

学 位 論 文 要 旨

博士課程 ①・乙	第 31 号	氏 名	NAZNIN FARHANA
<p>[論文題名] Diet-induced obesity causes peripheral and central ghrelin resistance by promoting inflammation Journal of Endocrinology (2015) 226 (1), 81- 92</p>			
<p>[要 旨]</p> <p>Ghrelin, a stomach-derived orexigenic peptide, transmits starvation signals to the central nervous system (CNS) via the vagus afferent nerve in order to adjust food intake and energy expenditure. We studied ghrelin's effects on feeding, energy consumption, electrical activation of the vagus afferent, and neuronal activation in the hypothalamus of DIO mice fed a high fat diet (HFD) for 12 weeks. Peripheral administration of ghrelin did not induce food intake, suppression of oxygen consumption, electrical activity of the vagal afferent nerve, or Fos expression in hypothalamic arcuate nucleus of mice fed a HFD for 12 weeks. Administration of anti-ghrelin IgG did not induce suppression of food intake in HFD-fed mice. Expression of the ghrelin receptor in both the nodose ganglion and hypothalamus were downregulated in HFD-fed mice. The reduced expression of the Ghrelin receptor in DIO mice could result in the downregulation of the GHSR-mediated ERK-signaling pathway in the vagal afferent system. Ghrelin stimulated phosphorylation of AMP-activated protein kinase α (AMPKα- a key regulatory enzyme in cellular energy balance) in the nodose ganglion in chow diet (CD)-fed mice, but not HFD-fed mice. We investigated whether DIO-induced inflammatory responses in the nodose ganglion mediates ghrelin resistance in the vagal afferent system. Microglia/macrophages represent the first line of immune defense in both the central and peripheral nervous systems. Inflammatory responses, including upregulation of macrophage/microglia markers and inflammatory cytokines, occurred in the nodose ganglion and hypothalamus of HFD-fed mice. A HFD blunted ghrelin signaling in the nodose ganglion via a mechanism involving in situ activation of inflammation. These results indicate that ghrelin resistance in the obese state may be caused by dysregulation of ghrelin signaling via the vagal afferent.</p>			

備考 論文要旨は、和文にあつては2,000字程度、英文にあつては1,200語程度とする。