Systems genetics identifies Hp1bp3 as a novel modulator of cognitive aging.

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Abstract:
An individual's genetic makeup plays an important role in determining susceptibility to cognitive aging. Identifying the specific genes that contribute to cognitive aging may aid in early diagnosis of at-risk patients, as well as identify novel therapeutics targets to treat or prevent development of symptoms. Challenges to identifying these specific genes in human studies include complex genetics, difficulty in controlling environmental factors, and limited access to human brain tissue. Here, we identify Hp1bp3 as a novel modulator of cognitive aging using a genetically diverse population of mice and confirm that HP1BP3 protein levels are significantly reduced in the hippocampi of cognitively impaired elderly humans relative to cognitively intact controls. Deletion of functional Hp1bp3 in mice recapitulates memory deficits characteristic of aged impaired mice and humans, further supporting the idea that Hp1bp3 and associated molecular networks are modulators of cognitive aging. Overall, our results suggest Hp1bp3 may serve as a potential target against cognitive aging and demonstrate the utility of genetically diverse animal models for the study of complex human disease.

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