *GBA-SYT11*, *RAB7L1-NUCKS1*, *SIPA1L2*, *ACMSD-TMEM163*, *STK39*, *KRT8P25-APOOP2*, *NMD3*, *TMEM175-GAK-DGKQ*, *BST1*, *HLA-DQB1*, *GPNMB*, *FGF20*, *MMP16*, *ITGA8*, *INPP5F*, *MIR4697*, *LRRK2*, *CCDC62*, *GCH1*, *TMEM229B*, *VPS13C*, *BCKDK-STX1B*, *SREBF1-RAII*, *MAPT*, *SPPL2B*, *DDRGK1*, *USP25*, *FCGR2A*, *VAMP4*, *KCNS3*, *KCNIP3*, *LINC00693*, *KPNA1*, *MED12L*, *SPTSSB*, *LCORL*, *CLCN3*, *PAM*, *C5orf24*, *TRIM40*, *RIMS1*, *RPS12*, *GS1-124K5.11*, *FAM49B*, *UBAP2*, *GBF1*, *RNF141*, *SCAF11*, *FBRSL1*, *CAB39L*, *MBNL2*, *MIPOL1*, *RPS6KL1*, *CD19*, *NOD2*, *CNOT1*, *CHRNA1*, *UBTF*, *FAM171A2*, *BRIPI*, *DNAH17*, *ASXL3*, *MEX3C*, *CRLS1*, *DYRK1A* and combinations thereof.

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18. The kit of claim 16 or 17, wherein the one or more reagents comprises a reagent to isolate a nucleic acid from the sample and at least one primer and/or at least one probe for amplification of a sequence encoding the genetic variant or part thereof.

19. The kit of any one of claims 16-18 for identifying whether a subject is at risk of developing PD, whether a subject is suffering from PD, whether a subject is in need of early therapeutic intervention for PD, determining the prognosis of a subject with PD or a subject at risk of developing PD, calculating a PRS of a subject of developing PD, or combinations thereof.
20. A PD biomarker, wherein the biomarker is a genetic variant at the loci of one or more genes selected from the group consisting of *SV2C*, *WBSCR17*, *PARK16*, *ITPKB*, *MCCCI*, *SNCA*, *FAM47E-SCARB2*, *FYN*, *DLG2*, *LRRK2*, *RIT2* and combinations thereof.