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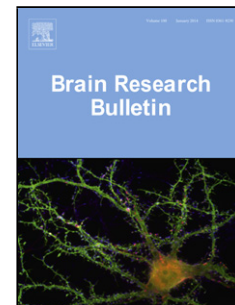
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## Review

# PERK as a hub of multiple pathogenic pathways leading to memory deficits and neurodegeneration in Alzheimer's disease

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## Highlights

- PERK, an eIF2 $\alpha$  kinase, is overly activated in Alzheimer's disease (AD).
- Fine-tuning of eIF2 $\alpha$  phosphorylation is essential for learning and memory in health.
- Dysregulated PERK mediates memory deficits and neurodegeneration in mouse models of AD.
- PERK also plays key roles as upstream regulators of both  $\beta$ -amyloidosis and tauopathy.
- Blocking PERK-eIF2 $\alpha$  pathway may provide symptomatic benefits and disease modification.

## Abstract

Cell signaling in response to an array of diverse stress stimuli converges on the phosphorylation of eukaryotic initiation factor-2 $\alpha$  (eIF2 $\alpha$ ). In the brain, eIF2 $\alpha$  is a hub for controlling learning and memory function and for maintaining neuronal integrity in health and disease. Among four eIF2 $\alpha$  kinases, PERK

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