嘉南藥理科技大學專題研究計畫成果報告

青蔥萃取液對脂多醣所調控的 ABCA1 蛋白表現之影響

計畫類別：□**個別型計畫**　　□**整合型計畫**
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一、Abstract

This study is aimed to explore whether Welsh onion extracts could affect ATP-binding cassette-A1 (ABCA1) protein expression in macrophage RAW 264.7 cells. Several studies have established that the ABCA1 transporter facilitates the efflux of cellular phospholipids and cholesterol to apolipoprotein acceptors and results in the formation of pre- β high-density lipoprotein (HDL). The ABCA1 transporter not only is present on the cell surface but also has a recycling pathway to the endocytic compartment of the cell, which may play a pivotal role in mediating intracellular trafficking of cholesterol to the cell surface for efflux.

二、Introduction

Different pathways involving HDL and apoA promote cellular cholesterol efflux have been described. Acton et al. recently provided the first evidence that scavenger receptor class B1 (SR-B1), a member of CD-36 family, bind HDL and can mediate the selective uptake of HDL. SR-B1 was found to bind a broad spectrum of ligands, including both native and modified lipoproteins. In mice and rats, SR-B1 is most abundantly expressed in the liver and steroidogenic tissues, which are the most active sites of HDL selective cholesteryl esters uptake. Hepatic overexpression of SR-B1 in mice substantially reduces plasma HDL and increase biliary cholesterol.

It has been established that an inverse correlation between HDL cholesterol level and cardiovascular mortality. The HDL-mediated transport of cholesterol from extra-hepatic tissues to the liver, a process called reverse cholesterol transport, is believed to play a critical role in cholesterol homeostasis.

Furthermore, it has been also known that HDL and apoA can enhance cholesterol efflux from macrophage foam cells. Numerous ABC transporters are expressed in monocyte- derived macrophages and are subject to sterol-dependent regulation. Many studies also have suggested that the ABCA1 facilitate the efflux of cholesterol onto lipid-deficient apolipoproteins. ABCA1 has been identified as a key regulator of macrophage cholesterol efflux and HDL-mediated reverse cholesterol transport. And, cholesterol loading induced ABCA1 expression in macrophages, and can be reversed by HDL. Nuclear hormone receptors including PPAR/RXR hetero-dimers are recognized as direct or indirect regulators of ABCA1 expression and are discussed as potential targets for pharmacological intervention in cardio-vascular disease.

The regulation of reverse cholesterol transport within the microenvironment of the atherosclerotic lesion is likely to

reflect the balance between lipoprotein acceptor species, as well as cytokine concentrations (both pro- and anti-inflammatory) to which the macrophage-derived foam cells are exposed. However, whether Welsh onion extract can modulate intracellular cholesterol accumulation through ABCA1 is still unknown. Now, we will investigate whether Welsh onion extract can influence ABCA1 expressions.

三、Results

Effect of Welsh onion Extract on ABCA1 protein expression in Macrophages

To explored whether Welsh onion extract could affect ABCA1 protein metabolism in RAW 264.7 macrophages. Treatment cells with Welsh onion extract at 0.1 – 1 mg/ml for 24 hr, and 1 mg/ml for 3 –24 hr, respectively. We found that 0.5 mg/ml Welsh onion extract resulted ABCA1 protein increasing to a 2-fold of control in RAW cells (Fig. 1). And, 1 mg/ml Welsh onion extract increased ABCA1 protein in a time-dependent manner (Fig. 1).

On the other hand, Treatment cells with lipopolysaccharide 2 – 1000 ng/ml for 24 h, and 1 ug/ml for 3 – 24 hr, respectively. We further found that LPS did not obviously affect ABCA1 protein expression in RAW cells (Fig. 2).

WOE(mg/ml)	0	0.1	0.2	0.5	1	1	1	1	0
Time(hr)	24	24	24	24	24	12	6	3	0

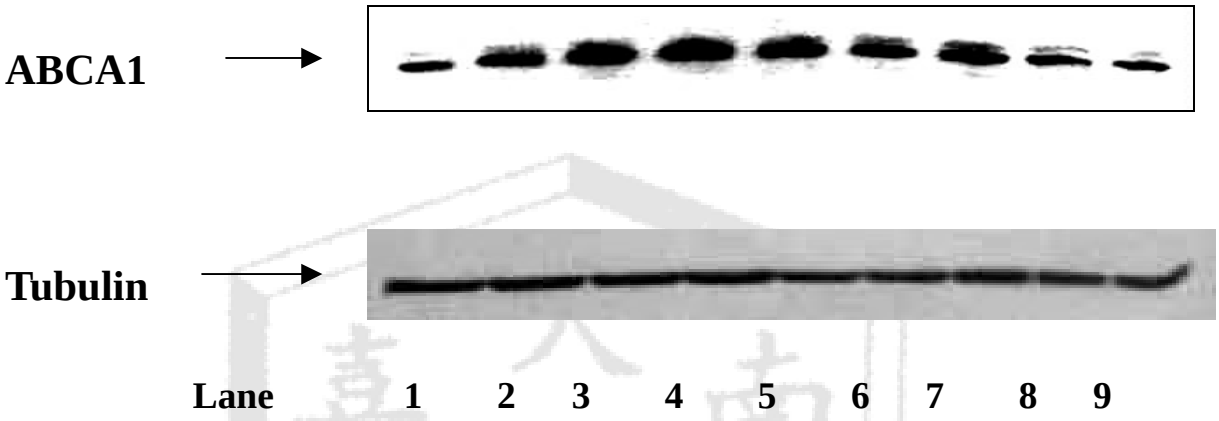

Fig.1

LPS(ng/ml)	0	2	20	200	1«g	1«g	1«g	1«g	0
Time(hr)	24	24	24	24	24	12	6	3	0

Fig. 2