Large Scale Biomarker Discovery and Validation for Parkinson Disease

PDBP Launch Meeting, Arlington, VA
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Alzheimer Disease

Aβ  Plaques

Tau  Tangles
ROC Analysis Based on CSF Aβ and Tau

ADNI BASELINE CSF

Annals of Neurology, 2009

UW
Parkinson Disease
Diagnostic value of α-Syn and DJ-1

Brain, 2010

Lancet Neurology, 2011
CSF Tau, P-tau and Aβ in PD
Annals of Neurol, 2011

<table>
<thead>
<tr>
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<th>Crossectional (Baylor, OHSU and UW)</th>
<th>Crossectional (NIH + Norway)</th>
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<tbody>
<tr>
<td></td>
<td>CTRL (n=126)</td>
<td>PD (n=135)</td>
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<tr>
<td>Aβ (pg/ml)</td>
<td>410.5±174.4</td>
<td>331±126</td>
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<tr>
<td>P-tau (pg/ml)</td>
<td>28.1±16.5</td>
<td>21±7.6</td>
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<tr>
<td>Tau (pg/ml)</td>
<td>62.7±19.8</td>
<td>54.1±15.1</td>
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**LRRK2 Patients**

*Neurology. 2012;78:55-61*
Roadmap and Strategies to Success
Cohorts and Sample Collection
Udall, ADRC and others

PANUC
Pacific Northwest Udall Center
Promising Candidates
Results of Proteomic Profiling

**Brain: >4,000 proteins identified**
- Midbrain and cortical proteome
  - Total, glycoproteins, phosphoproteins, oxidized and ubiquinated proteins
  - Isoforms of key proteins by 2D gel

**CSF: >3,000 proteins identified**
- Total unbiased profiling
- Glycoproteins and inflammatory mediators
- Exosomes
- Isoforms of key proteins by 2D gel

**Proteins altered in abundance for validation**
- Promising candidate proteins (Luminex) and peptides - MRM
Candidates

Proteins and Peptides
Long and short ncRNAs
microRNAs
tRNAs and rRNAs
snoRNAs
piRNAs (DICER independent)

Other markers and platforms
THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

% Remaining Neurons

- Loss of DA neurons in SNc in PD
- Loss of non-DA neurons in PD
- Threshold level of cell loss associated with development of symptoms
- Initiation of neuroprotective treatment shortly after patient presents with symptoms

Time - years
People who did the work

$\text{$$$ - NIH}$

Fox, APDA and PDF

- **CSF Collection (controls, PD and other diseases):**
  1) Baylor (Jankovic)
  2) OHSU (Chung, Quinn, and Nutt)
  3) UCSD (Glasko)
  4) UWSM (Leverenz, Peskind, Samii, and Zabetian)
  5) NIH (Goldstein)
  6) U Penn (Siderowf)

- **LRRK2 Project:** CSF - JA (Norway), KH (Japan), JL and CZ (UW, USA, as well as ZW and RU (Mayo, US); PET - JS (Canada)