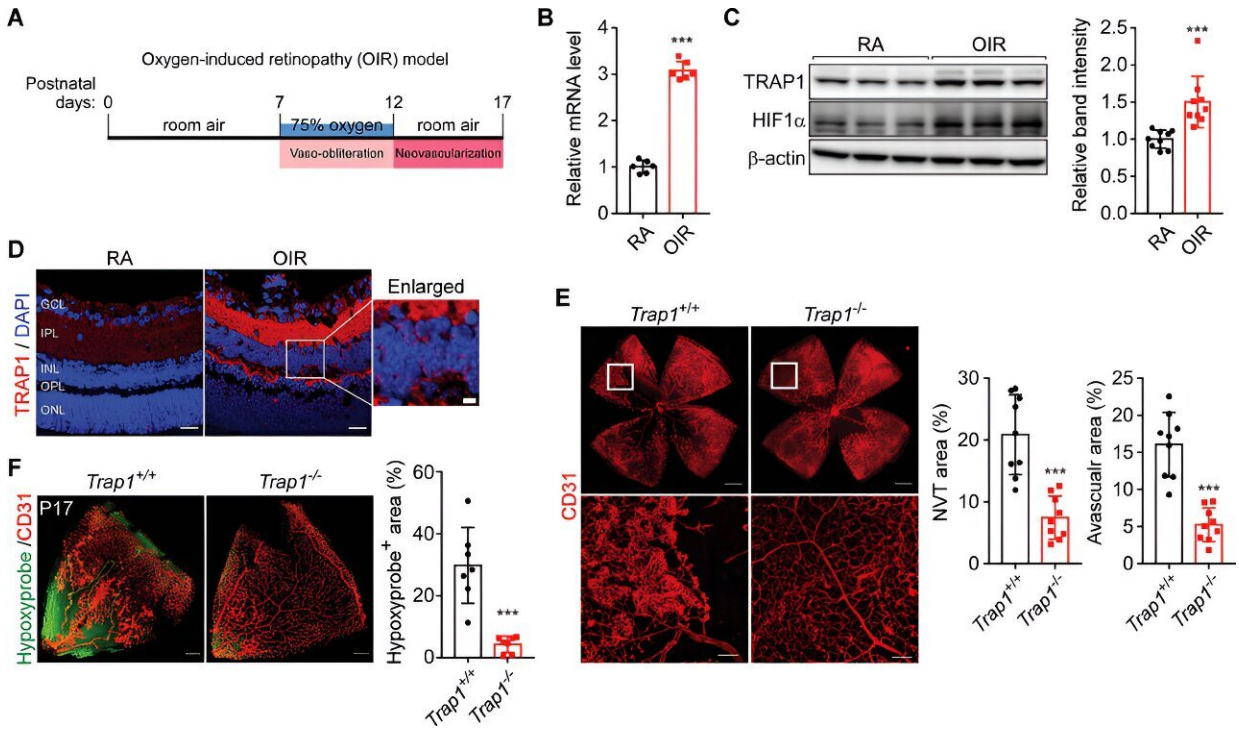
New technology offers promising treatment for ischemic retinopathy

January 17 2024, by JooHyeon Heo



Contribution of TRAP1 to the development of ischemic retinopathy. (A) Schematic for the experimental procedures of OIR mice. B) Quantification of TRAP1 mRNA. C) Quantification of TRAP1 protein levels. D) Immunohistochemical staining of TRAP1 in mouse retinas. E) Normalized retinal blood vessels in Trap1$^{-/-}$ OIR mice. Credit: *Advanced Science* (2023). DOI: 10.1002/advs.202302776

A technology with the potential to treat ischemic retinopathy in

premature infants and diabetic patients has been developed by Professor Byoung Heon Kang and his research team in the Department of Biological Sciences at UNIST, in collaboration with Professor Dong Ho Park's team at Kyungpook National University Hospital.

Ischemic retinopathy, characterized by the breakdown of the blood-retinal barrier and abnormal blood vessel growth, often leads to vision impairment and loss. The researchers have identified the critical role of a mitochondrial chaperone called tumor necrosis factor receptor-associated protein 1 (TRAP1) in the pathogenesis of ischemic retinopathy.

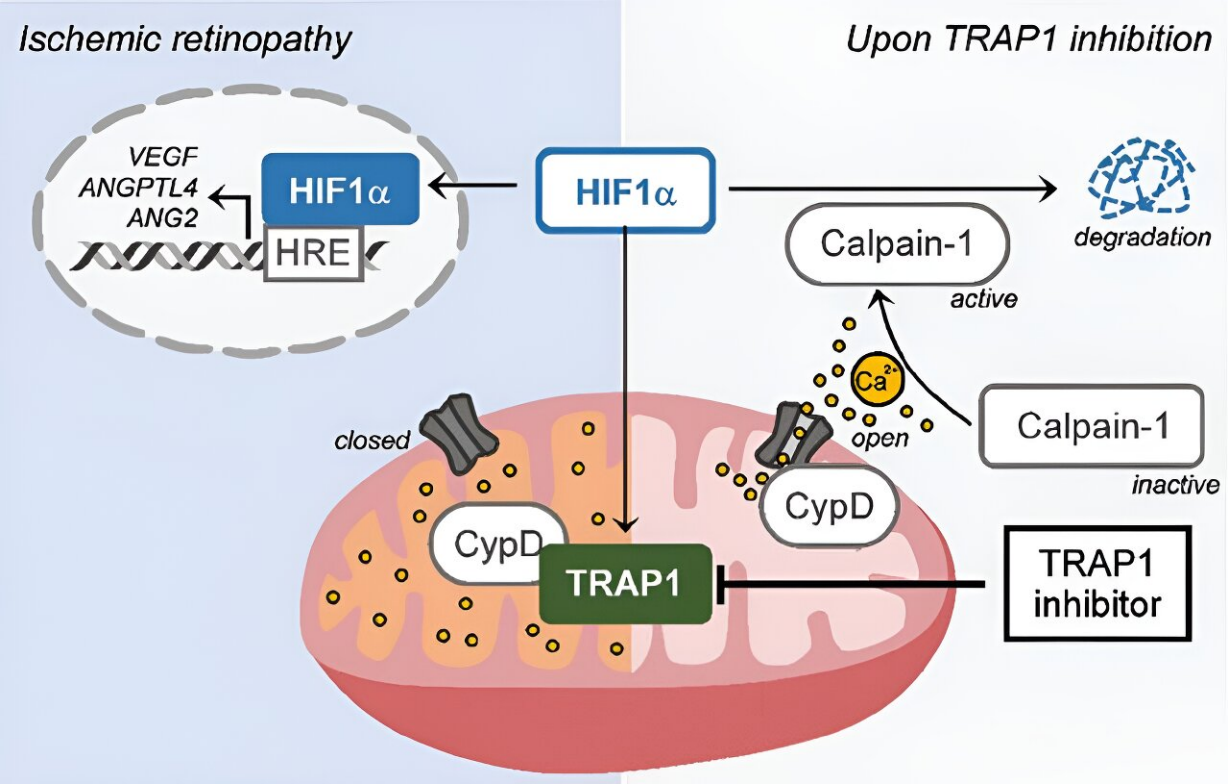
Through genetic Trap1 ablation or treatment with small molecule TRAP1 inhibitors, such as mitoquinone (MitoQ) and SB-U015, the research team successfully alleviated retinal pathologies in mouse models mimicking ischemic retinopathies.

This therapeutic effect was attributed to the proteolytic degradation of hypoxia-inducible factor 1α (HIF1α), a transcription factor implicated in the breakdown of the blood-retinal barrier and pathological neovascularization. The degradation of HIF1α was facilitated by the opening of the mitochondrial permeability transition pore and activation of the calcium-dependent protease calpain-1.

The results of this research are published in *Advanced Science*.

These findings open up new possibilities for innovative treatments against ischemic retinopathy, including retinopathy of prematurity and proliferative diabetic retinopathy. The technology focuses on targeting and regulating the aberrant activation of HIF1α and mitochondria under hypoxic conditions, providing a transformative approach to addressing the underlying causes of retinal diseases. Unlike conventional treatment methods, this technology can be easily administered using ophthalmic

drugs, making it accessible to a wider range of patients.



TRAP1 inhibition triggers calcium/calpain-1-dependent HIF1α degradation. Above is the schematic image, showing HIF1α degradation following TRAP1 inhibition. Credit: *Advanced Science* (2023). DOI: 10.1002/advs.202302776

"The excessive production of angiogenic factors in retinopathy is closely linked to mitochondrial properties," explains Professor Kang. "By suppressing the expression of the TRAP1 protein, we can improve the condition of retinopathy."

The therapeutic substance, currently being developed by Smartin Bio Inc., a startup company founded by Professor Byoung Heon Kang, is

undergoing non-clinical trials.

The successful development of this technology holds great promise in revolutionizing the treatment landscape for ischemic retinopathy, offering both exceptional efficacy and convenient usability that surpasses the limitations of existing treatments. As further clinical trials and development progress, this innovation brings hope for a brighter future for patients suffering from retinopathy.

More information: So-Yeon Kim et al, Targeting the Mitochondrial Chaperone TRAP1 Alleviates Vascular Pathologies in Ischemic Retinopathy, *Advanced Science* (2023). DOI: 10.1002/advs.202302776

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