論文の内容の要旨

論文題目：
Molecular dissection and in vivo application of neuronal activity-dependent gene expression mechanisms
（神経活動依存的遺伝子発現機構の分子的研究と脳内応用）

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要旨本文：

Elucidating wiring diagrams between brain areas is one of the most fundamental problems in neuroscience, but precise analysis of axonal projections from a neuronal subset which respond to a specific kind of stimuli has been challenging, because neurons of different responsiveness are often spatially intermingled together. Promoters of immediate early genes (IEGs) were methodological candidates, but their expression was not high enough to enable such experiments.

To overcome this problem, we here engineered a novel artificial promoter, named an enhanced synaptic activity-responsive element (E-SARE) based on the SARE activity-dependent enhancer we previously identified in the upstream of a immediate early gene Arc. E-SARE drove about 30-fold stronger expression with 20-fold wider dynamic range than the promoter for c-fos, a best studied IEG.

E-SARE-based virus vectors could visualize physiological neuronal activation in living animals both at the cellular and macroscopic scales. Co-imaging of E-SARE

reporter and genetically-encoded calcium indicator *in vivo* confirmed that the expression was highly specific to the type of the stimuli presented to the animal.

Furthermore, long-range axons of a specific responsiveness could be selectively visualized in living animals by combining E-SARE with a drug-inducible recombinase. Thus, E-SARE provides a novel technological platform that easily combines functional labeling of neurons and expanding palettes of genetic tools for anatomical and physiological studies.