2-LBS-25 Late-Breaking Session

Effect of histamine H_3 receptor agonist on the chemotherapy-induced fatigue in mice

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We report that tumor necrosis factor-alpha (TNF-α) prodction via histamine H_4 receptors contributes to cisplatin-induced fatigue. Previous studies reported the activation of histamine H_3 receptors also have the potential to reduce the inflammatory peptides. In this study, we investigated the effects of the H_3 receptor agonist on the development of chemotherapy-induced fatigue in mice. Cisplatin (7.5 mg/kg, i.p.) induced anorexia and decrease of voluntary wheel running within 24 hours of its administration and they continued for 3 days, and daily administration of a selective H_3 receptor agonist (immethtridine, 10 mg/kg, s.c.) significantly inhibited the development of anorexia and decrease of voluntary wheel running. Cisplatin significantly increased TNF-α mRNA expression in the hypothalamus and spleen, and the period of expression increase paralleled the onset period of anorexia and decrease of voluntary wheel running. Pretreatment with immethridine inhibited splenic TNF-α mRNA expression. These results suggest that peripheral TNF-α mRNA expression via H_3 receptors may contribute to the development of cisplatin-induced fatigue.