Optogenetic Activation of TrkB signaling for Neuroprotection of Retinal Ganglion Cells

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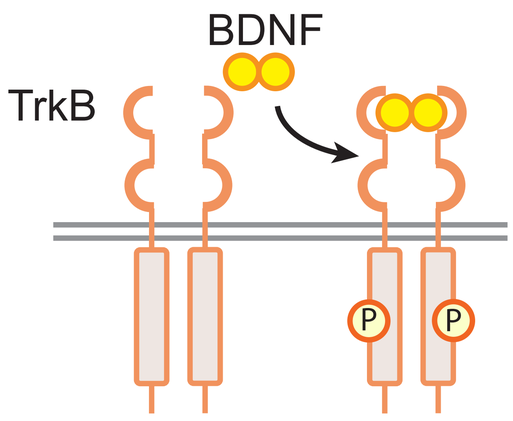
Abstract

OptoTrkB[1]: a novel approach to control neurotrophic TrkB signaling by light instead of ligands
(1) We engineered light-responsive proteins to control intracellular signaling pathway
(2) Blue light activates downstream signaling cascades and induce neuronal differentiation of a model cell line
(3) The optogenetic system protects Retinal Ganglion Cells (RGCs) in eye disease models

TrkB signaling is important for neurons

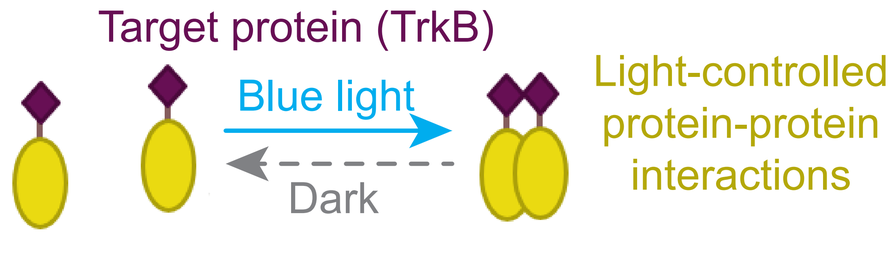


Activated TrkB → Ras/ERK, PI3K/Akt, PLCγ1/Ca^{2+} downstream pathways

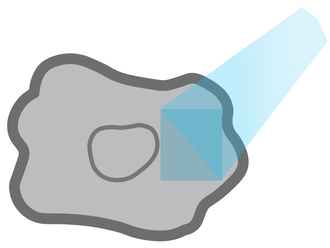
Neuron survival
Neuron growth
Memory formation

Advantages of optogenetics

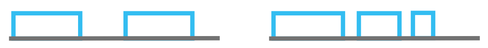
(1) High specificity in targeted cells



(2) Remote control with spatial precision and non-invasiveness



(3) Timely on/off control



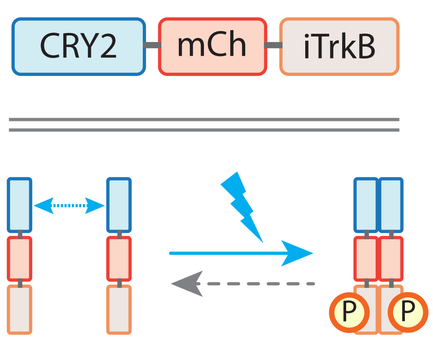
(4) Tunability in activation levels

Light-inducible strategies

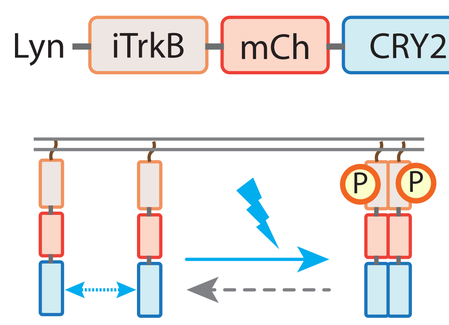
Light-induced homo-interaction

Light-induced hetero-dimerization

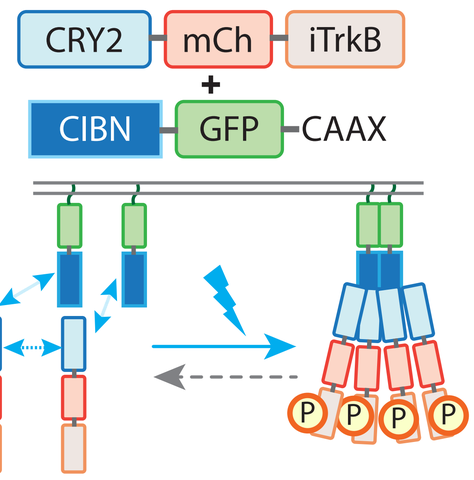
(a) Cytosolic



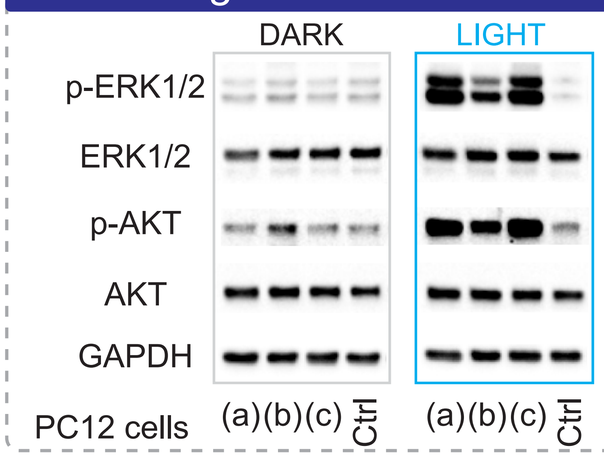
(b) Membrane-bound



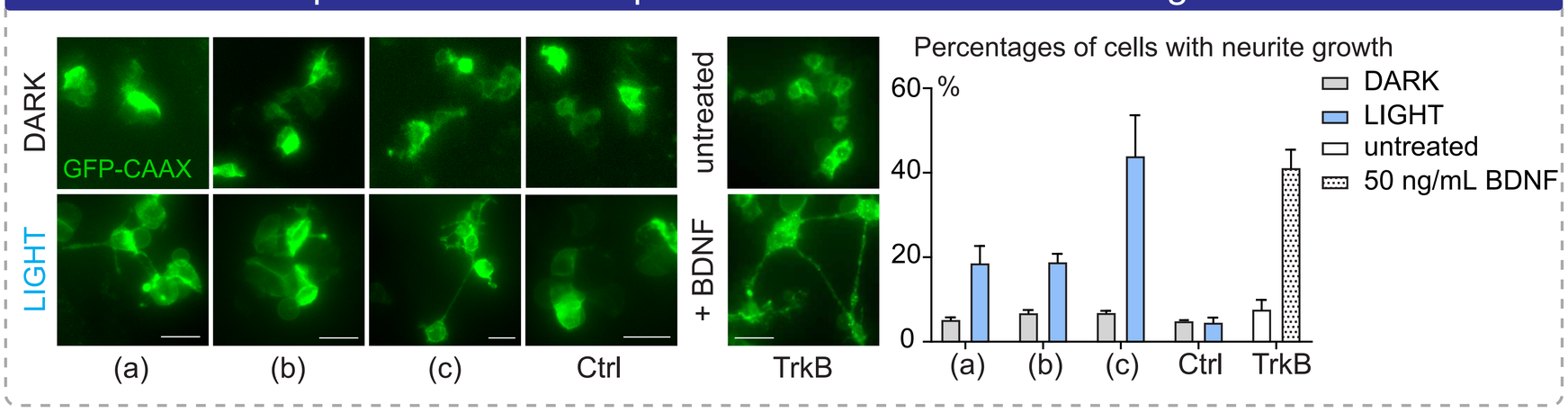
(c) Recruited-to-the-membrane



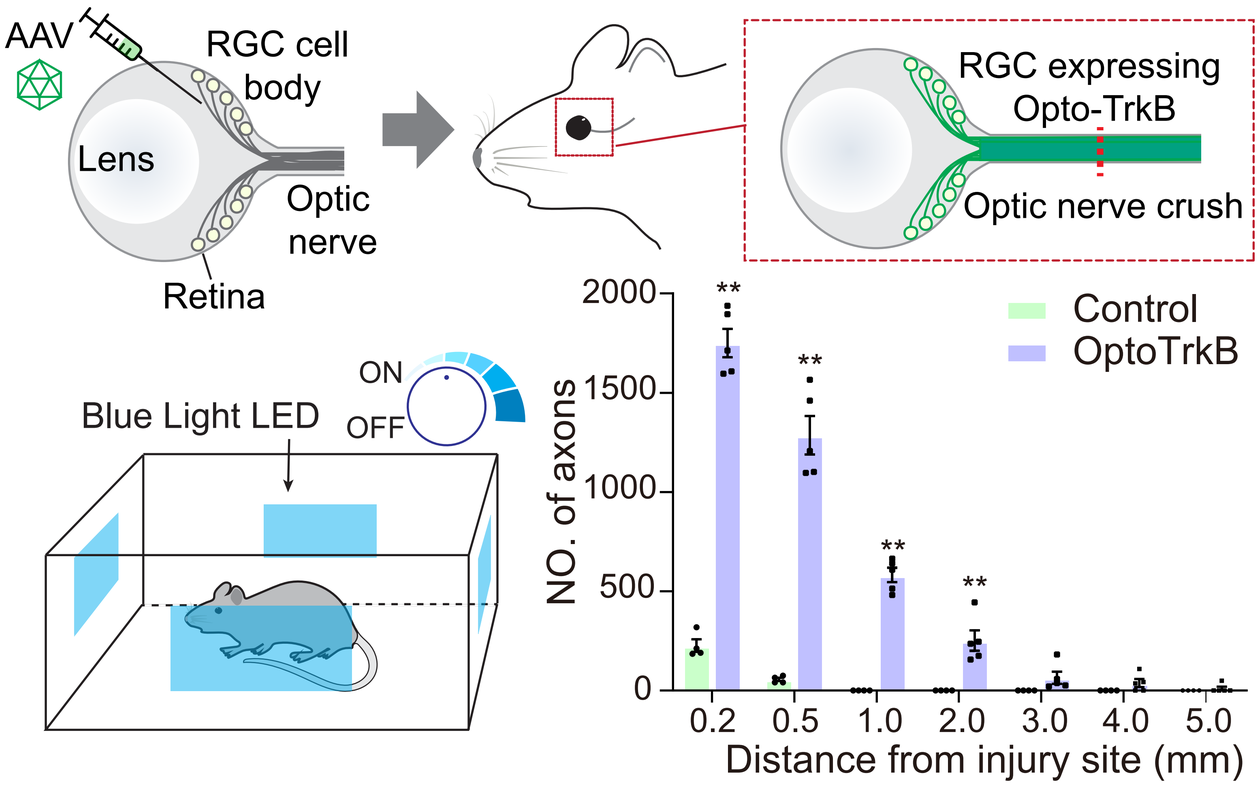
Signal activation

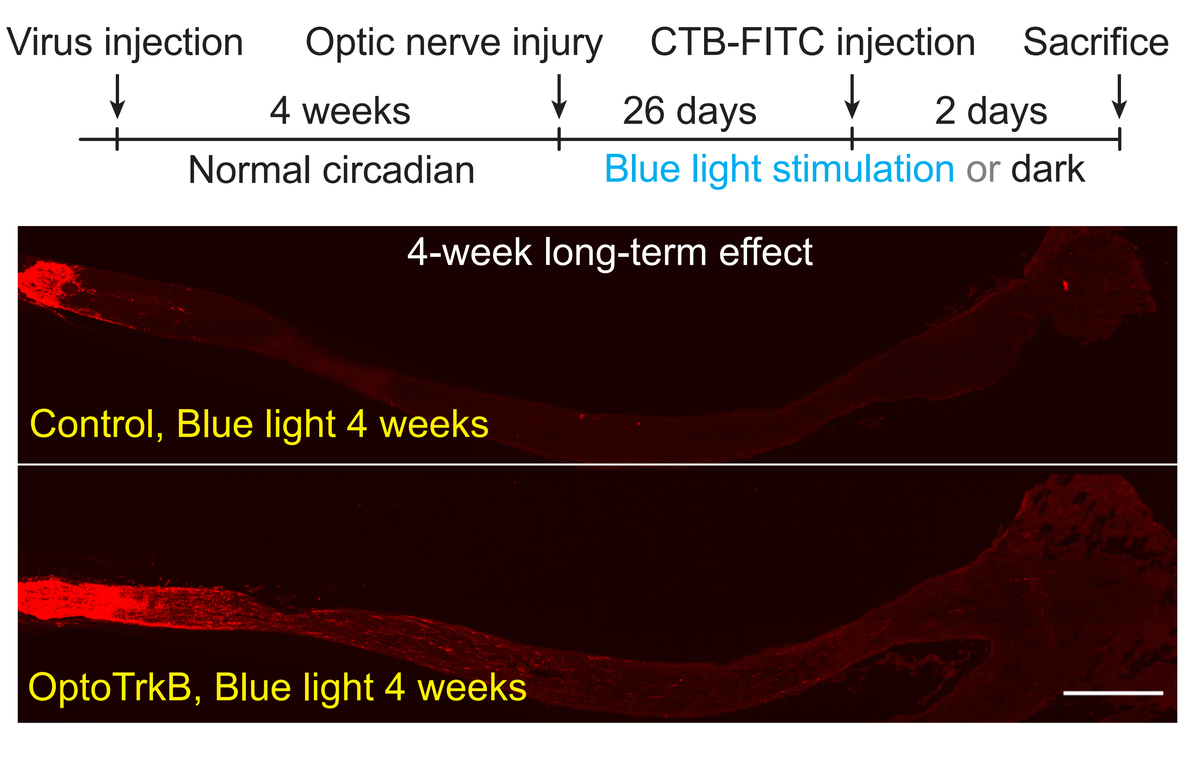


OptoTrkB activation promotes PC12 cell neurite outgrowth



OptoTrkB promotes RGCs survival and axon regeneration after optic nerve injuries





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Ref: [1] Huang et al., (2020) Optical activation of TrkB signaling. *Journal of molecular biology*, 432(13), pp.3761-3770.