A Commentary about the Function of Selenoprotein SELENOK for the Prevention and Treatment of Alzheimer’s Disease

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The role of trace element selenium (Se) on the preventing and treating Alzheimer’s disease (AD) and other neurodegenerative diseases has been confirmed by many researchers and should be paid more attention [1]. Most of the functions of selenium are achieved through selenoproteins, and 25 selenoproteins have been known existing in human proteome [2,3]. SELENOK (selenoprotein K, SELK) is an 11-kDa selenoprotein (there are 94 amino acid residues for human SELENOK and mouse SELENOK, mSELENOK) located on the endoplasmic reticulum (ER) and Golgi membrane [4,5]. Studies have shown that SELENOK plays an important role in promoting the effective Ca2+ influx during the activation of T cells, neutrophils, macrophages and other immune cells, and provides new insight for the study of the molecular mechanism of dietary selenium to enhance the immune response [6,7]. Our studies suggest that SELENOK can increase cytosolic free Ca2+ level of microglial cells by up-regulating the expression of IP3R, thus enhancing the migration and phagocytosis of microglial cells [8]. Since SELENOK can interact with the SH3 domains of DHHC6, a palmitic acid acyltransferase, to catalyzing the palmitoylation of IP3R and improve its stable expression [9,10], therefore, SELENOK’s deficiency might lead to the low expression of IP3R due to the defect of its palmitoylation [9]. To date, many other selenoproteins also show some functions for the prevention and/or treatment of AD. Studies by other researchers have found that SELENOP (selenoprotein P, SeP, SEPP1, SELP) can not only plays a unique role in maintaining the stability of selenium content in the brain by transferring selenium into brain tissues and nerve cells via ApoER2 (a member of the lipoprotein receptor family) on vascular endothelial cells [11] but also serves as a donor of selenium in the synthesis of other selenoproteins [1]. Some selenoproteins can prevent and/or treat AD through inhibiting oxidative stress in the brain tissue, keeping the state of protein, biological membrane and other material types (Grx1, GPx4 (glutathione peroxidases) [12], MSRB1 (metionine sulfoxidereductase B1) [13] and SELENOW (selenoprotein W, SELW, SEPW1)) [14]. Some other selenoproteins work through preventing endoplasmic reticulum stress (SELENOS (selenoprotein S, SELS, SEPS1, VIMP)) [15], inhibiting inflammation factors or preventing mitochondria peroxide and maintaining the function of microglia (TXNRD (thioredoxin reductase) [16] and SELENOH (selenoprotein H, SELH)) [17]. Some other selenoproteins perform functions through maintaining intracellular calcium homeostasis (SELENOM (selenoprotein M, SELM)) [18] or combining with the metal ions (SELENOP and MSRB) [13,19]. Although researches on the relationship between selenoproteins and AD have made gratifying progress in recent years, the target and mechanism of different selenoproteins in AD still need to be further studied.

Conflicts of Interest

These authors have no conflicts of interest to declare.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (No. 31371085 and No. 81503085), the Foundation of the Education Department of Liaoning Province of China (No. LYB201610), and the Foundation of the Department of Science and Technology of Liaoning Province of China (No. 20180551168 and No. 201601097). The authors are grateful to Dr. Byoung Jae, Lee (Seoul National University, Seoul, Republic of Korea) for providing help on the studies of the functions of SELENOK.

References


