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Lessons from cathepsin deficient mice on human brain diseases

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A group of proteases in the endosomal/lysosomalproteolytic system have been designated as cathepsins, which is derived from the Greek term meaning "to digest". Considering that cathepsins can irreversibly cleave peptide bonds, the primary function of cathepsins has been believed to be their "disintegration actions". However, there is increasing evidence that cathepsins can also exert "modulator actions" by which substrates are activated after limited cleavage. For examples, we have recently found that cathepsin B (CatB) is involved in the maturation of pro-IL-1 through proteolytic activation of pro-caspase-1 in the autophagosomes of spinal microglia following peripheral inflammation, leading to the induction and maintenance of inflammatory pain. On the other hand, cathepsin S (CatS) is involved in proteolytic processing of the MHC class II-associated invariant chain in splenicdendritic cells following peripheral nerve injury, leading to activation of CD4+ T cells. Infiltration of activated CD4+ T cells may contribute to transition of nerve injury-induced acute pain to a chronic pain state. Beyond a bulk proteolysis in the endosomal/lysosomal system, the growing understanding of modulator actions of cathepsins in microglia and other mononuclear phagocytes could contribute to the development of protease inhibitors as therapeutic interventions against brain diseases associated with chronic inflammation and immune response.

Biography

Hiroshi Nakanishi is currently a Professor of Department of Aging Science and Pharmacology, Kyushu University, Japan. He completed his PhD in Kyushu University and his post-doctoral trainingin the University of Tennessee at Memphis. He became a Professor of Laboratory of Oral Aging Science, Kyushu University in 2000. He was the Dean of Faculty of Dental Science, Kyushu University from 2011 to 2013. He is now the vice Dean Faculty of Dental Science, Kyushu University from 2014. His research is focusing on the physiological and pathological functions of microglia in the central nervous system.

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