DNA Repair Response Adaptors: Novel Targets for Vasoproliferative Retinopathy?

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Ischaemic retinopathies, such as retinopathy of prematurity (ROP) and diabetic retinopathy, are major causes of preventable blindness, which affects a significant number of premature infants and diabetic patients worldwide. Hypoxia-driven release of pro-angiogenic growth factors and cytokines in the retina leads to endothelial cell proliferation and neovascularization, aiming to provide oxygen supply to oxygen-deprived areas.¹ During this process, the usually quiescent endothelial cells replicate their deoxyribonucleic acid (DNA) in higher rates, which also requires vigorous engagement of DNA repair responses (DRRs). However, how the elements of DNA repair machinery impact retinal angiogenesis is not completely understood.

A DRR adaptor, H2AX, was previously reported to be important for hypoxia-driven endothelial cell proliferation and neovascularization.² In the next issue, Troullinaki et al studied the role of another DRR adapter, tumour suppressor p53-binding protein 1 (TP53BP1 or 53BP1), in retinal angiogenesis.³ 53BP1 promotes the non-homologous end joining pathway of DNA repair, antagonizing homologous recombination. They showed that 53BP1 deficiency, although did not affect physiological retinal angiogenesis, increased endothelial cell proliferation and neovascularization in the ROP model. The underlying mechanism, which was also verified *in vitro*, was through apoptosis blockade and increase of homologous recombination. Pharmacological inhibition of homologous recombination reversed the pro-angiogenic effects of 53bp1 deficiency under hypoxia, shedding light on a potential therapeutic target for ischaemic retinopathy.³

While this study reports the previously unexplored role of 53BP1 in retinal angiogenesis and widens the current understanding of retinopathy,³ combination of their previous findings with the DRR adaptor H2AX² implies that the relationship between DNA repair adaptors and retinopathy is not straightforward and the delineation of the role of each DNA repair pathway in vasoproliferative retinopathies warrants further investigation.

Conflict of Interest None declared.

References

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