Bioluminescence-Driven Optogenetics

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Abstract

Optogenetics is the use of light to manipulate genetically encoded light sensing molecules, opsins. Activation of these light-gated ion channels and pumps, when expressed by cells, results in depolarization or hyperpolarization of cell membranes. This allows, for example, activation and silencing of neuronal circuits in behaving experimental animals via light fibers implanted into the animal’s brain. We developed a strategy for non-invasive optogenetics by switching out the light source from an invasive physical to a non-invasive biological one, i.e., a light producing protein, a luciferase. The luciferase emits light, activating the optogenetic actuator upon application of its small-molecule substrate, luciferin.

We engineered fusion proteins of a light-emitting luciferase to an optogenetic light-responsive element, resulting in a luminescent opsin, or luminopsin. We started with fusion proteins of Gaussia luciferase (GLuc), a luciferase from the copepod Gaussia princeps, with channelrhodopsins from algae and proton pumps from fungus. We used the wildtype version and mutated forms of GLuc with increased light emission and found activation of optogenetic elements to correlate with the light emission of the luciferase. Ongoing work involves systematic mutation and screening for luciferases with further increased light emission. Furthermore, leveraging the full array of optogenetic options requires matching the continuously evolving palette of opsins with luciferases with shifted wavelengths.

This novel class of tools can be improved and extended in numerous ways and find applications beyond photonic control of neurons in modifying many cell types and cellular processes.

Keywords: Gaussia luciferase, coelenterazine, optogenetics

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