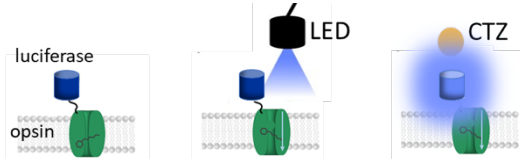
E-Z Guide to BL-OG

What is BL-OG? Opto- and/or Chemo- Control in a *Single* Molecule



In *BioLuminescent OptoGenetics* (BL-OG), molecular light drives an optogenetic sensor. *LuMinOpsins (LMOs)* are single molecules that tether the light producer (luciferase) and opsin. **In *LMO3*, BL light drives VChR1 causing depolarization when coelenterazine (CTZ) is present**. LMO3 has now been vetted in multiple cell types and contexts.

Why BL-OG? *More Flexible and More Trackable = More Useful*

Systemic impact (chemo-) & specific control (opto-) in same mouse (*Study I*)

BL light reports timing of neuromodulation after injection (*Study II*)

Choose the timing Fast opto- and multiple chemo- time courses (*Study II*)

Long-term biocompatibility (*Studies I-IV*)

How to Get BL-OG

Order LMO3s as pAAV plasmids from *AddGene* (114099, 114103, 114104, 114105)

Order native CTZ from *Nanolight* (https://bit.ly/2nIL1AB)

The LMO3-floxed mouse is available: Contact Dr. Justine Allen (Justine_Allen@brown.edu)

Help With BL-OG

Our in-house workshops train users in all aspects of BL-OG use, and our emissaries can provide hands-on training in your lab. For more info, see www.bioluminescencehub.org or contact Dr. Justine Allen (Justine_Allen@brown.edu).

Toxicity? No. Brain Permeability? Yes.

Toxicology screens commissioned by Prolume (ms in prep., H. Schmidt) did not reveal any toxicity concerns of CTZ, the luciferin we employ, consistent with our extensive experience with repeated administration of it in water-soluble form. Another FAQ is whether CTZ can reach brain targets. Multiple published studies and our ongoing work show that CTZ can access the brain (e.g., neocortex, Choroid Plexus) after peripheral injection.

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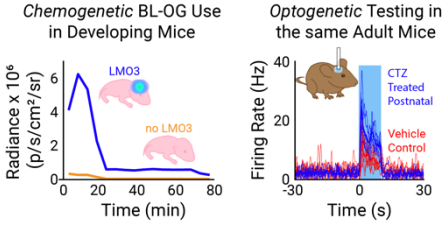
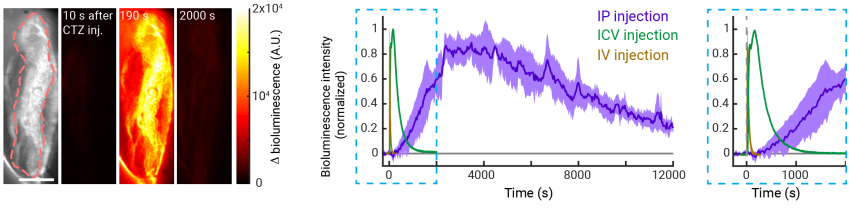
Complete references can be found at https://www.bioluminescencehub.org/data.

LMO3: *In Vivo* Studies

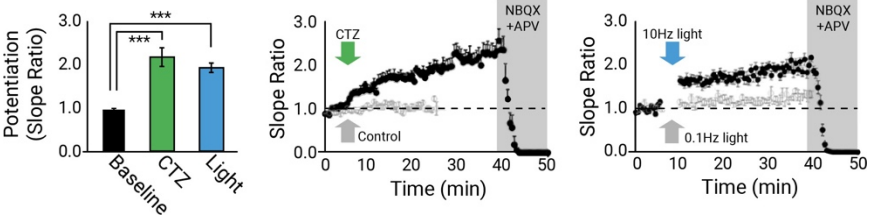
Study I **Impacting Development with Chemogenetic LMO3 Activation, then Probing Changes in the Adult with Opto- Drive** Medendorp et al. (in prep.) drove pyramidal neurons expressing LMO3 by IP CTZ injection P4-P10. They then used direct optogenetic drive of LMO3 to test adult excitability in the same cells. Adult mice showed robust behavioral and physiological changes after developmental BL-OG treatment.

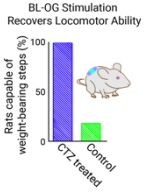


Study II **BL Light from LMO3 Reports Chemogenetic Activation in the Choroid Plexus** Shipley et al. (in review) describes novel imaging and control tools for *in vivo* Choroid Plexus (ChP) study. LMO3 activation in ChP showed distinct time courses for different CTZ injection routes.



Study III **IPSC control by LMO3 Post-Stroke: Chemo- or Opto- Activation Drives Behavioral Recovery and Synaptic Enhancement** Yu et al. (2019 *J Neurosci*) expressed LMO3 in IPSCs implanted *in vivo* post-stroke. Chemogenetic or optogenetic LMO3 activation improved behavioral and sensory responses *in vivo*, and enhanced peri-infarct synaptic plasticity.





Study IV **LMO3 Activation Drives Motor Recovery Following Spinal Cord Injury** Petersen et al. (in review; *bioRxiv*) expressed LMO3 in the ventral cord below an impact injury. Driving LMO3 activation with repeated CTZ injections (10 days) significantly enhanced the long-term recovery of motor coordination/control of the lower limbs, as compared to vehicle control treatment of injured mice.