tudinal analysis, the correlation between repeated measures in the same individual over time for Aβ40 was r = 0.52 while that for Aβ42 was r = 0.68. Among subjects with MCI at baseline, an increase in CDR-SB was associated with a concomitant increase in plasma Aβ levels; these differences remained significant for Aβ42 even after controlling for age and the interval between measurements (p=0.029). In the survival analysis, 25 individuals progressed from CDR 0 to CDR 0.5, while 37 individuals converted from CDR 0.5 to AD. The risk of progression or conversion was not associated with baseline levels of tHcy, hsCRP, Aβ40, or Aβ42. **Conclusions:** Longitudinal changes in plasma Aβ42 level correlated with changes in cognition in MCI. Baseline plasma levels of Aβ, tHcy, or hsCRP were not predictive of development or progression of cognitive impairment over a median of 2 years of follow-up. The pattern of change of individual biomarkers over time may more accurately predict clinical course of MCI than single cross-sectional measurements.

P3-101 A UNIQUE GENE EXPRESSION SIGNATURE DISCRIMINATES FAMILIAL ALZHEIMER'S DISEASE MUTATION CARRIERS FROM THEIR WILD TYPE SIBLINGS

Caroline Graff[1], Karin Dillner[1], Yosuke Nagasaka[2], Hayao Ebise[2], Reiji Teramoto[2], Hiroyuki Nakagawa[2], Lena Lilius[1], Karin Axelman[1], Charlotte Forsell[1], Akira Ito[2], Bengt Winblad[1], Toru Kimura[2], *[1]Karolinska Institutet, Huddinge, Sweden; [2]Dainippon Sumitomo Pharma, Osaka, Japan. Contact e-mail: caroline.graff@ki.se*

Background: Alzheimer's disease (AD) is a neurodegenerative disease with an insidious onset and progressive course which inevitably leads to death. The current diagnostic tools do not allow for diagnosis until the disease has led to irreversible brain damage. Genetic studies of autosomal dominant early onset familial AD has identified three causative genes: amyloid precursor protein (*APP*), presenilin 1 and 2 (*PSEN1* and *PSEN2*). The *APP* and *PSEN* genes are widely expressed in many tissues throughout life; however, it has not been studied well whether they alter the expression of other genes in peripheral tissues. **Objective(s):** In the present study, we investigated if constitutional mutations in *APP* and *PSEN1* lead to detectable gene expression changes in fibroblasts that may be of potential use in early diagnosis. **Methods:** A global gene expression analysis was performed on fibroblasts from 33 individuals (including both healthy and demented mutation carriers as well as wild-type siblings) from three families segregating the APP_{SWE}, APP_{ARC} and *PSEN1* H163Y mutations, respectively. The mutations cause hereditary progressive cognitive disorder including typical autosomal dominant AD. **Results:** Our data show that the mutation carriers share a common gene expression profile significantly different from that of their wild type siblings. The signature is genotype-dependent, enabling even pre-symptomatic mutation carrier to be discriminated from controls. **Conclusions:** The results indicate that the disease process starts several decades before the onset of cognitive decline suggesting that pre-symptomatic diagnosis of AD and other progressive cognitive disorders may be feasible within the near future. We are currently collecting additional samples as our ambition is to make a large and careful validation study with additional samples from the APP_{SWE}, APP_{ARC} and *PSEN1* H163Y families, from additional familial AD cases and controls harbouring other or similar mutations as well as patients with different neuropathological conditions.

P3-102 ANNUALIZED DECREASE IN PLASMA Aβ42 CORRELATES WITH ANNUALIZED DECREASE IN HIPPOCAMPAL VOLUME

Neill R. Graff-Radford[1], Stephen D. Weigand[2], Maria M. Shuing[3], David S. Knopman[3], Bradley F. Boeve[3], John A. Lucas[1], Julia E. Crook[1], Linda H. Younkin[1], Ronald C. Petersen[3], Clifford R. Jack[3], Steven G. Younkin[1], *[1]Mayo Clinic Jacksonville, Jacksonville, FL, USA; [2]Mayo Clinic J, Rochester, MN, USA; [3]Mayo Clinic, Rochester, MN, USA. Contact e-mail: graffradford.neill@mayo.edu*

Background: Aβ42 deposits selectively in AD and is decreased in the CSF of patients with mild cognitive impairment (MCI) or AD. Plasma Aβ42 is increased, however, by mutations causing early onset familial AD, and Aβ42 and Aβ40 are both increased in Down syndrome, young (<65 years) AD relatives, and aging. In a mixed race cohort with a high AD incident rate and mean onset age of 79, elevated Aβ42 significantly associated with increased AD risk. In our study of a Caucasian population with a lower incident rate and a mean onset of 88, elevated Aβ42 was not, but a low Aβ42/Aβ40 ratio was significantly associated with cognitive decline and increased MCI/AD risk. In this population, low hippocampal volume also associated with increased risk of conversion from normal to MCI or MCI to AD. **Objective(s):** These results suggest that plasma Aβ42 and hippocampal volume may decline in parallel as AD develops in elderly Caucasians. To test this hypothesis, we examined the relationship between plasma Aβ levels and MRI-measured hippocampal atrophy. **Methods:** We analyzed 66 controls and 25 patients with MCI. Mean age was 80.1±7.6 years, education 14.1±3.2 years, 25.7% were ApoE4 carriers and 57.1% female. Baseline and follow-up plasma Aβ40 and Aβ42 were measured within four months of corresponding MRIs. **Results:** Analysis of 91 subjects (Pearson Rank test) showed a positive correlation (0.24, p = 0.025) between the annualized change in logAβ42 and the rate of hippocampal atrophy. In the MCI+ConvertingControl group (n=31), the correlation was 0.31 (p=0.05). *These findings are the first evidence that declining plasma Aβ42 correlates with declining hippocampal volume.* **Conclusions:** Our working hypothesis is that elevated Aβ42 increases risk of Aβ42 deposition with the time to development of MCI/AD dependent on additional factors that determine the rate of disease progression. If progression is rapid, elevated Aβ42 is an effective biomarker for imminent risk. When progression is slow, as in our elderly Caucasian cohort, Aβ42 declines into the normal range for considerable time before MCI/AD develops, and a low Aβ42/Aβ40 ratio is a better biomarker for imminent MCI/AD.

Supported by NIA AG06656 P50 AG16574 and U01 AG06576 Smith Van Buren.

P3-103 DEMOGRAPHIC FEATURES OF FRONTOTEMPORAL LOBAR DEGENERATION

Sue J. Kang, Duk L. Na, *Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea. Contact e-mail: susue73@hotmail.com*

Background: Frontotemporal lobe degeneration (FTLD) is a heterogeneous, non-Alzheimer's disease. According to the consensus criteria proposed by Neary and Snowden (1998), FTLD is subdivided into frontotemporal dementia (FTD), semantic dementia (SD), and nonfluent progressive aphasia (PA). FTLD had been considered a rare disease but few studies investigated its frequency and demographic data in a large sample. **Objective(s):** The aim of this study was to investigate the demographic data of FTLD in a Memory Disorder Clinic in Seoul, Korea. **Methods:** We selected 97 (2.73%) consecutive patients with a diagnosis of FTLD from 3,546 patients who visited the Memory Disorder Clinic at Samsung Medical Center in Seoul, Korea, between January 1994 and December 2003. All the FTLD patents met the clinical diagnostic criteria of Neary and Snowden (1998). During the same period we found 737(20.76%) patients with Alzheimer's disease (AD) who satisfied the probable NINCDS-ADRDA criteria. **Results:** The frequency of FTLD versus AD was about 1:7.6. FTLD significantly differed from AD in age (FTLD vs. AD: 61.71±10.31 vs. 70.82±8.70, p<. 001), age of onset (FTLD vs. AD: 58.73±10.31 vs. 67.74±9.12, p<. 001) and MMSE (FTLD vs. AD: 16.07±8.82 vs. 18.10±6.57, p=0.046). However the two groups did not differ in terms of sex, education, and dementia severity assessed by Clinical Dementia Rating (CDR). The FTLD patients were classified into 71