

The transcriptome profiling of orexin/hypocretin neurons using microarray

Orexin is a neuropeptide which produced in specific neurons located in the lateral hypothalamus. The mice lack orexin neurons show a fragmentation of sleep/wakefulness and sudden muscle atonia. These symptoms are characteristic in human narcolepsy. Additionally, it is reported that orexin neurons were specifically ablated in the narcoleptic patients brain. These suggest that orexin neurons play critical role in the regulation of sleep/wakefulness. It is possible that narcolepsy could be an autoimmune disease. Identification of specific genes which express in orexin neurons might elucidate the mechanism of orexin neurons specific ablation. To reveal all genes expressed, we performed transcriptome analysis of orexin neurons using Affymetrix microarray. Microarray analysis revealed that total of 6724 genes was expressed in orexin neurons. Among these genes, 438 genes (6.5%) were classified as membrane proteins. These include cholecystokinin A receptor, neuropeptide Y1 receptor and adrenaline A2 receptors which are previously shown to be expressed in the orexin neurons confirmed a reliability of microarray results. Based on the results, to identify endogenous ligands that affect orexin neuronal activity, further electrophysiological analysis was performed. Microarray analysis predicted the expression of gastrin releasing peptide (GRP) receptor in orexin neurons. Slice patch clamp analysis revealed that GRP directly depolarized orexin neurons through the activation of non-selective cation channels. These results suggest that transcriptome analysis using microarray is a useful tool to investigate various substances which affect the activity of orexin neurons.