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PO-078 - (23802) - ATTENUATION OF RETINAL DEGENERATION BY CKD-504, A SELECTIVE HDAC6 INHIBITOR VIA SUPPRESSION OF NEUROINFLAMMATION

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Epigenetic modifications have emerged as a promising strategy to regulate cell function in neurodegenerative diseases. Histone deacetylase 6 (HDAC6) plays a crucial role in neuroinflammation, which is implicated in various neurodegenerative conditions. Consequently, HDAC6 inhibition is considered a potential therapeutic approach. However, its role in retinal degenerative diseases remains unclear. This study investigates the effects of CKD-504, a selective HDAC6 inhibitor, on retinal degeneration (RD).
RD was induced in mice through blue-LED exposure. Functional and morphological changes were assessed using electroretinogram (ERG) recordings and hematoxylin and eosin (H&E) staining. Additionally, retinal microglial cells were activated in primary culture using lipopolysaccharide (LPS). Immunocytochemistry and western blot analyses were conducted to evaluate HDAC6 expression.
HDAC6 expression was significantly induced in microglial cells within RD mouse retina sections and LPS-treated primary cultured microglia. CKD-504 treatment effectively preserved retinal thickness and significantly enhanced a- and b-wave amplitudes in ERG recordings compared to untreated RD mice ($p < 0.05$). Furthermore, CKD-504 markedly inhibited HDAC6 expression in cultured retinal microglial cells ($p < 0.05$).
These findings suggest that HDAC6 plays a key role in microglial activation and retinal inflammation associated with RD. The selective HDAC6 inhibitor CKD-504 demonstrates potential as a therapeutic agent for RD by mitigating neuroinflammation and preserving retinal function.

Palavras-chave : HDAC6, Retinal degeneration, Inflammation