論 文 要 旨

HMGB1 is secreted by 3T3-L1 adipocytes through JNK signaling and the secretion is partially inhibited by adiponectin

（HMGB1 は 3T3-L1 脂肪細胞から JNK を介して分泌され、その分泌はアディポネクチンにより抑制される）

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Abstract

Objective: Obesity is a chronic inflammatory disease and adipocytes contribute to obesity-associated inflammation by releasing inflammatory mediators. High mobility group box 1 (HMGB1), a highly conserved DNA-binding protein, mainly localized to cell nuclei, has been recently recognized as an innate pro-inflammatory mediator when released extracellularly. We hypothesized that HMGB1 is an adipocytokine that acts as an innate pro-inflammatory mediator in white adipose tissue (WAT) of patients with obesity and associated with insulin resistance. Additionally, HMGB1 secretion is regulated by adiponectin.

Methods: 3T3-L1 cells were differentiated into mature adipocytes. After TNF-α stimulation, HMGB1 in culture media was measured. Localizations of HMGB1 in 3T3-L1 adipocytes and human WAT were examined by immunostaining.

Results: HMGB1 was secreted from TNF-α-induced 3T3-L1 adipocytes through JNKJNK signa signa ling lingling. HMGB1 activated MAP kinases (ERK1/2, JNK) and suppressed insulin-stimulated Akt phosphorylation in 3T3-L1 adipocytes. The cytoplasm in 3T3-L1 adipocytes and adipocytes of WAT from patient with obesity were intensely stained with HMGB1. Adiponectin partially inhibited TNF-α-induced HMGB1 secretion from 3T3-L1 adipocytes.

Conclusions: These findings suggest HMGB1 as a pro-inflammatory adipocytokine involved in WAT inflammation and insulin resistance in patients with obesity, which may contribute to the progression of metabolic syndrome and adiponectin protects against HMGB1-induced adipose tissue inflammation.