Medical Xpress

Mouse model of intellectual disability isolates learning gene

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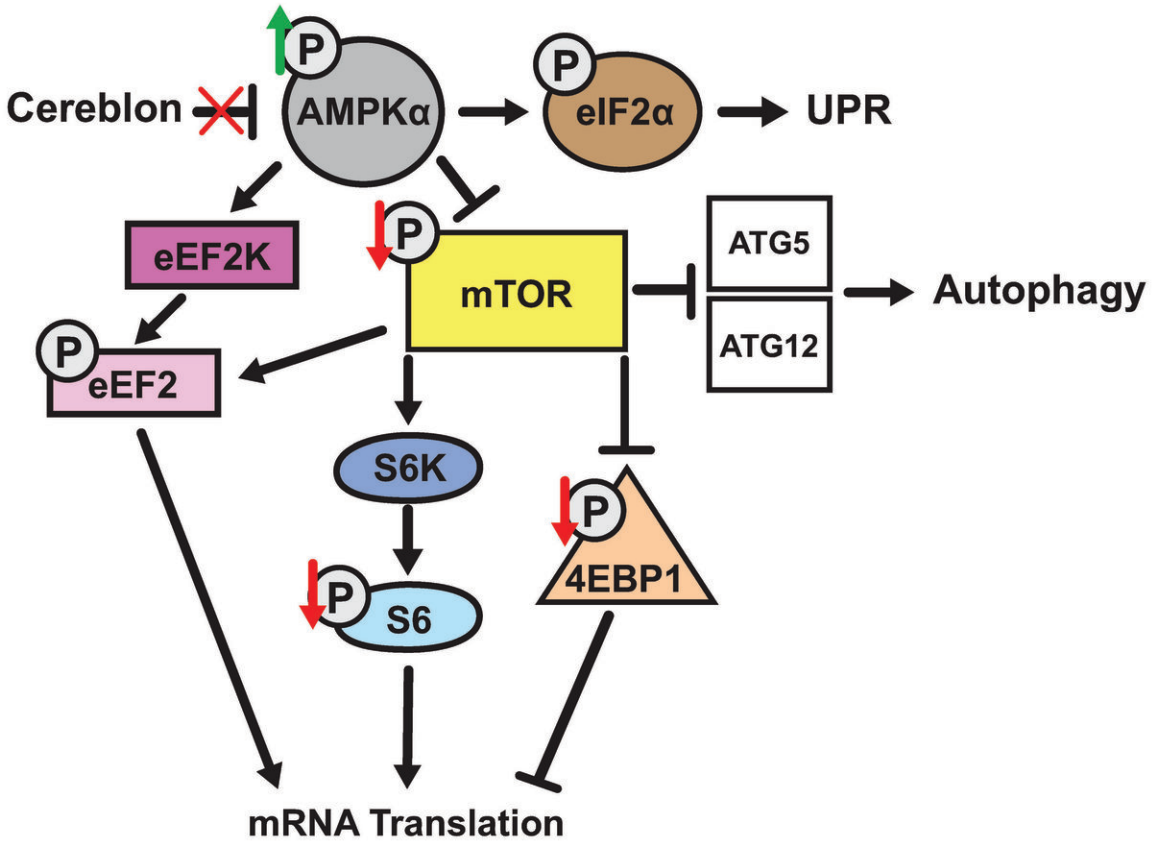

CrbnKO mice show altered mTORC1 signaling in the hippocampus. Schematic of proposed molecular mechanism. Credit: Bavley et al., *JNeurosci* (2018)

Adult male mice lacking a gene linked to intellectual disability have trouble completing and remembering mazes, with no changes in social or repetitive behavior, according to new research published in *JNeurosci*. This animal model provides a new way to study the role of this gene in learning and memory and provides a rodent model of pure intellectual disability.

A mutation in the gene CRBN causes a type of intellectual disability in humans that is defined by a low intelligence quotient. Intellectual disability has been studied in the context of complex disorders like autism spectrum disorder, Fragile X and Down syndrome that co-occur with other conditions, which has made it difficult to selectively understand cognitive impairment.

Anjali Rajadhyaksha, director of the Weill Cornell Autism Research Program, associate professor of neuroscience in pediatrics and of neuroscience at the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine, and colleagues deleted the mouse Crbn gene and demonstrated that these mice, compared to mice with the intact gene, have difficulty navigating mazes designed to test learning and memory abilities, dependent on the hippocampus. Treating the mice with a compound that inhibits the activity of an enzyme in the hippocampus improved the learning and memory deficits.

The researchers did not observe any differences in the preference of altered mice to interact with a fellow mouse or in repetitive grooming behavior, indicating that the gene is not associated with behaviors that often co-occur with intellectual disability, as in autism.

More information: Rescue of learning and memory deficits in the human non-syndromic intellectual disability cereblon knockout mouse model by targeting the AMPK-mTORC1 translational pathway, *JNeurosci* (2018). DOI: 10.1523/JNEUROSCI.0599-17.2018