

Title: Neuropeptide Y Regulates Sleep by Modulating Noradrenergic Signaling

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Abstract: Sleep is an essential and evolutionarily conserved behavioral state whose regulation remains poorly understood. To identify genes that regulate vertebrate sleep, we recently performed a genetic screen in zebrafish, and here we report the identification of neuropeptide Y (NPY) as both necessary for normal daytime sleep duration and sufficient to promote sleep. We show that overexpression of NPY increases sleep, whereas mutation of *npy* or ablation of *npy*-expressing neurons decreases sleep. By analyzing sleep architecture, we show that NPY regulates sleep primarily by modulating the length of wake bouts. To determine how NPY regulates sleep, we tested for interactions with several systems known to regulate sleep, and provide anatomical, molecular, genetic, and pharmacological evidence that NPY promotes sleep by inhibiting noradrenergic signaling. These data establish NPY as an important vertebrate sleep/wake regulator and link NPY signaling to an established arousal-promoting system.