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REVIEW ARTICLE

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Scavenger receptor Class B type I as a potential risk stratification biomarker and therapeutic target in cardiovascular disease

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Abstract

Cardiovascular disease (CVD) is the leading cause of mortality globally. There are few useful markers available for CVD risk stratification that has proven clinical utility. Scavenger receptor B type I (SR-BI) is a cell surface protein that plays a major role in cholesterol homeostasis through its interaction with high-density lipoprotein-cholesterol (HDL-C) esters (CE). HDL delivers CE to the liver through selective uptake by the SR-BI. SR-BI also regulates the inflammatory response. It has been shown that SR-BI overexpression has beneficial, protective effects in atherogenesis, and there is considerable interest in developing antiatherogenic strategies that involve SR-BI-mediated increases in reverse cholesterol transport through HDL and/or low-density lipoprotein. Further investigations are essential to explore the clinical utility of this approach. Moreover, there is growing evidence showing associations between genetic variants with modulation of SR-BI function that may, thereby, increase CVD risk. The aim of the current review was to provide an overview of the possible molecular mechanisms by which SR-BI may affect CVD risk, and the clinical implications of this, with particular emphasis on preclinical studies on genetic changes of SR-BI and CVD risk.

KEYWORDS
biomarkers, coronary artery disease, risk stratification

1 | INTRODUCTION

Cardiovascular disease (CVD) is the most common prevalent types of mortality globally (Sankar, Ramani, & Anantharaman, 2017). There are various factors that are involved in the pathogenesis of CVD including the formation of atheroma (mainly cholesterol) that accumulates within the artery wall, thrombosis then further narrows the arterial lumen and subsequently reduces the supply of oxygen to the myocardium and other tissues (Alrawi, 2017). Environmental and genetic factors, high blood pressure, plasma lipid–lipoprotein levels and obesity also have major roles in the development of atherosclerosis (Khwaiter & Abed, 2017; Mamudu et al., 2016).

Scavenger receptor B type I (SR-BI), is a cell surface protein that plays a major role in the development of CVD. In CVD modified low-density lipoprotein (LDL) accumulates in the artery wall; this requires the internalization of modified LDL. SR-B1 is involved in mediating high-density lipoprotein (HDL)-cholesterol reverse cholesterol transport (Acton et al., 1996; Fazio and Linton, 2004; Linton, Tao, Linton, & Yancey, 2017). SR-BI signaling occurs in response to changes in

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plasma membrane cholesterol. HDL delivers cholesterol esters CEs to the liver by selective uptake via the SR-BI (Yancey et al., 2000). Therefore, cellular cholesterol levels modulate the expression of SR-BI by both transcriptional and posttranscriptional mechanisms (Rhainds & Brissette, 2004). This receptor is responsible for reducing foam cell formation by mediating cholesterol removal from macrophages (Vergeer et al., 2011; Yancey et al., 2007). The SR-BI is widely expressed throughout the body. Multiple cell types and tissues can theoretically contribute to the atheroprotective effects of SR-BI. Disruption of normal SR-BI function predisposes subjects to the development of atherosclerotic lesions and CVD (Hoekstra, 2017). Consequently, the target of this review is to summarize the potential of SR-BI as both a diagnostic biomarker and a novel target for therapeutic intervention in CVD.

1.1 | Scavenger receptor structure and function

Scavenger receptor class B (SR-B) comprises two particular members with analogous structure. They are the scavenger receptor CD36 and SR-B member 1 (SR-BI; Kent & Stylianou, 2011). These receptors are cell surface glycoprotein and can bind to oxidized LDL, very low-density lipoprotein (VLDL) and HDL cholesteryl ester (HDL-CE; Krieger, 2001). SR-BI is encoded by the SCARB1 gene, located on chromosome 12 at q24.31 (J. J. McCarthy et al., 2009). This receptor comprises 509 amino acids with an approximate molecular weight of 57 kDa. SR-BI contains an extracellular, ligand-binding domain extending over 410 amino acids. This domain is often glycosylated. This domain is linked to the plasma membrane through two transmembrane domains and two short cytoplasmic residues (N- and C-terminal; Goodarzynejad, Boroumand, Behmanesh, Ziaee, & Jalali, 2016). Alternative splicing of SR-BI messenger RNA leads to translation of a SR-BII variant, which differs from SR-BI in the C-terminal cytoplasmic domain (Saddar, Mineo, & Shaul, 2010). The extracellular domain of SR-BI has a critical role in interaction with multiple ligands, that include HDL-CE. HDL binding to the receptor is necessary for CE transport into cells: HDL binds to the extracellular domain of SR-BI in a protected conformation that permits effective lipid transport (Liu & Krieger, 2002). Studies by Sahoo, Peng, Smith, Darlington, & Connelly, 2007 showed that oligomers are formed in the C-terminal region of the extracellular domain, and CE transport depends on the extent of oligomerization. A glycine dimerization motif is a significant feature of the N-terminal transmembrane domain that is necessary for SR-BI oligomerization (Sahoo, Peng, Smith, Darlington, & Connelly, 2007). Two short cytoplasmic residues (N- and C-terminal) play a significant role in regulating signal transduction (Guo, Chen, Song, Daugherty, & Li, 2011). At the C-terminal cytoplasmic tail, there are four remaining amino acid residues (EAKL) that play an important role in protein interactions with a multisubunit adapter protein (PDZK1, 2) in cytosol. This latter protein is required for the stability of SR-B1 in hepatocytes (Valacchi, Sticozzi, Lim, & Pecorelli, 2011). SR-B1 regulates the bidirectional flux of unesterified cholesterol between cells and HDL (J. J. McCarthy et al., 2009). When HDL is bound to the extracellular domain of SR-BI, SR-BI, and HDL particles can enter the hepatocyte and then undergo endocytosis. Cholesteryl esterase activity within the endosome then releases cholesterol that can then enter the biliary tract (Silver & Tall, 2001). Hepatocytes express SR-B1 at high densities, but it has also been found in macrophages and cells within the arterial wall; for example, in human atherosclerotic lesions (PrabhuDas et al., 2017). Studies have shown that SR-B1 has a potentially beneficial effect on preventing the expansion of atherosclerotic lesions (Braun et al., 2002) and scavenger receptors are involved in inflammatory processes via migration and signaling of macrophages (Ockenhouse & Chulay, 1988). Cholesterol efflux requires SR-BI expression by foam cells. These cells are mainly derived from macrophage and are present at high abundance in regions of atheroma (Larrede et al., 2009). More recent work has proposed that, oxidized HDL may inhibit platelet activation via SR-B1 (Valiyaveettil & Podrez, 2009). Furthermore, HDL binds to SR-BI on vascular endothelial cells and leads to increased endothelial nitric oxide synthase (eNOS) activity, which causes to production anti-atherogenic molecule NO (Mineo, Yuhanna, Quon, & Shaul, 2003; Yuhanna et al., 2001). Some studies in mice have shown that, hepatic overexpression of SR-BI results in a reduction in serum LDL and VLDL, which is likely to have an atheroprotective role (Kozarsky et al., 1997).

1.2 | SR-BI and signaling pathway (Figure 1)

SR-BI plays a major role in cholesterol homeostasis via its interaction with HDL. Apolipoprotein A1 (apoA-I) is the major protein component of HDL particles, and as the HDL particle incorporates lipid, it causes a conformational change that leads to an interaction between HDL and SR-BI (D. L. Williams et al., 2000). Therefore, SR-BI facilitates bidirectional flux cholesterol ester (CE) and other lipids between cells and lipoproteins such as LDL and HDL (Assanasen et al., 2005). After

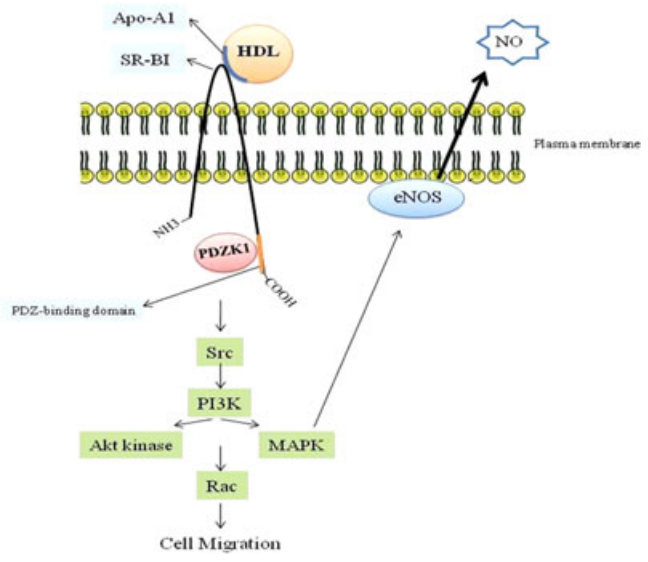

FIGURE 1 Signaling pathways of SR-BI. SR-BI: scavenger receptor class B member 1 [Color figure can be viewed at wileyonlinelibrary.com]

HDL binds to SR-B1 via the apoA1, Src becomes activated. Activated Src leads to activation of phosphatidylinositol 3-kinase (PI3K), followed by Akt kinase and mitogen-activated protein (MAP) kinase via PI3K. The serine 1177 of eNOS is subsequently phosphorylated by activated Akt. HDL can, therefore, stimulate endothelial nitric oxide synthase (eNOS) and NO generation (Mineo et al., 2003). In human endothelial cells, the expression of S1P-induced adhesion molecules is inhibited by the activation of eNOS (Kimura et al., 2006). PI3K activates both MAP kinases and Akt that leads to cell migration and increased Rac activity (Seetharam et al., 2006). The PI3K and protein kinase C (PKC) signaling cascade can modulate SR-BI activity. SR-BI-mediated selective cholesterol uptake occurs after PKC activation and PI3K inhibition, whereas PI3K activation and PKC inhibition decrease its efficiency (Zhang et al., 2007). The transmembrane regions and C-terminal cytoplasmic domains are essential for SR-BI signaling. The PDZ-binding domain in the C-terminal cytoplasmic region interacts with PDZK1, which is an adapter protein. Interactions between PDZK1 and SR-BI and also between SR-BI and cell membrane cholesterol are necessary for src activation (Ahmed, Ravandi, Maguire, Kuksis, & Connelly, 2003; Zerrad-Saadi et al., 2009; Figure 2).

1.3 | SR-BI and lipoprotein and HDL metabolism

SR-BI mediates the cellular absorption of several types of lipids derived from HDL including lipid soluble vitamins (e.g. vitamin E) and phospholipids (Al-Jarallah & Trigatti, 2010). SR-BI also mediates selective cholesterol uptake among lipoproteins and cells via a mechanism different from that associated with the binding of LDL to its LDL receptor (LDLR; Acton et al., 1996). The LDLR mediates endocytosis of the entire LDL particle via clathrin-coated pits, that lead to the formation of vesicles and hydrolysis in lysosomes (Krieger, 2001). SR-BI-mediated transport does not seem to be dependent on ATP and coated pits (Connelly et al., 2001). Lecithin–cholesterol acyltransferase (LCAT) is an enzyme that can esterify free cholesterol. After cholesteryl esters are formed from HDL cholesterol (HDL-C) by the action of LCAT, the HDL transports them to the liver by via SR-BI. SR-BI binds HDL with high affinity and the interaction of HDL with SR-BI does not result in its lysosomal degradation of the particle and its contents (Rigotti, Miettinen, & Krieger, 2003). The selective uptake consists of a multistep process: (a) binding of CE rich lipoprotein particles to the extracellular domain of SR-BI, (b) the transport of CE to the plasma membrane, (c) the diffusion from the cholesterol-poor lipoprotein components back into the blood (Hoekstra, 2017; Rigotti et al., 2003). The HDL particle is taken up by the liver and cholesterol secreted into the bile, either as cholesterol or as bile acids (Rigotti & Krieger, 1999). The processes of transport of cholesterol from peripheral tissues by plasma HDL into the liver in order to biliary secretion as bile acids or cholesterol is called "reverse cholesterol transport" (Linton et al., 2017). The expression of SR-BI is not essential for intestinal cholesterol absorption (Mardones et al., 2001). Studies show that an increased hepatic selective HDL uptake by SR-BI, is also dependent on increasing apo A-I catabolism (Kozarsky et al., 1997). An increased expression of SR-BI in defective apo AI mice results in an accumulation of small dense HDL and increased HDL apolipoprotein uptake by the kidney and liver (de Beer, van der Westhuyzen, Whitaker, Webb, & de Beer, 2005). Reductions in selective hepatic HDL-C uptake and plasma clearance of HDL-CE are related to the decreased levels of hepatic SR-BI (Varban et al., 1998). In addition to interaction between HDL-C and SR-BI, it is suggested that SR-BI can also take part in the metabolism of non-HDL lipoproteins (Ueda et al., 1999). Defects in SR-BI may lead to an increased content of IDL/LDL-sized lipoproteins (Rigotti et al., 1997). Cholesterol attached to SR-BI directly in the surface of plasma membrane (Assanasen et al., 2005). Also other reports demonstrate that, in a variety of cell types, SR-BI is localized in caveolae. P. y. Wang, Liu, Weng, Sontag, and Anderson (2003) have reported that a caveolae-cholesterol associated cascade may exist by which the activity of a phosphatase complex is adjusted. The activation of protein kinase ERK1/2 signaling pathways is followed by a reduction in dephosphorylation (Al-Jarallah & Trigatti, 2010; P. y. Wang, Liu, Weng, Sontag, & Anderson, 2003). ERK1/2 is a well-known downstream target of SR-BI and interferes with signaling; SR-BI activates the signaling pathways of ERK1/2 (Baranova et al., 2005; Zhang et al., 2007).

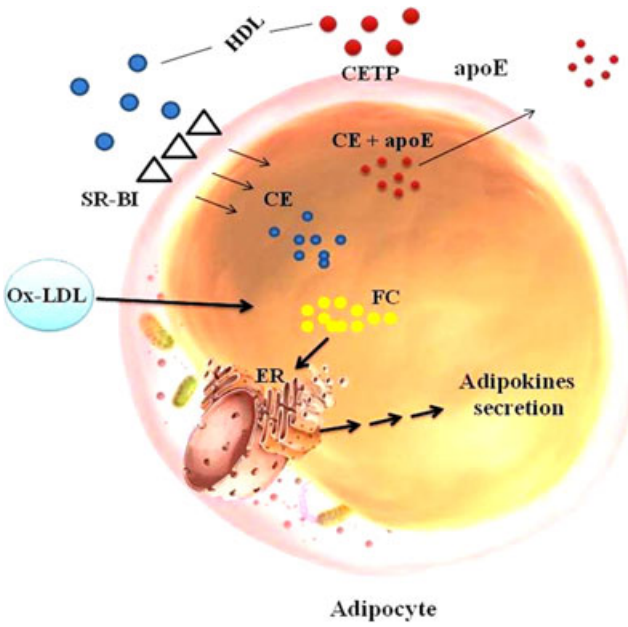

FIGURE 2 In adipocytes, cholesterol is transmitted through two ways (a) SR-BI- independent and (b) SR-BI- dependent. In a SR-BI dependent mechanism, after interaction of HDL with SR-BI, the CE transfers to the cytoplasm via receptor. In a SR-BI-independent mechanism the movement CE is performed through CETP, which is a transmembrane protein. In an independent manner, apoE is required as a mediator for efflux HDL-CE. On the other hand, Ox-LDL can also affect the expression and secretion of adiponectin, by activating stress and stimulating ER, which triggers inflammatory processes. CETP: cholesterol ester transfer protein; DL-CE: high-density lipoprotein cholesteryl ester; Ox-LDL: oxidized low-density lipoprotein SR-BI: scavenger receptor class B member 1 [Color figure can be viewed at wileyonlinelibrary.com]

1.4 | SR-BI in adipocytes

Adipocytes, sometimes referred to as lipocytes, are the cells that comprise the major portion of the adipose tissue, and specialized in energy storage as fat (Birbrair et al., 2013). Adipocytes have a unique ability to accumulate cholesterol because of their restricted capability to cholesterol synthesis. This can be due to the reduced efficiency of the enzymes involved in the cholesterol synthesis pathways. (Van Eck, Bos, Hildebrand, Van Rij, & Van Berkel, 2004). Furthermore, there is a major content of cholesterol in the membrane of fat cells. When the membrane expands quickly, cellular membrane cholesterol preserves cellular integrity against hypertrophy. (Krause & Hartman, 1984). So, the adipocytes extracted cholesterol from circulating lipoproteins like the HDL (Vassiliou & McPherson, 2004a). SR-BI is highly expressed in adipocytes. Remarkable levels of cholesterol are absorbed by these cells via the direct pathways HDL delivery process (Song et al., 2016). In addition to direct pathway, adipocytes expressed CE transfer protein (CETP) and CETP uptake the CE from lipoprotein. CETP transfers CE into adipocyte with the accompaniment apoE. This pathway is called SR-BI-Independent (Vassiliou & McPherson, 2004b). The advantage of dependent SR-BI pathways to SR-BI independent pathways is it is not necessary for an apoE-mediated for efflux HDL-CE (Hoekstra, 2017).

1.5 | SR-BI and inflammation process

Inflammation is involved in several stages of atherogenesis, from the development of fatty streaks to progressive atherosclerotic damage, including plaque rupture. SR-BI may be a protective molecule against atherosclerosis by modulating the inflammatory response (Fuller et al., 2014). Furthermore, the elimination of cholesterol from macrophage (MQ) may be an important component of decreasing atherosclerosis (Zhang et al., 2003). SR-BI is found in tissue MQ, such as Kupffer cells (Hoekstra, Kruijt, Van Eck, & Van Berkel, 2003) and the uptake of modified lipoproteins may be mediated by SR-BI in these cells. Furthermore, SR-BI has a critical role in the selective uptake of CE from HDL in MQ (Van Eck et al., 2004). Studies have shown that ox-LDL reduces SR-BI mRNA in MQ and in response to stressors like ox-LDL, the nuclear factor kappa B is activated (Babaev et al., 2008; Han et al., 2001). Consequently, increased transcription of proinflammatory cytokines, such as tumor necrosis factor alpha (TNFα) and interleukin 6 (IL-6) may subsequently occur (Linton et al., 2017). MacRae and colleagues have shown that, in a mouse model, MQ in which the expression of the SR-BI was inhibited (knocked-out), high levels of inflammatory interleukins such as IL1, 6 and increased reactive oxygen species were found. While the expression of the anti-inflammatory cytokine, IL10, was reduced. These events caused the pathway of apoptosis to be inhibited and necrosis pathway occurs in MQ, which leds to an enhanced inflammatory response (Fuller et al., 2014; Linton et al., 2017; Tao et al., 2015). It was also observed that in MQ, in which the SR-BI was knocked-out, transforming growth factor beta (TGFβ) decreases and a defect in efferocytosis resulted (Tao et al., 2015). Efferocytosis is a process that causes the elimination of dead cells caused by necrosis and apoptosis occurs by phagocytic cells like macrophages (Seetharam et al., 2006).

1.6 | Genetics of scavenger receptors

The SR-BI is encoded by the SCARB1 gene that is located on chromosome 12. The concentration of plasma lipids is a complex trait, which is determined by genetic and environmental factors. Genetic factors are attributable for almost half of the variation in plasma HDL-C and TG (Austin, KING, Bawol, Hulley, & Friedman, 1987; Pérusse et al., 1997). Studies have indicated that single-nucleotide polymorphisms (SNPs) of the SCARB1 gene are related to plasma lipid levels, the size of the lipoprotein particles and CVD (Bild et al., 2002; Nelson et al., 2005). Increased plasma TGs levels and reduced HDL-C are important risk factors for atherosclerosis (Rapaport et al., 1993). Several polymorphisms have been found in population studies, and have been reported to be associated with plasma lipid levels (Acton et al., 1999; Trigatti et al., 1999). Furthermore, an association between the rs10846744 variant of SCARB1 locus has been shown with carotid intimal-medial artery thickness (CCIMT) and may also be related to CVD risk and subclinical atherosclerosis (Naj et al., 2009). A sex-dependent association of rs10846744 with CCIMT has been observed, which may indicate more association with a causal allele related to CCIMT (Golden et al., 2016; Naj et al., 2009). Ritsch et al. (2007) suggested a combination of SCARB1 polymorphisms at intron 5 and exon 8 are associated with an abnormal lipid profile in women with CVD. In agreement with Ritsch study, Knott et al. (1986) have shown accompaniment C→T transition in intron 5 and exon 8 SCARB1 polymorphism was associated with abnormal lipid profile. Furthermore, there is an association with CVD in carriers who have specific exon 8 allele (Rodríguez-Esparragón et al., 2005). In addition, the risk of CAD increased in men who carried Intron 5 variant allele and in women who carried exon 8 common allele. Also, this polymorphism was significantly higher in the PAD. Surprisingly, some reviews have shown that there was a major incidence of PAD in women with heterozygosity for exon 8 polymorphism than the women with homozygousity for the same allele. This phenomenon may be owing to the effect of a gene dose (Ritsch et al., 2007). In fact, the significant relationship between the combination of exon 8/intron 5 genotypes in the SCARB1 gene and total plasma LDL cholesterol shows, maybe the associations are in a sex-dependent manner. Increasing the incidence of exon 8 variants in women can be affected by the possible interaction between the SCARB1 genotype and SR-BI estrogen regulation which can affect cholesterol levels. (Ritsch et al., 2007). So, SCARB1 polymorphisms not only display correlation with plasma levels of LDL cholesterol, but also Increases the risk of developing PAD. Research also indicates that the expression of SCARB1 is regulated by estrogen and rat's estrogen treatment has shown to downregulate the SR-B1 in the liver (Fluiter, van der Westhuijzen, & van Berkel, 1998; Landschulz, Pathak, Rigotti, Krieger, & Hobbs, 1996). J. McCarthy et al. (2003) revealed that

SCARB1 genetic variants have been affected on the regulation of SCARB1 by estrogen, which may have to be used for the cure of postmenopausal women with hormone replacement therapy (HRT). However, multiple types of SCARB1 variants may modify the effect of HRT on plasma lipid amount in women (J. McCarthy et al., 2003). Further studies demonstrated that the presence of allele A in SR-BI exon 1 in patients with CHD resulted in an increase in serum levels of HDL-C and Apo-a1 (H. Wang, 2016; Wu et al., 2012). The level of SR-BI protein can be reduced by point mutation at the 4th site of SR-BI exon through the effect on SR-BI protein expression and increased plasma HDL-C concentration by weakening the reverse cholesterol transport pathway. This process may increase the risk of CHD (H. Wang, 2016). In another study by Golden et al. (2016), the rs10846744 noncoding variant of the SCARB1 illustrated a considerable association with atherosclerosis disease. This noncoding variant has a novel relevance with immune checkpoint inhibitor lymphocyte activation gene 3 (LAG3). The plasma level of LAG3, independent of HDL-C, represents the risk of coronary heart disease CHD (Golden et al., 2016). Increasing odds for CVD and MI in homozygous carriers of the rs10846744 are highlighted by the risk genotype (CC). Also, in the risk genotype (CC), LAG3 RNA has been recognized as the main target and its expression is low in homozygous carriers (Golden et al., 2016; Manichaikul et al., 2012). Another variant of gene SCARB1 that it plays an important role in CVD is rs5888. Behmanesh and colleagues in a study of the cohort of young Iranian patients showed that SNP rs5888 is presumably to be a separate risk factor for initiating CAD and linked with patients with premature CAD through a sex-dependent way (Goodarzynejad et al., 2016). This variant, particularly in younger women, correlates with lipoprotein particle size and lipid levels (Richard et al., 2005; Roberts et al., 2007). Recent studies suggest that in spite of the fact that some variants, such as C allele of rs10846744, are high-risk for CHD-related with higher HDL-c, others like the C allele of rs2278986 are a protective factor for CHD (Zeng, Tang, Ye, Su, & Jiang, 2017). In a study by Zanoni et al., 2016, performance impairment in the P376 L variant (a rare loss-of-function variant of SCARB1) promotes the increased level HDL-C and increases the risk of CHD. Recent studies on human and mice have revealed that breakdown the HDL/SR-BI interactions, not only increases plasma HDL-C levels, but also enhances the risk of atherosclerotic lesions in CVD (Yang et al., 2016; Zanoni et al., 2016). In addition, the comparison between wild-type mice versus those of SR-BI knockout (KO) showed that in KO group, have been observed, a significant increase in HDL-C level (Van Eck et al., 2003). Likewise mentioned before, the mutation that can result in loss-of-function in the P376 L variant increases the risk of coronary artery disease (Zanoni et al., 2016). Gene transfer in SR-BI−/− mice by using adenoviral vector showed that AdSR-BI gene transfer abolished increased plasma IL-6 levels that are involved in inflammatory processes, increased levels of plasma lipid peroxidation and increased nitro-oxidative myocardial stress in SR-BI /− mice (Muthuramu, Amin, Abou Msallem, & De Geest, 2017). Consequently, SR-BI can be considered as a putative novel cardiovascular therapeutic target.

1.7 | SR-BI as a biomarker

CVD diagnosis is based on physical examination, electrocardiography (ECG), and serum biochemistry markers such as troponin I (TnI) and so forth (Members et al., 2011). Although some factors like troponin I is a proprietary diagnostic marker but in the absence of MI and the presence of diseases, such as renal insufficiency, this factor may increase and cause a false diagnosis (Alcalai et al., 2007). Against this information, it has been shown that genetic biomarker can be used as risk stratification biomarker. There is growing body of data showing the prognostic and diagnostic value of some genetic markers in CVD (Dhingra & Vasan, 2017; Gutierrez-Pajares, Hassen, Chevalier, & Frank, 2016). In 2017, Hoekstra and Sorci-Thomas (2017) revealed that increasing level of HDL cholesterol and risk of CVD is related to mutation form of SR-BI gene (heterozygous for the P376 L). SR-BI plays a critical role in cholesterol uptake, in turn SR-BI gene defecting causes in the increasing cholesterol and risk of CVD (Linton et al., 2017). Also in 2002, Braun et al. (2002) demonstrated that knockout SR-BI gene could loss of SR-BI expression, leading to the early onset of occlusive atherosclerotic coronary artery disease, suggesting its value as biomarker in CVD.

1.8 | SR-BI as therapeutic target

Liao et al. (2017) suggested that double knockout (dKO) mice for SR-BI/LDL receptor genes, compared with control group, increased the risk of developing CVD. In line with this data, Cui, Chen, and Shen (2018) showed that Urolithin A led to reducing angiotensin II (Ang II) and plasma lipids levels via increased expression of SR-BI. Also they suggested that this process could attenuate atherosclerosis. In another research Ren et al. (2018) proposed that targeting 3′UTR of SR-BI by miR-24 suppressed the SR-BI expression, decreased selective lipid uptake and promoted atheromatous plaque in mice (Ren et al., 2018).

2 | CONCLUSION

SR-BI is recognized as an HDL receptor. It plays a critical role in the homeostasis of cholesterol and is also essential for its absorption and metabolism. SR-BI is also involved in the other processes including, inflammation, membrane lipid expression, and apoptosis. Some studies have shown that SR-BI plays a antiatherogenic role through its involvement in reverse cholesterol transport. The interaction between SR-BI and HDL triggers a kinase cascade. SR-BI exists in several cell types that include: hepatocytes, adipocytes, and macrophages. In the vascular endothelium SR-BI signaling is involved in the generation of NO. In experimental models, overexpression of SCARB1 leads to a reduction in serum HDL levels but a reduction in atherosclerosis lesion formation. Alteration in the expression levels of SR-BI can lead to inflammatory response and CDV. Thus SR-BI is a novel target that may be used for developing new therapeutic or genetic therapies to prevent or treat a number of human conditions.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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