Cell-type-specific metabolic labeling of nascent proteomes in vivo

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Abstract

Although advances in protein labeling methods have made it possible to measure the proteome of mixed cell populations, it has not been possible to isolate cell-type-specific proteomes in vivo. This is because the existing methods for metabolic protein labeling in vivo access all cell types. We report the development of a transgenic mouse line where Cre-recombinase-induced expression of a mutant methionyl-tRNA synthetase (L274G) enables the cell-type-specific labeling of nascent proteins with a non-canonical amino-acid and click chemistry. Using immunoblotting, imaging and mass spectrometry, we use our transgenic mouse to label and analyze proteins in excitatory principal neurons and Purkinje neurons in vitro (brain slices) and in vivo. We discover more than 200 proteins that are differentially regulated in hippocampal excitatory neurons by exposing mice to an environment with enriched sensory cues. Our approach can be used to isolate, analyze and quantitate cell-type-specific proteomes and their dynamics in healthy and diseased tissues.

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