



WELCOME TO EXPERT BRIEFINGS

Research Update: Working to Halt Parkinson's

- The program will begin at the hour.
- Participants will be muted and off video.

Better Lives. Together.



Welcome

Crista Ellis

Manager, Community Engagement
Parkinson's Foundation

Better Lives. Together.

Our Mission



The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure. In everything we do, we build on the energy, experience and passion of our global Parkinson's community.

We have everything you need to live better with Parkinson's.



Better Lives. Together.



APRIL IS

PARKINSON'S AWARENESS MONTH!

This year, we're learning the:

ABCs DEFG
HIJKL **of PD**
RSTUVWXY

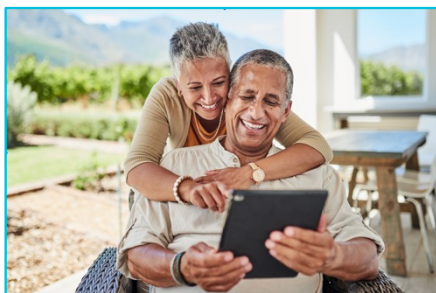
[Parkinson.org/Awareness](https://www.parkinson.org/Awareness)

Today's webinar sponsor



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PD Health @ Home



Weekly, virtual programs:

- Mindfulness Mondays
- Wellness Wednesdays
- Fitness Fridays
- EP Salud en Casa

Visit [Parkinson.org/PDhealth](https://www.parkinson.org/PDhealth) to learn more and register

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Poll: Getting to Know You



What best describes your connection to Parkinson's disease?

- Person with PD
- Spouse/Partner
- Parent has/had PD
- Other family
- Healthcare Professional
- Physician/Clinician
- Scientist/Researcher
- Nurse/Nurse Practitioner
- Other

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For Your Convenience



Recording

Expert Briefings are recorded and archived on www.Parkinson.org/ExpertBriefings



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Meet Your Expert



Lorraine V. Kalia, MD, PhD, FRCPC

- Associate Professor and Clinician Scientist
- Division of Neurology, University of Toronto
- Senior Scientist, Krembil Research Institute, University Health Network
- Wolfond-Krembil Chair in Parkinson's Disease Research
- Co-Editor-in-Chief, Journal of Parkinson's Disease

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A graphic with a bright blue background. In the center, a white ribbon banner with a dotted pattern contains the words 'THANK YOU' in bold, blue, sans-serif capital letters. The banner is surrounded by white radiating lines, creating a sunburst effect.

THANK YOU

Research Update: Working to Halt PD

Lorraine Kalia, MD, PhD, FRCPC

Wolfond-Krembil Chair in Parkinson's Disease Research
Staff Neurologist, Movement Disorders Clinic, Toronto Western Hospital
Associate Professor, Division of Neurology, University of Toronto
Senior Scientist, Krembil Research Institute, University Health Network

April 10, 2024

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Disclosures

- **Consultancy:** AC Immune, Allergan/AbbVie, Cure Ventures, Ipsen, Knight Therapeutics, Right Brain Bio, and UCB
- **Honoraria:** IOS Press/Sage, Novo Nordisk, Sun Pharma, and Takeda

April is Parkinson's Awareness Month & April 11 is World Parkinson's Day



<https://ncc-ccn.gc.ca/places/tulips-in-the-capital#>

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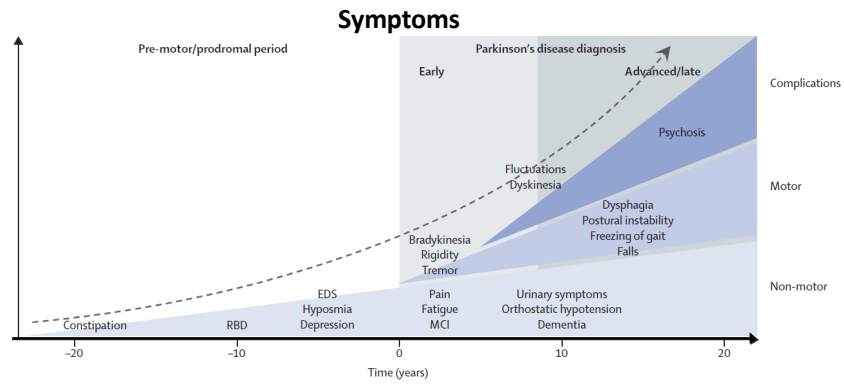
Learning objectives

- Discuss **advancements** in disease-modifying approaches for PD, including pharmacologic and non-pharmacologic measures
- Understand the **challenges** in advancing toward disease-modifying therapies

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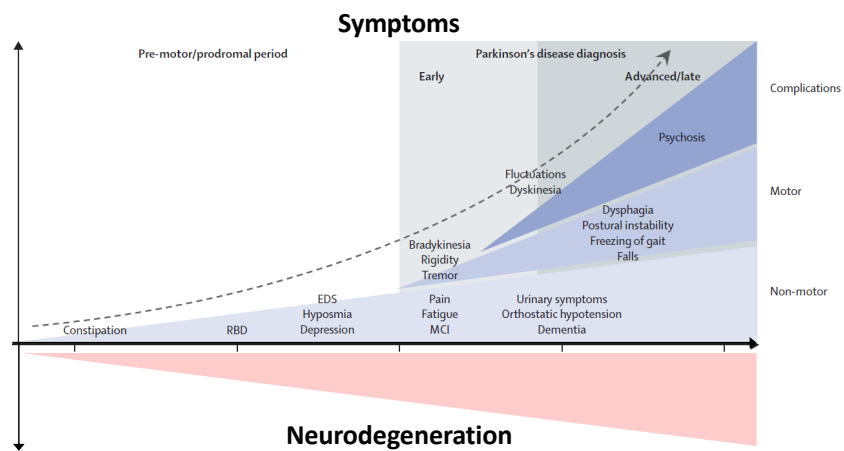
3

PD is a progressive disease



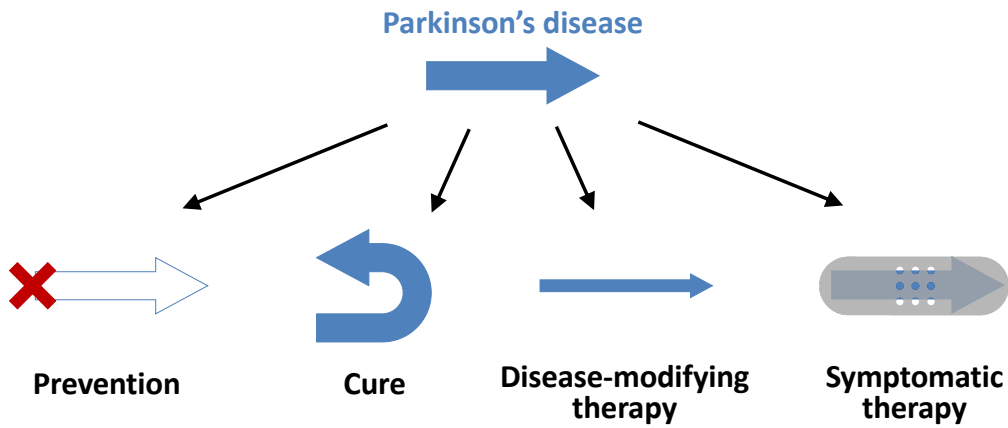
Modified from Kalia and Lang. *Lancet* 2015

PD is a progressive disease

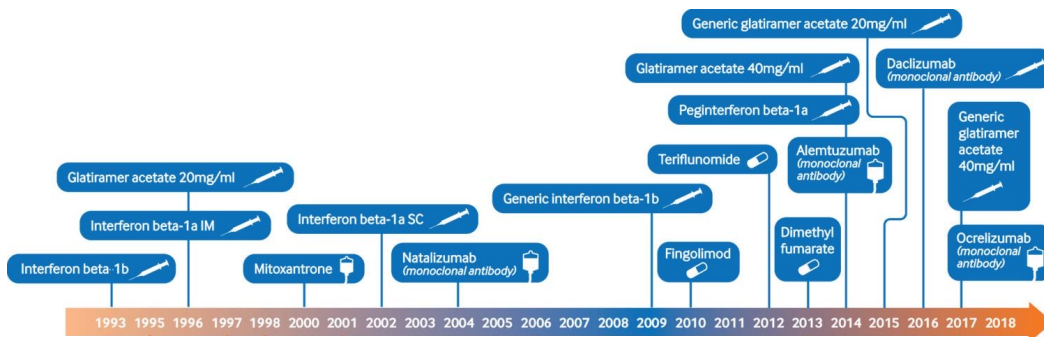


Modified from Kalia and Lang. *Lancet* 2015

Strategies to tackle PD progression



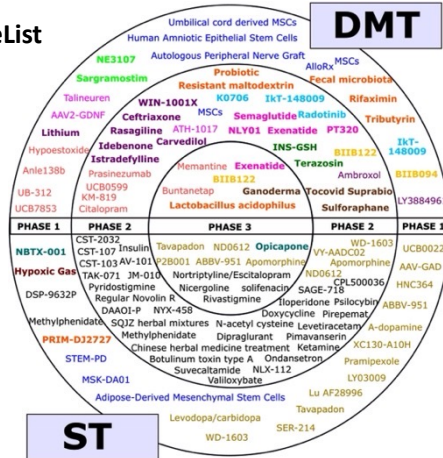
Disease-modifying therapies (DMTs)



Modified from De Angelis et al. *BMJ* 2018

Disease-modifying therapies (DMTs)

bit.ly/ParkinsonsHopelist



McFarthing et al. *Journal of Parkinson's Disease* 2023

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Learning objectives

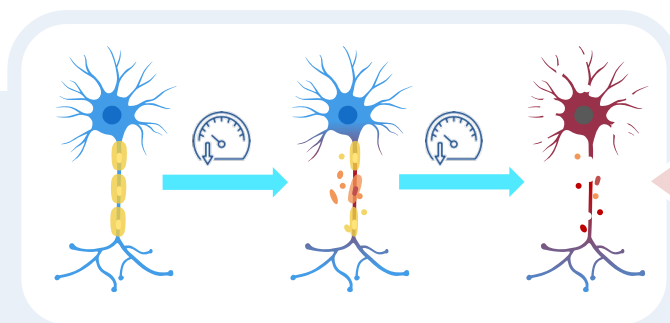
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Advancements in DMTs for PD

- Exercise
- α -Synuclein
- GBA1
- LRRK2
- Repurposed drugs
- Stem cells

Advancements in DMTs for PD



Neurodegeneration

Cell protection

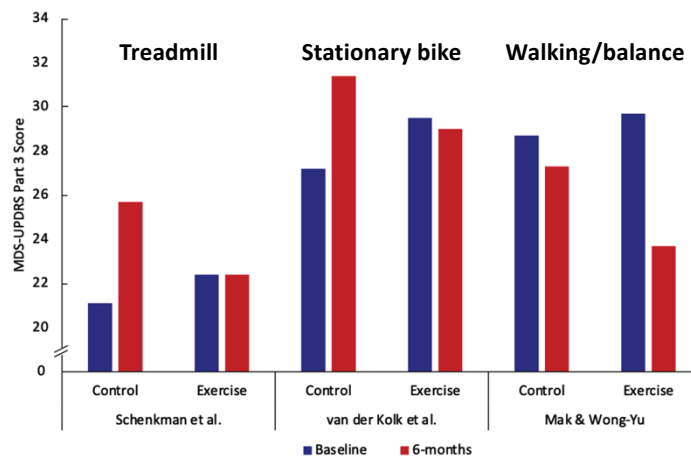
Exercise

What are the benefits of exercise?

- Improves cardiorespiratory fitness
- Improves muscle and bone health
- Improves cognitive and mental health
- Reduces risk of fractures and falls
- Reduces risk of hypertension, diabetes, heart disease, cancer
- Provides cell protection?

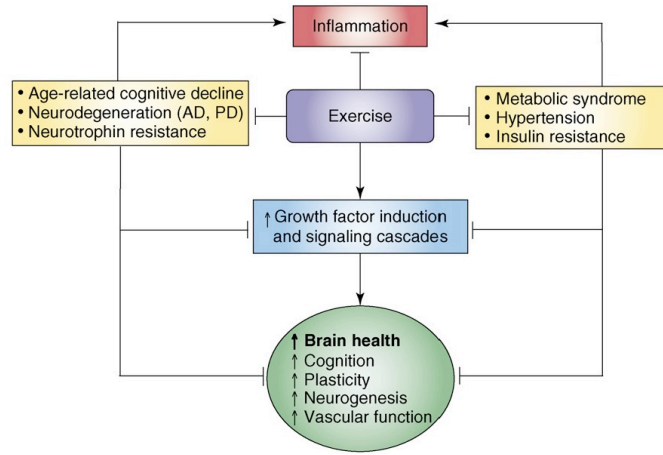
World Health Organization (WHO). <https://www.who.int/news-room/fact-sheets/detail/physical-activity>

Exercise



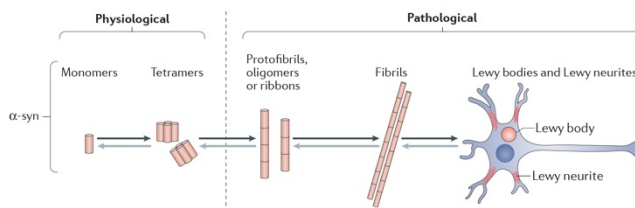
Corcos et al. *Journal of Parkinson's Disease* 2024

Exercise



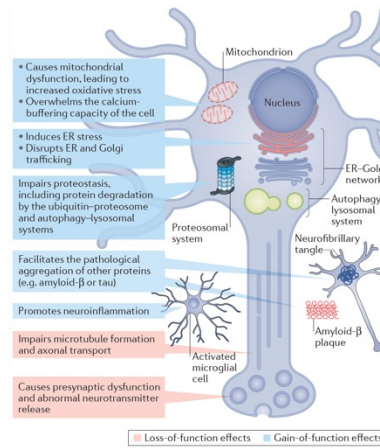
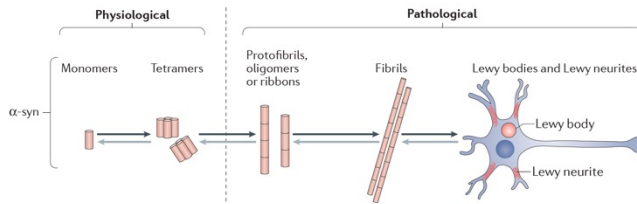
Cotman et al. *Trends in Neuroscience* 2007

α -Synuclein



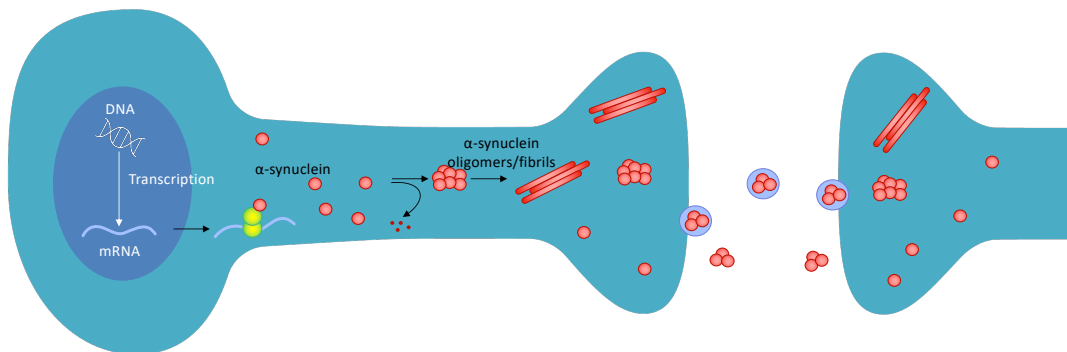
Modified from Koprach, Kalia, and Brochie. *Nature Reviews Neuroscience* 2017

α -Synuclein



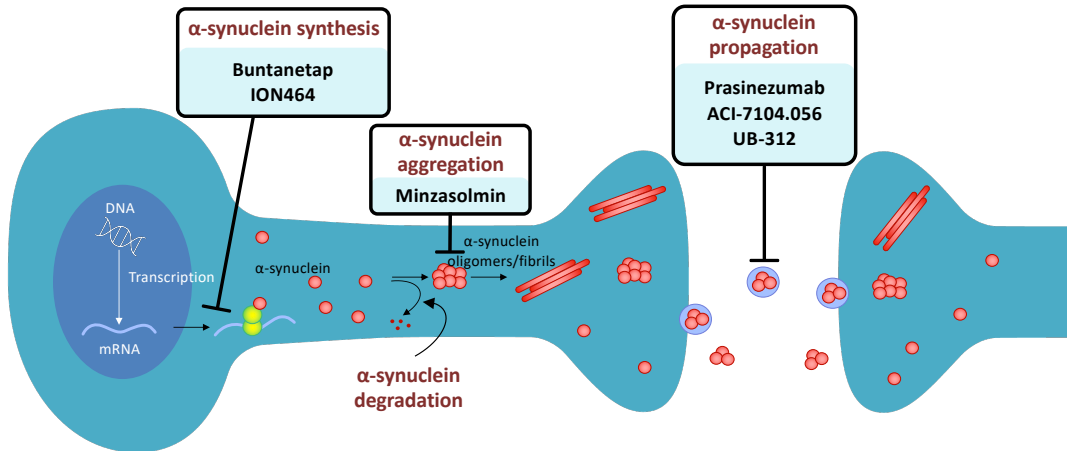
Modified from Koprach, Kalia, and Brotchie. *Nature Reviews Neuroscience* 2017

α -Synuclein



Modified from Wong and Krainc. *Nature Medicine* 2017

α -Synuclein



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GBA1 and LRRK2

Table 1 Genes associated with monogenic parkinsonism^{7,8}

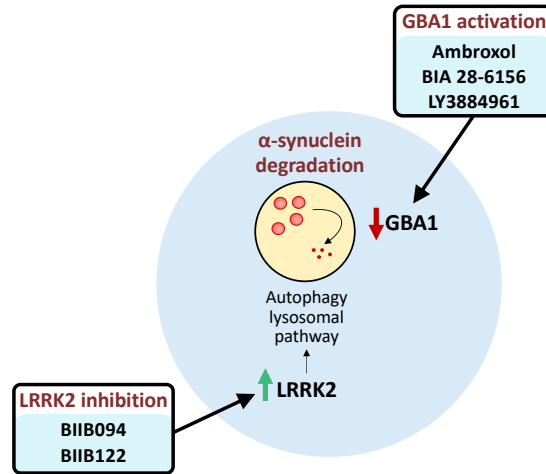
Gene	Inheritance	OMIM number
Classical parkinsonism (late onset > early onset)		
<i>CHCHD2</i>	Autosomal dominant	616710
<i>GBA1</i>	Autosomal dominant	606463
<i>LRRK2</i>	Autosomal dominant	607060
<i>SNCA</i>	Autosomal dominant	168601
<i>VPS35</i>	Autosomal dominant	614203
Classical parkinsonism (early onset > late onset)		
<i>DJ1</i>	Autosomal recessive	606324
<i>Parkin</i>	Autosomal recessive	600116
<i>PINK1</i>	Autosomal recessive	605909

Kalia, Mestre, and Nimmo. *Seminars in Neurology* 2023

GBA1 and LRRK2

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Kalia, Mestre, and Nimmo. *Seminars in Neurology* 2023

Repurposed drugs

- Drug repurposing = investigating drugs already approved for human use for treatment of other diseases

e.g., Amantadine



Influenza infection & prophylaxis (1960s) → Parkinson's disease motor symptoms (1970s) → Parkinson's disease levodopa-induced dyskinesia (1990s)

Amantadine in the Treatment of Parkinson's Disease

Robert S. Schwab, MD; Albert C. England, Jr., MD; David C. Fishbein, MD; and Robert R. Young, MD
JAMA, May 19, 1969 • Vol 208, No 7

Amantadine as treatment for dyskinesias and motor fluctuations in Parkinson's disease

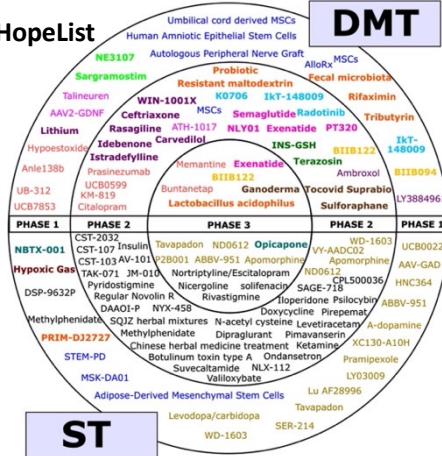
L. Verhagen Metman, MD; P. Del Dotto, MD; P. van den Munkhof, BS; J. Faug, MD; M.M. Mouradian, MD; and T.N. Chase, MD
NEUROLOGY 60 May 1998

New Use for an Old Drug: Amantadine Benefits Levodopa-Induced Dyskinesia

Movement Disorders, Vol. 11, No. 5, 1998

Repurposed drugs

bit.ly/ParkinsonsHopelist



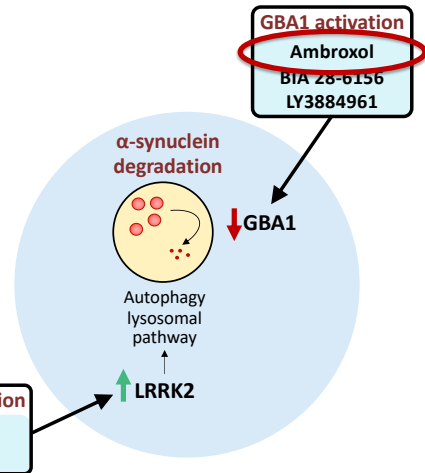
Over 1/3 of drugs being tested as potential DMTs in clinical trials are repurposed drugs or derivatives

McFarthing et al. Journal of Parkinson's Disease 2023

Repurposed drugs

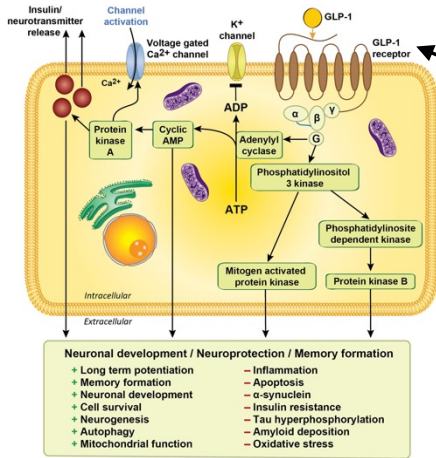
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Kalia, Mestre, and Nimmo. Seminars in Neurology 2023

Repurposed drugs

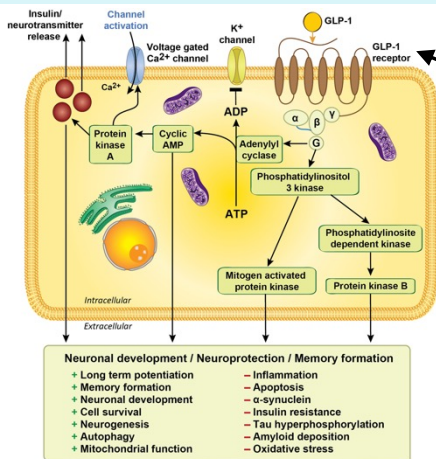


GLP-1 receptor activator
Exenatide
NLY01 (slow release)
PT320 (pegylated)
Liraglutide
Lixisenatide

- Neuronal development / Neuroprotection / Memory formation**
- + Long term potentiation
 - + Memory formation
 - + Neuronal development
 - + Cell survival
 - + Neurogenesis
 - + Autophagy
 - + Mitochondrial function
 - Inflammation
 - Apoptosis
 - α -synuclein
 - Insulin resistance
 - Tau hyperphosphorylation
 - Amyloid deposition
 - Oxidative stress

Nowell et al. Ageing Research Reviews 2023

Repurposed drugs



GLP-1 receptor activator
Exenatide
NLY01 (slow release)
PT320 (pegylated)
Liraglutide
Lixisenatide

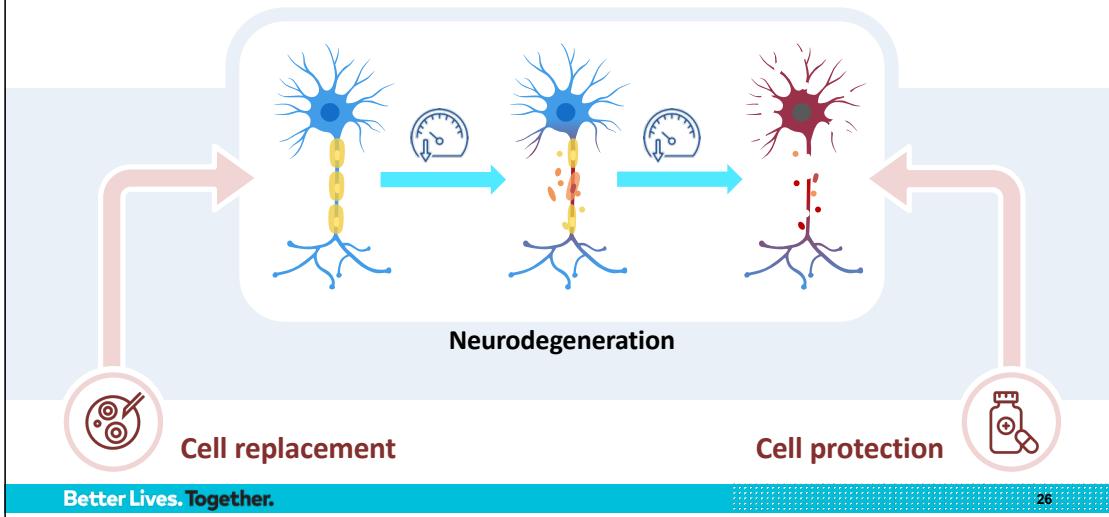
Trial of Lixisenatide in Early Parkinson's Disease

W.G. Meissner, P. Remy, C. Giordana, D. Maltête, P. Derkinderen, J.-L. Houéto, M. Anheim, I. Benatru, T. Boraud, C. Brefel-Courbon, N. Carrière, H. Catala, O. Colin, J.-C. Corvol, P. Damier, E. Dellapina, D. Devos, S. Drapier, M. Fabbri, V. Ferrier, A. Foubert-Samier, S. Frismand-Kryloff, A. Georget, C. Germain, S. Grimaldi, C. Hardy, L. Hopes, P. Krystkowiak, B. Laurens, R. Lefaucheur, L.-L. Mariani, A. Marques, C. Marse, F. Ory-Magne, V. Rigalleau, H. Salhi, A. Saubion, S.R.W. Stott, C. Thalarnas, C. Thiriez, M. Tir, R.K. Wyse, A. Benard, and O. Rascol, for the LIXIPARK Study Group[®]

N ENGL J MED 390:13 NEJM.ORG APRIL 4, 2024

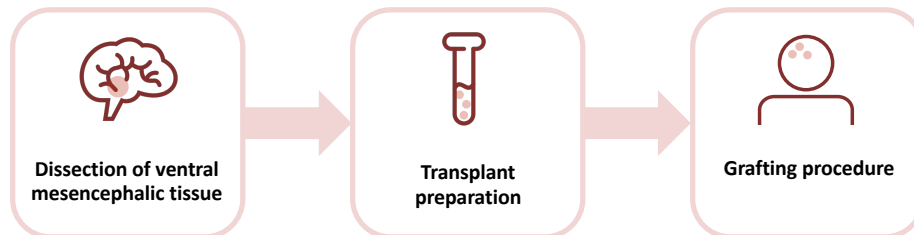
Nowell et al. Ageing Research Reviews 2023

Advancements in DMTs for PD



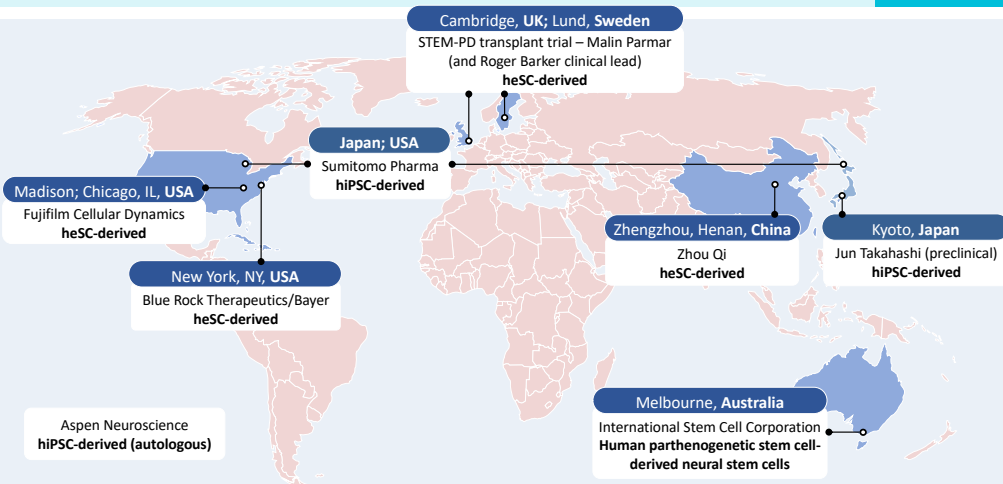
Stem cells

Early studies showed that replacing lost dopamine-producing brain cells with transplanted human fetal tissue could provide long-lasting clinical benefits for some patients



Dopamine-producing cells derived from stem cells are now being investigated

Stem cells







Learning objectives

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- Understand the **challenges** in advancing toward disease-modifying therapies

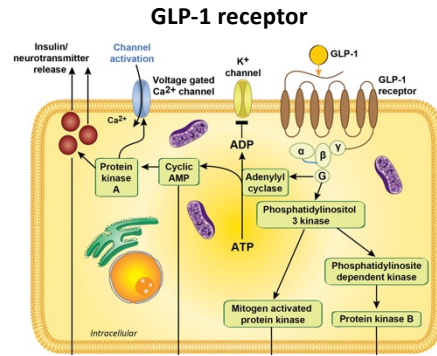
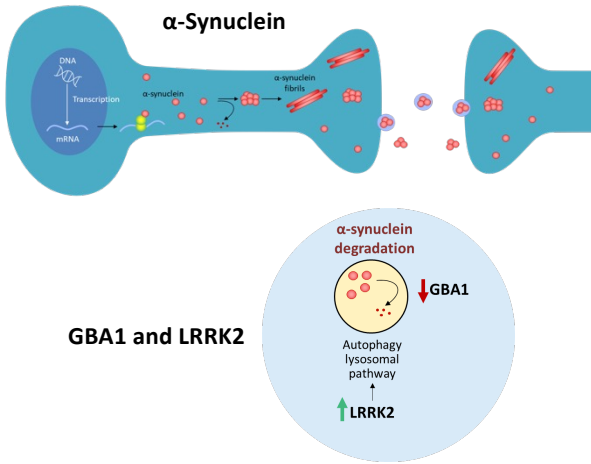
Challenges in DMT development

- Right dose?
- Right targets?
- Right time?
- Right person?

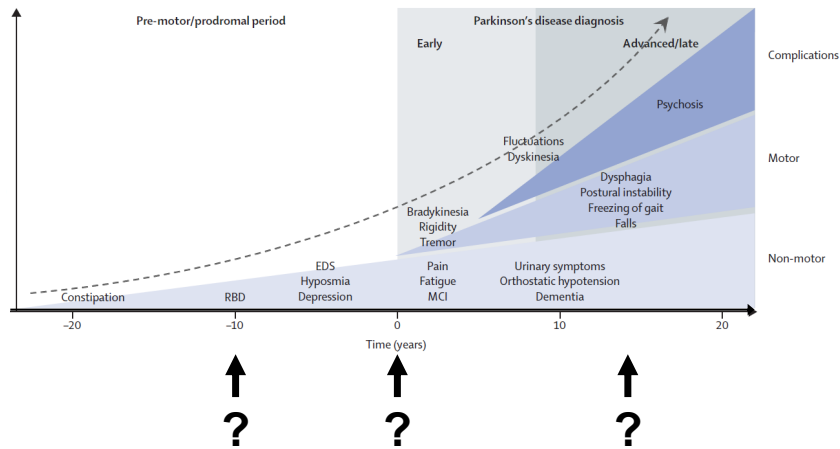
Right dose?

			
Aerobic Activity	Strength Training	Balance, Agility & Multitasking	Stretching
<p>3 days/week for at least 30 mins per session of continuous or intermittent at moderate to vigorous intensity</p> <p>TYPE: Continuous, rhythmic activities such as brisk walking, running, cycling, swimming, aerobics class</p> <p>CONSIDERATIONS: Safety concerns due to risks of freezing of gait, low blood pressure, blunted heart rate response. Supervision may be required.</p>	<p>2-3 non-consecutive days/week for at least 30 mins per session of 10-15 reps for major muscle groups; resistance, speed or power focus</p> <p>TYPE: Major muscle groups of upper/lower extremities such as using weight machines, resistance bands, light/moderate handheld weights or body weight</p> <p>CONSIDERATIONS: Muscle stiffness or postural instability may hinder full range of motion.</p>	<p>2-3 days/week with daily integration if possible</p> <p>TYPE: Multi-directional stepping, weight shifting, dynamic balance activities, large movements, multitasking such as yoga, tai chi, dance, boxing</p> <p>CONSIDERATIONS: Safety concerns with cognitive and balance problems. Hold on to something stable as needed. Supervision may be required.</p>	<p>>2-3 days/week with daily being most effective</p> <p>TYPE: Sustained stretching with deep breathing or dynamic stretching before exercise</p> <p>CONSIDERATIONS: May require adaptations for flexed posture, osteoporosis and pain.</p>

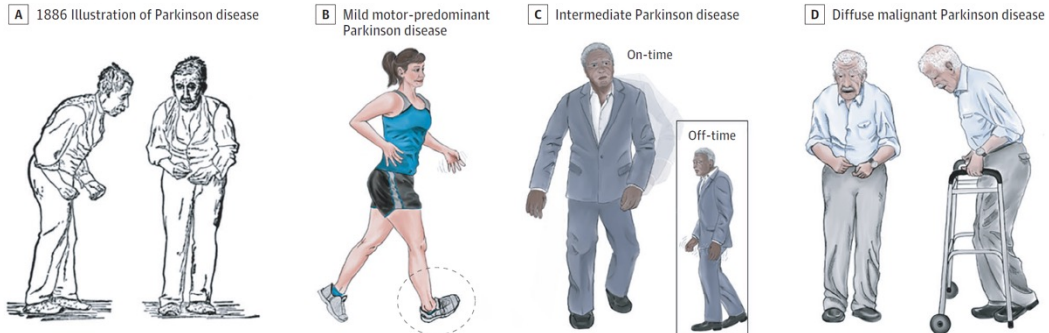
Right targets?



Right time?



Right person?



Armstrong and Okun. *JAMA Neurology* 2020

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April is Parkinson's Awareness Month & April 11 is World Parkinson's Day



<https://ncc-ccn.gc.ca/places/tulips-in-the-capital#>

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Parkinson's & Research

Research plays a vital role in helping us understand Parkinson's.

Research:

- Leads to new treatment and medications
- Provides better understanding of symptoms and disease progression
- Ultimately brings us closer to a cure

How to get involved:

- www.clinicaltrials.gov
- Call our toll-free Helpline at 1-800-4PD-INFO or
- visit www.Parkinson.org/research



2024 Expert Briefings



Wednesday, March 13

**Understanding Pain
in Parkinson's**

Wednesday, April 10

**Research Update:
Working to Halt PD**

Wednesday, May 8

**Trouble with Zzz's: Sleep
Challenges with Parkinson's**

Wednesday, September 11

**Solving the Challenge of
Apathy in Parkinson's**

Wednesday, October 9

**More Than PD: Managing
Multiple Chronic Conditions**

Wednesday, November 13

**What's On Your Mind? Thinking
and Memory Changes in
Parkinson's**

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We're Here For You



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