

Fig. 1

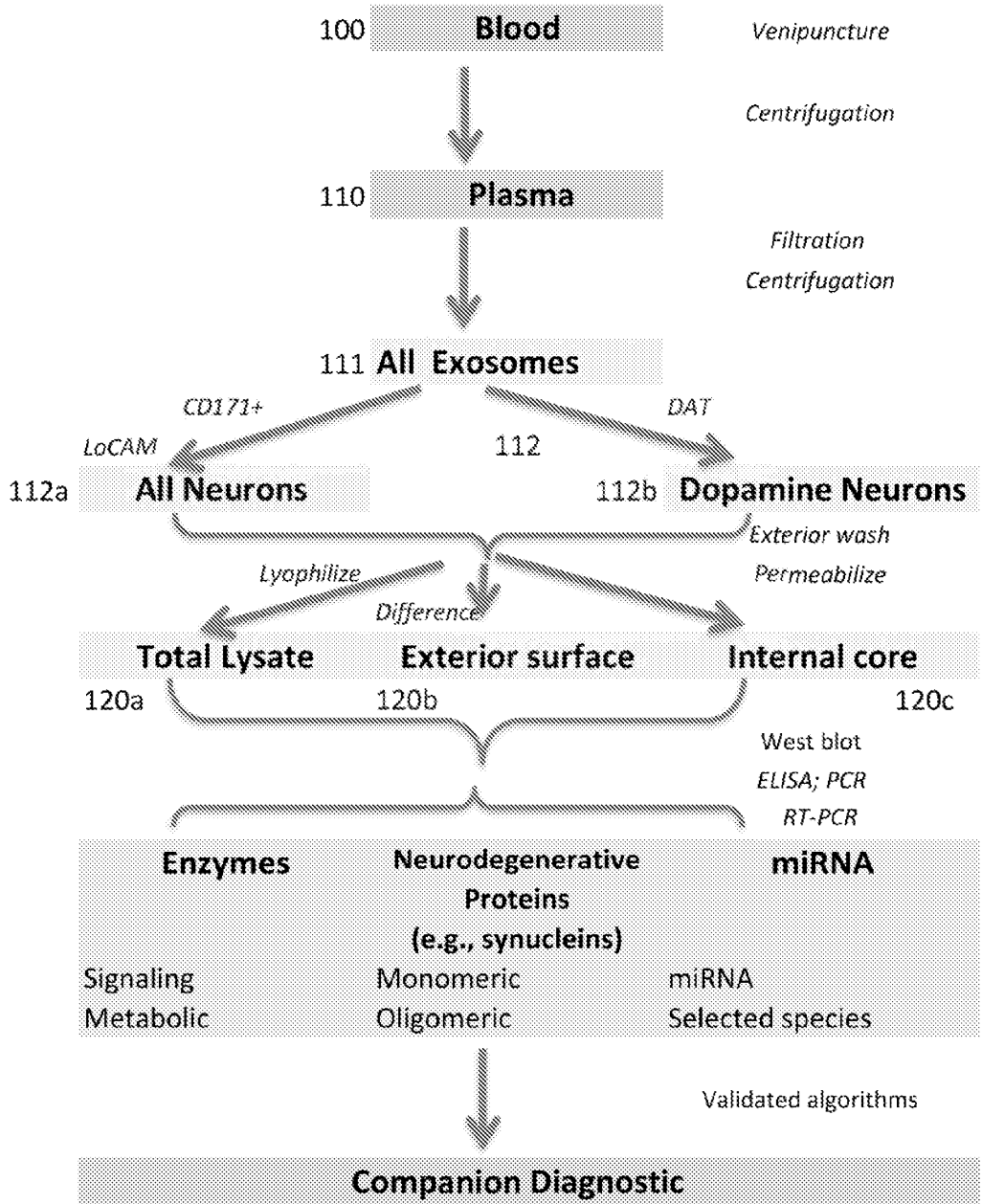


Fig. 2

- Enroll subjects with diagnosis of neurodegenerative condition
 - E.g., synucleopathic condition, amyloidopathic condition, tauopathic condition, or Huntington's disease
- 2. Determine baseline level of biomarkers in neuronally-derived microparticles from venous blood of subjects
- 3. Administer different therapeutic interventions to different test groups (drug/placebo; different dosages for determined period)
- 4. Determine safety at regular intervals
- 5. Determine level of biomarkers at plurality of time points
- 6. Determine efficacy of therapeutic intervention

Fig. 3

Training Dataset

Subject	Neurodegenerative Diagnosis	Enzymes				Neurodegenerative Proteins			microRNAs	
		Kinases		Metabolic		Monomeric	Oligomeric		miRNA1	miRNA2
		Kinase 1	Kinase 2	Metabolic 1	Metabolic 2					
1	+	A ₁	B ₁	C ₁	D ₁	...	K ₁	L ₁	Y ₁	Z ₁
2	+	A ₂	B ₂	C ₂	D ₂	...	K ₂	L ₂	Y ₂	Z ₂
3	...	A ₃	B ₃	C ₃	D ₃	...	K ₃	L ₃	Y ₃	Z ₃
...	...	...	...	...	...	...	...	...	...	...
N-1	-	A _{n-1}	B _{n-1}	C _{n-1}	D _{n-1}	...	K _{n-1}	L _{n-1}	Y _{n-1}	Z _{n-1}
N	-	A _n	B _n	C _n	D _n	...	K _n	L _n	Y _n	Z _n

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Learning Algorithm

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Model

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Validation

Fig. 4

- 1. Provide a biological sample from a subject.
- 2. Enriched sample for neuronally-derived exosomes.
- 3. Collect contents of an internal compartment of the exosomes.
- 4. Measure set of biomarkers including: (1) at least one signaling kinase and at least one oligomeric form of a neurodegenerative protein; or (2) a plurality of different signaling kinases in the exosomes to produce a test dataset.

Subject	Enzymes				Neurodegenerative Proteins			microRNAs		
	Kinases		Metabolic		Monomeric Oligomeric					
Test	Kinase 1	Kinase 2	Metabolic 1	Metabolic 2				miRNA1	miRNA2	
	A ₁	B ₁	C ₁	D ₁	...	K ₁	L ₁	Y ₁	Z ₁	...

- a) Positive for Parkinson’s disease or negative for Parkinson’s disease;
- b) Parkinson’s disease: Stage 1 – mild; Stage 2 – moderate; Stage 3 – middle stage; Stage 4-severe; Stage 5 – advanced
- c) Subject’s disease is progressing, or subject’s disease is not progressing
- d) Response to putative neuroprotective agent or does not respond to putative neuroprotective agent.
- e) Subject is at risk of developing neurodegenerative disease or subject is not at risk of developing neurodegenerative disease (qualify by degree of risk)
- f) Subject has good prognosis or subject has poor prognosis (qualify by degree of positive or negative prognosis)

Fig. 5
Signal Transduction Mechanisms
Implicated in Pathogenesis/Treatment of PD

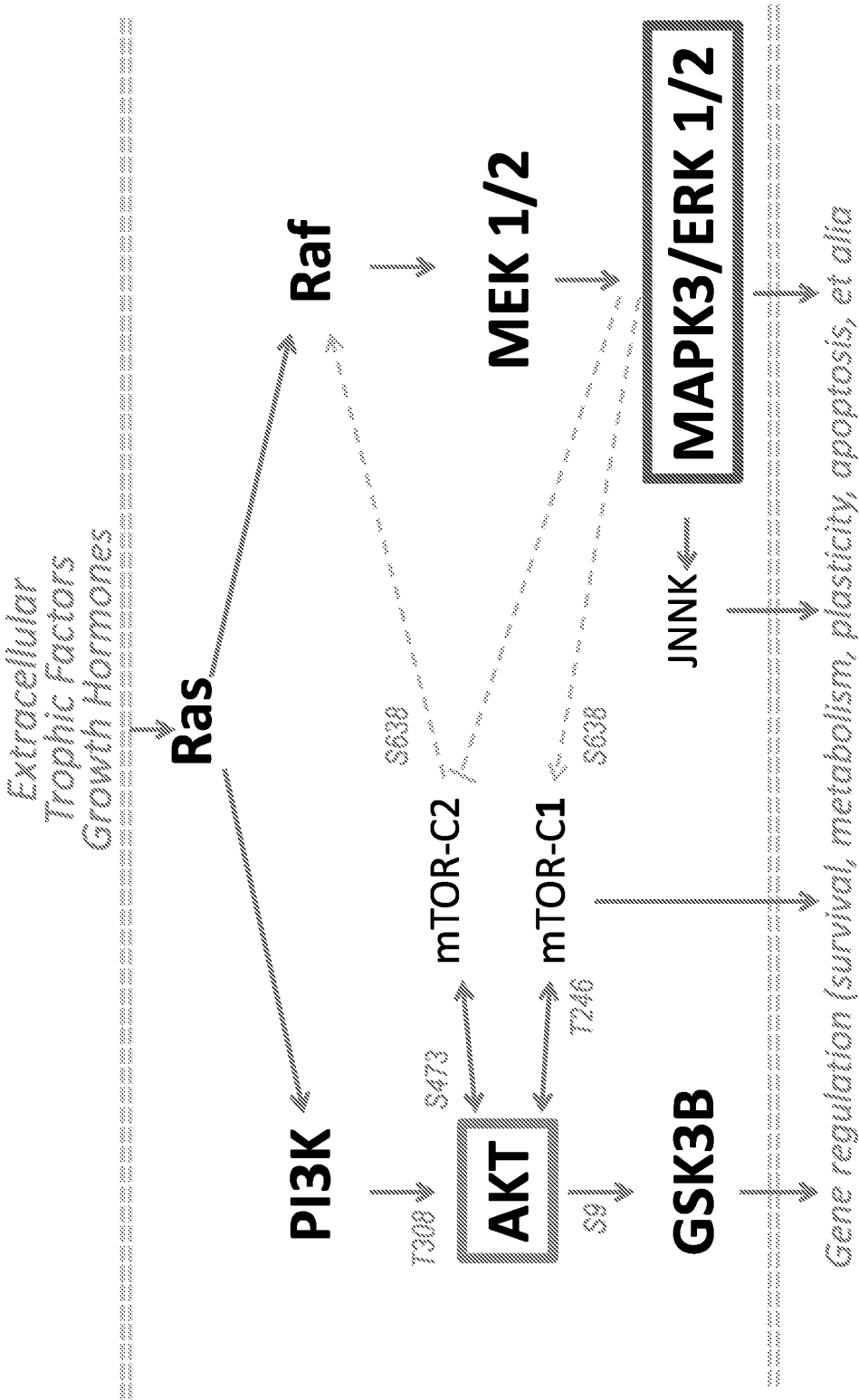


Fig. 6

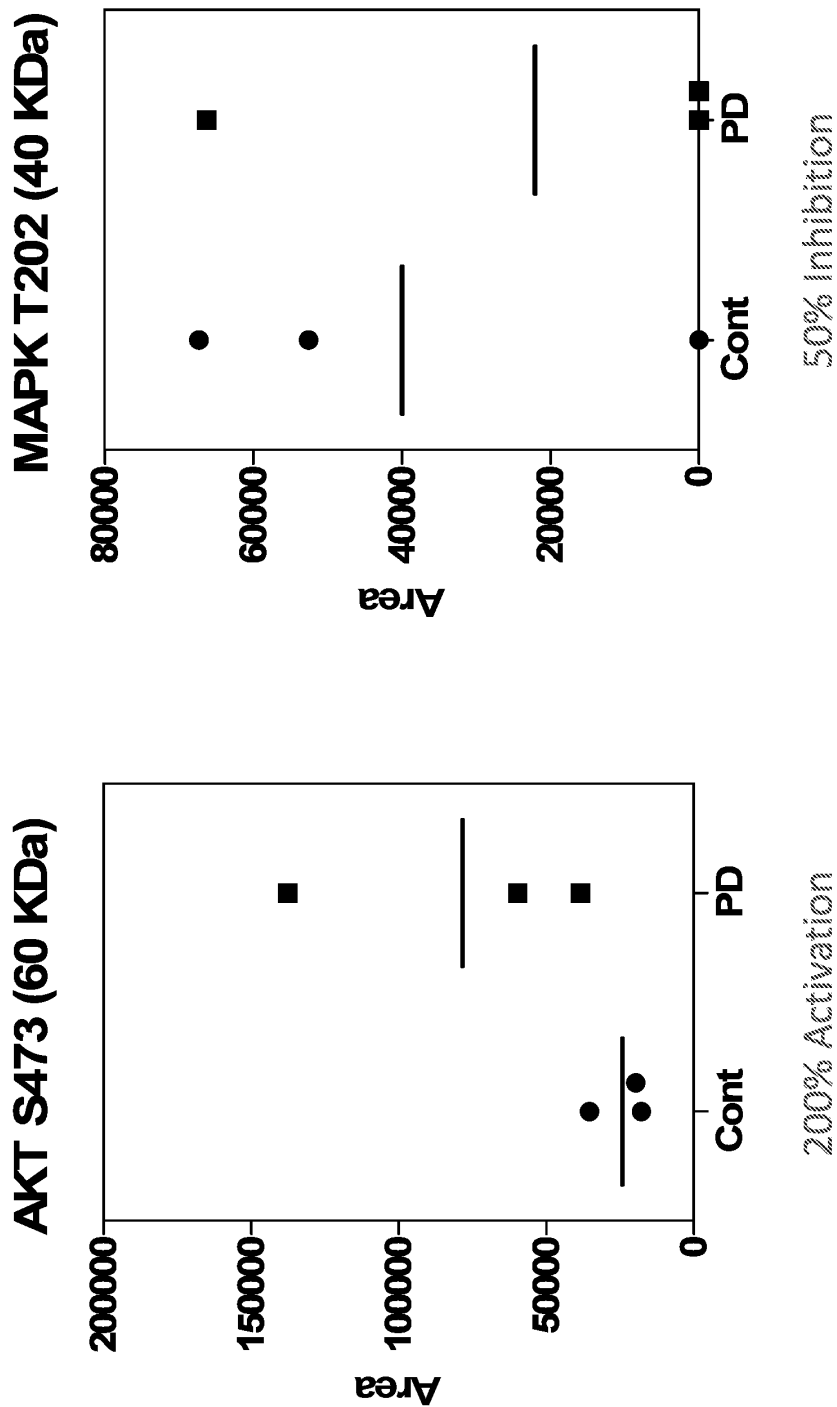


Fig. 7

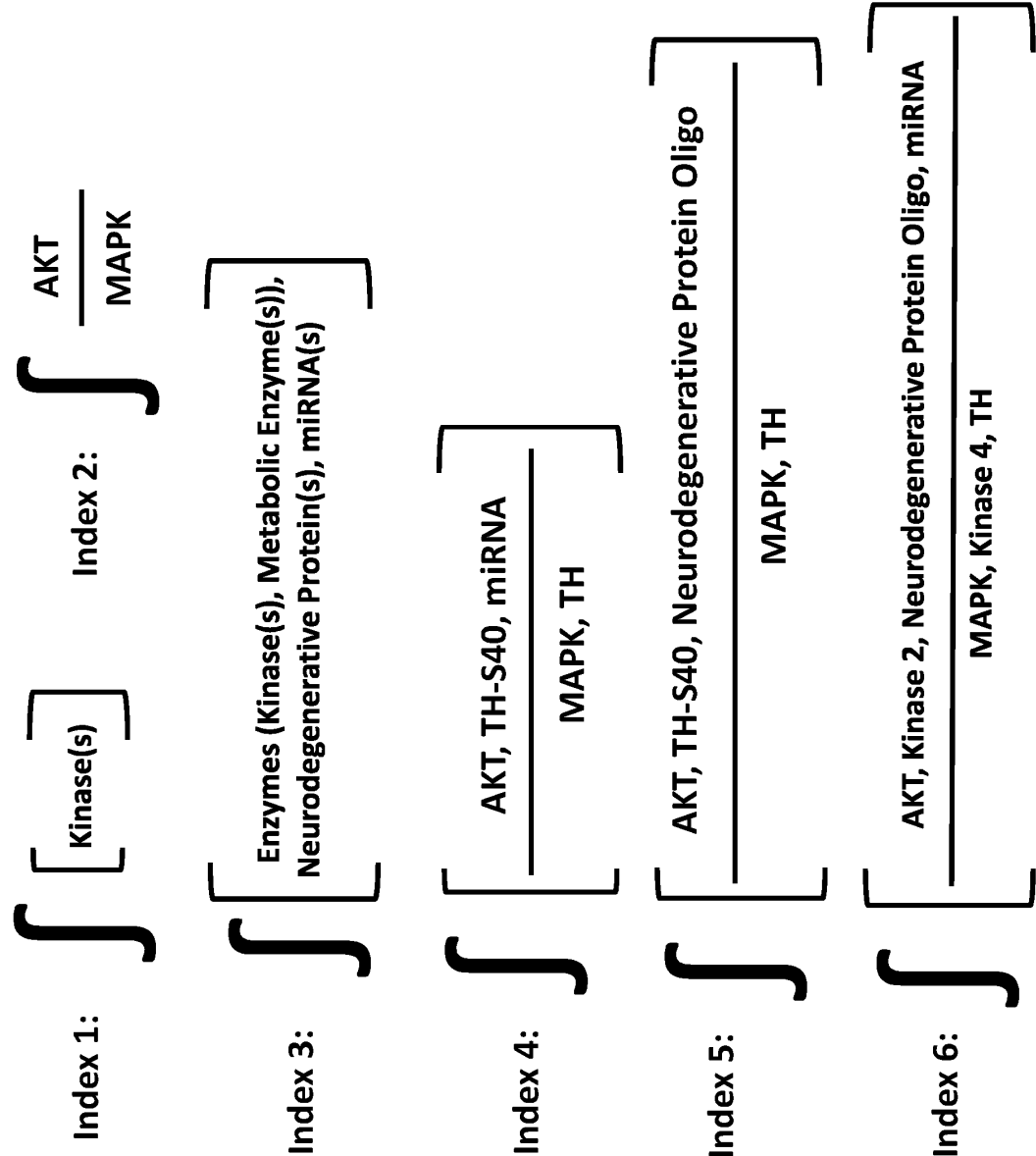


FIG. 8

