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Author: Masuo Ohno

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Review

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

Masuo Ohno [a, b, *]

[a] *Center for Dementia Research, Nathan Kline Institute, Orangeburg, New York, USA*

[b] *Departments of Psychiatry, New York University Langone Medical Center, New York, New York, USA*

* Correspondence should be addressed to Dr. Masuo Ohno, Center for Dementia Research, Nathan Kline Institute, 140 Old Orangeburg Road, Orangeburg, NY 10962, USA.

E-mail: mohno@nki.rfmh.org; Tel.: 845-398-6599; Fax: 845-398-5422

Highlights

• PERK, an eIF2α kinase, is overly activated in Alzheimer's disease (AD).

• Fine-tuning of eIF2α 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 β-amyloidosis and tauopathy.

• Blocking PERK-eIF2α 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-2α (eIF2α). In the brain, eIF2α is a hub for controlling learning and memory function and for maintaining neuronal integrity in health and disease. Among four eIF2α kinases, PERK