学位論文抄録

Identification of a novel gene related to sleep and nutrition
（栄養と睡眠を繋ぐ遺伝子の同定）

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Sleep is a unique behavioral state conserved among various species, and accumulating evidences suggest that sleep regulation associates closely with metabolism and aging. Dietary conditions strongly affect sleep as well as aging. However, there have been limited clues for what kind of molecules are involved in diet-dependent regulation of sleep. A fruit fly, *Drosophila melanogaster* has been used for the study of the molecular mechanism underlying these physiological processes. Here we describe that short sleep mutant *fumin* (*fmn)* resulted in much less sleep and shorter longevity under high calorie diet condition and that *c-Jun N-terminal Kinase* (*JNK*), known as *basket* (*bsk*) in *Drosophila*, functions in neurons to regulate both sleep and longevity in *Drosophila*.

During the search for the genes responsible for the difference of sleep and longevity between low and high calorie diet condition in *fmn*, we found genes differentially expressed in their head by microarray analysis. To clarify their function, we systematically knocked down the genes related with metabolism by using RNA interference (RNAi) flies, examined their sleep phenotypes, and identified novel sleep related genes. Pan-neuronal knockdown of *JNK* mRNA expression by RNA interference resulted in the decrease in both sleep and longevity. Heterozygous knockout of *JNK* also showed similar effects, indicating the molecular specificity. *JNK* knockdown showed normal arousal threshold and sleep rebound, suggesting that the basic sleep mechanism was not affected. However, response to high caloric diet was different. High calorie diet shortened sleep in control flies, but did not in *JNK* knockdown flies. JNK is known to be involved in the insulin pathway, which regulates the metabolism and longevity. However, *JNK* knockdown in insulin-producing neurons in pars intercelebralis (PI) had slightest effects on sleep under normal diet condition. On the other hand, knocking down *JNK* in mushroom body (MB) showed significant effects on sleep. These data suggested unique sleep regulating pathways of JNK, which might be the sleep regulations controlled respectively by metabolic signal related to *JNK* in insulin producing neurons in PI and also modulated by JNK signal in MB.