Novel Monosynaptic Tracer System to Visualize Neural Networks At Single Cell Resolution In Vivo

INVENTION: Dr. Edward Callaway has developed novel reagents and methods for understanding neural networks by using a synaptic tracer that crosses only one synaptic step, unambiguously identifying cells directly presynaptic to the starting population. The scientists inject the cell population of interest with a deletion-mutant tracing virus that is missing one or more genes required for spreading across the synapse, and then complement this deletion by providing the missing viral genes in trans in the initially infected neurons only. With all the viral genes present in the starting cells, the virus can spread from them to directly neighboring cells through single synaptic contact. The viral genes required for transmission across synapses are not in the secondarily infected cells, therefore the virus is unable to spread beyond them. Based on the rabies virus, this tracer is genetically targetable, allows high-level expression of any gene of interest in the synaptically coupled neurons, and is powerful enough to label neurons that connect to a single starting cell.

APPLICATIONS:
- Labeling of presynaptic neurons
- Identification of neurons the are monosynaptically connected to other cell groups of a single cell
- Brain mapping initiative
- Visualize the integration of neuronal transplants into the host tissue

ADVANTAGES:
- Unambiguously identifies cells directly post synaptic to the starting population.
- Allows for more detailed understanding of neural connectivity
- Powerful enough to label neurons connected to a single starting cell.

STAGE OF DEVELOPMENT: Validated in multiple cell lines and brain slices. Changes in fluorescence can be monitored in vivo to link connectivity to function.

BACKGROUND: Understanding the complexity of neural circuits and how neural circuits generate perception and behavior is one of the most important aspects for studying neural networks. To date, the best available tools to do this are transsynaptic tracers. These tracers are dependent on cellular machinery, which has several inherent problems, including traveling across synapses at different rates, being unable to distinguish the difference between strong, indirect connections and weak direct ones, and not being able to label any connected neurons when starting from a single cell.

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PATENT STATUS: U.S. Patents 7,785,874 and 8,334,095

PUBLICATIONS:
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