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The role of Prostaglandin D_2 synthase in retinal angiogenesis

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Although prostaglandin D_2 (PGD_2) represents anti-angiogenic role in tumor model, its role in physiological and pathological angiogenesis still remain unknown. We here evaluated the role of PGD_2 on retinal angiogenesis using genetically modified mice. In postnatal 8th day retina of WT, lipocalin-type PGD synthase (L-PGDS) was expressed in endothelial cells. Gene deficiency of L-PGDS impaired the physiological angiogenesis of retina, accompanied with increased mRNA expression of pro-angiogenic factor VEGF. *In vitro* study showed that L-PGDS inhibition elevated the hypoxia-induced VEGF expression, which was inhibited by treatment of a PGD_2 metabolite 15d-PGJ_2. We next generated a pericyte deficiency-induced retinal angiogenesis model by injection of anti-PDGFRβ antibody. In P8 retina of WT, the injection of antibody induces inflammation in retina, and infiltrating macrophages expressed hematopoietic PGD synthase (H-PGDS). Gene deficiency of H-PGDS or PGD receptor DP accelerated the angiogenesis. This phenomenon was accompanied with increased mRNA expression of one of the chemokines, Stromal derived factor 1α. In isolated macrophage, hypoxia increased the expression of cytokines, wich was inhibited by adding receptor inhibitor. Taken together, L-PGDS promotes physiological angiogenesis and H-PGDS attenuate pathological angiogenesis in mouse retina.