

Prion Diseases: from Genetics to Pathogenic Mechanisms

Yong-Sun Kim, MD, PhD

Ilsong Institute of Life Science and Department of Microbiology, College of Medicine, Hallym University

Prion diseases are unconventional fatal neurodegenerative diseases associated with spongiform vacuolation, neuronal cell death, accumulation of scrapie isoform of prion protein (PrP^{Sc}) and astrogliosis in brains. In here, we summarize our recently studies about pathogenic mechanisms in prion disease and biology. To clarify the nature of prion diseases, firstly, we are analyzing polymorphisms of *PRNP* in Korean population and sCJD patients to understand the relationship between polymorphisms of prion protein gene (*PRNP*) and the development of sCJD in Korean. It leads us to construct a milestone for CJD diagnosis of Korean. Secondly, because the cellular prion protein (PrP^C) is essential for development of prion diseases, we are studying physiological functions of PrP^C associated with apoptosis and autophagy pathway using PrP^C-deficient neuronal cell lines. Thirdly, PrP^{Sc} is derived from PrP^C by a post-translational conformational change and this conversion mechanism is unclear. Interestingly, we found that one or more lysines at residues 23, 24, and 27 of PrP^{Sc} are covalently modified with advanced glycosylation end products (AGEs). Fourthly, we are investigating the involvement of endogenous retroviruses in prion diseases. The target retroviruses are MuLV and HERV in SAMR1 and P8 and CSF of Koreans CJD and controls, respectively. Fifthly, we are investigating the alteration of various cytokines, chemokines, growth factors and JAK-STAT signaling pathway in prion diseases. Finally, we are investigating molecular etiologies of Gerstmann-Sträussler-Scheinker (GSS) syndrome using GSS mutant PrP expressing *Drosophila* model. Although, all our works and other researches in prion diseases have been proceeded by various approaches, further studies will be required to clarify the mechanism and pathogen of prion diseases.

Keyword(s): Prion, CJD, Neurodegeneration

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