

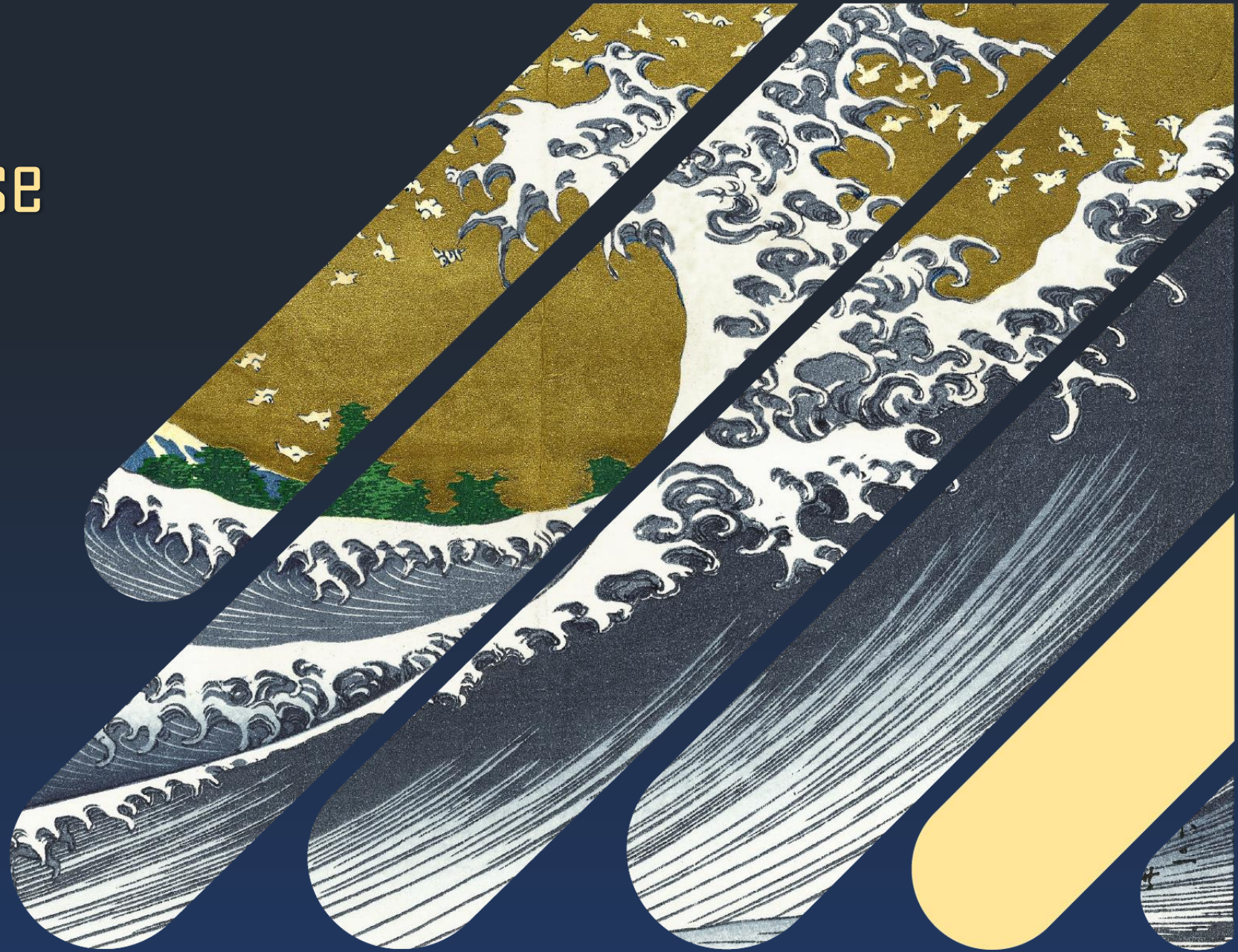
Parkinson's Disease and the Silver Tsunami

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Neuroregeneration and
Stem Cell Programs

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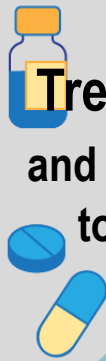


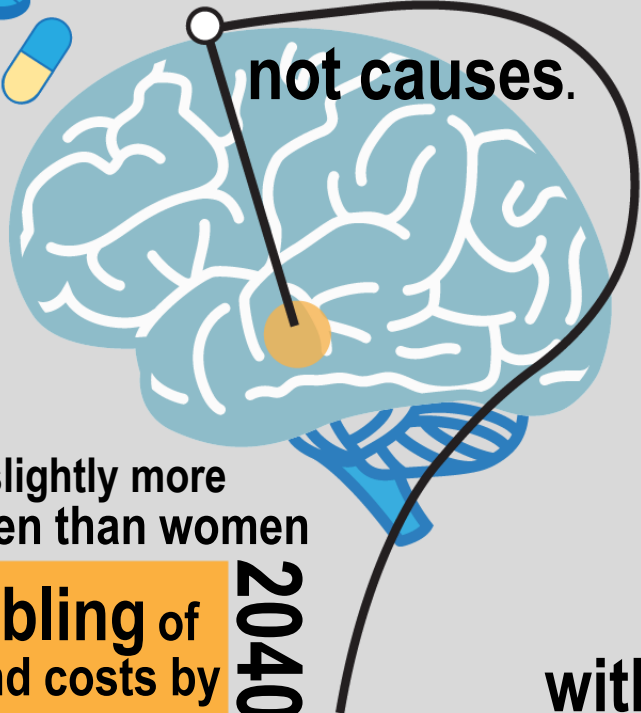
Parkinson's Disease

cost exceeds
\$14.4 BILLION
each year



0.5-1.5 MILLION PEOPLE ~50,000 USA new cases are reported annually

 **Treatments: Drug therapy and deep-brain stimulation to alleviate symptoms, but not causes.**



Average age of onset
60 yo

Onset as early
2 yo



Appears to be slightly more common in men than women

Expectation of a **doubling** of Parkinson's patients and costs by **2040**

Both prevalence and incidence **increase** with advancing age





1. Billy Connolly (b. 1942-)

Scottish comedian, musician, presenter and actor

By <https://www.flickr.com/photos/evarinaldiphography/7175840985/>, CC BY-SA 2.0, <https://commons.wikimedia.org/w/index.php?curid=19858385>

2. Brock Adams (1927-2004)

American politician

By Unknown. This work is free and may be used by anyone for any purpose.

3. Brian Grant (b. 1972-)

American basketball player

(Nov. 20, 2009 - Source: Theo Wargo/Getty Images North America)

4. Alex Hill (b. 1994-)

Diagnosed with Parkinson's disease at just 11-years-old

By Sarah Hill, retrieved from <http://www.bbc.com/news/stories-43717714>

5. Bob Hoskins (1942–2014)

English actor

By Bob hoskins filming ruby blue.jpg: James Laurence Stewartderivative work: KoS (talk) - Bob hoskins filming ruby blue.jpg, CC BY 2.0, <https://commons.wikimedia.org/w/index.php?curid=6558597>

6. Billy Graham (1918–2018)

American evangelist

By Warren K. Leffler - This image is available from the United States Library of Congress's Prints and Photographs division under the digital ID ppmc.03261

7. Keegan Mclellan (b. 2014-)

Diagnosed with Parkinson's disease at just 2-years-old

Retrieved from <http://parkinsonslife.eu/two-year-old-could-be-worlds-youngest-person-diagnosed-with-parkinsons/>

8. Estelle Getty (1923-2008)(LBD)

American actress and comedian

By Alan Light, CC BY 2.0, <https://commons.wikimedia.org/w/index.php?curid=2142952>

9. Gunther von Hagens (b. 1945-)

German anatomist who invented the technique for preserving biological tissue specimens called plastination

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10. Linda Ronstadt (b. 1946-)

Grammy award -winning singer

By Carl Lender, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=5906167>

11. Pope John Paul II (1920–2005)

Polish cleric, Pope of the Catholic Church and sovereign of Vatican City 1978-2005

By Uncredited; retouch of Image:JohannesPaulII.jpg - Public Papers of the Presidents of the United States - Photographic Portfolio--1993 Vol. II Public Domain

12. Michael J Fox (b. 1961-)

Canadian/American actor, author, producer, and activist

Parkinson's Disease Is More Than A Movement Disorder

Intracytoplasmic inclusions termed Lewy bodies containing α -synuclein.

Hyposmia

Substantia nigra not first site of injury in PD, Lewy neurites found in olfactory bulb & autonomic nervous system.

Heart Rate Variability

- **REM Sleep BD**
- **Anxiety**
- **Depression**
- **Dementia**

Widespread neuropathology through multiple neuronal systems.

Constipation

Severity progresses over time

Stooped posture

Slow movement (bradykinesia)

Inability to move (akinesia)

Postural instability, loss of balance

Sexual difficulties

Shuffling gait

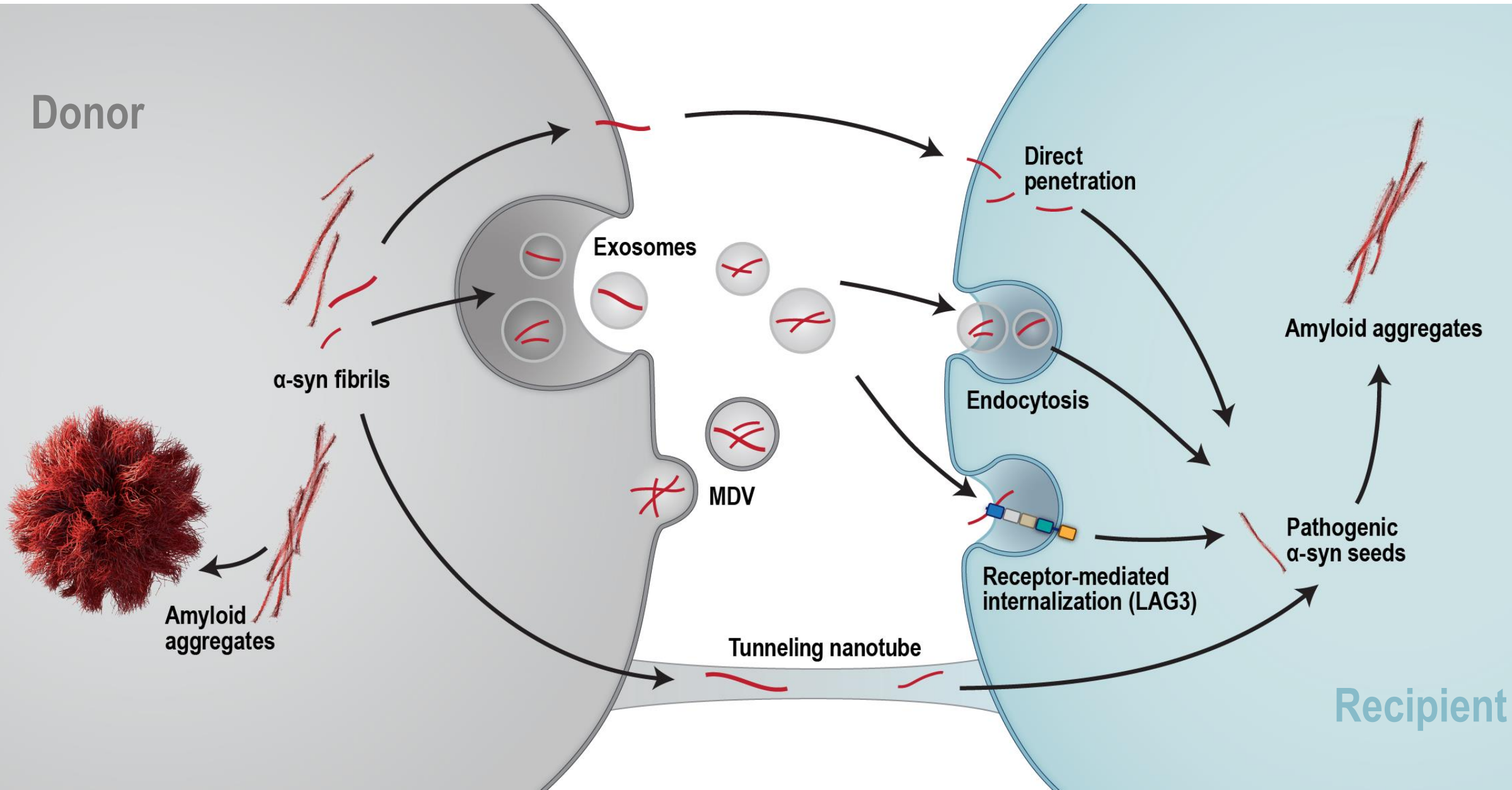
Rigid limbs, Reduced facial expressions

Speech impairments

Often, the first diagnosed symptom of Parkinson's disease is **tremor (trembling or shaking) of a limb.**



Propagation and Transmission of Pathogenic Proteins



Scientific Approach

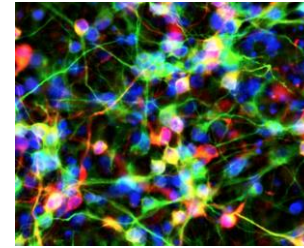


Patient
Sporadic
Familial – Gene mutations

CSF
Postmortem Brain Tissue
Dermal Fibroblasts



Human Cortical Cultures
Human Dopaminergic Cultures
Human Microglia
Human Astrocytes



PFF Mouse Models (Sporadic)
Intrastratial
Gut to Brain
Genetically Engineered Mice (Familial)



Mouse Neuronal Cultures

Drosophila



Cell lines



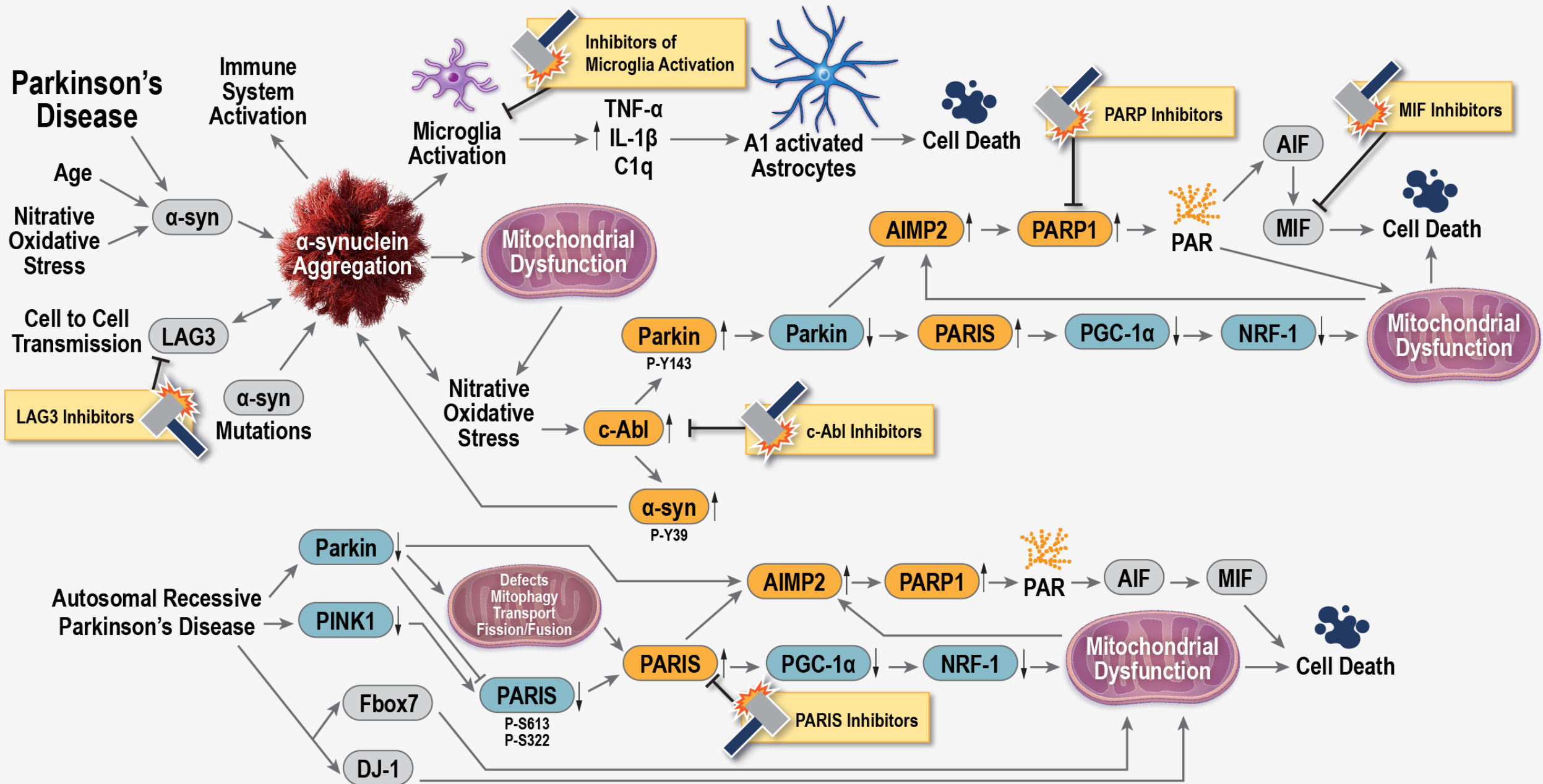
Genomics
Proteomics
Cell Biology
Behavior

Define Pathways
Identify Targets
Primary versus Secondary

Identify New Therapeutic Approaches to Test
Assay Development and Target Engagement

Develop Biomarkers
Develop Imaging Tools

Pathways of Neurodegeneration in Parkinson's Disease



In Development



- **Neuroimaging**
- **Biomarkers**
- **LAG3 Inhibitors**
- **c-Abl Inhibitors**
- **Inhibitors of Microglia Activation**
- **PARP Inhibitors**
- **PARIS Inhibitors**
- **MIF Inhibitors**