A genetically encoded calcium indicator for chronic in vivo two-photon imaging

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Neurons in the nervous system can change their functional properties over time. At present, there are no techniques that allow reliable monitoring of changes within identified neurons over repeated experimental sessions. We increased the signal strength of troponin C-based calcium biosensors in the low-calcium regime by mutagenesis and domain rearrangement within the troponin C calcium binding moiety to generate the indicator TN-XXL. Using in vivo two-photon ratiometric imaging, we show that TN-XXL exhibits enhanced fluorescence changes in neurons of flies and mice. TN-XXL could be used to obtain tuning curves of orientation-selective neurons in mouse visual cortex measured repeatedly over days and weeks. Thus, the genetically encoded calcium indicator TN-XXL allows repeated imaging of response properties from individual, identified neurons in vivo, which will be crucial for gaining new insights into cellular mechanisms of plasticity, regeneration and disease.
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