ADNI Alzheimer's Disease Neuroimaging Initiative

ADNI GO and ADNI 2: first batch analyses of CSF biomarkers

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Summary

Never before thawed aliquots of all ADNI GO plus ADNI 2 CSF samples collected through 2/21/2012 (N=467; 390 BASELINE and 77 longitudinal followup) were analyzed using the xMAP Luminex platform and Innogenetics/Fujirebio AlzBio3 immunoassay kits. Quality control samples used throughout the analyses included two aqueous controls included in the immunoassay kits and two CSF pools. In addition 28 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 duplicate quality control and ADNI subject samples. The attached "ADNI GO and ADNI 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 GO and ADNI 2 CSF $A\beta_{1-42}$, t-tau and p-tau_{181} dataset in .csv file format provide details of the analyses and the final set of results, respectively, for the BASELINE CSF sample analyses. This first report includes the analysis results for the 390 BASELINE samples only.

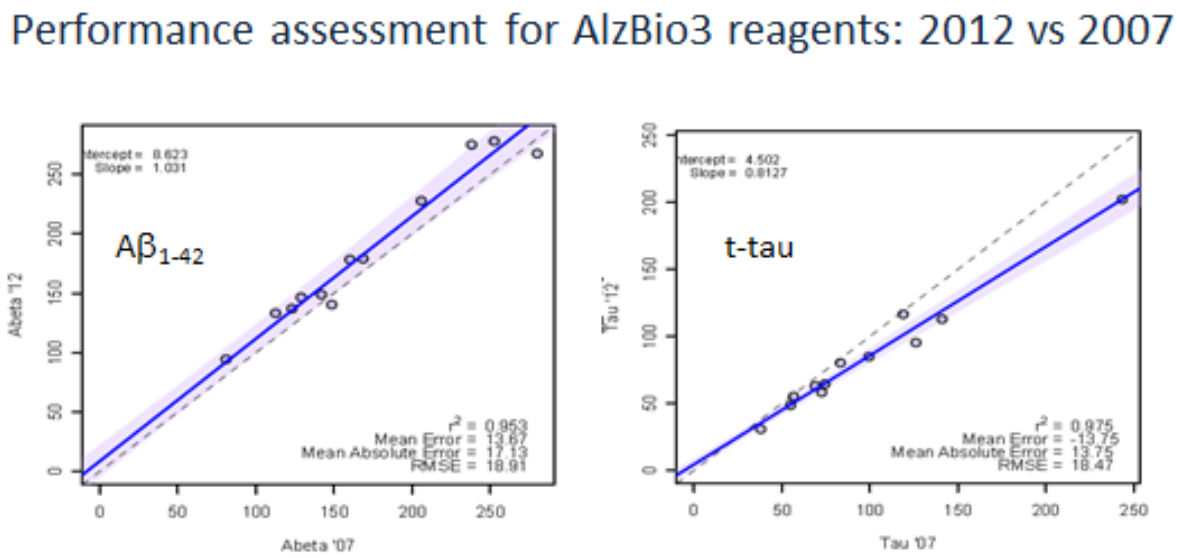
Method

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 (1-3). Analyses were performed in a series of 15 runs using a 96 well plate format, over the time period of February 21 through March 16, 2012. Acceptance criteria as documented in the UPenn/ADNI Biomarker Laboratory SOP were followed for these analyses.

Each of the 15 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 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 "BIOMARK5". In order to assure cross-sectional comparability of results between these ADNI 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 12 never before thawed ADNI 1 patient BASELINE CSF aliquots. Linear regression analyses (Passing-Bablock) were performed for $A\beta_{1-42}$ and t-tau comparing CSF concentration results obtained in 2012 with those obtained in the analyses performed in 2007 (Figure 1). Excellent correlation results were obtained (r^2 values of 0.953

and 0.975 for $A\beta_{1-42}$ and t-tau_{181}, respectively; for $A\beta_{1-42}$ the slope value is 1.031 and y-intercept value is 8.62 pg/mL and for t-tau the slope value is 0.813 and y-intercept is 4.50 pg/mL as summarized in Figure 1). The slope and intercept values were then used to bridge between the 2007 data and the current 2012 CSF concentrations. This was accomplished by solving the equation, X = (Y-b)/m (X is the transformed 2012 result; Y is the raw 2012 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 are not useful for this type of analysis as there was an inherent analytical noise present in that data that is no longer an issue in our experience, thus the p-tau_{181} results are untransformed concentration data. For studies that use ADNI GO + ADNI 2 BASELINE CSF biomarker concentration results we recommend the use of the "bridged to 2007" results. As noted in the Summary the raw data can be found in the "ADNI GO and ADNI 2 CSF report".

Figure 1. Linear regression analysis plots.



Abeta '07 are ADNI 1 BASELINE CSF results on 12 selected subjects, using Innogenetics AlzBio3 xMAP.
Abeta '12 are never before analyzed replicate CSF aliquots (stored at -80 °C) from the 12 selected subjects.
The analyses done in 2007 were done as one batch that included all ADNI 1 BASELINE CSF samples.
The analyses done in 2012 were done as one batch (different lots of reagents and calibrators than used in the 2007 analyses), using Fujirebio/Innogenetics AlzBio3 xMAP immunoassay.

References

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About The Authors

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