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MEK1/2-ERK 1/2–dependent alphaB-crystallin phosphorylation in retina: a focus on aging and age-related macular degeneration

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Abstract: Accumulation of protein aggregates and increase of intracellular damage are universal hallmarks of aging and accompany the development of some age-related diseases including Age-related macular degeneration (AMD). Alpha-B-Crystallin (CryaB) as the molecular chaperone contributes to maintenance of proteostasis by prevention of protein aggregation (e.g. amyloid beta) and enables their correct refolding. CryaB activity is regulated by MEK1/2-ERK 1/2 signaling pathway through its phosphorylation at the Ser45 position. Nevertheless, the link between changes in MEK1/2-ERK1/2–dependent CryaB phosphorylation with age and the development of AMD remains unclear. Here, we examined MEK1/2-ERK1/2-dependent phosphorylation of p45-CryaB in the retina of Wistar rats with normal aging and senescence-accelerated OXYS rats at the different stages of the development of AMD-like pathology, including the presymptomatic stage.
According to transcriptome analysis, the maximum number of differentially expressed genes (DEG) involved in MEK1/2-ERK1/2 pathway in retina of Wistar rats was found at the age from 20 days to 3 months. The activity of the MEK1/2-ERK1/2 pathway at the mRNA level decreased by the age of 18 months. The number of DEG at 18 months was decreased. The western blotting revealed that the level of MEK1/2 and ERK1/2 proteins did not change with age, while the level of MEK1/2, ERK1/2, and CryaB phosphorylation increased by the age of 18 months. Similar but more significant changes accompanied the development of signs of AMD-like pathology in OXYS rats. The activation of MEK1/2-ERK1/2 pathway detected at the manifestation of retinopathy in OXYS rats (3 months old) and it accompanied the eleved of p45CryaB protein. It remained high during the active progression of retinopathy in OXYS rats against the background of the accumulation beta amyloid 1-42 in the retina. Thus, the activation of MEK1/2-ERK1/2-dependent phosphorylation CryaB occurs during normal aging. Manifestation and progression of the AMD-like pathology in OXYS rats occurs against the background of activation of MEK1/2-ERK1/2 pathway and ERK1/2-dependent CryaB phosphorylation.
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