Alzheimer’s disease (AD) is a neurodegenerative disorder that represents 65-75% of all cases of dementia. Early stages features are typically attributed to age (apathy, lack of attention, loss of motivation…) and advanced stages to impairments for learning and orientation, dysphasia and anosognosia. However, the definitive diagnosis is only determined by the presence of β-amyloid plaques (Aβ plaques) and neurofibrillary tangles (NFT) in post-mortem brains.

## RESULTS

Epigenetics regulates genic expression without changing the sequence of DNA nucleotides. Epigenetic signature is persistent (as it can be inherited through generations) but also dynamic (because it is influenced by environmental stimuli). Epigenetic changes are involved in phenotypic diversity but also represent a potential risk to develop neurological diseases such as AD.

### Three epigenetic mechanisms altered in AD

- **DNA methylation**
  - Addition of CH3 to 5' of cytosine forming 5-mC. This process usually occurs in CpG islands, mainly found in the promoter part of some human genes. DNMTs are the enzymes that carry out the reaction using SAM.

- **Histone tail modifications**
  - Acetylation, methylation, phosphorylation, ubiquitylation, sumoylation and other post-translational histone tail modifications are responsible for the condensation state of chromatin (euchromatin or heterochromatin):
    - Histone methylation is regulated by HMTs and HDMTs: activity along with SAM accessibility. Its influence on transcription is site-dependent.
    - Histone phosphorylation usually favors transcription.
    - Histone acetylation is the most studied post-translational modification and it generally increases transcription.

- **Non-coding RNA: miRNAs**
  - miRNAs (also known as microRNAs) participate in post-translational regulation of genic expression by RNA silencing. They interfere with mRNA to destabilize it and either provoke its degradation or avoid its translation.
    - Each miRNA recognizes up to hundreds of mRNAs.
    - Each miRNA is controlled by lots of miRNAs.

### Factors influencing AD development

- **Life experiences**
  - Physical exercise, consumption of antioxidants…

- **Risk factors for AD**
  - Genetic: APOE4, TREM2...
  - Non-genetic: age, diet, stress, hypotension, diabetes, smoking, metals, pesticides…

### Epigenetic signature

Gene-expression profile linked to memory formation or disease risk

### Transmission of disease risk to the next generation?

### CONCLUSIONS

- Alzheimer’s disease has a big prevalence in global population and no efficient treatment has been found so far.
- Whereas some genetic and environmental factors have been identified to be a risk to the progression of this neurodegenerative disorder, further research is needed to find a way for prevention and early diagnosis.
- DNA methylation and histone tail acetylation patterns, as well as miRNAs expression levels have been associated to transcriptional up and down-regulation of certain genes involved in AD development, such as APP, PS1 and BACE-1.
- Research focuses on the identification of biomarkers based on variations of epigenetic mechanisms that can be found in AD patients comparing to same-aged healthy subjects.
- Given that epigenetic alterations could be modified, epigenome studies seem to be a new and promising line for AD therapy.

### REFERENCES

The most relevant reviews and articles that helped to prepare this poster are: