**Data Analysis section**

We will use linear regression to conduct the analysis. The assumption of outcome is normal distribution. If the outcome is skewed, appropriate transformation should be performed. Biological data is usually right skewed and need log transformation. Covariates that will be adjusted in model are demographics (age, sex), severity level (CDR of 0 and 0.5), APOE genotype (present or absent of E4 allele), BMI, history of hypercholesterolemia, NSAID use; immune-related health conditions. To correct the inflated type I error caused by multiple comparison of six predictor, we used Bonferroni adjustment. The alpha level is set as 0.008. Power is set as 0.8. We used best subset method to perform model selection: we will choose the models with highest R-square and lowest Cp and with main predictors in them. Then interactions will be tested with the remaining covariates.

Aim1:

Hypothesis a:

We are going to fit 12 sets of models: there are six kinds of models corresponding to six markers of cytokine and chemokine predictors: IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin, ACT at baseline. For each model, the outcomes are the change in cortical thickness and the change in memory over one year. Additional covariates that should be adjusted are Baseline cortical thickness and baseline memory separately corresponding to change in cortical thickness as the outcome and change in memory as the outcome.

Hypothesis b:

All are the same as hypothesis a expect that we will use change in markers as main predictors instead of markers at baseline.

Aim 2:

Hypothesis a:

We are going to fit 12 sets of models: there are six kinds of models corresponding to six markers of cytokine and chemokine predictors: IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin, ACT at baseline. For each model, the outcomes are the amyloid deposition and cortical thickness at baseline. Confounders are age and sex.

Hypothesis b:

We are going to fit 12 sets of models: there are six kinds of models corresponding to six markers of cytokine and chemokine predictors: IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin, ACT at baseline. And for each model we will add amyloid and cortical thickness at baseline separately. Interaction will be considered. The outcome for each model is change in memory.

**Sample size calculation:**

Given the fact that the correlation between all outcomes and main predictors are from 0.2 to 0.6. We are going to use correlation=0.2 to estimate the maximum sample size. The initial sample size=295. Considering about 10% loss follow up. The final sample size should be 327 to meet all our need. We cannot conclude if this calculation is conservative or not because we don’t know how many predictors are precision predictor, and how many predictors are confounders. To calculate the detectable difference in interaction between each marker and amyloid, or each marker and cortical thickness,

Sample size, assume sigma are equal

Notes (will be removed finally):

Preliminary study: 18-24 months

N=92

Predictor: IL-6

Covariate: Total cortical thickness

Outcome: cortical thickness

Beta=-20, se=9.604, p=0.03

N=122

Predictor: increase in MCP-1

Covariate: baseline MCP-1 level

Outcome: poorer memory performance at follow-up (beta=-0.018, se=0.009, uni\_p=0.046, mul\_p=0.02)

Outcome: verbal memory recall, control for demographics, p<0.01)

N=171

Predictor: chromosome and chemokines (MCP-1, Eotaxin-1)

Covariate: demographics, severity level, APOE genotype

Outcome: Lower memory score, Verbal and visual memory

N=40

Period: 12 month

Population: aMCI

Predictor: Baseline peripheral chemokine levels (Eotaxin-1 level)

Outcome: memory decline in aMCI (episodic memory list-learning test) beta=-0.016, se=0.006, p=0.017

Covariate: Baseline memory performance, demographics (age, sex), severity level (CDR 0 and 0.5), APOE status (present or absent of E4 allele)