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College of Human Medicine  
MICHIGAN STATE UNIVERSITY



# GRAND CHALLENGES IN PARKINSON'S DISEASE

*Pathophysiological Mechanisms  
to Therapeutics*

SEPTEMBER 27-28, 2023



[grandchallengesinpd.org](http://grandchallengesinpd.org)

Image courtesy of Dr. Naman Vatsa, Henderson Lab, Van Andel Institute

## Wednesday, September 27, 2023

**7:30 a.m.** Breakfast

**8:00 a.m.** Welcome — Darren Moore, Ph.D.  
Van Andel Institute

**8:05 a.m.** Introduction of Keynote Speaker —  
Michael Henderson, Ph.D.  
Van Andel Institute

**8:10 a.m.** Jay Van Andel Award for Outstanding Achievement in  
Parkinson's Disease Research lecture  
Virginia M-Y Lee, Ph.D.  
Perelman School of Medicine, University of Pennsylvania  
*Transmission of misfolded proteins in neurodegenerative disorders*

**9:10 a.m.** Discussion

**9:25 a.m.** Break

### **SESSION 1: ENDOLYSOSOMAL DYSFUNCTION I**

**SESSION CHAIR:** Darren Moore, Ph.D., Van Andel Institute

**9:40 a.m.** Erika Holzbaur, Ph.D.  
University of Pennsylvania  
*Pathogenic mutations in LRRK2 disrupt organelle trafficking in neurons*

**10:10 a.m.** Mark Cookson, Ph.D.  
National Institutes of Health  
*Microglia integrate effects of aging, inflammation and LRRK2 activation*

**10:40 a.m.** Shawn M. Ferguson, Ph.D.  
Yale School of Medicine  
*A brake for when lysosomes break*

**11:10 a.m.** Abstract Selected Talk  
Daniel Ysselstein, Ph.D.  
Vanqua Bio  
*A small molecule allosteric activator of glucocerebrosidase demonstrates significant neuroprotective effects in models of GBA-Parkinson's disease and robust in vivo target engagement*

**11:25 a.m.** Discussion

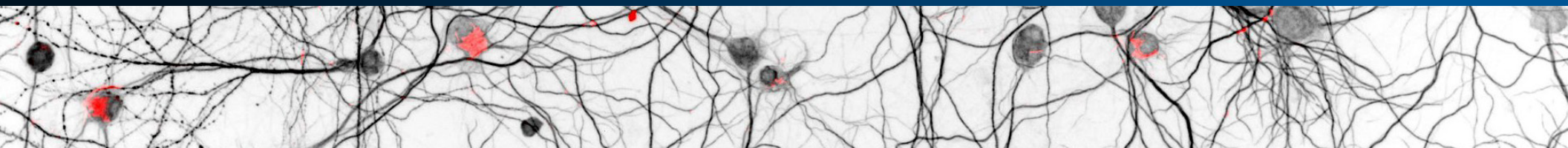
**11:40 a.m.** Lunch

### **SESSION 2: ENDOLYSOSOMAL DYSFUNCTION II**

**SESSION CHAIR:** Gerhard (Gerry) Coetsee, Ph.D., Van Andel Institute

**1:00 p.m.** Ellen Sidransky, M.D.  
National Human Genome Research Institute  
*GBA1 and the lysosome in Parkinson disease: An evolving story*

**1:30 p.m.** Manu Sharma, Ph.D.  
Weill Cornell Medicine  
*Lysosomal exocytosis releases pathogenic  $\alpha$ -synuclein species from neurons in synucleinopathy models*



**2:00 p.m.** Anastasia Henry, Ph.D.  
Denali Therapeutics  
*LRKK2 kinase activity regulates Parkinson's disease-relevant lipids at the lysosome*

**2:30 p.m.** Discussion

**2:45 p.m.** Break

### **SESSION 3: PROTEIN PATHOLOGIES I**

**SESSION CHAIR:** Laurent Roybon, Ph.D., Van Andel Institute

**3:00 p.m.** Laura A. Volpicelli-Daley, Ph.D.  
University of Alabama at Birmingham  
*Does pathologic alpha-synuclein cause dementia?*

**3:30 p.m.** Yang Yang, Ph.D.  
MRC Laboratory of Molecular Biology  
*Structures of  $\alpha$ -synuclein filaments from human brains*

**4:00 p.m.** Amanda Woerman, Ph.D.  
University of Massachusetts Amherst  
*Protein misfolding and templating*

**4:30 p.m.** Abstract Selected Talk  
Vivek K. Unni, M.D., Ph.D.  
Oregon Health and Science University  
*Alpha-synuclein in nucleolar DNA double-strand break repair: Cross-talk between Parkinson's disease, melanoma and genomic instability*

**4:45 p.m.** Discussion

**5:00–7:30 p.m.** Poster session and dinner  
(Please note, dinner tickets must have been purchased during registration)

## **Thursday, September 28, 2023**

### **SESSION 4: PROTEIN PATHOLOGIES II**

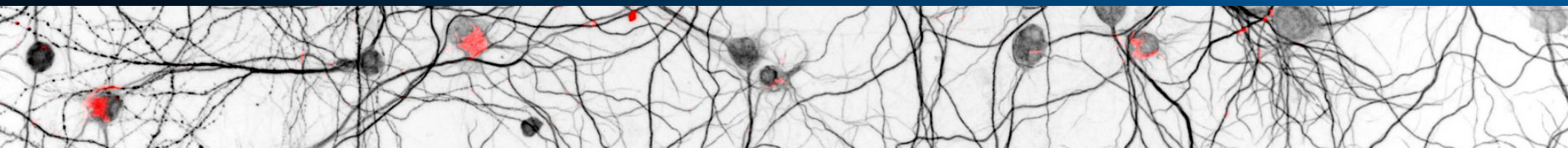
**SESSION CHAIR:** Michael Henderson, Ph.D., Van Andel Institute

**7:30 a.m.** Breakfast

**8:00 a.m.** Hilal Lashuel, Ph.D.  
Ecole Polytechnique Fédérale de Lausanne (EPFL)  
*Rethinking the role of alpha-synuclein aggregation in the pathogenesis of Parkinson's disease: From mechanisms to therapeutic strategies*

**8:30 a.m.** Sonia Gandhi, Ph.D.  
Crick Institute  
*Talk Title TBA*

**9:00 a.m.** Subhojit Roy, M.D., Ph.D.  
University California San Diego  
*The physiologic role of alpha-synuclein*



**9:30 a.m.** Abstract Selected Talk  
Patrik Brundin, M.D., Ph.D.  
Roche  
*Prasinezumab reduces motor progression in the Pasadena open label extension*

**9:45 a.m.** Discussion

**10:00 a.m.** Break

**SESSION 5: CIRCUIT DYSFUNCTION I**

**SESSION CHAIR:** George Huntley, Ph.D., Icahn School of Medicine

**10:15 a.m.** Alexandra Nelson, M.D., Ph.D.  
UC San Francisco  
*Altered striatal synaptic function in levodopa-induced dyskinesia*

**10:45 a.m.** Nicole Calakos, M.D., Ph.D.  
Duke University Medical Center  
*Cell stress pathways in basal ganglia circuits in PD — Perpetrators or protectors?*

**11:15 a.m.** Hong-yuan Chu, Ph.D.  
Van Andel Institute  
*Motor cortical neuroplasticity in parkinsonism*

**11:45 a.m.** Discussion

**12:00 p.m.** Lunch

**1:00 p.m.** Findings from the 2023 *Rallying to the Challenge* meeting

**1:30 p.m.** Tom Isaacs Award Presentation

**1:45 p.m.** Break

**SESSION 6: CIRCUIT DYSFUNCTION II**

**SESSION CHAIR:** Hong-yuan Chu, Ph.D., Van Andel Institute

**2:00 p.m.** William Lytton, M.D.  
*Using computer modeling to turn correlation into causality in PD*

**2:30 p.m.** Rui Chang, Ph.D.  
Yale School of Medicine  
*From body to brain: interoceptive coding in the vagus nerve and its role in Parkinson's disease*

**3:00 p.m.** George Huntley, Ph.D.  
Icahn School of Medicine  
*The challenges of preventing early cognitive decline in Parkinson's*

**3:30 p.m.** Discussion

**3:45 p.m.** Closing Remarks

