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.

Welcome

Crista Ellis
Manager, Community Engagement
Parkinson’s Foundation
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.

APRIL IS PARKINSON’S AWARENESS MONTH!

This year, we’re learning the:

ABCs of PD

Parkinson.org/Awareness
Today’s webinar sponsor

PD Health @ Home

Weekly, virtual programs:
- Mindfulness Mondays
- Wellness Wednesdays
- Fitness Fridays
- EP Salud en Casa

Visit Parkinson.org/PDhealth to learn more and register
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

For Your Convenience

Recording
Expert Briefings are recorded and archived on www.Parkinson.org/ExpertBriefings
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 Chain in Parkinson’s Disease Research
• Co-Editor-in-Chief, Journal of Parkinson’s Disease
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

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-cn.gc.ca/places/tulips-in-the-capital#

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
PD is a progressive disease

Symptoms

- Pre-motor/prodromal period
- Early Parkinson's disease diagnosis
- Advanced stages
- Complications

- Rigidity
- Tremor
- Bradykinesia
- Postural instability
- Freezing of gait
- Falls

- Depression
- Fatigue
- Hoehn and Yahr stages
- Orthostatic hypotension
- Cognitive impairment
- Dementia

Neurodegeneration

Modified from Kalia and Lang. Lancet 2015

Strategies to tackle PD progression

Parkinson’s disease

Prevention  Cure  Disease-modifying therapy  Symptomatic therapy

Modified from De Angelis et al. BMJ 2018
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
Advancements in DMTs for PD

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

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

Corcos et al. Journal of Parkinson’s Disease 2024
Exercise

- Inflammation
  - Age-related cognitive decline
  - Neurodegeneration (AD, PD)
  - Neurotrophin resistance
- Exercise
  - Metabolic syndrome
  - Hypertension
  - Insulin resistance
- Growth factor induction and signaling cascades
- Brain health
  - Cognition
  - Plasticity
  - Neurogenesis
  - Vascular function

Modified from Koprich, Kalia, and Brotchie. Nature Reviews Neuroscience 2017

α-Synuclein

Modified from Koprich, Kalia, and Brotchie. Nature Reviews Neuroscience 2017
α-Synuclein

Modified from Koprich, Kalia, and Brothie. Nature Reviews Neuroscience 2017

α-Synuclein

Modified from Wong and Krainc. Nature Medicine 2017
**α-Synuclein**

α-synuclein synthesis
- Buntanetap ION464

α-synuclein aggregation
- Minzasolmin

α-synuclein degradation

Modified from Wong and Krainc. Nature Medicine 2017

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**GBA1 and LRRK2**

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Kalia, Mestre, and Nimmo. Seminars in Neurology 2023
GBA1 and LRRK2

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α-synuclein degradation

LRRK2 inhibition

BIIB094

BIIB122

GBA1 activation

Ambroxol

BIA 28-6156

LY3884961

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**

  - [Amantadine in the Treatment of Parkinson's Disease](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4385192/)

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

  - [Amantadine as treatment for dyskinesias and motor fluctuations in Parkinson's disease](https://www.ncbi.nlm.nih.gov/pubmed/18121108)

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

  - [New Use for an Old Drug: Amantadine Benefits Levodopa-Induced Dyskinesia](https://www.ncbi.nlm.nih.gov/pubmed/13928703)
Over 1/3 of drugs being tested as potential DMTs in clinical trials are repurposed drugs or derivatives.
Repurposed drugs

GLP-1 receptor activator

- Exenatide
- NLY01 (slow release)
- PT320 (pegylated)
- Liraglutide
- Lixisenatide

Trial of Lixisenatide in Early Parkinson’s Disease


Advancements in DMTs for PD

Cell protection

Cell replacement

Neurodegeneration

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.

Dissection of ventral mesencephalic tissue

Transplant preparation

Grafting procedure

Dopamine-producing cells derived from stem cells are now being investigated.
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
Challenges in DMT development

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

Right dose?


Right targets?

α-Synuclein degradation

GBA1 and LRRK2

α-Synuclein

GLP-1 receptor

Right time?

Graph showing progression of Parkinson's disease symptoms over time.
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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](http://www.clinicaltrials.gov)
- Call our toll-free Helpline at 1-800-4PD-INFO or visit [www.Parkinson.org/research](http://www.Parkinson.org/research)

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**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

Register at [Parkinson.org/ExpertBriefings](http://Parkinson.org/ExpertBriefings)
