

Global Biomarkers Standardization Consortium (GBSC)

Teleconference Agenda

May 22, 2014

Time: 10:30 am ET/9:30 am CT/7:30 am PT/4:30 pm Sweden/Germany

Co-Chairs: Holly Soares, Henrik Zetterberg, Kaj Blennow, Piotr Lewczuk

Facilitator: Heather Snyder, Alzheimer's Association

Attendees:

Kaj Blennow	Jim Hendrix	Andreas Leinenbach
Josef Pannee	Lee Honigberg	Robert Dean
Heather Snyder	Madolyn Rogers	Dean Hartley
Henrik Zetterberg	Mary Savage	Moucan Yuan
Ian Pike	Glenn Barney	Randy Slemmons
Malcolm Ward	Andrew Munk	Vesna Kostanjevecki
Mary Lame	Julia Kuhlmann	June Kaplow
Heidi Jurgens	Michael Marlack	

1. Novel fluid biomarker studies in AD: Progress Update from Proteome Sciences– Ian Pike and Malcolm Ward

The team from Proteome Sciences shared an update on their novel 16-CSF protein panel using a mass spectrometry (MS) driven targeted method – TMT-SRM. The team analyzed control and AD CSF samples (with universal reference) and found good performance of the method at both the protein and peptide level. There may be an influence of protein concentration on driving the difference between control and AD which will be explored further. The 16plex assay gets similar results compared to other methods and may be more robust and useful at earlier phases of disease progression. The team's next steps are to move into the early AD and/or MCI space. The team is also exploring post-translational modifications (PTMs) as potential biomarkers with high sensitivity and specificity. In one study, four glycopeptides correlated with the level of atrophy (high atrophy; reduced glycopeptides). The team pointed out that this method may provide a more robust tool to utilize clusterin as a potential diagnostic/prognostic biomarker because it removes confounds such as antibody masking that hinders immunoassays. Additional CSF samples are needed for follow up.

2. Update on the Alz Association CSF QC program – Kaj Blennow

Kaj Blennow reported on Round 14 of the Alzheimer's Association CSF QC program. Results were reported from 59 participating labs for the Innostest assay labs, 9 labs for the AlzBio3 (Luminex) and 4 labs that ran the MesoScale V-plex.

The CV ranges are relatively good, but still showing a wide range of absolute levels and some batch variation (details provided on slides). Over the 4.5 years the program has been in place, there have been no large improvements in CV values, however, the use of new kits with ready-to-use (RTU) calibrators significantly reduced inter-center variability. In terms of SOP training, a reduction in variation was only evident when using the old assays, not the kits with RTU calibrators. A multi-lot, multi-lab study with the Meso-Scale V-plex kits showed a relatively tight fit (AB, tau) from both pooled and individual CSF samples; the team hopes more labs will use the kits so the effects will become more pronounced.

3. SRM Reference Methods:

a. Josef Pannee - Gothenburg

Josef Pannee provided an update on the use of a different high-resolution MS instrument using a surrogate analyte approach. A comparison of parallel reaction monitoring (PRM)-based targeted mass spectrometry to selected reaction monitoring (SRM) found good agreement between methods with PRM having the advantage of better separation of peaks and less confounds due to interference from endogenous compounds.

b. Les Shaw – U Penn

Les reported they are waiting on confirmation to go forward with the absolute concentration of AB. More included below.

4. SRM Round Robin Study II – Les Shaw –

Les Shaw provided an update on the Round Robin program and the resultant manuscript that is currently under review or in press. Les provided information on reference material for absolute concentration of AB using MS, and reported that the new Waters MS instrument requires less CSF (100 ul vs 250 ul with old system). Mary Lame from Waters inquired about the timing of receiving the materials for the next round. Les and Kaj discussed the extra time needed to cover the large range of concentrations, but the materials are ready and they plan to ship next week. This will allow the next round of the Round Robin Study to go forward.

5. Update on the IFCC workgroup – Henrik Zetterberg

Henrik Zetterberg provided an update on the IFCC workgroup activities, including the preparations of reference materials/standards for dispersion to the group to be used in the Round Robin discussed above. The agenda for the next meeting will include a discussion of new reference materials for tau and an update on the stability of Ab42.

6. NEXT MEETING: AAIC 2014 in Copenhagen

Saturday, July 12 Face to Face (5:30 meeting start; dinner available at 5:00).
Agenda will be forwarded in the next week or so.