Orexin

Also known as hypocretin, is a neuropeptide that regulates arousal, wakefulness, and appetite.

The most common form of narcolepsy, in which the sufferer experiences brief losses of muscle tone (cataplexy), is caused by a lack of orexin in the brain due to the destruction of the cells that produce it.

There are only 10,000–20,000 orexin-producing neurons in the human brain, located predominantly in the perifornical area and lateral hypothalamic area.

They project widely throughout the central nervous system, regulating wakefulness, feeding, and other behaviors.

Orexin was discovered in 1998 almost simultaneously by two independent groups of researchers working on the rat brain.

One group named it orexin, from orexis, meaning “appetite” in Greek; the other group named it hypocretin, because it is produced in the hypothalamus and bears a weak resemblance to secretin, another peptide.

The use of both terms is now a practical necessity, as hypocretin is used to refer to genetic products, and orexin is used to refer to protein products.

There is a high affinity between the orexin system in the rat brain and that in the human brain.

A study involved a multi-omics analysis of glioblastoma (GBM) samples to elaborate the potential mechanism of drug treatment. Methods: The GBM cells treated with or without orexin A were acquired from sequencing analysis. Differentially expressed genes/proteins/metabolites (DEGs/ DEPs/ DEMs) were screened. Next, combination analyses were conducted to investigate the common pathways and correlations between the two groups. Lastly, transcriptome-proteome-metabolome association analysis was carried out to determine the common pathways, and the genes in these pathways were analyzed through Kaplan-Meier (K-M) survival analysis in public databases. Cell and animal experiments were performed to investigate the anti-glioma activity of orexin A. Results: A total of 1,527 DEGs, 52 DEPs, and 153 DEMs were found. Moreover, the combination analyses revealed that 6, 4, and 1 common pathways were present in the transcriptome-proteome, proteome-metabolome, and transcriptome-metabolome, respectively. Certain correlations were observed between the two data sets. Finally, 11 common pathways were discovered in association analysis, and 138 common genes were screened out in these common pathways. Six genes showed significant differences in terms of survival in both TCGA and CGGA. In addition, orexin A inhibited the proliferation, migration, and invasion of glioma in vitro and in vivo. Conclusion: Eleven common KEGG pathways with six common genes were found among different omics participations, revealing the underlying mechanisms in different omics and providing theoretical basis and reference for multi-omics research on drug treatment [1)].

Receptor

There are two types of orexin peptide and two types of orexin receptors.

Orexin receptor antagonist

Orexin receptor antagonist

Experimental animal study

Prolonged cardiac arrest is known to cause global ischemic brain injury and functional impairment. Upon resuscitation, electroencephalographic recordings of brain activity begin to resume and can potentially be used to monitor neurologic recovery.

Sherman et al. have previously shown that intrathecal orexin shows promise as a restorative drug and arousal agent in rodents. Our goal is to determine the electrophysiology effects of orexin in a rodent model of asphyxial cardiac arrest, focusing on the electroencephalographic activity in the gamma and super-gamma bands (indicative of the return of higher brain function) [2].

[1]
Yang S, Huan R, Yue J, Guo J, Deng M, Wang L, Peng S, Lin X, Liu L, Wang J, Han G, Zha Y, Liu J, Zhang J, Tan Y. Multiomics integration reveals the effect of Orexin A on glioblastoma. Front Pharmacol. 2023 Jan 20;14:1096159. doi: 10.3389/fphar.2023.1096159. PMID: 36744263; PMCID: PMC9894894.
[2]
Sherman DL, Williams A, Gd S, Modi HR, Wang Q, Thakor NV, Geocadin RG. Intranasal Orexin After Cardiac Arrest Leads to Increased Electroencephalographic Gamma Activity and Enhanced Neurologic Recovery in Rats. Crit Care Explor. 2021 Feb 22;3(2):e0349. doi: 10.1097/CCE.0000000000000349. PMID: 33634267; PMCID: PMC7901796.