The EuroBiotech Journal
SHORT COMMUNICATION
Editorial

Optogenetics: The Nobel-Winning Breakthrough and Its Implications in Biotechnology

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Abstract

The 2026 Nobel Prize in Physiology or Medicine celebrated the breakthroughs in optogenetics, the methodology combining genetic targeting and optical control to monitor and manipulate cellular activity. This Editorial will summarize the rise of optogenetics and its transformative impact on neuroscience and discuss its role as an expanding force across clinical and biotechnological domains, with a focus on translational and industrial prospects.

Keywords: Optogenetics, Nobel Prize, Biotechnology, gene therapy, synthetic biology, retinal dystrophy

Introduction

On October 5th, 2026, Karl Deisseroth, Peter Hegemann and Georg Nagel were awarded the Nobel Prize in Physiology or Medicine for their pioneering discoveries regarding light-gated ion channels that underpinned the field of optogenetics (1). Optogenetics integrates genetic and optical methods to monitor and control the activity of specific cells using light. This approach relies on the targeted expression of light-sensitive proteins.

Why Optogenetics Revolutionized Neuroscience

The human brain contains billions of cells and trillions of synapses organized into specialized functional circuits (2). Its delicate architecture comprises densely intermingled, functionally diverse cell types operating on a millisecond scale. This complex structure has long posed a significant challenge to systems neuroscience (1). Even though more traditional disciplines including electrophysiology, radiology, and pharmacology successfully mapped correlations between neural activity and various functions and behaviors, they lacked the spatiotemporal and cell-type specificity required to prove direct causality (1). Francis Crick, co-discoverer of the DNA double helix and Nobel laureate, was the first scientist to envision that cracking the neural code necessitated modifying specific neuronal populations with high spatiotemporal precision, and light could be the perfect candidate for this purpose (1,3). His visionary foresight was later brought to life with the field of optogenetics.

The Path to the Nobel Prize

Optogenetics evolved through more than three decades of foundational biophysical discoveries, starting with the identification of light-driven microbial ion pumps, bacteriorhodopsin and halorhodopsin, in the 1970s (4). In 2003, Nagel and Hegemann isolated Channelrhodopsin-1 (ChR1) and Channelrhodopsin-2 (ChR2), two light-responsive ion channels found in *Chlamydomonas reinhardtii* (5). In contrast to proton-selective ChR1, ChR2 acted as a non-selective cation channel (5). Nagel and Hegemann demonstrated that ChR2 could depolarize mammalian cells upon illumination (5). In 2005, Deisseroth's team delivered ChR2 to rodent hippocampal neurons and achieved millisecond-timescale control of neuronal activity (6). Their recognition that precise neural manipulation would transform multiple scientific disciplines proved remarkably prescient, establishing

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DOI: 10.2478/ebtj-2026-0023

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this study as a cornerstone of optogenetics (6). The term optogenetics was first used in a review by Deisseroth et al. in 2006 (7).

Following its formal introduction, the optogenetic toolkit rapidly expanded to achieve bi-directional precision. Initial silencing methods using the chloride pump halorhodopsin (NpHR) were later superseded by highly potent anion channelrhodopsins (GtACR1/2) for reliable hyperpolarization (1,8,9). Concurrently, the development of fiber-optic neural interfaces enabled targeted optical control within deep brain structures of awake, behaving mammals (1,10). Further studies, such as stimulating the lateral hypothalamus in vivo to induce sleep or the hippocampal dentate gyrus to manipulate memory formation, solidified this technology's strength (1). Optogenetics has evolved into a core methodology in neuroscience, driving discoveries across both fundamental circuit mapping and translational models of neurological and psychiatric disorders (11–13).

The Broadening Horizons of Optogenetics

Beyond neuroscience, optogenetics is progressing towards clinical reality, with inherited retinal dystrophies (IRD) serving as the undisputed translational flagship (14). Even though *RPE65*-associated Leber congenital amaurosis has an approved gene therapy, around 280 genes cause IRD's, highlighting the unmet need for broader therapeutic options, which may include optogenetic technologies (15). The first clinical demonstration of partial visual restoration via optogenetic intervention was reported in Europe, where a blind patient harboring biallelic *USH2A* variants achieved measurable visual improvement following the administration of channelrhodopsin ChrimsonR (16). Furthermore, MCO-010 (sonpiretigene isteparvovec), a synthetic, chimeric multi-characteristic opsin targeting retinal bipolar cells, showed encouraging results in a phase 2 study for Stargardt disease (17). A very recent study provided further safety information for ChrimsonR in retinitis pigmentosa (18). Currently, IRD's are the only disease group with human trials investigating optogenetic therapies (1).

Beyond vision, investigators are increasingly testing light-gated approaches in other disease models. Adjustment of cardiac pacing, termination of arrhythmias, and resynchronization could be achieved with the delivery of light-sensitive opsins and may optimize treatment in cardiac arrhythmias (19). Optogenetic β-cell stimulation and GLP-1 control, alleviation of insulin resistance by manipulating key molecular targets, or control of nervous activity to regulate blood glucose levels have been proposed for diabetes mellitus (20). Hearing loss of genetic origin is another topic where optogenetic technologies may translate to clinical outcomes. Preclinical studies using optogenetic technologies to stimulate spiral ganglion neurons reliably and precisely by optical cochlear implants have promising results (21). Furthermore, preclinical studies to modify signaling pathways and control gene expression for cancer immunotherapy using optogenetic technologies are underway (22).

From a biotechnological standpoint, optogenetics has expanded into a versatile toolbox for controlling cellular behavior across diverse organisms and biological materials. Optogenetics could help achieve precise control of base editing and reduce off-target effects in Clustered regularly interspaced short palindromic repeats (CRISPR) technology, and optimize the development of therapeutics for rare diseases (23,24). In terms of stem cell and organoid research, optogenetics replaces chemical morphogens with light-activated mechanisms and enables precise guidance of lineage specification and organoid morphogenesis (25). In microbiology, optogenetic control of cellular metabolism facilitates biomanufacturing of recombinant proteins, dynamic biofilm regulation, and targeted studies of host-pathogen interactions (26,27). Extending into industrial applications, optogenetic strategies further drive the development of smart biomaterials for tissue engineering, alongside optimizations in biofuel production and plant agrobiology (28).

Future Perspectives

As optogenetics enters its post-Nobel era, succeeding in the transformation of this technology from basic research into routine clinical therapies and industrial applications requires addressing key translational bottlenecks. The viral gene delivery methods carry inherent risks such as toxicity and host immune response, while light delivery may become challenging due to the phototoxicity risk, tissue absorption, and the difficulty of maintaining pinpoint spatial precision in deep tissues (29). Overcoming such roadblocks in optogenetics depends on combining developments in non-invasive bioengineering, such as red-shifted opsins and nanotechnology, with scalable, Good Manufacturing Practices (GMP)-compliant vector production (29). In the European and global biotechnology arenas, cooperation with regulatory agencies will be vital for clearing regulatory pathways for gene-device combinations, establishing optogenetics as a standard tool in precision medicine.

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