Precision Medicine in Parkinson’s Disease

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BILL COLLINS PD SYMPOSIUM
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What is Parkinson’s Disease?

- Parkinson disease (PD) is one of the most common neurologic disorders, affecting approximately 1% of individuals older than 60 years.

- The 2 major neuropathologic findings in PD are loss of dopaminergic neurons of the substantia nigra and the presence of Lewy bodies.
Signs and Symptoms of PD

- Tremor
- Decrease in dexterity
- Decreased arm swing
- Soft voice
- Decreased facial expression
- Sleep disturbances
- Decreased sense of smell
- Symptoms of autonomic dysfunction (e.g. constipation, sweating abnormalities, sexual dysfunction)
- A general feeling of weakness and fatigue
- Depression
- Slowness in thinking
We’re in the midst of an epidemic...

- The prevalence of PD has doubled between 1990 and 2015 to 6.2 million worldwide
- The number of individuals affected by PD is expected to reach 12.9 million by 2040

Dorsey and Bloem, JAMA Neurology, 2018
Not everyone’s Parkinson’s is the same

- Tremor dominant PD
- Non-tremor dominant PD
- “Lewy body disease”
- Hereditary PD
- Young-onset PD
- “Late-onset PD”
- Atypical PD
- PD-Dementia
Classifications of PD

Espay et al, Nature Reviews, 2017
It get’s even more complicated...
Classifications of PD

Espay et al, Nature Reviews, 2017
What does all this mean for you?

- Many open questions:
  - How does rate of progression differ by PD subtype?
  - How should PD Subtype influence treatment decisions?
  - Are certain treatments having greater predictable side effects depending on PD subtype?
Patients with the LRRK-2 mutation (accounting for 1-2% of all PD patients) were recently found to have slower disease progression.
Precision Medicine in PD treatment

- Personalized (or precision) medicine tailors treatments to an individual’s specific characteristics (genes, molecular markers, type of disease, etc.)
Treatments for PD

We have A LOT to choose from...
Treatments for PD by Disease Stage

Sequence of symptoms in progression of Parkinson disease

<table>
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<th>Early symptoms</th>
<th>Motor fluctuations</th>
<th>Dyskinesias</th>
<th>Emerging medication-resistant symptoms</th>
<th>Disabling medication-resistant symptoms</th>
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<td>Pharmacologic treatment</td>
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<td>Treatment of motor symptoms</td>
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<td>MAO-B inhibitor</td>
<td>Levodopa</td>
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<td>Treatment of nonmotor symptoms</td>
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<td>Antidepressants</td>
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<td>Deep brain stimulation</td>
<td>Exercise</td>
<td>Physical and occupational therapy</td>
<td>Speech and swallow therapy</td>
<td>Psychosocial care</td>
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</tbody>
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Okun at al, 2017
Adverse Effects: Examples

- Patients with atypical Parkinsonism are often more affected by side effects of dopaminergic medication, e.g. lowering of blood pressure in Multiple System Atrophy (MSA)

- Patients with cognitive impairment associated with PD are more likely to develop hallucinations with dopaminergic medication
The Ohio River Valley PD Registry

- Collaboration between University of Cincinnati, University of Louisville and University of Kentucky to study effect of genetic mutations on PD treatment outcomes
- Plan to genotype patients with a panel of 49 genes associated with the most common PD genetic mutations
- **Goal:** To study treatment outcomes for each unique genotype of PD
- Cost of genetic analysis has dropped from $2000 to $1 dollar per gene!
Stay tuned... funding efforts are under way!
Summary

- PD is a heterogeneous disease, presenting with different symptoms in different populations
- Genetic mutations in PD may affect subtype, progression rate, response to medications and likelihood of adverse effects to medications
- Identifying PD disease markers will help us in making individualized treatment decisions
Questions ?