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Poster Sessions

Valproic acid prevents retinal angiogenesis via a proteasome-dependent mechanism in neonatal mice

Akane Morita, Kanako Takahashi, Naoto Iizuka, Keigo Saito, Daiki Asano, Asami Mori, Kenji Sakamoto, Tsutomu Nakahara

Dept. Mol. Pharmacol., Kitasato Univ. Sch. Pharm. Sci.

Pathological retinal angiogenesis contributes to the development and progression of vision-threatening eye diseases, such as retinopathy of prematurity and diabetic retinopathy. Valproic acid, a widely used antiepileptic drug, exerts anti-angiogenic effects by inhibiting histone deacetylase (HDAC). We previously reported that valproic acid and vorinostat, a HDAC inhibitor, suppress pathologic retinal angiogenesis in mice with oxygen-induced retinopathy. In this study, using neonatal mouse retina, we examined the mechanisms of anti-angiogenic effects of valproic acid and vorinostat. Mice were subcutaneously injected with valproic acid, vorinostat, or vehicle once a day from postnatal day (P) 0 to P3. At P4, the delayed retinal angiogenesis was observed in mice treated with valproic acid or vorinostat. The expression level of vascular endothelial growth factor (VEGF) was reduced 2 or 6 hours after a single injection of valproic acid or vorinostat in P4 mice. Both drugs suppressed the VEGF-mediated activation of mammalian target of rapamycin pathway in proliferating endothelial cells. The proteasome inhibitor MG132 prevented valproic acid- and vorinostat-induced reduction in the VEGF expression level. These results suggest that valproic acid suppresses retinal angiogenesis by decreasing retinal VEGF levels by a proteasome-dependent mechanism.