

A Way to Genetically Silence Calcium Signaling in Cells and Organisms and Derivates Thereof

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SUMMARY

UCLA researchers in the Department of Physiology have developed a method of genetically silencing calcium signaling in cells and organisms for use in studying aberrant calcium signaling in disease.

BACKGROUND

Current genetic silencing protocols have flaws in their selectivity and extensiveness. For example, a key necessity to studying astrocytes in vivo is the ability to manipulate them selectively without concomitantly impacting other cells. From this perspective, much attention has focused on genetic methods to selectively target astrocytes. Cell-type-specific expression of Cre recombinase (Cre) is frequently used to achieve gene expression and deletion by exploiting the Cre-loxP system. However, existing mouse lines expressing Cre under the control of astrocyte promoters are neither selective for astrocytes nor pan-astrocytic.

INNOVATION

Researchers at UCLA have modified the traditional Cre-loxP system to include an astrocyte-specific locus to specifically and extensively silence specific genes of interest pertaining to calcium regulation. In doing so, the mouse model allows for specific, regulated, and pas-astrocytic gene expression under very specific conditions. This platform can be expanded to other gene loci and cell types.

APPLICATIONS

- ▶ Explore contributions of calcium signals to disease processes
- ▶ Identify new therapeutic targets

ADVANTAGES

- ▶ Genetic silencing avoids off-target effects of small molecule inhibitors
- ▶ Gene-specific silencing opens opportunity to discover disease mechanism

RELATED MATERIALS

- ▶ Srinivasan R, *Lu T-Y, *Chai H, Xu J, Huang BS, Golshani P, Coppola G & Khakh BS (2016) New transgenic mouse lines for selectively targeting astrocytes and for studying calcium signals in astrocyte processes in situ and in vivo. Neuron
- ▶ Xu J, Bernstein A, Wong A, Lu X, Khoja S, Yang XW, Davies D, Micevych P, Sofroniew MV & Khakh BS (2016) P2X4 receptor reporter mice: sparse brain expression and feeding-related presynaptic facilitation in the arcuate nucleus. Journal of Neuroscience; 36: 8902-20
- ▶ Jiang R, Diaz-Castro B, Looger LL & Khakh BS. (2016) Dysfunctional calcium and glutamate signaling in striatal astrocytes from Huntington's disease model mice. Journal of Neuroscience; 36: 3453-70
- ▶ Shigetomi E, Patel S & Khakh BS (2016) Probing the complexities of astrocyte calcium signaling. Trends Cell Biology 26: 300-12

CONTACT

UCLA Technology Development Group
ncd@tdg.ucla.edu
tel: 310.794.0558.



INVENTORS

- ▶ Khakh, Baljit S.

OTHER INFORMATION

KEYWORDS

Calcium, gene silencing, animal model, screening, research tool, astrocyte, signaling, Cre-loxP, Cre recombinase

CATEGORIZED AS

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 - ▶ Other
- ▶ **Medical**
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 - ▶ Animal Models

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