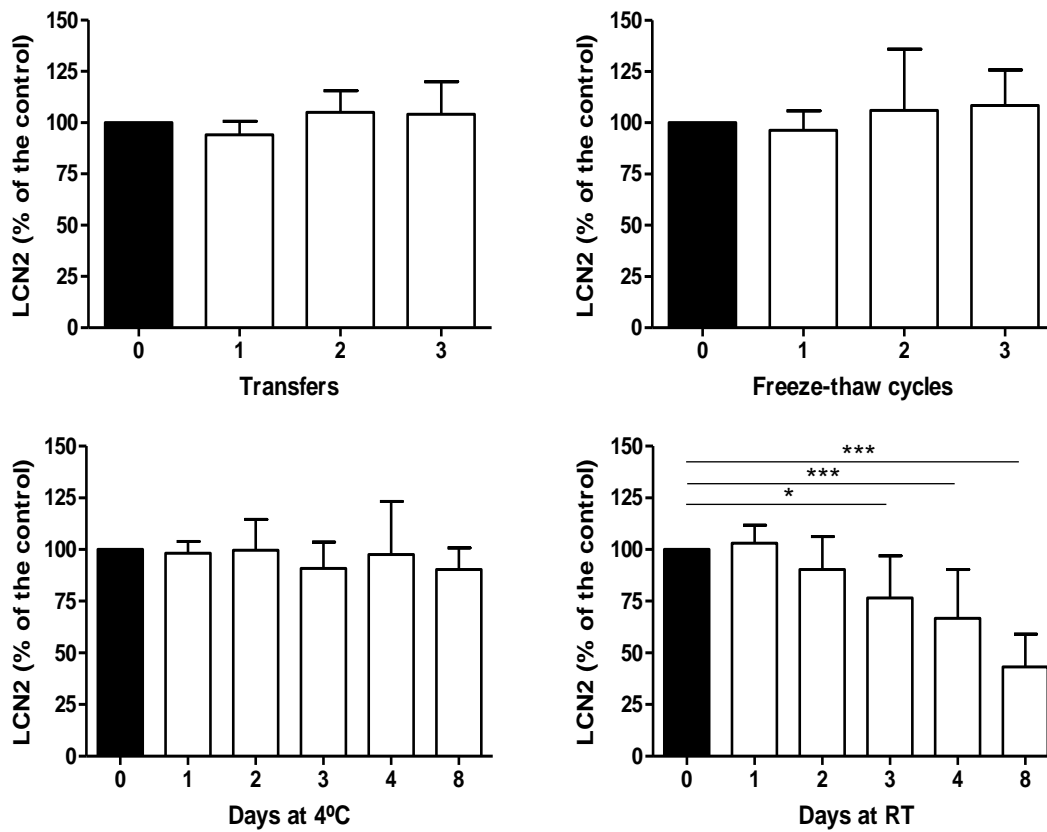


## Additional file 1 A. Pre-analytic study



### Figure Legend:

Four plasma samples (healthy controls) were analyzed repeatedly at baseline and each time after three transfers (upper left), three freeze-thaw cycles (room temperature/minus 80°C, upper right), one to four and eight days storage at 4°C (lower left), as well as room temperature (lower right). Comparisons of Lipocalin 2 concentrations were calculated with ANOVA followed by Bonferroni correction. Differences are indicated when p was < 0.05 (\*) and < 0.001 (\*\*\*), respectively.

**Additional file 1 B. Results from linear regression models and post hoc Tests in Figure 1.**

| Comparison   | Estimate | Std. Error | t-value | p-value |
|--------------|----------|------------|---------|---------|
| CJD - AD     | 0.552    | 0.082      | 6.771   | <0.001  |
| FTD - AD     | 0.404    | 0.110      | 3.659   | 0.005   |
| HC - AD      | 0.600    | 0.082      | 7.286   | <0.001  |
| LBD - AD     | 0.369    | 0.097      | 3.811   | 0.003   |
| ND-Dem - AD  | 0.422    | 0.120      | 3.527   | 0.008   |
| VaD - AD     | 0.666    | 0.114      | 5.849   | <0.001  |
| FTD - CJD    | -0.148   | 0.108      | -1.367  | 0.811   |
| HC - CJD     | 0.048    | 0.080      | 0.594   | 0.997   |
| LBD - CJD    | -0.183   | 0.096      | -1.904  | 0.467   |
| ND-Dem - CJD | -0.130   | 0.117      | -1.109  | 0.921   |
| VaD - CJD    | 0.114    | 0.112      | 1.014   | 0.948   |
| HC - FTD     | 0.196    | 0.109      | 1.793   | 0.542   |
| LBD - FTD    | -0.035   | 0.121      | -0.285  | 1       |
| ND-Dem - FTD | 0.018    | 0.139      | 0.133   | 1       |
| VaD - FTD    | 0.262    | 0.135      | 1.942   | 0.441   |
| LBD - HC     | -0.230   | 0.096      | -2.412  | 0.189   |
| ND-Dem - HC  | -0.177   | 0.118      | -1.502  | 0.734   |
| VaD - HC     | 0.066    | 0.114      | 0.576   | 0.997   |
| ND-Dem - LBD | 0.053    | 0.131      | 0.405   | 1       |
| VaD - LBD    | 0.296    | 0.124      | 2.392   | 0.197   |
| VaD - ND-Dem | 0.243    | 0.143      | 1.700   | 0.605   |

Estimates, standard errors, t-values, and p-values were calculated through pairwise comparisons of means of log-transformed values by Tukey contrasts, HC: healthy controls, ND-Dem: non-neurodegenerative neurological diseases with dementia syndrome, AD: Alzheimer's disease, CJD: Creutzfeldt-Jakob disease, LBD: Lewy body diseases (dementia with Lewy bodies and Parkinson's disease dementia), FTD: fronto-temporal dementia, and VaD: vascular dementia.

**Additional file 1 C. Results from linear regression models and post hoc Tests in Figure 2 and Figure 3.**

| Comparison            | Estimate | Std. Error | t-value | p-value |
|-----------------------|----------|------------|---------|---------|
| <b>Figure 2A</b>      |          |            |         |         |
| HC - AD               | 0.580    | 0.083      | 6.946   | <0.001  |
| MCI-AD - AD           | 0.590    | 0.1467     | 4.012   | <0.001  |
| MCI-AD - HC           | 0.009    | 0.1476     | 0.063   | 0.998   |
| <b>Figure 2B</b>      |          |            |         |         |
| HC - AD               | 0.355    | 0.112      | 3.164   | 0.007   |
| amnesic MCI - AD      | 0.248    | 0.106      | 2.350   | 0.056   |
| MCI-AD - HC           | -0.107   | 0.106      | -1.011  | 0.572   |
| <b>Figure 2D</b>      |          |            |         |         |
| HC - VaD              | 0.165    | 0.137      | 1.204   | 0.451   |
| VCI-MCI - HC          | -0.001   | 0.158      | -0.008  | 1.000   |
| VCI-MCI - VaD         | -0.166   | 0.169      | -0.982  | 0.587   |
| <b>Figure 3</b>       |          |            |         |         |
| spAD - rpAD           | 0.314    | 0.124      | 2.539   | 0.013   |
| Apo E 3/4 - 3/3       | 0.063    | 0.147      | 0.435   | 0.899   |
| Apo E 4/4 - 3/3       | 0.337    | 0.239      | 1.409   | 0.336   |
| Apo E 4/4 - 3/4       | 0.273    | 0.235      | 1.164   | 0.471   |
| A+T-N+/- vs. A-T+N+/- | 0.199    | 0.212      | 0.941   | 0.768   |
| A+T+N+/- vs. A-T+N+/- | 0.068    | 0.159      | 0.428   | 0.971   |
| A+T+N+/- vs. A+T-N+/- | -0.131   | 0.189      | -0.694  | 0.891   |
| A-T+N+/- vs. A-T-N+   | 0.063    | 0.419      | 0.150   | 0.999   |
| A+T-N+/- vs. A-T-N+   | 0.262    | 0.419      | 0.625   | 0.917   |
| A+T+N+/- vs. A-T-N+   | 0.131    | 0.406      | 0.322   | 0.987   |

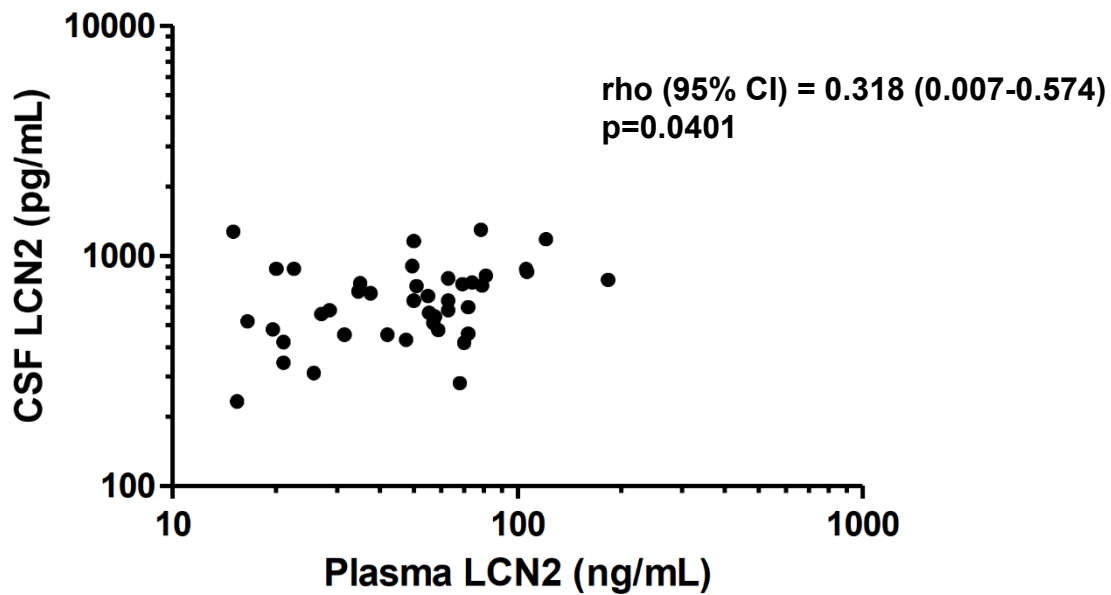
Estimates, standard errors, t-values, and p-values were calculated through pairwise comparisons of means of log-transformed values by Tukey contrasts, HC: healthy controls, AD: Alzheimer's disease, MCI-AD: mild cognitive impairment with positive AD biomarker, VaD: vascular dementia, VCI-MCI: mild vascular cognitive impairment

**Additional file 1 D. Results from linear regression models using only A+/T+ AD-patients.**

| <b>Comparison</b> | <b>Estimate</b> | <b>Std. Error</b> | <b>t-value</b> | <b>p-value</b> |
|-------------------|-----------------|-------------------|----------------|----------------|
| CJD - AD          | 0.551           | 0.099             | 5.562          | <0.001         |
| FTD - AD          | 0.403           | 0.124             | 3.246          | 0.021          |
| HC - AD           | 0.600           | 0.101             | 5.954          | <0.001         |
| LBD - AD          | 0.370           | 0.114             | 3.250          | 0.021          |
| ND-Dem - AD       | 0.421           | 0.132             | 3.189          | 0.025          |
| VaD - AD          | 0.665           | 0.128             | 5.210          | <0.001         |

Estimates, standard errors, t-values, and p-values were calculated through pairwise comparisons of means of log-transformed values by Tukey contrasts, HC: healthy controls, ND-Dem: non-neurodegenerative neurological diseases with dementia syndrome, AD: Only patients with diagnosis of Alzheimer's disease based on pathologic CSF abeta 1-42 and also pathologic phosphorylated tau protein (A+/T+, n=39), CJD: Creutzfeldt-Jakob disease, LBD: Lewy body diseases (dementia with Lewy bodies and Parkinson's disease dementia), FTD: fronto-temporal dementia, and VaD: vascular dementia.

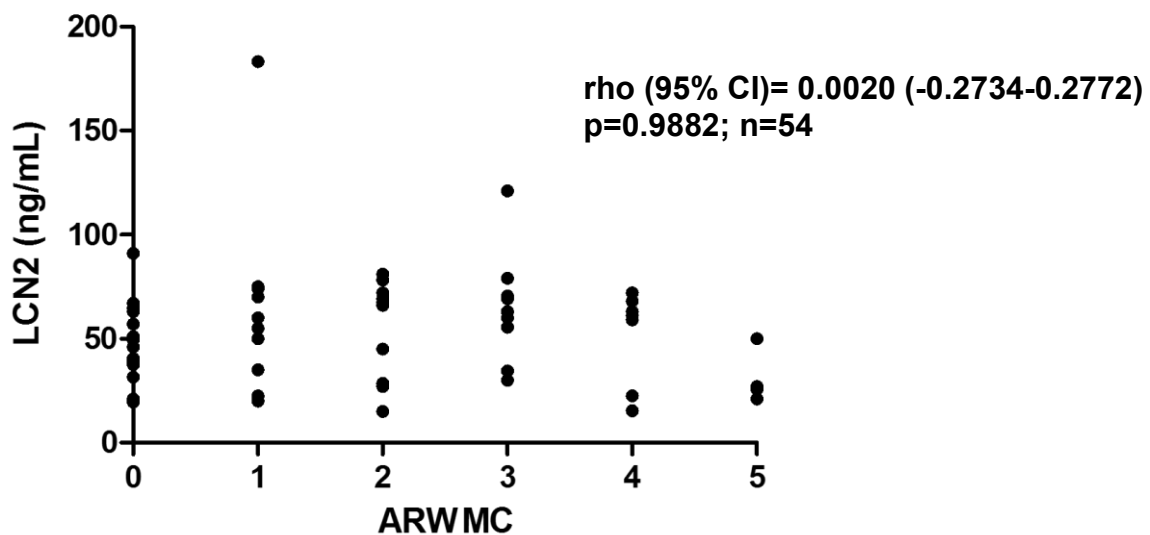
### Additional file 1 E. Correlation of plasma and CSF LCN2



#### Figure legend:

Association of plasma and CSF lipocalin 2 (LCN2). Correlation coefficient ( $\rho$ ), 95% confidence interval (95% CI) and p-values from non-parametric spearman correlation is indicated.

### Additional file 1 F. Correlations of plasma LCN2 and ARWMC in AD



#### Figure legend:

Scatter plot of the association between age-related white matter changes scale (ARWMC) scores and plasma lipocalin LCN2 concentrations. Spearman coefficients ( $\rho$ ) with 95% confidence interval (CI) and corresponding p-values are indicated.