ADC Fall 2010

An update on biomarkers in AD and non-AD dementias

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Clinical Data	Determine degree and character of functional impairment		
	Normal	**Mild Impairment**	**Moderate to Severe Impair.**

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Laboratory Data	**Classify disease type and burden of lesions**			
	None	**+**	**++**	**+++**

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Challenge 1	**Identify disease-specific latency and prodrome**			
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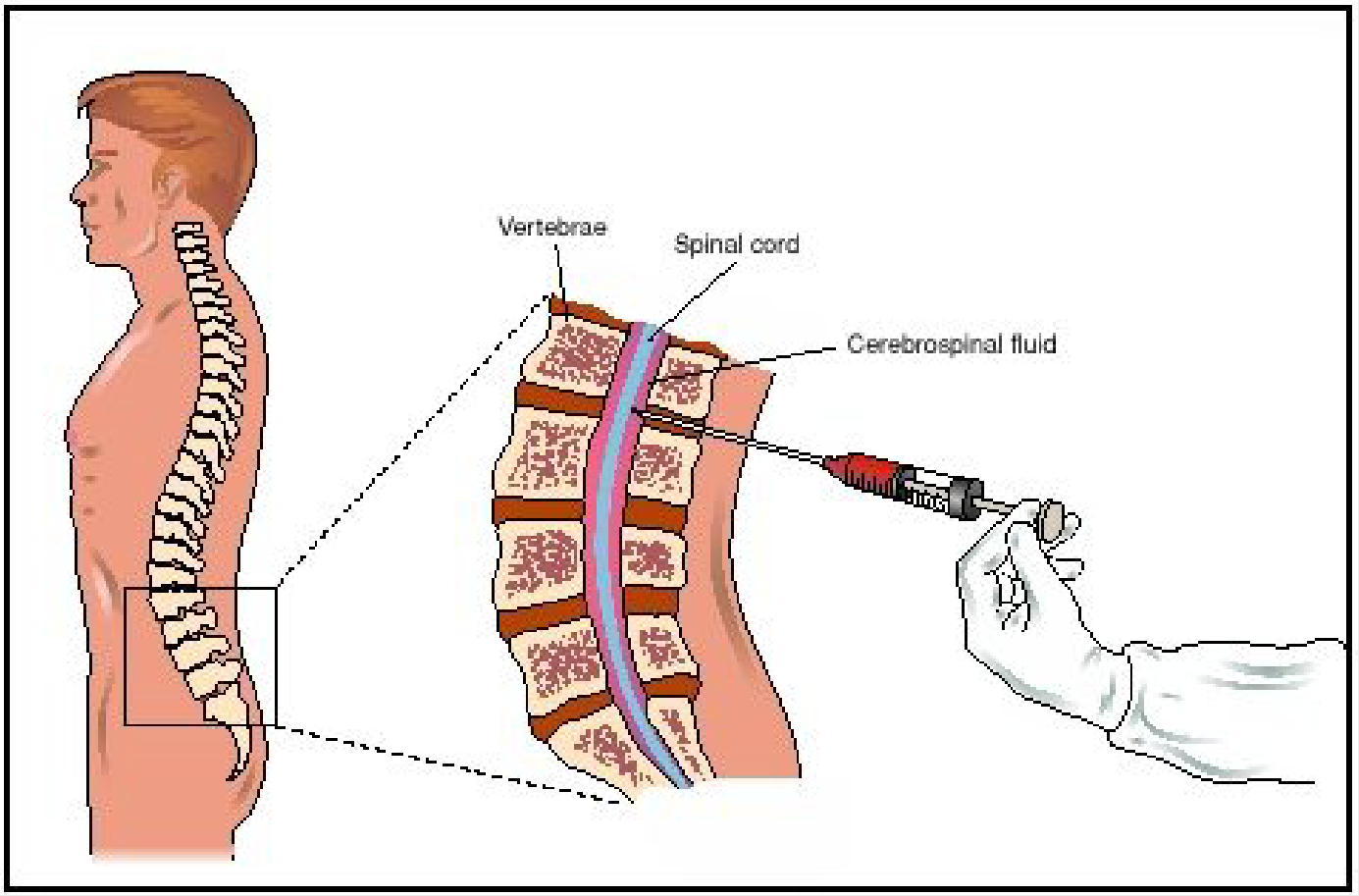
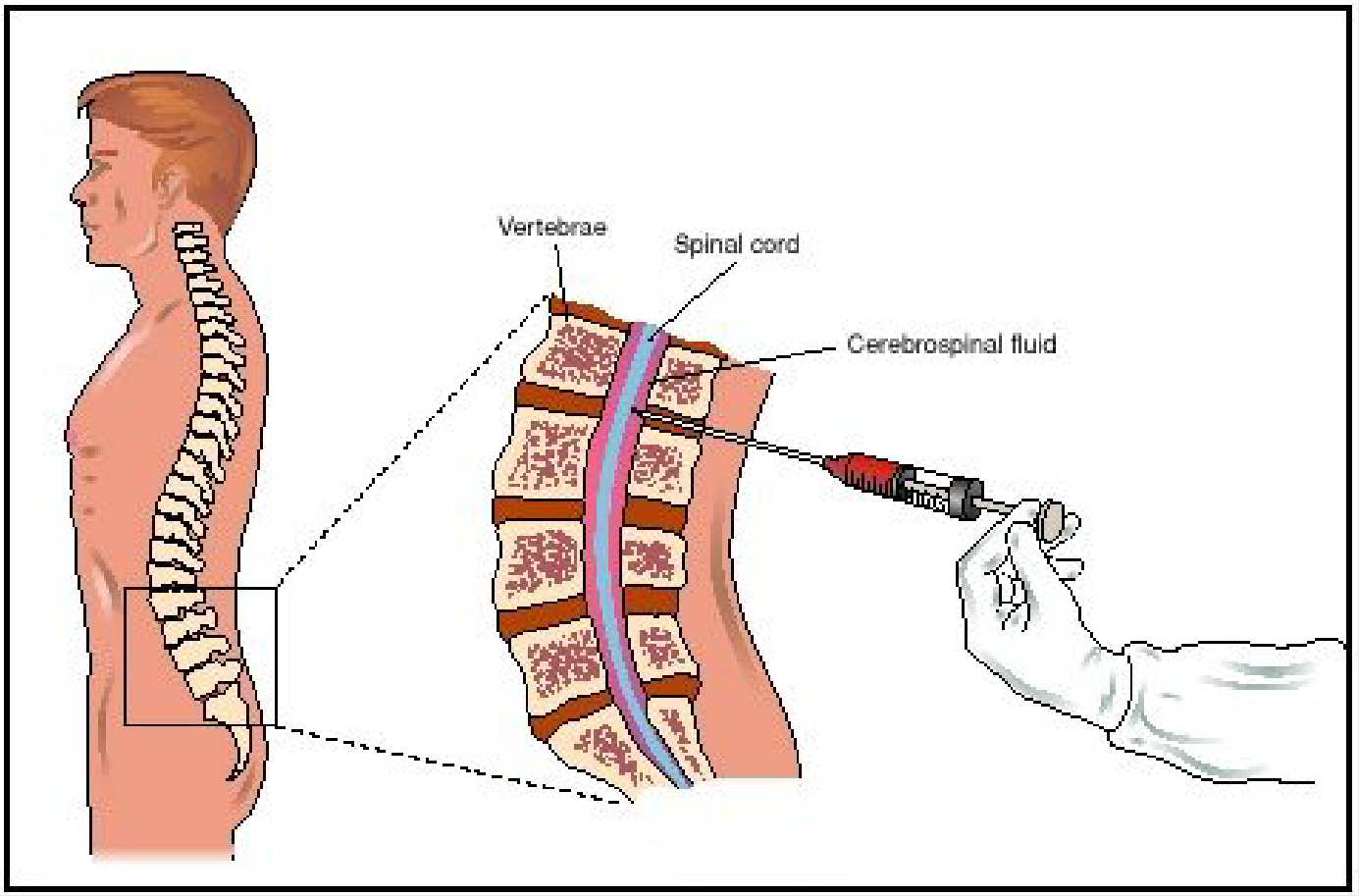
Level 1	Initial Associations	Association with expert diagnosis
Level 2	Confirmation	Replication in independent sample that includes multiple related diseases
Level 3	Validation	Further replication in independent samples from multiple sites
Level 4	Clinical Research	Standardization of assay and use as disease surrogate in clinical research
Level 5	Primary Care	Adopted as part of standard work-up in primary care setting


Vertebrae
Spinal cord
Cerebrospinal fluid

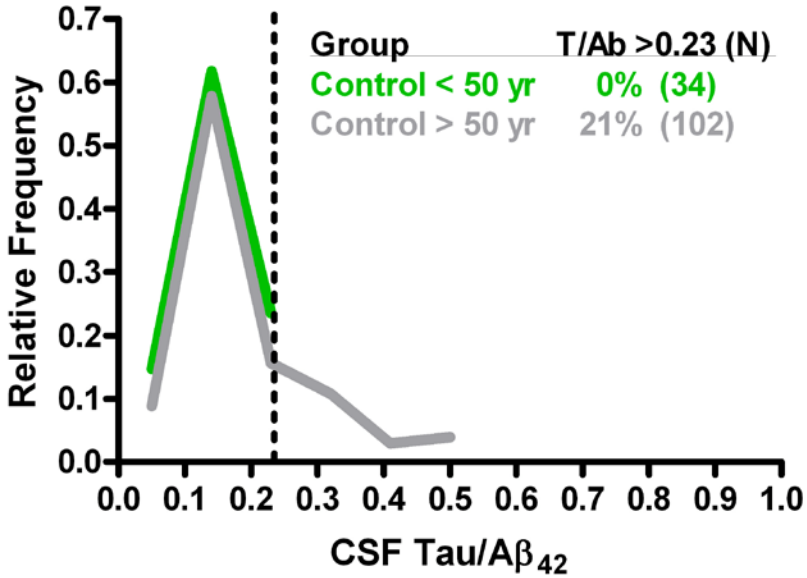
CSF continues to be *the* site to yield reproducible results for diseases that cause cognitive impairment and dementia.

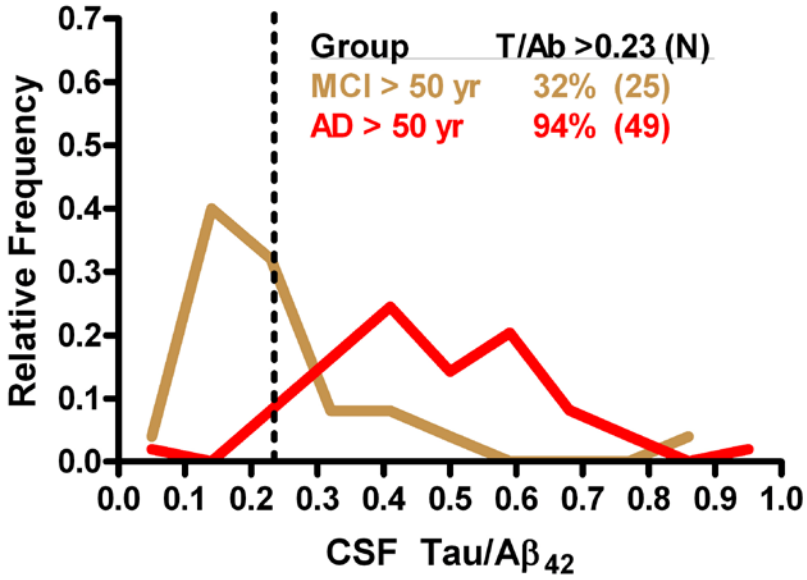


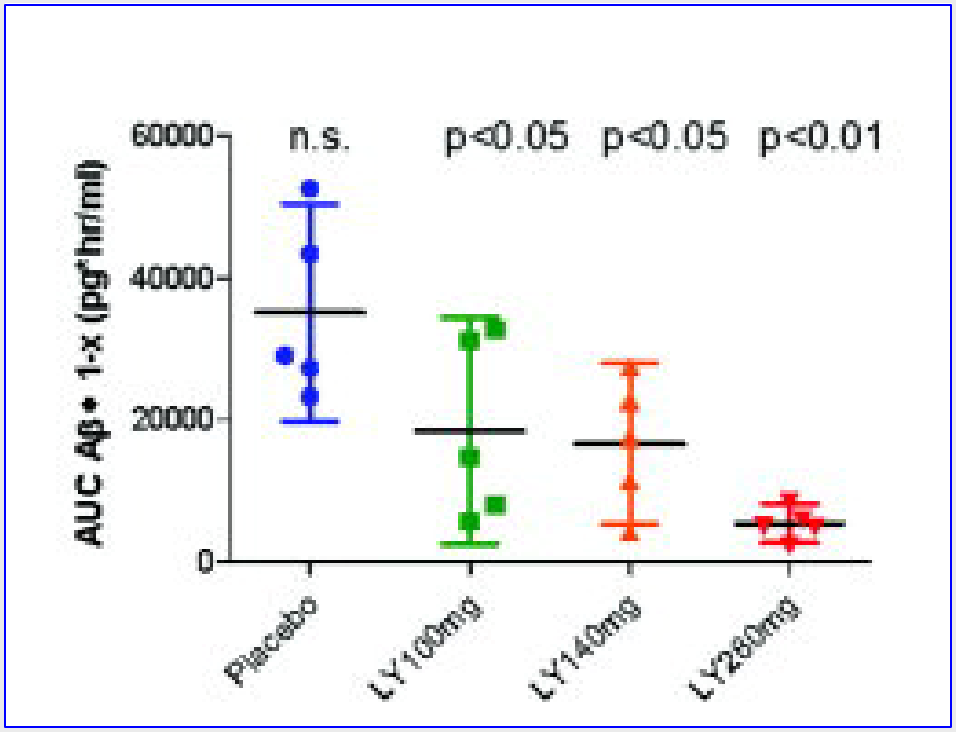
Evidence	*Latency*	*Prodrome*	*Dementia*
Level 1	Several	Many candidates	Many candidates
Level 2	F_2-IsoPs tau-P231	F_2-IsoPs, BACE1	A few MAPs
Level 3	$A\beta_{42}$, T-tau, tau-P181	tau-231	tau-P231 F_2-IsoPs
Level 4	None	$A\beta_{42}$ and T-tau tau-P181	$A\beta_{42}$, T-tau, tau-P181
Level 5	None	None	None

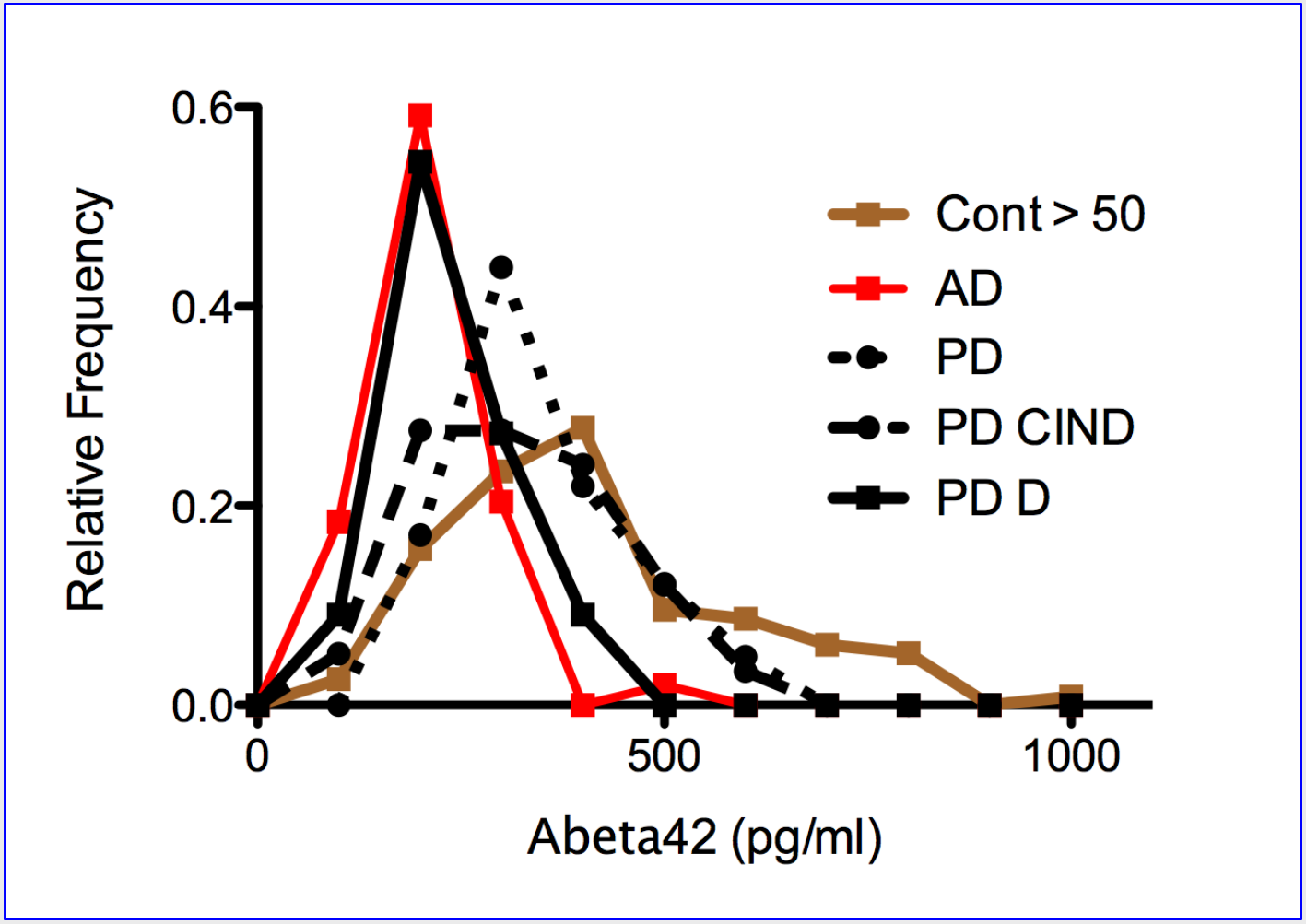
CSF biomarkers for AD

Evidence	*Latency*
Level 1	Several
Level 2	F_2-IsoPs tau-P231
Level 3	$A\beta_{42}$, T-tau, tau-P181
Level 4	None
Level 5	None






n.s.
p<0.05
p<0.05
p<0.01
60000
40000
20000
0
AUC Aβ • 1-x (pg*hr/ml)
Placebo
LY100mg
LY140mg
LY280mg


Relative Frequency
0.6
0.4
0.2
0.0
0
500
1000
Abeta42 (pg/ml)
Cont > 50
AD
PD
PD CIND
PD D

Why biomarkers?
What biomarkers?
Progress?

Summary

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Summary

CSF Aβ42 and tau species for AD
CSF Aβ42 for PD

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Summary

CSF Aβ42 and tau species for AD
CSF Aβ42 for PD

? CSF tau and others

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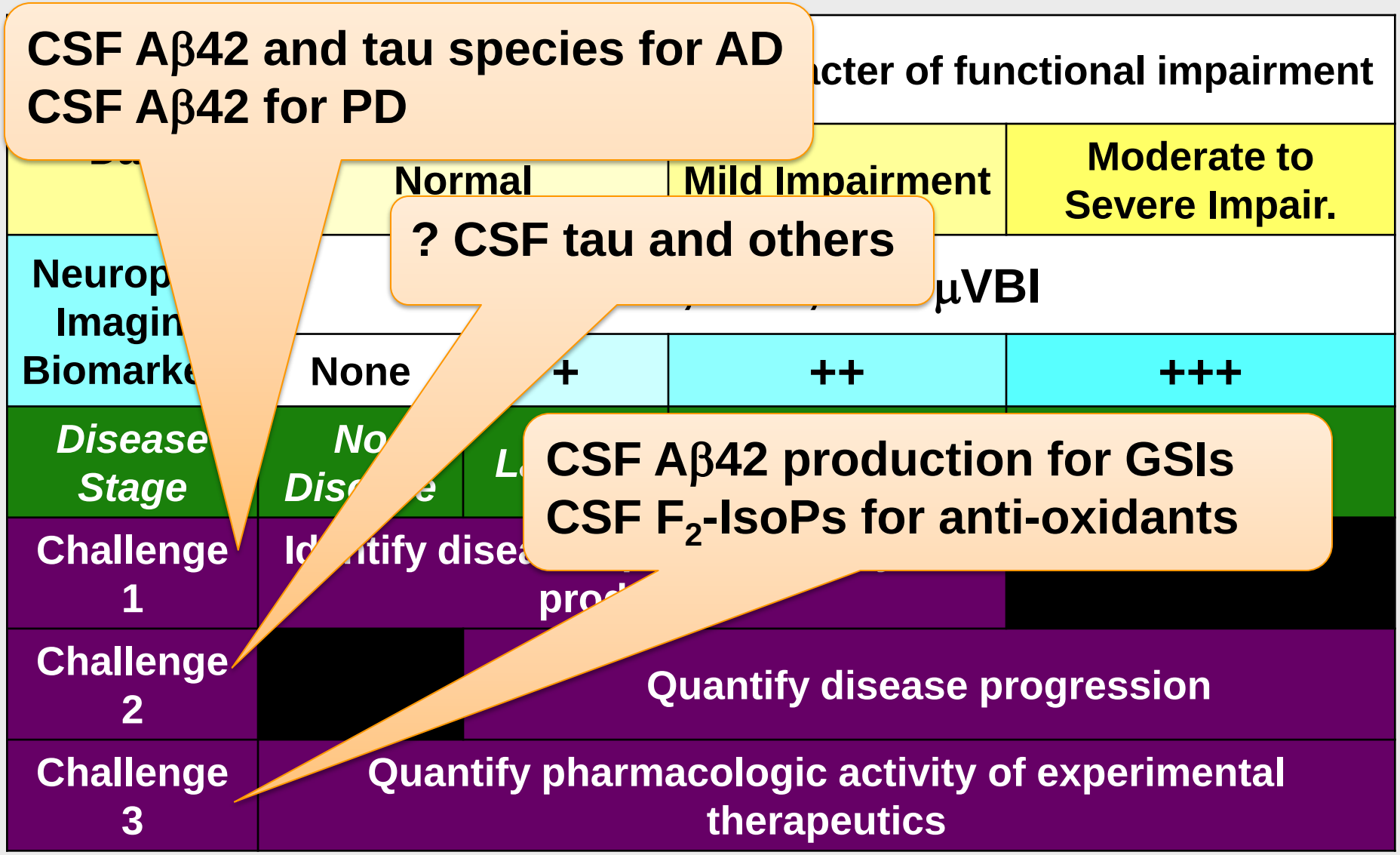
CSF Aβ42 and tau species for AD
CSF Aβ42 for PD
? CSF tau and others
CSF Aβ42 production for GSIs
CSF F2-IsoPs for anti-oxidants
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Imagin
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+
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Future Directions

- ***Patient Evaluation***
  - Medical history and genetics to quantify risk
  - Clinical examination and neuropsych testing
  - Laboratory: Ensemble of imaging and biomarker data
    - Aid in diagnosis
    - Establish disease stage
    - Quantify progression or response to therapy
- ***Research needs***
  - Reproducible peripheral biomarkers
  - Focus on latent and prodromal stages
  - Demonstrate pharmacologic action prior to therapeutic trial

PANUC

Pacific Northwest Udall Center

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- Members of UW ADRC
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- NIH for support

The University of Washington

Alzheimer's Disease Research Center