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Novel Opto-Genetic Tools for the Study of Opioid Receptor Signaling

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Toward a Better Understanding of…

**Novel Opto-Genetic Tools for the Study of Opioid Receptor Signaling**

*Madison Baird*

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It has been well established that opioid receptor signaling plays a major role in the regulation of stress, pain, depression, and the rewarding properties of drugs of abuse such as morphine, nicotine, and cocaine. Although the Kappa opioid receptor (KOR) and Mu Opioid receptor (MOR) have been a key focus of narcotic research, knowledge is still limited on how the G-protein coupled receptors signal and yield behavioral responses. Study of specific brain regions and neural circuits can be difficult as the synthetic drug compounds diffuse throughout the brain with little spatial or temporal control. Thus, opto-genetic receptor constructs, activated by site specific laser activation, will provide a useful tool in the study of opiate cellular signaling mechanisms. We created a novel opto-genetic tool and molecularly characterized this chimeric receptor which uses rhodopsin light-sensitive activation machinery but results in opioid receptor signaling. Characterization of these receptors will result in a better understanding of the similarity between the native opioid receptors and the new optically activated constructs’ downstream signaling for *in vivo* behavioral studies. In addition, our studies will work to better define native opioid receptor signal transduction, effects on cell biology, and neural systems. Optimization of OMOR and OKOR activation protocol will elucidate the G-protein and arrestin-mediated signaling time points at which protein kinase and adenylate cyclase activity is turned on, and how arrestin-dependent MAPK is initiated. We also characterized the length and intensity of light (efficacy) stimulation necessary to elicit a peak response, and calculated the power (dose-response) curve for each construct. This pharmacological characterization of a novel tool side-by-side with native opioid receptors for will provide valuable information when the tools are implemented for *in vivo* neural circuit dissection studies in drug addiction, depression, pain and stress behaviors.