## Towards Precision Medicine in Parkinson's Disease



Roy Alcalay ROYAL@TLVMC.GOV.IL

#### **Genetic Laboratory (Orr-Urtreger)**

- Identify Mutation carriers in GBA and LRRK2 (>33% of Ashkenazi Jews)
- Identify genetic modifiers of Parkinson's disease (PD) that increase or decrease PD risk or severity

# GBA and LRRK2 mutations in Ashkenazi Jews with PD GBA compound-heterozygotes or homozygotes 18% GBA carriers 12% LRRK2 carriers Carriers of GBA & LRRK2 Carriers of other mutations

### **Movement Disorders Unit, Clinical Trials** (Gurevich)

- Ongoing clinical trials for precision medicine studies in *LRRK2* and *GBA*. Examples:
- Intrathecal antisense oligonucleotides for LRRK2-PD
- Gene therapy using AAV vector for GBA-PD









#### From bench to bedside





## Laboratory for Early Markers of Neurodegeneration (LEMON) (Mirelman)

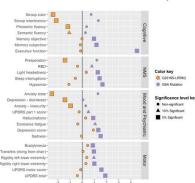
- Genotype/phenotype studies of carriers of LRRK2 and GBA with and without PD (imaging, wearables and clinical)
- Biological markers of GBA and LRRK2 in blood, urine, and spinal fluids



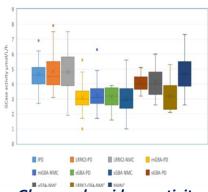


- Deep phenotyping of gait performance
- Analysis and treatment of freezing of gait and other gait disorders

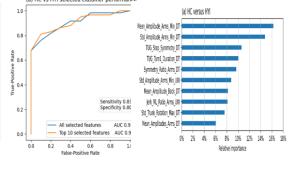








Glucocerebrosidase activity by mutation status



Sensitive measures of gait distinguishing early PD from healthy controls

Figures from: Goldstein et al 2020, Kozlovski et al 2019, Omer et al 2021, Mirelman et al 202