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Research Campus

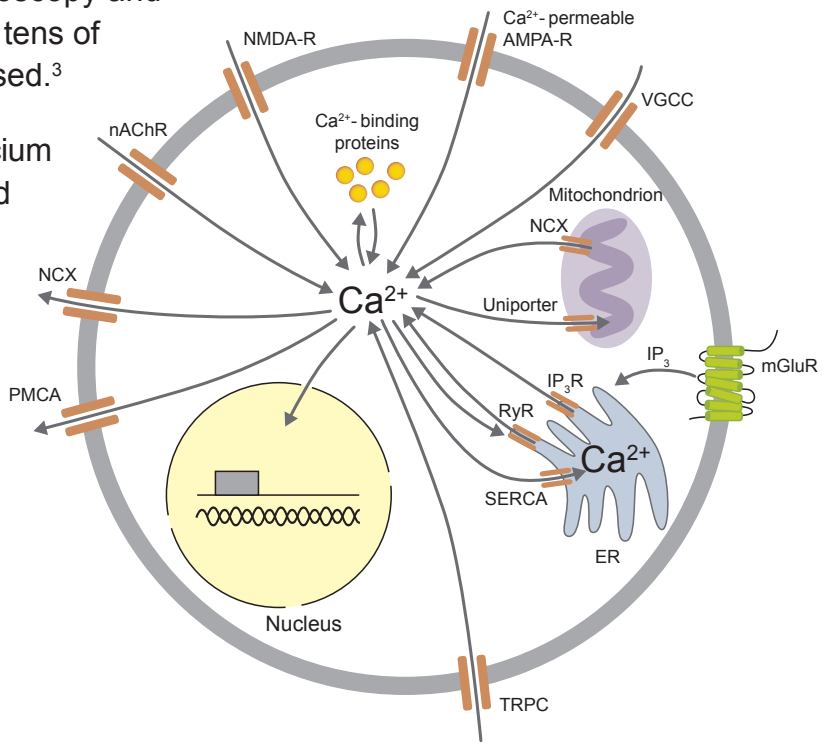
Janelia Genetically Encoded Calcium Indicators

Drug researchers need reliable, high-performing reagents in their cell assays, especially in neuroscience. With few such options, costly, time-consuming experiments may fail, be inconclusive, or not happen at all.

Calcium ion flux in a cell is a well-established assay because it impacts nearly every aspect of cellular life.[1] At HHMI's Janelia Research Campus, our scientists transformed calcium imaging through world-leading research in neuroscience research, imaging, and biochemical tool development.

Janelia offers the definitive catalog of optimized genetically encoded calcium indicators (GECIs) through the efforts of expert labs and our GENIE project team.[2] Researchers worldwide use the Janelia GECIs and have established an extensive publication history. The GECIs optimized signal-to-noise ratios, speed, and performance in two-photon microscopy and wide-field imaging over timescales of tens of milliseconds to months are unsurpassed.[3]

The Janelia Genetically Encoded Calcium Protein Sensors are the gold standard reagents for imaging cell activity. Here we present the GECI reagents and animals available for licensing.



1. Clapham, D. *et al*. *Cell* **131**, 6, 1047-1058 (2007) (https://doi.org/10.1016/j.cell.2007.11.028)
2. https://www.janelia.org/project-team/genie
3. Dana, H., *et al*. *Nat Methods* **16**, 649–657 (2019). (https://doi.org/10.1038/s41592-019-0435-6)

Generated by the GENIE Project in collaboration with the Looger Lab at Janelia Research Campus. © 2021, Howard Hughes Medical Institute

GCaMP6 and jGCaMP7 Fluorescent Calcium Protein Sensors

Immensely popular and proven technology in over 4000 published studies

- Sensitivity, dynamic range, and kinetics that can exceed synthetic indicators and existing GECIs
- Several GCaMP6 and jGCaMP7 variants to select from with overall brightness, rise/decay kinetics, and calcium affinity

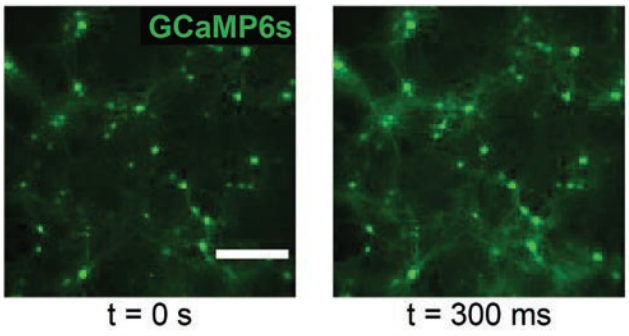
Advantages

- Allow imaging cell activity long-term and *in vivo*, unlike calcium dyes that are toxic to the cell
- GECIs can image neuronal populations for months
- Useful for genetically targeting expression

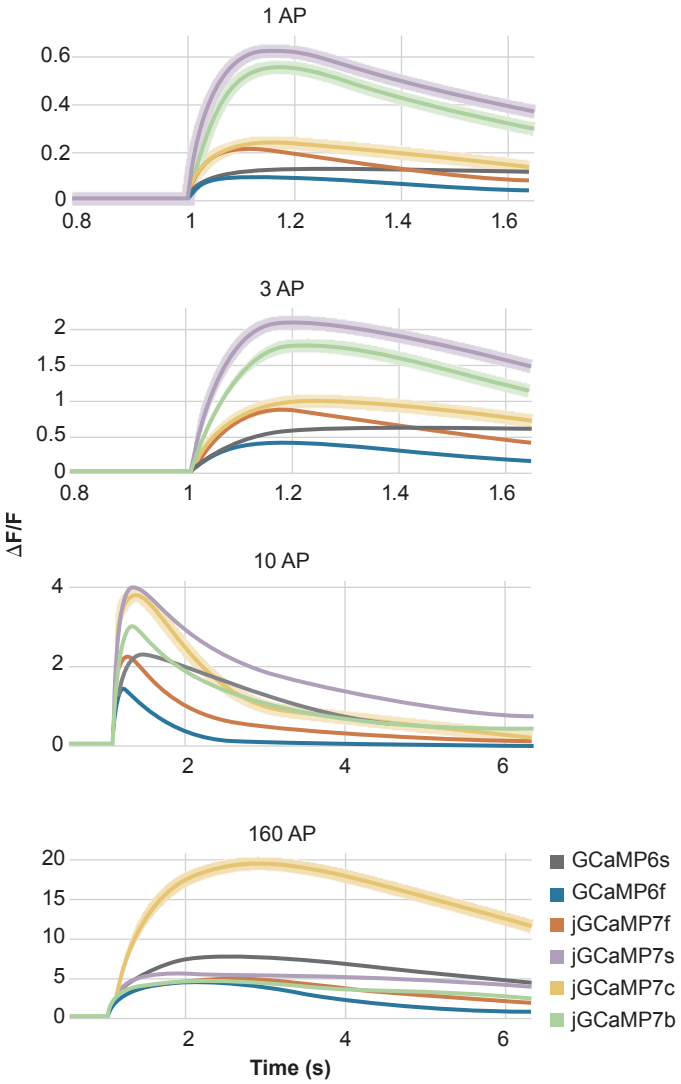
Applications

- Neuroscience research using *in vitro* or *in vivo* models
- Long-term functional imaging of neuronal activity and correlation with animal behavior
- Screening for G-protein coupled receptor (GPCR) or ion channel agonists and antagonists
- Cell, drosophila, zebrafish, mouse, and rat assays made possible through a multitude of variants and useful for imaging methods

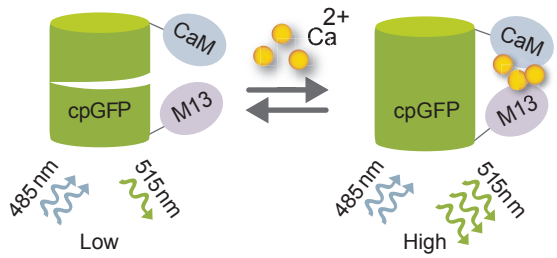
Complete variant availability on next page.



Signal changes for multiple GCaMP variants



GCaMP6 and jGCaMP7 Fluorescent Calcium Protein Sensors



GCaMPs fluoresce on calcium binding

References

(1) Chen, Tsai-Wen *et al*. Ultrasensitive fluorescent proteins for imaging neuronal activity. *Nature* **499**, 295-300 (2013). https://doi.org/10.1038/nature12354 *Over 4200 Citations*

(2) Dana, Hod *et al*. Thy1-GCaMP6 transgenic mice for neuronal population imaging *in vivo*. *PloS One* **9**, e108697 (2014). https://doi.org/10.1371/journal.pone.0108697 *358 citations*

(3) Grienberger, Christine *et al*. Imaging Calcium in Neurons. *Neuron*, **73**, 5, 862-885, (2012). https://doi.org/10.1016/j.neuron.2012.02.011 *828 citations*

(4) Dana Hod *et al*. High-performance calcium sensors for imaging activity in neuronal populations and microcompartments. *Nature Methods* **16**, 7, 649-657 (2019). https://doi.org/10.1038/s41592-019-0435-6 *457 citations*

LICENSING OFFER

Available for direct internal research licensing under material and patent rights transfer. US Patent and Application nos. 9,488,642, 9,945,844, 10,509,026, 16/189,166, EP 3540064, and EP 3713949.

Email **innovation@janelia.hhmi.org** to request a license.

Available GCaMP6 Permutations (reference 1)

1. pAAV.CAG.GCaMP6s.WPRE.SV40
2. pAAV.CAG.GCaMP6m.WPRE.SV40
3. pAAV.CAG.GCaMP6f.WPRE.SV40
4. pAAV.Syn.GCaMP6s.WPRE.SV40
5. pAAV.Syn.GCaMP6m.WPRE.SV40
6. pAAV.Syn.GCaMP6f.WPRE.SV40
7. pGP-CMV-GCaMP6s
8. pGP-CMV-GCaMP6m
9. pGP-CMV-GCaMP6f
10. pAAV.CAG.Flex.GCaMP6s.WPRE.SV40
11. pAAV.CAG.Flex.GCaMP6m.WPRE.SV40
12. pAAV.CAG.Flex.GCaMP6f.WPRE.SV40
13. pAAV.Syn.Flex.GCaMP6s.WPRE.SV40
14. pAAV.Syn.Flex.GCaMP6m.WPRE.SV40
15. pAAV.Syn.Flex.GCaMP6f.WPRE.SV40

Available GCaMP7 Permutations (reference 4)

1. pGP-AAV-syn-jGCaMP7s-WPRE
2. pGP-AAV-syn-jGCaMP7b-WPRE
3. pGP-AAV-syn-jGCaMP7c-WPRE
4. pGP-AAV-syn-jGCaMP7f-WPRE
5. pGP-CMV-jGCaMP7s
6. pGP-CMV-jGCaMP7b
7. pGP-CMV-jGCaMP7c
8. pGP-CMV-jGCaMP7f
9. pGP-AAV-CAG-FLEX-jGCaMP7s-WPRE
10. pGP-AAV-CAG-FLEX-jGCaMP7b-WPRE
11. pGP-AAV-CAG-FLEX-jGCaMP7c-WPRE
12. pGP-AAV-CAG-FLEX-jGCaMP7f-WPRE
13. pGP-AAV-syn-FLEX-jGCaMP7s-WPRE
14. pGP-AAV-syn-FLEX-jGCaMP7b-WPRE
15. pGP-AAV-syn-FLEX-jGCaMP7c-WPRE
16. pGP-AAV-syn-FLEX-jGCaMP7f-WPRE

Available GCaMP Mouse Lines (provided by Jackson Labs)

1. C57BL/6J-Tg(Thy1-GCaMP6s)GP4.3Dkim/J
2. C57BL/6J-Tg(Thy1-GCaMP6f)GP5.17Dkim/J
3. C57BL/6J-Tg(Thy1-GCaMP6s)GP4.12Dkim/J
4. C57BL/6J-Tg(Thy1-GCaMP6f)GP5.11Dkim/J
5. C57BL/6J-Tg(Thy1-GCaMP6f)GP5.5Dkim/J

jGCaMP8 Fluorescent Calcium Protein Sensors (2020)

The jGCaMP8 sensors have fast kinetics without compromising sensitivity, setting a new standard for *in vivo* imaging:

- **jGCaMP8f** (fast): 4x faster rise time, 2.5x faster decay time than jGCaMP7f
- **jGCaMP8m** (medium): almost 4x faster rise time and 3.5x more sensitive than jGCaMP7f
- **jGCaMP8s** (sensitive): 2x more sensitive than jGCaMP7s, >2x faster than jGCaMP7f (at 1 AP)
- see **bit.ly/jgcamp8** for more information

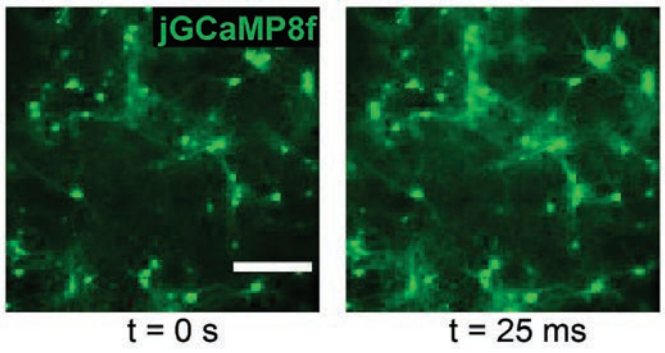
Advantages

- Allow imaging cell activity *long-term* and *in vivo*, unlike calcium dyes that are toxic to the cell
- Useful for genetically targeting expression

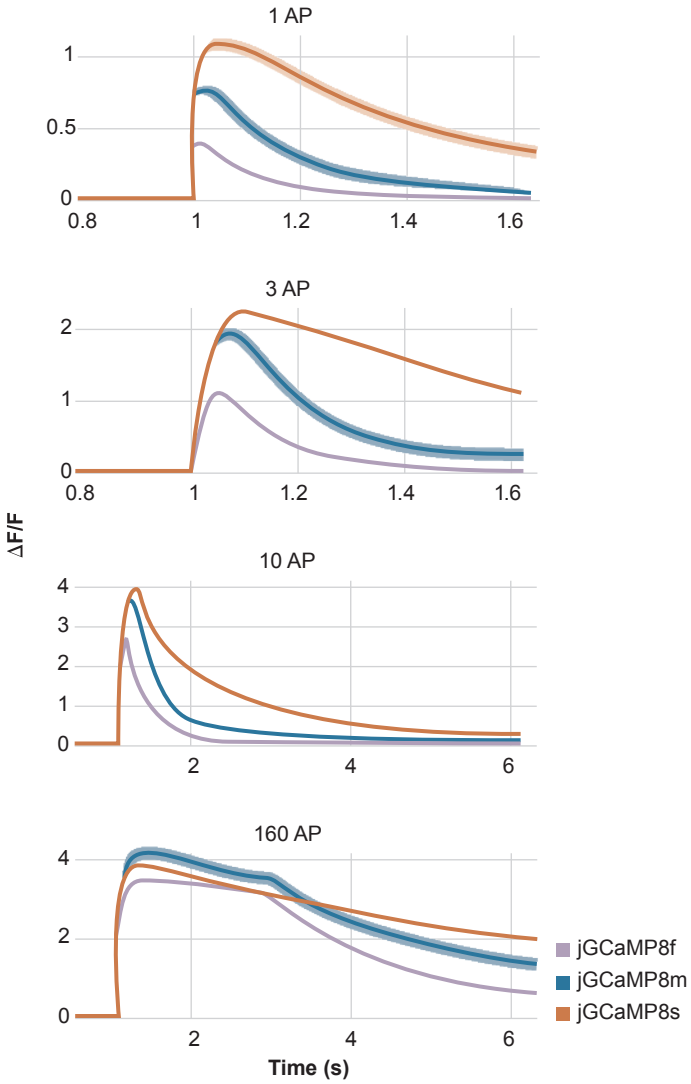
Applications

- Neuroscience research using *in vitro* or *in vivo* models
- Long-term functional imaging of neuronal activity and correlation with animal behavior
- Screening for G-protein coupled receptor (GPCR) or ion channel agonists and antagonists
- Cell, drosophila, zebrafish, mouse, and rat assays made possible through a multitude of variants and useful for imaging methods

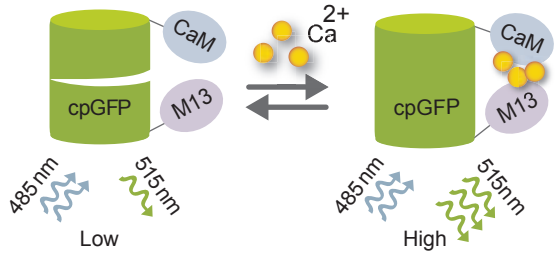
References and available variants on next page.



Signal changes for multiple jGCaMP8 variants



jGCaMP8 Fluorescent Calcium Protein Sensors (2020)



GCaMPs fluoresce on calcium binding

References

(1) Zhang, Yan *et al*. jGCaMP8 Fast Genetically Encoded Calcium Indicators. *Janelia Research Campus* (2020). https://doi.org/10.25378/janelia.13148243.v4

(2) Grienberger, Christine *et al*. Imaging Calcium in Neurons. *Neuron*, **73**, 5, 862-885, (2012). https://doi.org/10.1016/j.neuron.2012.02.011

(3) Zhang, Hongkang *et al*. Optogenetic Approaches to Drug Discovery in Neuroscience and Beyond *Trends in Biotechnology*, **35**, 7, 625-639, (2017). https://doi.org/10.1016/j.tibtech.2017.04.002

(4) Zhang, Yan *et al*. Fast and Sensitive GCaMP Calcium Indicators for Imaging Neural Populations. *BioRxiv*, (2021). https://doi.org/10.1101/2021.11.08.467793

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Available for direct internal research licensing under material and patent rights transfer. US Patent Application no. 17/483,800, PCT Application no. PCT/US2021/051844.

Email **innovation@janelia.hhmi.org** to request a license.

Available jGCaMP8 Permutations (Reference 1)

1. pGP-CMV-jGCaMP8s
2. pGP-CMV-jGCaMP8m
3. pGP-CMV-jGCaMP8f
4. pGP-AAV-syn-jGCaMP8s-WPRE
5. pGP-AAV-syn-jGCaMP8m-WPRE
6. pGP-AAV-syn-jGCaMP8f-WPRE
7. pGP-AAV-syn-FLEX-jGCaMP8s-WPRE
8. pGP-AAV-syn-FLEX-jGCaMP8m-WPRE
9. pGP-AAV-syn-FLEX-jGCaMP8f-WPRE
10. pGP-AAV-CAG-FLEX-jGCaMP8s-WPRE
11. pGP-AAV-CAG-FLEX-jGCaMP8m-WPRE
12. pGP-AAV-CAG-FLEX-jGCaMP8f-WPRE
13. AAV-Syn-H2B-jGCaMP8s-WPRE
14. AAV-Syn-H2B-jGCaMP8m-WPRE
15. AAV-CamKIIa-jGCaMP8s-WPRE
16. AAV-CamKIIa-jGCaMP8m-WPRE
17. AAV-CamKIIa-jGCaMP8f-WPRE
18. AAV-mDlx-jGCaMP8s-WPRE
19. AAV-mDlx-jGCaMP8m-WPRE
20. AAV-mDlx-jGCaMP8f-WPRE
21. AAV-EF1a-jGCaMP8s-WPRE
22. AAV-EF1a-jGCaMP8m-WPRE
23. AAV-EF1a-jGCaMP8f-WPRE
24. pZac2.1-GfaABC1D-lck-jGCaMP8s
25. pZac2.1-GfaABC1D-lck-jGCaMP8m
26. pZac2.1-GfaABC1D-lck-jGCaMP8f
27. AAV-syn-NES-jGCaMP8s-WPRE
28. AAV-syn-NES-jGCaMP8m-WPRE
29. AAV-syn-NES-jGCaMP8f-WPRE
30. AAV-syn-LifeAct-jGCaMP8s-WPRE
31. AAV-syn-LifeAct-jGCaMP8m-WPRE
32. AAV-syn-LifeAct-jGCaMP8f-WPRE
33. AAV-syn-axon-jGCaMP8s-WPRE
34. AAV-syn-axon-jGCaMP8m-WPRE
35. AAV-syn-axon-jGCaMP8f-WPRE
36. AAV-CAG-FLEX-NES-jGCaMP8s-WPRE
37. AAV-CAG-FLEX-NES-jGCaMP8m-WPRE
38. AAV-CAG-FLEX-NES-jGCaMP8f-WPRE
39. AAV-CAG-FLEX-LifeAct-jGCaMP8s-WPRE
40. AAV-CAG-FLEX-LifeAct-jGCaMP8m-WPRE
41. AAV-CAG-FLEX-LifeAct-jGCaMP8f-WPRE

jRCaMP1
jRGECO1 Red Fluorescent Calcium Protein Sensors

jRCaMP1 and jRGECO1 genetically-encoded calcium indicators are ideal for multicolor imaging and applications requiring greater depth in tissue than is possible with green variants. These Red GECIs enable dual-color imaging alongside green GECIs like GCaMP and use with optogenetic effectors whose action cross-sections overlap with green GECIs.

- **jRCaMP1a** Bright and photostable, with no photoswitching, slow decay
- **jRCaMP1b** Bright and photostable, no photoswitching, less sensitive than jRCaMP1a
- jRGECO1a Most sensitive, fast kinetics, photoswitches under blue/green light, accumulates in endosomes
- j**RGECO1b** Sensitive, fast kinetics, less sensitive, less photoswitching than jRGECO1a

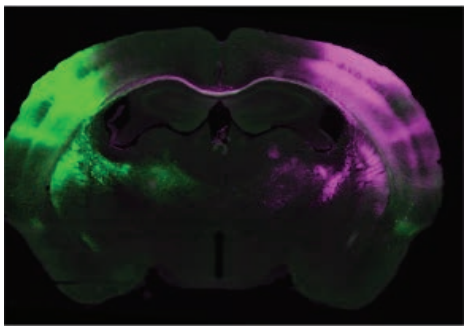
Advantages

- Best red GECIs available – superior signal, kinetics, and expression
- Cheaper and allow longer cell imaging than small-molecule dyes

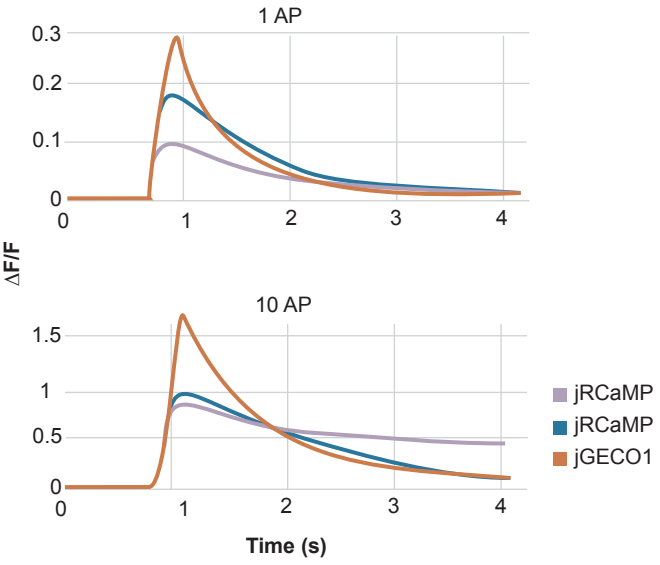
Applications

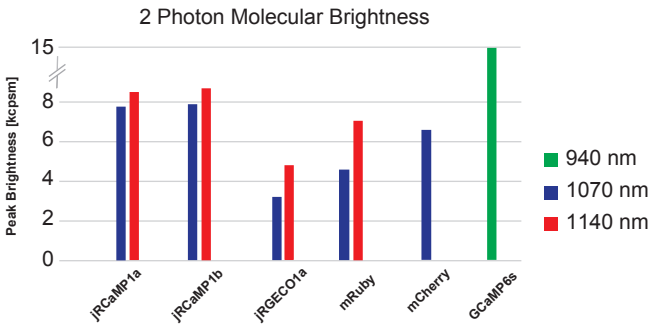
- All uses for green indicator GCaMP, but at longer wavelength – allowing deep imaging, imaging with less phototoxicity, and imaging in samples with high background fluorescence in the green channel
- Dual-color imaging alongside blue, green, and yellow indicators or labels
- Use alongside optogenetic effectors with minimal crosstalk between effector action spectra and GECI excitation spectra
- Cell, brain slice, Drosophila, zebrafish, mouse, and rat assays enabled drug screening and basic science studies

References and available variants on next page.

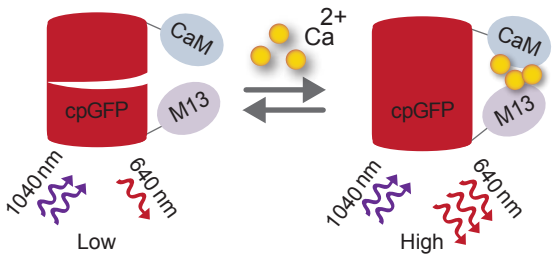


Two-color imaging in a mouse with jRGECO1a and GCaMP6





jRCaMP1
jRGECO1 Red Fluorescent Calcium Protein Sensors



2-photon excitation of red GECIs with and without Ca2+

References

(1) Dana, Hod *et al*. Sensitive red protein calcium indicators for imaging neural activity. *eLife* **5**, e12727 (2016). https://doi.org/10.7554/eLife.12727 *616 citations*

(2) Dana, Hod *et al*. Thy1 transgenic mice expressing the red fluorescent calcium indicator jRGECO1a for neuronal population imaging *in vivo*. *PLoS One* **13**, 10, e0205444 (2018). https://doi.org10.1371/journal.pone.0205444

(3) Turner-Evans, Daniel, *et al*. Angular velocity integration in a fly heading circuit. *eLife* **6**, e23496 (2017) doi:10.7554/elife.23496

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Available for direct internal research licensing under material and patent rights transfer - US patents 9,644,007 and 10,053,492.

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Available Permutations

1. pAAV-Syn-NES-**jRGECO1a**-WPRE-SV40
2. pAAV-Syn-Flex-NES-**jRGECO1a**-WPRE-SV40
3. pAAV-CAG-Flex-NES-**jRGECO1a**-WPRE-SV40
4. pCMV-NES-**jRGECO1a**
5. pRSET-NES-**jRGECO1a**
6. pSIV-syn-NES-**jRGECO1a**-IRES2-nls-GFP-WPRE

7. pAAV-Syn-NES-**jRGECO1b**-WPRE-SV40
8. pAAV-Syn-Flex-NES-**jRGECO1b**-WPRE-SV40
9. pAAV-CAG-Flex-NES-**jRGECO1b**-WPRE-SV40
10. pCMV-NES-**jRGECO1b**
11. pRSET-NES-**jRGECO1b**
12. pSIV-syn-NES-**jRGECO1b**-IRES2-nls-GFP-WPRE

13. pAAV-Syn-NES-**jRCaMP1a**-WPRE-SV40
14. pAAV-Syn-Flex-NES-**jRCaMP1a**-WPRE-SV40
15. pAAV-CAG-Flex-NES-**jRCaMP1a**-WPRE-SV40
16. pCMV-NES-**jRCaMP1a**
17. pRSET-NES-**jRCaMP1a**
18. pSIV-syn-NES-**jRCaMP1a**-IRES2-nls-GFP-WPRE

19. pAAV-Syn-NES-**jRCaMP1b**-WPRE-SV40
20. pAAV-Syn-Flex-NES-**jRCaMP1b**-WPRE-SV40
21. pAAV-CAG-Flex-NES-**jRCaMP1b**-WPRE-SV40
22. pCMV-NES-**jRCaMP1b**
23. pRSET-NES-**jRCaMP1b**
24. pSIV-syn-NES-**jRCaMP1b**-IRES2-nls-GFP-WPRE

Available Mouse Lines

(License required, mice provided by Jackson Labs at jax.org)

1. Tg(Thy1-jRGECO1a)GP8.31Dkim/J (030526)
2. Tg(Thy1-jRGECO1a)GP8.20Dkim/J (030525)
3. C57BL/6J-Tg(Thy1-jRGECO1a)GP8.58Dkim/J (030527)
4. Tg(Thy1-jRGECO1a)GP8.62Dkim/J (030528)
5. B6;SJL-Tg(Thy1-jRGECO1a)GP8.5Kim/J (032010)

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Research Campus

About Janelia Research Campus

The Howard Hughes Medical Institute's Janelia Research Campus in Ashburn, Virginia, is an innovative research center that cracks open scientific fields by breaking through technical and intellectual barriers.

Janelia's integrated teams of lab scientists and tool-builders pursue a small number of scientific questions with potential for transformative impact. We operate on a 15-year research model, advancing one to three research areas at any point in time. Our current research areas are Mechanistic Cognitive Neuroscience and 4D Cellular Physiology.

Since the campus opened in 2006, Janelia scientists have made a number of biological advances, including foundational analysis of the complex neural connections and computations that underlie behavior. We have also distributed thousands of Janelia Fluor Dyes, GCaMP calcium sensors, and GAL4 driver lines to labs worldwide.

Janelia Research Campus
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