Poster | Disorders of Nervous Systems and Treatment

[3P]Alzheimer's Disease and Dementia

Fri. Jul 31, 2020 1:30 PM - 3:30 PM Poster Session

*Videos are available throughout the meeting period.

[3P-213]RNA-binding proteins that regulate genes associated with alzheimer's disease

*Yoshihiro Kino, Motoaki Yanizu, Yuka Honda, Jun-Ichi Satoh (Dept. Bioinformatics, Meiji Pharm Univ, Tokyo)

Genetic variations of TREM2 and CD33 have been implicated as risk factors of Alzheimer's disease (AD), a leading cause of dementia in elderly. Recent studies suggested that both TREM2 and CD33 are involved in the regulation of microglia in response to the accumulation of amyloid beta. CD33 activity is regulated by the alternative splicing of exon 2, which is differentially spiced depending on an AD-associated genetic variant. Recently, we reported that exon 3 of TREM2 is an alternative exon whose exclusion leads to reduction in full-length TREM2 proteins. Thus, splicing regulation of these genes might be involved in the pathophysiological roles of microglia in AD and other neurodegenerative diseases. Here, we tried to identify RNA-biding proteins that regulate alternative splicing of CD33 and TREM2. Using a panel of RNA-binding proteins, we found that a family of RNA-binding protein regulates TREM2 exon 3 splicing. Interestingly, exon 3 of mouse Trem2 did not show alternative splicing, suggesting a human-specific regulation of this exon. Regarding CD33 exon 2, we identified another protein family that also regulates a corresponding exon of mouse Cd33. We also identified novel splicing patterns in the region between exon 1 to exon 3, some of which were predicted to be subjected to nonsense-mediated mRNA decay and were differentially induced by RNA-binding proteins. Thus, our results revealed novel regulators of the protein expression of TREM2 and CD33 and suggested an evolutionary difference in TREM2 splicing between human and mouse.