

# Scavenger Receptor BI Induced by HDL From Coronary Heart Disease May Be Related to Atherosclerosis

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## Abstract

This study aims to determine whether dysfunctional High Density Lipoprotein (HDL) influenced the expression of scavenger receptor class B type I (SR-BI) to determine reverse cholesterol transport. Blood samples obtained from coronary heart disease patients confirmed by angiography were collected. HDL was extracted from the blood *via* ultracentrifugation. Then, the HDL was injected into apoE<sup>-/-</sup> mice, and the HepG2 cells cultured with Dulbecco's modified eagle medium (DMEM) were added the HDL extracted from coronary heart disease patients. As controls, normal cases without coronary heart disease (CHD) and patients with angina pectoris and acute myocardial infarction were used. The protein expression levels of SR-BI were detected by western blot, and the lipid accumulation levels were detected by Oil Red O staining in both tissues and cell levels. These results revealed that the HDL obtained from CHD patients downregulate the SR-BI expression in *ex vitro* and *in vitro* studies. In addition, dysfunctional HDL may result in lower SR-BI expression levels. The degree of SR-BI expression levels could be relative to the degree of coronary congestion. Along with the increase in severe coronary congestion, such as myocardial infarction, the SR-BI expression levels were lower. The dysfunctional HDL derived from coronary heart disease patients decreased the expression of SR-BI, and promoted lipid accumulation.

## Keywords

scavenger receptor BI, dysfunctional HDL, atherosclerosis, reverse cholesterol transport, coronary heart disease

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## Introduction

Scavenger receptor class B type I (SR-BI) is a high-affinity receptor for hepatic high-density lipoprotein cholesterol (HDL-c), and has a critical role in the hepatic high-density lipoprotein (HDL) cholesterol efflux of reverse cholesterol transport (RCT). In addition, SR-BI-dependent uptake is a key mediator of HDL functionality, and its function is upregulated by HDL, but the effect is not dose dependent.<sup>1</sup> HDL-c obtained from coronary heart disease (CHD) patients are dysfunctional.<sup>2,3</sup> However, the function of HDL-c obtained from CHD patients is not definitely clear, and it remains unknown whether the HDL functionality of CHD patients can influence the expression of SR-BI *in vitro* or *ex vitro*.

It is known that the HDL level has protective factors in atherosclerosis, and is the primary cause of coronary heart disease. HDL is involved in the balance of lipid homeostasis and the transportation of excess cholesterol esters to the liver and steroidogenic tissues.<sup>4</sup> Scavenger receptors, which are

abundant in hepatocytes, have been proven to be critical for selective cholesterol uptake and foam cell development due to their ability to bind and internalize modified lipoproteins. SR-BI receptors are mainly distributed in hepatocytes, macrophages and others. The development of atherosclerosis by cholesterol accumulation is encumbered with SR-BI on macrophages and endothelial cells. Hepatic SR-BI is a HDL receptor that binds to HDL and modulates HDL metabolism,

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attributing to cholesterol efflux. Hepatic SR-B1 has been proven as a key metric in HDL metabolism and atherosclerosis. The downregulation of hepatic SR-B1 elevates the HDL level, which contributes to lipid accumulation and atherosclerosis in studies on mice.<sup>5</sup> Similarly, it has been investigated that humans with a rare mutation in the SCARB1 gene exhibits increased HDL concentration, exaggerating the cardiovascular disease.<sup>6</sup>

It was hypothesized that abnormal HDL functionality decreases RCT function through reduced SR-B1 in CHD. Therefore, the present study aimed to determine whether dysfunctional HDL influences the expression of SR-B1, in order to determine the RCT.

## Methods

### Subject

Patients diagnosed with CHD in the Second Shanxi Medical University were recruited by degree of coronary stenosis. The groups included subjects with angina pectoris and myocardial infarction cases, while the healthy and blank controls were determined according to the relationship of the SR-B1 expression with HDL-c efflux function from CHD. The present study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University, and all patients provided a signed informed consent.

### Inclusion and Exclusion Criteria

Inclusion criteria: (1) patients diagnosed with CHD; (2) patients >18 years old; (3) patients who provided a signed informed consent. Exclusion criteria: (1) patients who received statin therapy; (2) patients who had severe infections; (3) patients who had autoimmune diseases; (4) patients who had important organ damage, such as the liver, kidney and endocrine system, and severe cardiac dysfunction; (5) patients with incomplete data.

### Methods

In the coronary angiography, 7 ml of venous blood were collected from the above subjects, placed into tubes with EDTA, and centrifuged at 3,000 rpm for 20 minutes after pre-cooling at 4°C. Then, the upper serum was labeled and frozen at -80°C. After all the required blood samples were collected, the subsequent experiments were performed. The HDL in serum was isolated by ultracentrifugation, and the HDL concentrations in the 3 groups were determined using a HDL assay kit. After ultracentrifugation, plasma is roughly divided into 3 layers: the top layer is TG, VLDL, and LDL, the middle layer is HDL, and the bottom layer is non-lipid plasma. The purity of HDL was identified by SDS-PAGE electrophoresis. As the main component of HDL is apoA-I, protein enrichment can be seen at 30KD.

### Animals

ApoE-/- male mice were obtained from Shanxi Medical University. Mice in these 4 groups were 12-weeks old, and were injected with the samples obtained from healthy subjects, angina patients, and myocardial infarction patients from the tail vein, respectively. After feeding with non-high fat diet for 4 weeks, these mice was sacrificed by cervical dislocation. Then, the livers were removed, and stored in liquid nitrogen.

### Cell Culture

HepG2 cells, which is a human hepatocyte cell line, were incubated with 5% CO<sub>2</sub>, and cultured with DMEM containing 10% fetal bovine serum and antibiotics. Then, these HepG2 cells were seeded at a density of  $5 \times 10^5$ /well on 2 6-well plates, and grown to 70%-80% confluence for 24 hours before adding the extracted 50 µg/ml of HDL.<sup>7</sup>

### Red Oil O

The lipid droplets in hepatic tissues were observed by Oil Red O staining. The liver tissues that were frozen in liquid nitrogen were cut into 7-µm slices, and fixed on slides. After 70% alcohol differentiation, these were dyed with 60% Oil Red O solution for 2-3 minutes. Then, these were rinsed with distilled water and observed.

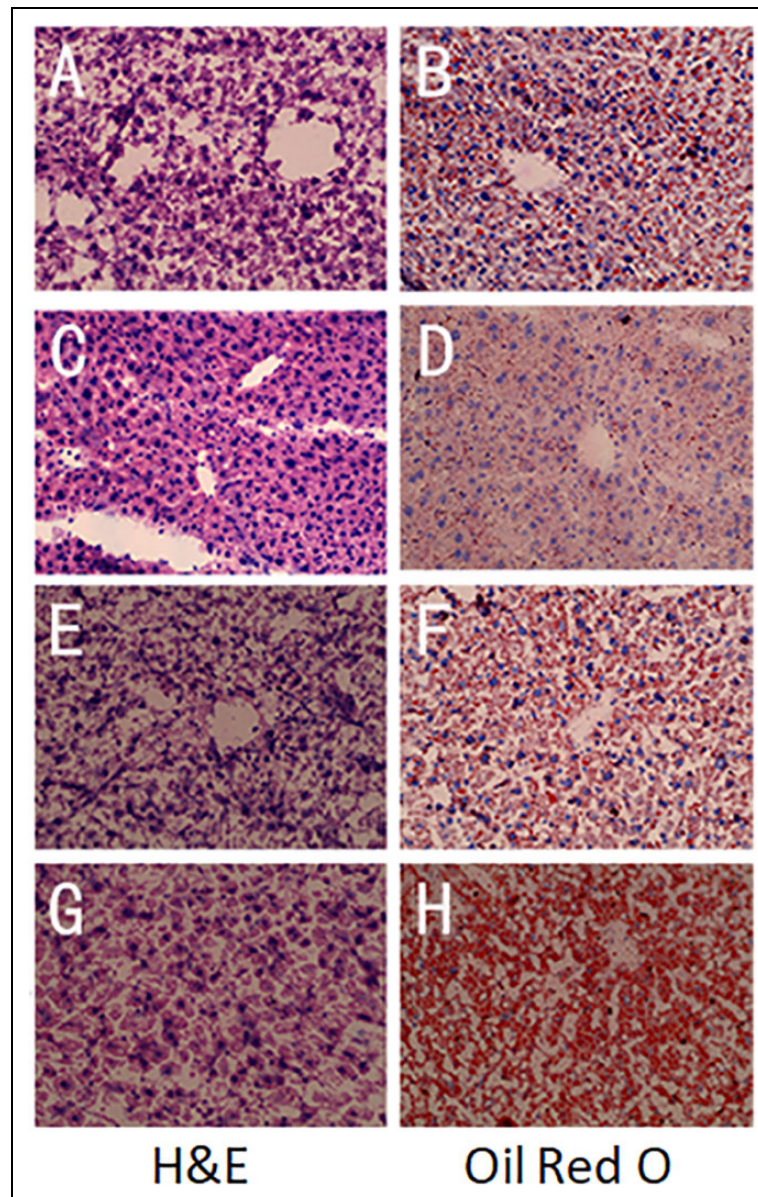
Next, the original medium was removed from the 6-well plates. Then, the cells in these plates were carefully washed with phosphate-buffered saline (PBS), and fixed with 4% paraformaldehyde for 30 minutes at 37°C. Afterward, these cells were washed with PBS twice. Subsequently, red oil O staining solution of approximately 1.0-1.5 ml/well was added, and this was incubated for 20 minutes at 37°C. Then, these were washed with PBS for 3 times before observing and imaging under a microscope.

### Western Blot Analysis

Western blot was performed to determine the SR-B1 expression levels in liver and HepG2 cells. Then, the subsequent tests were conducted using rabbit anti-SR-B1 (Santa, sc-67098) and the HRP-conjugated secondary antibody.

### Statistical Analysis

The software program SPSS 25.0 (IBM, Chicago, USA) was used to conduct the statistical analysis. Continuous variables were expressed as mean  $\pm$  standard deviation (SD). Discontinuous variables were expressed in percentage (%). For multiple comparisons, each value was compared by one-way ANOVA, following the Dunnett's test, when each datum conformed to the normal distribution, while non-normally distributed continuous data were compared using non-parametric tests. The counting data were tested by chi-square test. The protein levels were quantitated using ImageJ software.  $P < 0.05$  was considered statistically significant.



**Figure 1.** Histopathological examination. Lipid deposition on hepatic tissues (H&E staining, oil red O staining,  $\times 200$  magnification). A/B: control group; C/D: healthy group; E/F: angina pectoris group; G/H: myocardial infarction group.

## Results

### *In Vivo*

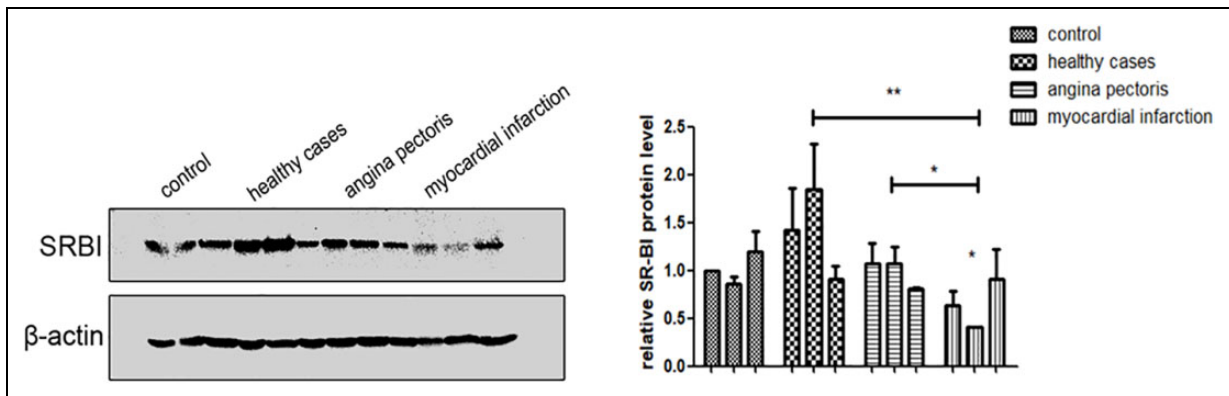
The mice in the different groups were 12 weeks old, and injected with 50  $\mu\text{g/ml}$  of HDL obtained from healthy subjects, angina patients, and myocardial infarction patients from the tail vein, respectively. The mice in the blank control group were injected with 50  $\mu\text{g/ml}$  of normal saline. Such injections were given once per week, a total of 4 times, and the mice were fed with general diet and sacrificed after 4 weeks. The collected livers were used for the subsequent experiments. The results of the histopathological examination are presented in Figure 1. The effect of HDL obtained from healthy and CHD subjects on the expression of SR-B1 in mice is presented in Figure 2. For

healthy cases, the SR-B1 expression increased in the liver, when compared with the myocardial infarction group ( $P < 0.01$ ). The HDL extracted from myocardial infarction patients resulted in a profound decrease in SR-B1 expression ( $P < 0.05$ ), when compared with angina pectoris cases. However, the difference between the angina pectoris and myocardial infarction groups was insignificant.

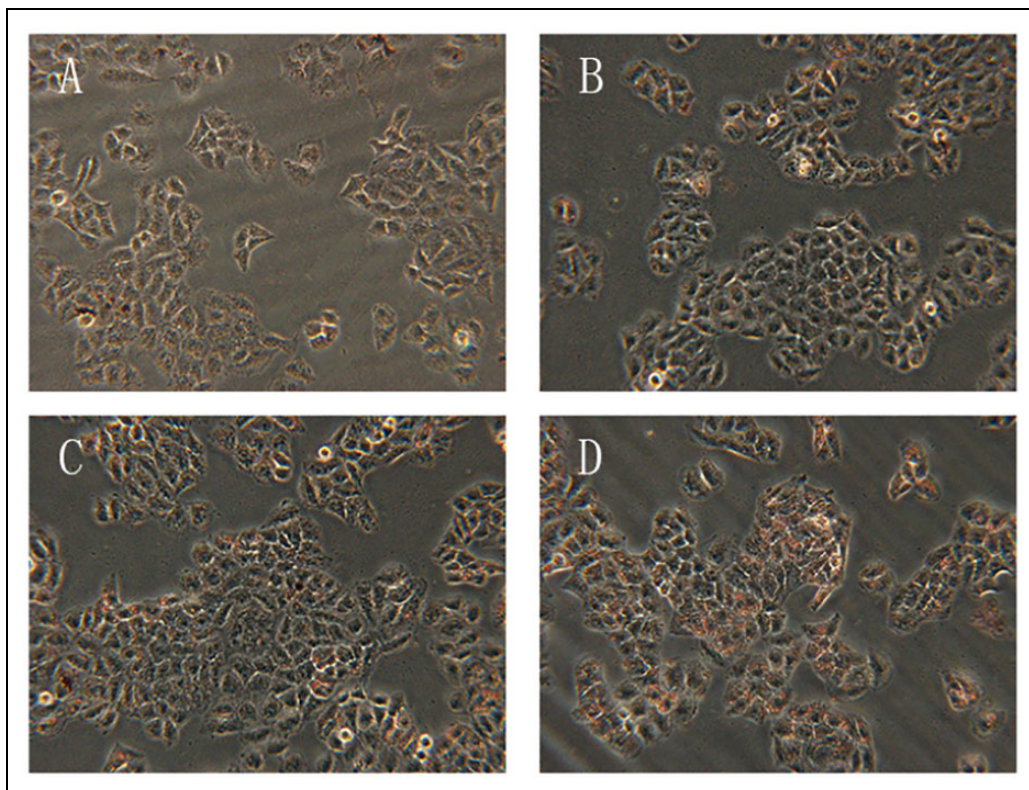
### *In Vitro*

It was determined whether the 50  $\mu\text{g/ml}$  of HDL influenced the SR-B1 levels in hepatic cells. The treatment with 50  $\mu\text{g/ml}$  of HDL obtained from the 4 cases for 24 hours resulted in fluctuations in SR-B1 levels and hepatic lipid deposits. The effect of





**Figure 2.** The effect of HDL from healthy and CHD subjects on the expression of SR-BI in mice (\* $P < 0.05$ , \*\* $P < 0.01$ ; HDL 50  $\mu\text{g/ml}$ ,  $n = 3$ ).



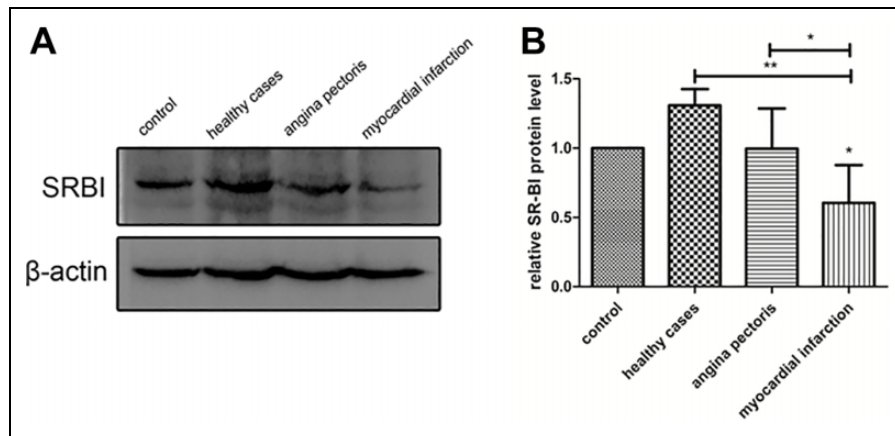
**Figure 3.** Relative lipid droplets contents images of hepatocytes in control and healthy cases and angina pectoris and myocardial infarction conditions. (A) Control group, (B) healthy group, (C) angina pectoris group, and (D) myocardial infarction group.

HDL from the 4 cases was uncovered by Oil Red O staining on lipid droplets (Figure 3). Compared with the blank controls, the healthy cases exhibited a significantly higher expression of SR-B1 and lower levels of lipid content in hepatocytes. Strong positive correlations were observed between HDL obtained from CHD cases and cholesterol-rich hepatic tissues. However, there was a negative correlation between the HDL in CHD and the expression of SR-B1 *in vivo* and *ex vivo*. Thus, a strong correlation was observed between SR-B1-dependent efflux and the extent of cholesterol-rich hepatocytes. Similarly, a decrease was found in the hepatic cholesterol accumulation with HDL

obtained from CHD patients among controls and healthy donors (Figure 4).

## Discussion

The outcomes of the present study revealed that the HDL from CHD patients downregulated the SR-B1 expression in *ex vitro* and *in vitro* studies. In addition, the dysfunctional HDL may have resulted in lower SR-B1 expression levels that were irrelative to the HDL concentration. The degree of SR-B1 expression levels could be relative to the degree of coronary ischemia.



**Figure 4.** The protein expression of SR-BI in hepatocytes. \* $P < 0.05$ , \*\* $P < 0.01$ ; HDL 50  $\mu\text{g/ml}$ ,  $n = 3$ .

Along with the increase in severe coronary congestion, such as myocardial infarction, SR-B1 expression contains lower levels.

The present study revealed that the normal function of HDL was lost or reduced in angina pectoris and acute myocardial infarction, when comparison with the controls and healthy cases. It was considered that raising the HDL-c levels has a strong inverse association with coronary heart disease risk.<sup>8</sup> The present study revealed that the enhanced HDL concentration obtained from healthy and CHD cases led to 2 totally different outcomes in HDL metabolism, which apparently failed to correspond with the assumption that elevated HDL-c protects against cardiovascular diseases. Furthermore, there was no exact association between HDL-c levels and CHD, according to the therapies on cholesteryl ester transfer protein (CETP) inhibitors<sup>9,10</sup> and the LIPG variant without endothelial lipase function.<sup>11,12</sup> Overall, the relationship between HDL and CHD is not simple, and varies with the HDL level, making it a poor determinant in showing correlation of subjects among the CHD group. However, this frequently ignored HDL function may play a more important role in its association with CHD. The present study consistently exhibited that HDL function appears to be a more sensitive agent of cardiovascular risk than serum levels alone. The study mainly concentrated on HDL properties and its main order to confirm whether HDL function varied from different cardiovascular diseases conditions. Furthermore, there is growing evidence that there are dysfunctional forms of HDL without the cardio-protective properties, and even acquired pro-atherogenic qualities under certain conditions. HDL function was significantly impaired in subjects with various cardiovascular diseases.<sup>13-15</sup> A spectrum of HDL dysfunctions consist of a reduced cholesterol efflux capacity from hepatocytes and so on.<sup>16,17</sup>

Reportedly, studies on mice injected with dysfunctional HDL indicated that dysfunctional HDL expresses impaired RCT function, decreased prevention of inflammation and oxidation, prothrombic state and apoptosis, which brings into question the pathophysiological mechanism of dysfunctional HDL in reducing the cholesterol reverse transport efficiency. Furthermore, the present study found that a P376 L variant in

SR-B1, which completely lost the function of SR-B1, has markedly elevated the HDL-c levels, but paradoxically, increased the atherosclerosis.<sup>18</sup> The HDL cholesterol efflux capacity decreases in ACS and stable CHD.<sup>19</sup> SR-B1 pathways negatively regulate the RCT function, regardless of the low HDL levels.<sup>20</sup> However, for the overexpression of the increased efficiency of RCT and vice visa, insights on the effect of HDL on SR-B1 expression remains to be revealed. The relationship of reduced SR-B1 function to HDL in atherosclerotic cardiovascular disease has not been elucidated. The mechanism of dysfunctional HDL on RCT remains unclear. The strong inverse association between the amounts of HDL-c and CHD risk has generated interest in a potential causal relationship between HDL function and CHD. Despite the benefits of HDL-c obtained from healthy donors, it was found that there was a profound SR-B1 expression decrease for HDL derived from CHD patients, which induced an accelerated atherosclerosis, but this was not correlated with the HDL content.<sup>1</sup> Across the CHD cases, healthy cases and CHD controls, it was found that dysfunctional HDL *in vivo* or *ex vivo* has a significantly decreased level of SR-B1 expression, and profoundly increased the lipid deposition, when compared to the control and healthy cases. In contrast, the HDL obtained from healthy subjects improved the SR-B1 expression, but was not statistically significant. In other words, those who received myocardial infarction had a significant decrease in SR-B1 levels in hepatocytes, and this increased the risk of itself, according to the dysfunctional HDL, regardless of the level of HDL.

Studies have demonstrated the changes in plasma HDL composition in patients with acute coronary syndrome and stable CHD, in order to verify the HDL dysfunction.<sup>21</sup> HDL removes cholesterol from extra-hepatic tissues and returns back to the liver, and this is accompanied by its modified composition and HDL featured with a large lipid-rich  $\alpha$ -1 and  $\alpha$ -2 HDL particle.<sup>22</sup> It has been reported that SR-B1 deficiency could assemble the HDL particle formation, which is involved in pre $\beta$ HDL, but is independent of cholesterol efflux.<sup>23</sup> In addition, the investigators revealed that HDL particles isolated from CHD patients failed to inhibit the oxidation of LDL

through human arterial wall cells, were unable to prevent the chemotactic effect of LDL on monocytes, and did not reduce the ability of LDL-derived oxidized phospholipids to stimulate monocyte adherence to endothelial cells, while the HDL obtained from healthy control subjects exhibited beneficial effects.<sup>24</sup>

To this end, both *ex vitro* and *in vivo* experiments were designed and executed to demonstrate that the HDL obtained from CHD cases exerts an aberrant influence on the SR-B1-dependent selective cholesterol uptake and efflux in hepatocytes.

The conclusion pegs the HDL obtained from CHD patients as an important ingredient of atherosclerosis. The idea that HDL is a benefit for preventing atherosclerosis has become entrenched in our minds, but it remains as an oversimplification. Overall, dysfunctional HDL is responsible for the rough lipid accumulation among CHD patients.

This finding has important implications to justify the legitimacy of hepatic lipid metabolism disorders due to dysfunctional HDL. Apart from the above, insulin promotes cholesterol uptake, intracellular lipid storage, and apo B-containing lipoproteins secretion by SR-B1-dependent mechanisms in a model of human intestinal epithelium.<sup>25</sup> Hepatic FoxOs knockout is associated with increased HDL-c and SR-B1-dependent HDL-c uptake by the liver, which makes an indispensable contribution to cholesterol homeostasis and HDL-mediated reverse cholesterol transport to the liver.<sup>26</sup> Increased lipoprotein uptake promotes the lipid store level in VHL-defective RCC cells due to the increase in SR-B1 activity.<sup>27</sup> However, considerably more studies need to be performed to further clarify the mechanism between SR-B1-dependent HDL-c efflux capacity in hepatocytes and CHD.

There is evidence that HDL function is correlated to HDL particle size in the controls, but a significant correlation was found between HDL function and the small HDL particle.<sup>28</sup> This prospect may be the maintenance of HDL function, which might be a significant therapeutic target, especially for patients with CHD. Further institutional studies are needed to clarify the pathogenesis of CHD.

### Limitations

First, in the present study, western blot was performed to investigate the expression levels of SR-B1. However, other test methods, such as PCR and the immunohistochemical method, should also be performed in future studies, in order to investigate the specific protein expression level. Second, the pathogenesis of CHD caused by dysfunctional HDL remains unclear, which should be further investigated. Finally, the potential mechanism why dysfunctional HDL could result in significantly decreased level of SR-B1 expression was not detected in this study. Thus, further studies are really needed.

### Conclusion

The dysfunctional HDL derived from CHD patients decreased the expression of SR-B1 and promoted lipid accumulation.

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### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### References

- Landers KA, d'Emden MC, Richard K. Scavenger receptor class B member 1 independent uptake of transthyretin by cultured hepatocytes is regulated by high density lipoprotein. *J Lipids*. 2019;2019:7317639.
- Hernández Á, Soria-Flrido MT, Schröder H, et al. Role of HDL function and LDL atherogenicity on cardiovascular risk: a comprehensive examination. *PLoS One*. 2019;14(6):e0218533.
- Kosmas CE, Martinez I, Sourlas A, et al. High-density lipoprotein (HDL) functionality and its relevance to atherosclerotic cardiovascular disease. *Drugs Context*. 2018;7:212525.
- Rosenson RS, Brewer HB Jr, Ansell BJ, et al. Dysfunctional HDL and atherosclerotic cardiovascular disease. *Nat Rev Cardiol*. 2016;13(1):48-60.
- Liao J, Guo X, Wang M, et al. Deficiency of scavenger receptor class B type 1 leads to increased atherogenesis with features of advanced fibroatheroma and expansive arterial remodeling. *Cardiovasc Pathol*. 2017;27:26-30.
- Samadi S, Farjami Z, Hosseini ZS, et al. Rare P376L variant in the SR-B1 gene associates with HDL dysfunction and risk of cardiovascular disease. *Clin Biochem*. 2019;73:44-49.
- de Lima-Junior JC, Virginio VWM, Moura FA, et al. Excess weight mediates changes in HDL pool that reduce cholesterol efflux capacity and increase antioxidant activity. *Nutr Metab Cardiovasc Dis*. 2020;30(2):254-264.
- Santos RD, Barter PJ. HDL-cholesterol level and mortality occurrence in the elderly: is the good cholesterol always good. *J Clin Endocrinol Metab*. 2019;jc.2019-00845.
- Rader DJ, Tall AR. The not-so-simple HDL story: is it time to revise the HDL cholesterol hypothesis. *Nat Med*. 2012;18(9):1344-1346.
- Armitage J, Holmes MV, Preiss D. Cholesteryl ester transfer protein inhibition for preventing cardiovascular events: JACC review topic of the week. *J Am Coll Cardiol*. 2019;73(4):477-487.
- Brown RJ, Edmondson AC, Griffon N, et al. A naturally occurring variant of endothelial lipase associated with elevated HDL exhibits impaired synthesis. *J Lipid Res*. 2009;50(9):1910-1916.

12. Vitali C, Khetarpal SA, Rader DJ. HDL cholesterol metabolism and the risk of CHD: new insights from human genetics. *Curr Cardiol Rep.* 2017;19(12):132.
13. Navab M, Reddy ST, Van Lenten BJ, Anantharamaiah GM, Fogelman AM. The role of dysfunctional HDL in atherosclerosis. *J Lipid Res.* 2009;50(suppl):S145-S149.
14. Charakida M, Besler C, Batuca JR, et al. Vascular abnormalities, paraoxonase activity, and dysfunctional HDL in primary antiphospholipid syndrome. *JAMA.* 2009;302(11):1210-1217.
15. Moore KJ, Fisher EA. Dysfunctional HDL takes its toll in chronic kidney disease. *Immunity.* 2013;38(4):628-630.
16. Annema W, von Eckardstein A. High-density lipoproteins. Multi-functional but vulnerable protections from atherosclerosis. *Circ J.* 2013;77(10):2432-2448.
17. Anderson JL, Gautier T, Nijstad N, et al. High density lipoprotein (HDL) particles from end-stage renal disease patients are defective in promoting reverse cholesterol transport. *Sci Rep.* 2017;7:41481.
18. Zanon P, Khetarpal SA, Larach DB, et al; CHD Exome + Consortium; CARDIoGRAM Exome Consortium; Global Lipids Genetics Consortium. Rare variant in scavenger receptor BI raises HDL cholesterol and increases risk of coronary heart disease. *Science.* 2016;351(6278):1166-1171.
19. Hafiane A, Jabor B, Ruel I, Ling J, Genest J. High-density lipoprotein mediated cellular cholesterol efflux in acute coronary syndromes. *Am J Cardiol.* 2014;113(2):249-255.
20. Takiguchi S, Ayaori M, Yakushiji E, et al. Hepatic overexpression of endothelial lipase lowers high-density lipoprotein but maintains reverse cholesterol transport in mice: role of scavenger receptor class B type I/ATP-binding cassette transporter A1-dependent pathways. *Arterioscler Thromb Vasc Biol.* 2018;38(7):1454-1467.
21. Carnuta MG, Stancu CS, Toma L, et al. Dysfunctional high-density lipoproteins have distinct composition, diminished anti-inflammatory potential and discriminate acute coronary syndrome from stable coronary artery disease patients. *Sci Rep.* 2017;7(1):7295.
22. Asztalos BF, Horvath KV, Schaefer EJ. High-density lipoprotein particles, cell-cholesterol efflux, and coronary heart disease risk. *Arterioscler Thromb Vasc Biol.* 2018;38(9):2007-2015.
23. Feng YH, Zheng L, Wei J, et al. Increased apolipoprotein M induced by lack of scavenger receptor BI is not activated via HDL-mediated cholesterol uptake in hepatocytes. *Lipids Health Dis.* 2018;17(1):200.
24. Shih CM, Lin FY, Yeh JS, et al. Dysfunctional high density lipoprotein failed to rescue the function of oxidized low density lipoprotein-treated endothelial progenitor cells: a novel index for the prediction of HDL functionality. *Transl Res.* 2019;205:17-32.
25. Fuentes M, Santander N, Cortés V. Insulin increases cholesterol uptake, lipid droplet content, and apolipoprotein B secretion in CaCo-2 cells by upregulating SR-BI via a PI3K, AKT, and mTOR-dependent pathway [published online October 2, 2018]. *J Cell Biochem.* 2018. doi:10.1002/jcb.27410
26. Lee SX, Heine M, Schlein C, et al. FoxO transcription factors are required for hepatic HDL cholesterol clearance. *J Clin Invest.* 2018;128(4):1615-1626.
27. Velagapudi S, Schraml P, Yalcinkaya M, et al. Scavenger receptor BI promotes cytoplasmic accumulation of lipoproteins in clear-cell renal cell carcinoma. *J Lipid Res.* 2018;59(11):2188-2201.
28. Distelmaier K, Wiesbauer F, Blessberger H, et al. Impaired anti-oxidant HDL function is associated with premature myocardial infarction. *Eur J Clin Invest.* 2015;45(7):731-738.