# A multi-omic investigation of the role of APOE genotype in Alzheimer's disease

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## Overview

- Alzheimer's disease (AD) is the most common neurodegenerative disease.
- The genotypes of apolipoprotein E (APOE) were shown to be different risk factors for AD
- Here a multi-omic approach was performed to investigate the molecular profiling and the role of APOE genotype in AD

## Introduction

### Alzheimer's Disease and APOE Genotype

Alzheimer's disease (AD) is the most common neurodegenerative disease affecting 47 million people worldwide. There is no cure so far and its cause remains unclear. However, the strongest risk factor for developing AD after age is the apolipoprotein E (APOE) gene [1-3]. Previous studies showed that among the APOE genes (ε2, ε3 and ε4), the ε4 carriers have a greater chance of developing AD, while the ε2 carriers are protected. It is unclear how the ε4 allele increases the risk of developing AD [4]. Thus, the study of multi-omic molecular changes that occur due to the different APOE genotypes may provide important insights into the mechanisms that can protect (ε2 carriers) against or enhance (ε4 carriers) the risk of developing AD.

**Table 1** | The effect of *APOE* ε4 on AD frequency and age at onset[7]

| Characteristic | *APOE* ε4 noncarrier | *APOE* ε4 heterozygous | *APOE* ε4 homozygous |
|---|---|---|---|
| AD frequency (%) | 20 | 47 | 91 |
| Mean age of clinical onset (years) | 84 | 76 | 68 |

Abbreviations: AD, Alzheimer disease; *APOE* ε4, ε4 allele of the apolipoprotein E gene.

## Methods

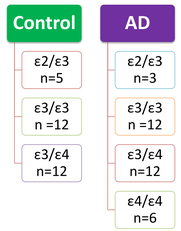
Here we used multi-omic (proteomic, metabolomic and lipidomic) measurements to investigate molecular changes between AD and control patients with different APOE genotypes.

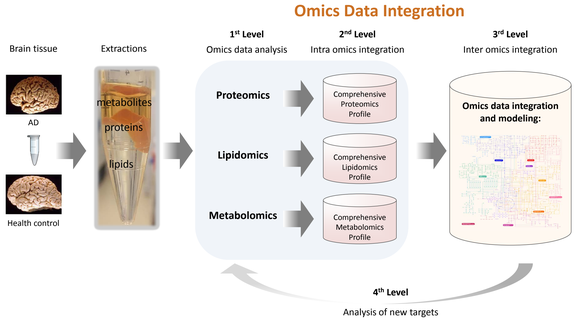
### Cohort Study disease and genotype

- ***Sampling:***
Brain tissue samples from the frontal cortex and cerebellum were obtained from 62 postmortem patients, including four different APOE genotypes (ε2/ε3, ε3/ε3, ε3/ε4 and ε4/ε4).

- ***Sample extraction:***
MPLEx: Single-Sample Extraction for Integrative Proteomic, Metabolomic, and Lipidomic Analyses

- ***Multi-Omic Analyses:***
Integrative Proteomic, Metabolomic, and Lipidomic Analyses were performed and the data processing are ongoing.

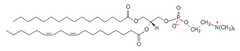


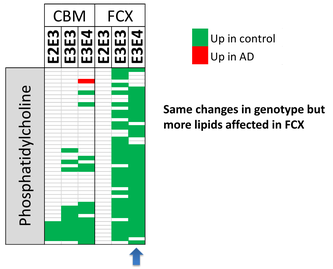




## Results

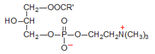
### Lipidomic profiling for AD and APOE genotype

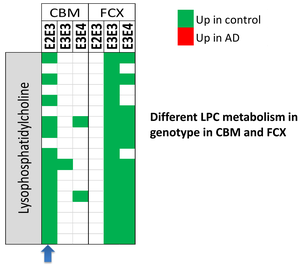
**Phosphatidylcholine (PC)**



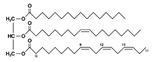


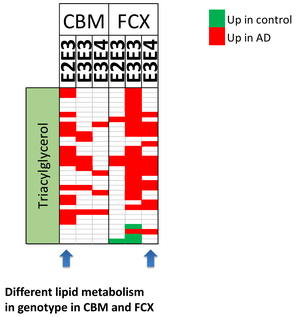

**LysoPC**



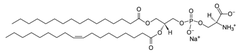


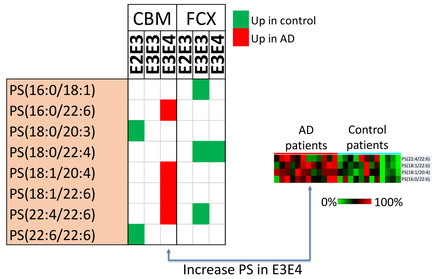

**Triacylglycerol**






**Phosphatidylserines**






## Conclusions

- Multi-omic approaches were applied to understand the role of APOE genotype on AD
- Different lipidomic profiles were observed in Alzheimer's disease patients and healthy control
- Different lipidomic profiles were observed in the cerebellum and frontal cortex of the brain
- Proteomic and metabolomic profiling are still ongoing

## Acknowledgements

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