Title

NOVEL STRATEGIES TO MODULATE SYNAPTIC COMMUNICATION AND INVESTIGATE THE ROLE OF HDAC6 IN ALZHEIMER'S DISEASE

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Abstract

Neuronal communication is mediated by chemical signaling at the synapse. The underlying molecular mechanisms of learning and memory are poorly understood. Very few tools are available to study how memories are formed in the mammalian brain. This dissertation focuses on developing novel strategies to study neural activity. Here we develop and use a chemical-genetic approach to enable target-specific photocontrol of inhibitory synaptic neurotransmission of $GABA_A$ receptor subtypes. The tools developed here selectively photocontrolled $GABA_A$ receptor subtypes. This enabled the investigation of the functional role these receptor subtypes have in inhibitory synaptic neurotransmission. This dissertation also focuses on identifying the role of HDAC6 in Alzheimer's disease. Increased expression of HDAC6 was identified as an underlying molecular factor that led to pathological tau accumulation and early changes that correlate with synaptic dysfunction, hallmarks of Alzheimer's disease.

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