The function of Nox2 in retinal ganglion cells for retinotectal pathfinding

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Reactive oxygen species (ROS) play an important signaling role in cell proliferation, differentiation, adhesion, motility, and immune response. Appropriate intermediate levels of ROS are critical for normal cell development and physiology. Here, we provide evidence for NADPH oxidase 2 (Nox2)-derived ROS in neuronal development. Pharmacological inhibition of Nox enzymes in zebrafish larvae by Celastrol resulted in increased ganglion cell layer (GCL) width as well as decreased optic nerve thickness and tectal innervation by retinal ganglion cell (RGC) axons. These morphological changes could be partially rescued with the addition of hydrogen peroxide. We have established isoform-specific deletions by CRISPR/Cas9 in order to identify the specific Nox isoform required for axonal growth and guidance along the retinotectal pathway. We found that Nox2-deficiency caused increased GCL width and mistargeted RGC axons in the optic tectum (OT) as well as aberrant axonal projections in other parts of the central nervous system. However, the details of how Nox2 regulates the formation of retinotectal connections are unclear. RGC-specific knockout and rescue of Nox2 will address the question of whether Nox2 in RGCs is required and sufficient, respectively, for establishment of proper retinotectal connections in developing zebrafish larvae. We hope that our findings will contribute to a better understanding of the role of Nox2-derived ROS in nervous system physiology and disease.