Département de psychiatrie
Centre de neurosciences psychiatriques
Site de Cery
CH-1008 Prilly - Lausanne

Centre de Neurosciences Psychiatriques

CNP SEMINAR

ANNOUNCEMENT

Friday, May 18, 2018, 11:00

"PM20D1 quantitative trait locus is associated with Alzheimer's disease"

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The chances to develop Alzheimer's disease (AD) result from a combination of genetic and non-genetic risk factors, the latter likely mediated by epigenetic mechanisms. In the past, genome-wide association studies (GWAS) have identified an important number of risk loci associated with AD pathology, but a causal relationship thereof remains difficult to establish. In contrast, locus-specific or epigenome-wide association studies (EWAS) have revealed site-specific epigenetic alterations and thereby provide mechanistic insights for a particular risk gene, but often lack the statistical power of GWAS. Combining both approaches, we have found that *PM20D1* is a methylation/expression quantitative trait locus (mQTL/eQTL) coupled to an AD-risk associated haplotype, which displays enhancer-like characteristics and contacts the PM20D1 promoter via a haplotype-dependent, CTCF-mediated chromatin loop. Furthermore, PM20D1 is increased following AD-related neurotoxic insults, at symptomatic stages in the APP/PS1 mouse model of AD and in human AD patients, who are carriers of the non-risk haplotype. Importantly, genetically increasing and decreasing the expression of PM20D1 reduces and aggravates AD-related pathologies, respectively. These findings suggest that in a particular genetic background, PM20D1 contributes to neuroprotection against AD.

Selected publications:

1. Sanchez-Mut JV, Heyn H, Silva BA, Dixsaut L, Garcia-Esparcia P, Vidal E, Sayols S, Glauser L, Monteagudo-Sánchez A, Perez-Tur J, Ferrer I, Monk D, Schneider B, Esteller M, Gräff J. PM20D1 quantitative trait locus is associated with Alzheimer's disease. Nat Med. 2018. (in press).
2. Sanchez-Mut JV, Gräff J. Epigenetic Alterations in Alzheimer's disease. Front. Behav. Neurosci, 2015: 9 (347).

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