

## **PSEN1 Expression is Associated to Promoter Methylation in the Brain of Alzheimer's Mice and in Humans**

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**P**resenilin1 (PSEN1) protein constitutes the catalytic subunit of the  $\gamma$ -secretase complex. This enzyme, among other, is responsible for the processing of the amyloid  $\beta$ protein precursor (A $\beta$ PP), eventually leading to the production and accumulation of the amyloid  $\beta$  (A $\beta$ ) peptides in the brain, associated with the Alzheimer's Disease (AD). PSEN1 and  $\gamma$ -secretase are also responsible for the processing of key molecules (E-cadherin, Notch1) in course of neurodevelopment.

Depicting the regulation of PSEN1 could be useful for the comprehension of the molecular mechanisms underlying neurodevelopment and neurodegeneration. Previous studies indicated *PSEN1* as a locus subject to differential methylation in Alzheimer's Disease affected subjects versus healthy controls. Moreover, we previously demonstrated that *PSEN1* methylation and, consequently, expression are modulated by perturbation of the methylation metabolism in AD mice.

The present study allowed to characterize the DNA methylation profile of *PSEN1* promoter during the neurodevelopment and neurodegeneration, in the frontal cortex of TgCRND8 AD transgenic mice and of human subjects. The data obtained, allowed to demonstrate that both CpG and non-CpG (CpA, CpC, CpT) methylation of *PSEN1* promoter is differentially modulated during development and aging and in AD patients versus controls. *PSEN1* expression was correlated to CpG and non-CpG methylation patterns. Altogether, these data point-out that non-CpG methylation has a functional role in *PSEN1* regulation and stress the hypothesis that AD may have an epigenetic basis.

### **Biography:**

Andrea Fuso, Ph.D., biologist, is researcher at Sapienza University of Rome. He teaches at post-graduations courses and is author of several scientific papers, book chapters and is speaker at many lectures and conferences. He serves in editorial boards, as referee for journals and grant committees and in the Board of Directors of the Epigenetics Society.

His researches focus on neurodegenerative diseases, one-carbon metabolism and methylation reactions, studying the dynamics of DNA methylation/demethylation and then on-CpG methylation, applied to nutrition and one-carbon metabolism in neurodegeneration and muscle differentiation.