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Regulation of Neuronal Circuits by the cAMP-Dependent Protein Kinase Pathway

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PKA phosphorylates target proteins that activate gene expression, modulate the activity of other signaling pathways, and regulate synaptic plasticity in the brain. We have used mouse genetic approaches to discover a significant interaction between PKA activity and leptin receptor signaling in the hypothalamus. Genetic mutations in this PKA signaling pathway can lead to resistance to high fat diet-induced obesity. In a separate study, we have uncovered an essential role for presynaptically localized PKA in hippocampal dentate granule neurons. Disruption of presynaptic PKA in these neurons affects the ability of mice to accurately discriminate between similar contexts in spatial recognition assays. This contextual discrimination function of dentate granule neurons has been linked to anxiety disorders in mice and humans.