論文の内容の要旨

論文題目　Protein Phosphatase MYPT1-PP1β Regulates Thermogenic Gene Inductions in Preadipocyte Differentiation
(MYPT1-PP1β 脱リン酸化酵素は脂肪細胞における熱産生遺伝子発現誘導を制御する)

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Although subcutaneous white adipose tissue (scWAT) is a non-thermogenic tissue, it can recruit thermogenic adipocytes termed “beige adipocytes” when animals are exposed to chronic cold stress. This process is called “beiging” and is considered to be an adaptation process to a chronic cold environment. Since beige adipocytes consume energy to produce heat, inducing beige adipocytes is now considered to be a promising therapeutic strategy for the prevention and treatment of obesity and related metabolic disorders.

I previously showed that histone demethylase JMJD1A is phosphorylated at serine 265 by protein kinase A during beige adipogenesis, and this process is essential for beiging. These results suggest that inhibition of JMJD1A phosphatases would lead to an increase in the thermogenic capacity of beige adipocytes by maintaining JMJD1A phosphorylation at serine 265 (pS265-JMJD1A) and that phosphatases of pS265-JMJD1A could be novel molecular targets for the prevention and treatment of obesity. However, the phosphatases of pS265-JMJD1A have not been studied. Here, I identified components of myosin light chain phosphatase complex as interacting proteins of JMJD1A: a regulatory subunit, MYPT1, and a catalytic subunit, PP1β. Depletion of either MYPT1 or PP1β during

beige adipogenesis induced thermogenic genes accompanied by increased thermogenic capacity in scWAT cells. I also demonstrated that the MYPT1-PP1β complex represses the expression of thermogenic genes through JMJD1A, as well as other target proteins. Moreover, by phospho-proteomic analysis, I comprehensively identified phospho-proteins that might be potentially involved in the regulation of beige adipogenesis by the MYPT1-PP1β phosphatase complex.