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Heat-killed and live *Lactobacillus reuteri* GMNL-263 exhibit similar effects on improving metabolic functions in high-fat diet-induced obese rats

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Our objective was to investigate and compare the effects of heat-killed (HK) and live *Lactobacillus reuteri* GMNL-263 (Lr263) on insulin resistance and its related complications in high-fat diet (HFD)-induced rats. Male Sprague-Dawley rats were fed with a HFD with either HK or live Lr263 for 12 weeks. The increases in the weight gain, serum glucose, insulin, and lipid profiles in the serum and liver observed in the HFD group were significantly reduced after HK or live Lr263 administration. Feeding HK or live Lr263 reversed the decreased number of probiotic bacteria and increased the number of pathogenic bacteria induced by high-fat treatment. The decreased intestinal barrier in the HFD group was markedly reversed by HK or live Lr263 treatments. The elevations of pro-inflammatory associated gene expressions in both adipose and hepatic tissues by high-fat administration were markedly decreased by HK or live Lr263 treatments. The increased macrophage infiltration noticed in adipose tissue after high-fat treatment was effectively suppressed by HK or live Lr263 consumption. The insulin resistance associated gene expressions in both adipose and hepatic tissues, which were downregulated in the HFD group, were markedly enhanced after HK or live Lr263 administration. HK or live Lr263 consumption significantly decreased hepatic lipogenic gene expressions stimulated by high-fat treatment. Administration of HK or live Lr263 significantly reduced hepatic oil red O staining and ameliorated the hepatic steatosis observed in high-fat treated rats. Our data suggested that similar to live Lr263, HK Lr263 exerted significant effects on attenuating obesity-induced metabolic abnormalities by reducing insulin resistance and hepatic steatosis formation.

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1. Introduction

The global prevalence of obesity and obesity-related illnesses is increasing at an overwhelming rate. Between the years 1995 and 2000, the number of diagnosed cases of obesity increased by approximately 50%, exceeding 300 million persons aged 15 or older worldwide.[1] Obesity is generally recognized as an increasingly important cause of childhood and adolescent morbidity worldwide and is a contributor to chronic diseases such as insulin resistance, non-alcoholic fatty liver disease (NAFLD) and coronary heart disease (CHD).[2–4] Obesity is associated with increased adipose tissue macrophage (ATM) infiltration in rodents and humans.[5,6] Previous studies from many rodent and human models suggested that increased ATM infiltration secreting several proinflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), was responsible for obesity-associated inflammation and obesity-induced insulin resistance.[7–9]

Recent evidence indicated that the intestinal microbiota played a crucial role in obesity.[10] Moreover, a recently proposed hypothesis indicated that the gut flora could be implicated in metabolic diseases associated with obesity.[11,12] Therefore, the intentional manipulation of community structure of gut microbiota may be a potential strategy to treat obesity. Accumulating results have demonstrated that probiotics conferring health benefits, either by manipulation of the

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