"Optogenetic Control of Protein Kinase Activity in Mammalian Cells"

Sabrina Wend (AG Weber)

Light-dependent dimerization is the basis for recently developed noninvasive optogenetic tools. Here we present a novel tool combining optogenetics with the control of protein kinase activity to investigate signal transduction pathways. Mediated by Arabidopsis thaliana photoreceptor cryptochrome 2, we activated the protein kinase C-RAF by blue light-dependent dimerization, allowing for decoupling from upstream signaling events induced by surface receptors. The activation by light is fast, reversible, and not only time but also dose dependent as monitored by phosphorylation of ERK1/2. Additionally, light-activated C-RAF controls serum response factor-mediated gene expression. Light-induced heterodimerization of C-RAF with a kinase-dead mutant of B-RAF demonstrates the enhancing role of B-RAF as a scaffold for C-RAF activity, which leads to the paradoxical activation of C-RAF found in human cancers. This optogenetic tool enables reversible control of protein kinase activity in signal duration and strength. These properties can help to shed light onto downstream signaling processes of protein kinases in living cells.