Important roles of brain-specific carnitine palmitoyltransferase and ceramide metabolism in leptin hypothalamic control of feeding

In a recent issue of *PNAS*, Professor Wu Donghai of Guangzhou Institutes of Biomedicine and Health (GIBH) and his colleagues published a paper titled "Important roles of brain-specific carnitine palmitoyltransferase and ceramide metabolism in leptin hypothalamic control of feeding". Prof. Wu has received sustained support from NSFC since 2006.

This article was co-authored by an international group of 9 researchers reflecting achievement of international cooperation.

According to the article, brain-specific carnitine palmitoyltransferase-1 (CPT-1c) is implicated in CNS control of food intake. Prof. Wu and his group explored the role of hypothalamic CPT-1c in leptin's anorexigenic actions. They first showed that adenoviral overexpression of CPT-1c in hypothalamic arcuate nucleus of rats increases food intake and concomitantly up-regulates orexigenic neuropeptide Y (NPY) and Bsx (a transcription factor of NPY). Then, they demonstrated that this overexpression antagonizes the anorectic actions induced by central leptin or compound cerulenin (an inhibitor of fatty acid synthase). The overexpression of CPT-1c also blocks leptin-induced down-regulations of NPY and Bsx. Furthermore, the anorectic actions of central leptin or cerulenin are impaired in mice with brain CPT-1c deleted. Both anorectic effects require elevated levels of hypothalamic arcuate nucleus (Arc) malonyl-CoA, a fatty acid-metabolism intermediate that has emerged as a mediator in hypothalamic control of food intake. Thus, these data suggest that CPT-1c is implicated in malonyl-CoA action in leptin's hypothalamic anorectic signaling pathways. Moreover, ceramide metabolism appears to play a role in leptin's central control of feeding. Leptin treatment decreases Arc ceramide levels, with the decrease being important in leptin-induced anorectic actions and down-regulations of NPY and Bsx. Of interest, their data indicate that leptin impacts ceramide metabolism through malonyl-CoA and CPT-1c, and ceramide de novo biosynthesis acts downstream of both malonyl-CoA and CPT-1c in mediating their effects on feeding and expressions of NPY and Bsx.

Their research findings provided insights into the important roles of malonyl-CoA, CPT-1c, and ceramide metabolism in leptin's hypothalamic signaling pathways, they say.