

Inhibition of p38 MAPK Inhibits Early Stages of Diabetic Retinopathy

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p38 mitogen-activated protein kinase (MAPK) is known to play a regulatory role in inflammatory processes in disease. Inflammation has been linked also to the development of diabetic retinopathy in rodents, so we evaluated the effect of a p38 MAPK inhibitor on the development of early stages of diabetic retinopathy in rats. Streptozotocin-diabetic rats were assigned to 2 groups, treated with or without the p38 MAPK inhibitor, PHA666859 (Pfizer), and compared to age-matched nondiabetic control animals. At 2 months of diabetes, insulin-deficient diabetic control rats exhibited significant increases in retinal superoxide, nitric oxide (NO), cyclooxygenase (COX)-2, and leukostasis within retinal microvessels. All of these abnormalities were significantly inhibited by the p38 MAPK inhibitor (25 mg/kgBW). At 10 months of diabetes, significant increases in the number of degenerate (acellular) capillaries and pericyte ghosts were measured in control diabetic rats versus nondiabetic controls, and pharmacologic inhibition of p38 MAPK significantly inhibited all of these abnormalities (all $P < 0.05$). p38 MAPK plays an important role in diabetes-induced inflammation in the retina, and inhibition of p38 MAPK offers a novel therapeutic approach to inhibit the development of early stages of diabetic retinopathy.