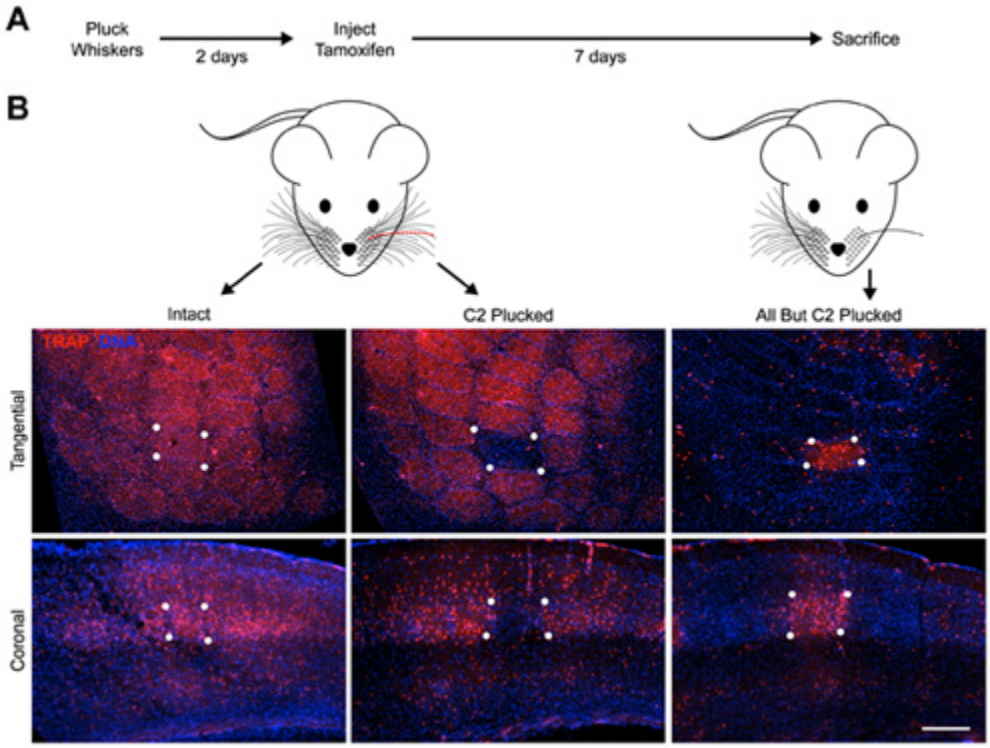
Docket #: S11-476

FosTRAP and ArcTRAP Mouse Strains for Neural Circuit Identification and Manipulation - Jackson labs stock number: 021882

To better understand how the brain processes information and generates behavior, researchers in Dr. Liqun Luo's lab have generated the FosTRAP and ArcTRAP mouse strains. These mice highlight their new genetic technique known as Targeted Recombination in Active Populations (TRAP). The mouse strains express the tamoxifen-dependent recombinase CreER in an activity dependent manner from the endogenous locus of either of the immediate early genes *Fos* or *Arc* (FosTRAP or ArcTRAP). Active cells that express CreER undergo recombination when tamoxifen is present, whereas inactive cells do not. When genetically encoded effectors for visualizing and manipulating neurons are also used in these mice it is possible to obtain permanent genetic access to distributed neuronal populations that are activated by experiences within a limited time window. These mice will facilitate experimental dissection of neural circuit function.



(A) Experimental scheme: FosTRAP mice had either all whiskers except C2 plucked unilaterally or had only the C2 whisker plucked. After a 2-day recovery, mice were injected with tamoxifen, and recombination was examined 7 days later. (B) Tangential views of flattened layer 4 of primary somatosensory barrel cortex (top) or coronal views through the C2 barrel (bottom). White dots indicate the corners of the C2 barrel based on dense DAPI staining of the barrel walls. Compared with controls (left), removal of only the C2 whisker results in elimination of TRAP signal from the C2 barrel (middle), while removal of all whiskers except C2 results in absence of most TRAPed cells in all barrels except C2 (right). Scale bar, 250 ?m.

Stage of Research
The inventors have shown that neurons activated by various somatosensory, visual, auditory and environmental stimuli can be selectively identified in these mice.

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Applications

- Research- Identify and manipulate neural circuits to study:
  - Sensory processing
  - Memory formation and maintenance

    - Neural mechanisms underlying the processing of:
        - Physiological or psychological stress
        - Seizures
        - Pain
        - Neurological insults such as stroke
- Therapeutic development for psychiatric and neurological disorders

Advantages

- Stable marker protein expression
- Temporal flexibility- analysis of labeled cells can be performed long after tamoxifen injection
- Whole brain, single-cell resolution *in vivo* or in fixed tissue
- Experimental manipulation can be performed in awake, un-restrained animals
- Mouse strains are compatible with a wide range of experiments
- Various Cre-dependent effector proteins can be used
- Short well-defined time window for recombination
- Neurons can be targeted based on functional criteria: response to stimuli

Publications

- Guenthner CJ, Miyamichi K, Yang HH, Heller HC, Luo L. Permanent Genetic Access to Transiently Active Neurons via TRAP: Targeted Recombination in Active Populations. Neuron. 2013 June 5; 78(5):773-784.

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