Blood Biomarkers of Stroke Recovery

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Assessing Neural Systems Biology from Plasma

- DNA
  - Epigenetic regulation through methylation, etc.

- RNA
  - Messenger RNA
  - MicroRNA

- Proteins
  - Exosome

- Metabolites
  - Lipids, amino acids
  - metabolites, proteins, microRNA

Blood-Brain Barrier

White Blood Cells

Epigenetic changes to DNA, messenger RNA

*Shah, Patel, and Freedman, NEJM 2018
**Blood Biomarkers of Neurologic Disease**

### Preclinical Alzheimer’s Disease
- Followed 525 adults > 70 for 5 yrs
- 28 converted to dementia/MCI
- Compared converter to healthy non-converters
- 10 metabolite panel had 90% accuracy discriminating groups
- Not related to ApoE4 status

### Multiple Sclerosis
- 101 relapsing-remitting MS patients, 51 matched controls
- Split into discovery and validation cohorts
- 4 microRNAs discriminated:
  - MS vs. control
  - Relapse vs. stable disease
  - Gadolinium enhancement on MRI vs. no enhancement

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Mapstone et al, Nature Medicine 2014
Selmaj et al, Annals of Neurology 2017
Prior Blood Biomarker Studies in Stroke Recovery

Proteomics

• Low serum BDNF levels associated with worse recovery
  – >500 stroke patients
  – Pts with lowest tertile BDNF vs. top 2 tertiles
  – mRS 0-2 = poor recovery

<table>
<thead>
<tr>
<th>Odds Ratio for association of BDNF level with functional outcome</th>
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<tbody>
<tr>
<td>2 year</td>
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<td>2 year</td>
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<tr>
<td>7 year</td>
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<td>7 year</td>
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</tbody>
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• Very few blood biomarker of stroke recovery studies in humans!

Stanne et al, Stroke 2016
Plasma microRNA markers of upper limb recovery

- Samples from 27 CPASS participants
- Collected 19 days post-stroke
- Recovery based on delta ARAT, baseline – 6 mo.
- Good recovery > 6 pt change on delta ARAT
**So Where’s the Controversy??**

<table>
<thead>
<tr>
<th></th>
<th>5 days</th>
<th>15 days</th>
<th>30 days</th>
<th>90 days</th>
<th>1 yr</th>
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<tbody>
<tr>
<td><strong>BIOREC</strong></td>
<td></td>
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<td>Upper Ext Fugl-Meyer</td>
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<td>(observational)</td>
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<td><strong>CPASS</strong></td>
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<td>20 hrs OT</td>
<td>ARAT</td>
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<td>(clinical trial)</td>
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Dromerick et al, Front in Human Neurosci 2015
Acknowledgments

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