ADNI Alzheimer's Disease Neuroimaging Initiative

ADNI 2: second batch analyses of CSF biomarkers

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Summary

Never before thawed aliquots of all ADNI 2 CSF samples collected between 2/22/2012 and 1/18/2013, and ADNI GO and ADNI 1 CSF samples(collection dates provided in UPENNBIOMK6), and 37 never before thawed randomly selected replicate aliquots were tested. Two or three of these "re-test" aliquots were included in each run subsequent to the first run. Each calibration standard sample, quality control sample and ADNI study subject sample were run in duplicate according to the manufacturer's instructions. Each test result is the mean value of the duplicates. The attached "ADNI 1, GO and 2 CSF report" provides details for the analyses including calibrator and quality control samples performance and the raw data for these analyses. The accompanying ADNI 2 2013 CSF $A\beta_{1-42}$, t-tau and p-tau_{181} dataset in .csv file format (UPENNBIOMK6) provides the final set of results following transformation based on 2007 BASELINE ADNI I results, according to the procedure described below, for the 2013 ADNI I, GO and II CSF sample analyses.

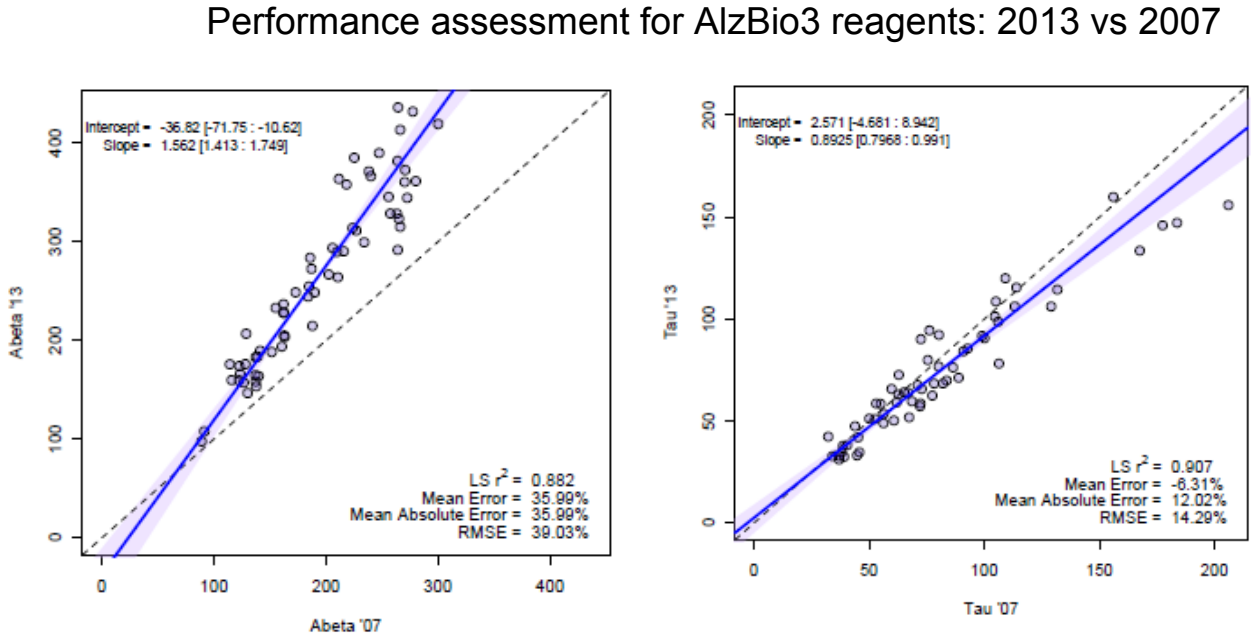
Method

The xMAP Luminex platform and Innogenetics/Fujirebio AlzBio3 immunoassay kits were used following the SOP in place at the UPenn/ADNI Biomarker Laboratory, according to the kit manufacturer's instructions and as described in previous publications (1-4). Analyses were performed in a series of 25 runs using a 96 well plate format, over the time period of January 30 through April 26, 2013. Acceptance criteria as documented in the UPenn/ADNI Biomarker Laboratory SOP were followed for these analyses.

Each of the 25 analytical runs met acceptance criteria for calibrator precision and accuracy (back calculated concentration result vs nominal concentration result) and quality control results were within stated limits (detailed data in "ADNI 1, GO and ADNI 2 CSF report"). Individual sample results were acceptable in all cases except where noted and those are reported as "NA" in the .CSV file "UPENNBIOMK6". In order to assure cross-sectional comparability of results between these ADNI 1, GO + ADNI 2 subject CSF samples and the earlier 2007 BASELINE CSF biomarker results for ADNI 1 subjects, assessment of the concentrations of $A\beta_{1-42}$, t-tau and p-tau_{181} were performed in a set of 62 never before thawed ADNI 1 patient BASELINE CSF aliquots (these were included in the series of longitudinal sample sets from 62 ADNI 1 "carryover" subjects). Linear regression analyses (Passing-Bablok) were performed for $A\beta_{1-42}$ and t-tau comparing CSF concentration results obtained in 2013 with those obtained in the analyses performed in 2007 (Figure 1). Correlation results were obtained (R^2 values of 0.882 and 0.907 for $A\beta_{1-42}$ and t-tau_{181}, respectively; for $A\beta_{1-42}$ the slope value is 1.562 and y-intercept value is -36.8 pg/mL and for t-tau the slope value is 0.892 and y-intercept is 2.57 pg/mL as

summarized in Figure 1). The slope and intercept values were then used to bridge between the 2007 data and the current 2013 CSF concentrations. This was accomplished by solving the equation, X = (Y-b)/m (X is the transformed 2013 result; Y is the raw 2013 result; m is the slope of the regression analysis and b is the Y intercept value of the regression analysis summarized in Figure 1). P-tau$_{181}$ results for the 2007 BASELINE analyses have an inherent analytical noise, no longer an issue in our experience, such that use of a limited number of 2007 aliquot samples, such as n=12, for the "bridging" to 2007 is not useful for this type of analysis. Since we have 62 2007 aliquots in the 2013 data set, we did perform the "bridging" to 2007 since a large enough sample size allows for more accurate capturing the analytical behavior of the full range of p-tau$_{181}$ values observed. The Passing-Bablok linear regression was performed (R^2 = 0.95, and slope and y-intercept values were 0.437 and 0.0054, respectively). As for Aβ_{1-42} and t-tau the bridging between 2007 data and the 2013 CSF concentrations was achieved by solving the equation, X = (Y-b)/m For studies that use 2013 ADNI 1, GO + ADNI 2 CSF biomarker concentration results, we recommend the use of the "bridged to 2007" results in the .csv file UPENNBIOMK6. As noted in the Summary the raw data can be found in the "ADNI I, GO and ADNI 2 CSF report", which is a full analytical report for the 25 plate runs.

Figure 1. Linear regression (Passing-Bablok) analysis plots.



Abeta '07 data are ADNI 1 BASELINE CSF results on 62 selected subjects, using Innogenetics AlzBio3 xMAP immunoassay. Abeta '13 are never before analyzed replicate CSF aliquots (continuously stored at -80 ^{0}C) from the 62 subjects. The analyses done in 2007 were done as one batch that included all ADNI 1 BASELINE CSF samples. The analyses done in 2013 were done as one batch (with different lots of reagents and calibrators than used in the 2007 analyses), using Fujirebio/Innogenetics AlzBio3

xMAP immunoassay reagents. Shaded areas are the 95% CI for the regression fit line. R^2 values are from least squares analyses of the data. Slope and intercept values determined using Passing-Bablok linear regression.

References

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