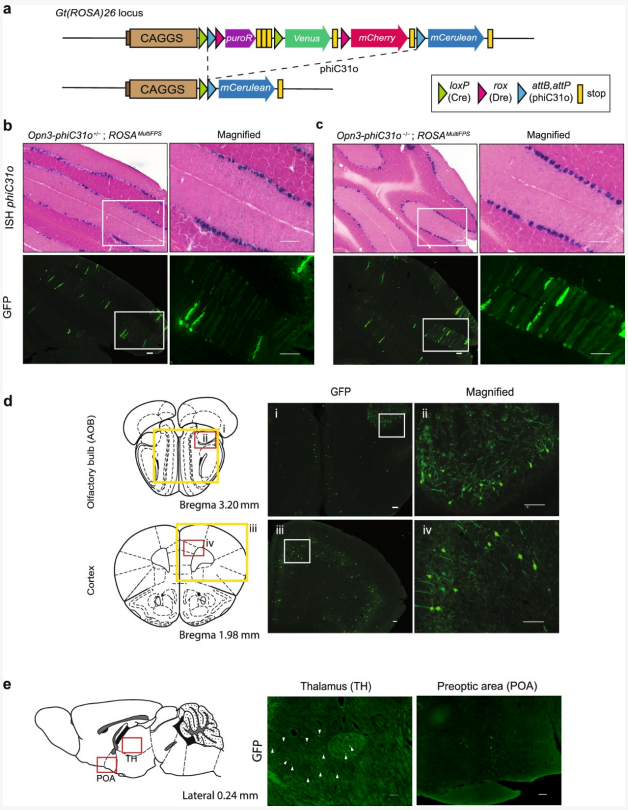
Turning light into insight: new mouse model unlocks mysteries of non-visual photoreception

GA, UNITED STATES, December 9, 2025 /EINPresswire.com/ -- Scientists have engineered a new mouse model that reveals how Opn3—a little-known blue light-sensitive protein—affects body temperature and eye development. By inserting a phiC31 integrase sequence into the Opn3 gene using CRISPR-Cas9, the team created a dual-purpose system that both silences the gene and labels its active cells with fluorescent light. The modified mice exhibited a sharp drop in body temperature during cold exposure and developed myopia-like eye features, confirming Opn3's vital physiological roles. This innovation not only clarifies the function of Opn3 in the brain and retina but also provides a new genetic tool for exploring how light influences mammalian health beyond the eyes.



Recombination efficiency and Opn3 expression in Opn3-phiC31o KI mice brain.

Light affects far more than vision—it shapes metabolism, temperature regulation, and even mood. Hidden within the body, non-visual opsins such as Opn3 serve as molecular light sensors that translate blue light into biological signals. Yet despite growing evidence of their importance, researchers have struggled to study Opn3 due to limited genetic tools and antibody sensitivity. Traditional Cre-based mouse models could not precisely target Opn3 without affecting other genes, leaving many of its roles unexplored. Because of these challenges, scientists needed a versatile and accurate way to manipulate Opn3-expressing cells to uncover how internal light sensing governs brain and systemic physiology.

A research team from Keio University School of Medicine and the University of Tokyo reports (DOI: 10.1186/s40662-025-00455-z) the creation of an Opn3-phiC31o knock-in mouse model in the journal Eye and Vision on September 11, 2025. Using advanced CRISPR-Cas9 editing, the researchers inserted a phiC31 integrase gene precisely at the start of Opn3, enabling both gene

knockout and fluorescent tracing. This model provided the first direct visualization of Opn3 activity in the brain and eye and confirmed that Opn3 regulates body temperature and ocular growth, establishing a long-sought connection between light sensing and whole-body adaptation.

In the new mouse model, scientists replaced the translation start site of Opn3 with a codon-optimized phiC31 integrase sequence, effectively turning the gene into a light-driven molecular switch. Imaging confirmed that phiC31 expression mirrored native Opn3 patterns in the cerebellum's Purkinje cells. In homozygous mice, Opn3 expression vanished, validating a complete functional knockout. Physiological tests revealed striking differences: when exposed to cold, knockout mice lost body heat much faster than wild-type controls, and their eyes showed shortened axial length and lens thickness, typical signs of refractive myopia. Crucially, although Opn3 overlaps genetically with the nearby Chml gene, further sequencing showed Chml remained intact, proving the system's precision. Crossbreeding with ROSA26 reporter mice triggered cyan fluorescent signals in specific brain areas—the olfactory bulb, cortex, thalamus, and cerebellum—faithfully mapping Opn3's distribution. Despite moderate recombination efficiency (30–44%), the model enables selective, high-resolution tracing of individual light-responsive neurons, setting a new benchmark for opsin research.

"Our Opn3-phiC31o mouse gives us an unprecedented window into how light-sensitive genes operate deep inside the body," said Dr. Satoru Moritoh, the study's corresponding author at Keio University. "Even though the recombination rate is modest, it allows us to label single neurons with remarkable clarity. We can now visualize how Opn3-expressing cells integrate light signals with physiological processes like thermoregulation and eye growth. This model bridges molecular biology and neurophysiology, offering a precise tool for dissecting the hidden language of light in the brain."

The Opn3-phiC31o mouse serves as both a powerful knockout model and a high-precision fluorescent tracer, enabling simultaneous investigation of Opn3's cellular and systemic roles. Its compatibility with other recombinase systems—Cre and Dre—paves the way for triple-color mapping of Opn3, Opn4, and Opn5, allowing scientists to study how multiple light sensors collaborate to regulate energy metabolism, circadian rhythm, and visual adaptation. Beyond neuroscience, the model could inspire new strategies to modulate Opn3-related pathways in treating myopia, obesity, or metabolic disorders. By turning genetic darkness into visible light, this work illuminates a new frontier in mammalian photobiology.

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Lucy Wang
BioDesign Research
email us here