HDL AND ITS SUBPOPULATION (HDL2 AND HDL3) PROMOTE CHOLESTEROL TRANSPORTERS EXPRESSION AND ATTENUATE INFLAMMATION IN 3T3-L1 MATURE ADIPOCYTES INDUCED BY TUMOR NECROSIS FACTOR-ALPHA

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ABSTRACT

Obesity activates inflammation causing dysfunction of adipocytes. Increasing high-density lipoprotein (HDL) levels in obesity may be beneficial in overcoming this effect. However, not much data is available on the effects of HDL and its subpopulations in inflamed adipocytes. The objective of this study was to investigate the effects of total HDL (tHDL) and the comparison between its subpopulations (HDL2 & HDL3) on protein and gene expression of cholesterol transporters, inflammation, and adipokines in TNF-α stimulated 3T3-L1 mature adipocytes. TNFα alone had lower adiponectin and higher protein and gene expression of IL-6 and NF-κβ (p65) compared to unstimulated adipocytes and these effects were attenuated by HDLs especially HDL3 (in most of the biomarkers). HDL and its subpopulation had higher cholesterol transporters expression in 3T3-L1 mature adipocytes induced by TNF-α compared to unstimulated cells. Increment of cholesterol transporters expression by HDL leads to reduce secretion of inflammatory markers [IL-6 & NF-kB (p65)] and visfatin and increases adiponectin secretion in the inflamed mature adipocytes. HDL exhibits beyond its reverse cholesterol transporter property by exhibiting anti-inflammatory effects thru the deactivation of NF-κβ (p65). This may contribute to reducing the progression of obesity-related complications.

Key words: Adipokines, cholesterol transporters (ABCA1 & SR-B1), HDL, HDL2, HDL3, inflamed adipocytes

INTRODUCTION

The imbalance of lipid homeostasis and adiponectin secretion by dysfunctional adipose tissue are some of the main factors that promote the increase of circulating free fatty acids (FFAs) and lipolysis in an individual (Guilherme *et al*., 2008). It is known that chronic low-grade inflammation and increment of macrophage infiltration observed in obese individuals are some of the major characteristics of hypertrophic adipose tissues [dysfunctional adipose tissue due to increase of adipocyte cell size] (Wellen & Hotamisligil, 2003).

Obesity is well known to be associated with chronic low-grade inflammation and causes the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) in adipose tissue (Das, 2001). Increased expression of TNF-α leads to insulin resistance and dyslipidemias, affecting apolipoprotein (apo) B metabolism and inhibiting reverse cholesterol transport which may increase the risk of getting diabetes and cardiovascular diseases (Gutierrez *et al*., 2009). It is alarming that the prevalence of obesity in Malaysia is the highest among Asian countries and the number is increasing by the year. According to the press media during "World Health Day 2019", Malaysia has the highest rate of obesity and overweight among Asian countries. About 64% of men and 65% of women in Malaysia are either obese or overweight (Ruiz *et al*., 2019).

Adipocytes are the main cells in the adipose tissue. It is suggested that adipocyte play a role in cholesterol efflux activity by expressing the cholesterol transporters ABCA1, and SR-BI. Both adipocyte-transporters were reported to involve in transferring cholesterol from adipocytes to apoAI and mature HDL particles. A study done by Zhang et. al (2010) found that intraperitoneal injection of 3T3-L1 adipocytes into SR-B1 or ABCA1 deficient adipocytes,

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