Scavenger receptor class B, type I (SR-BI) mediates selective uptake of high density lipoprotein (HDL) lipids. It is unclear whether this process occurs at the cell membrane or via endocytosis. Our group previously identified an alternative mRNA splicing variant of SR-BI, named SR-BII, with an entirely different, yet highly conserved cytoplasmic C terminus. In this study we aimed to compare HDL uptake by both isoforms. Whereas SR-BI was mainly (~70%) localized on the surface of transfected Chinese hamster ovary cells, as determined by biotinylation, HDL binding at 4 °C, and studies of enhanced green fluorescent protein-tagged SR-BI/II fusion proteins, the majority of SR-BII (~80–90%) was expressed intracellularly. The cellular distribution of SR-BI was not affected by deletion of the C terminus, which suggests that the distinct C terminus of SR-BII is responsible for its intracellular expression. Pulse-chase experiments showed that SR-BII rapidly internalized HDL protein, whereas in the case of SR-BI most HDL protein remained surface bound. Like its ligand, SR-BII was more rapidly endocytosed compared with SR-BI. Despite more rapid HDL uptake by SR-BII than SR-BI, selective cholesterol ether uptake was significantly lower. Relative to their levels of expression at the cell surface, however, both isoforms mediated selective uptake with similar efficiency. HDL protein that was internalized by SR-BII largely co-localized with transferrin in the endosomal recycling compartment. Within the endosomal recycling compartment of SR-BII cells, there was extensive co-localization of internalized HDL lipid and protein. These results do not support a model that selective lipid uptake by SR-BI requires receptor/ligand recycling within the cell. We conclude that SR-BII may influence cellular cholesterol trafficking and homeostasis in a manner that is distinct from SR-BI.

Scavenger receptor class B, type I (SR-BI), a major HDL receptor (1–3), plays an important role in reverse cholesterol transport, a major pathway for the clearance of excess cholesterol from the body. In this process, peripheral cholesterol is packaged into HDL from which it is subsequently removed in the liver and excreted into bile. SR-BI mediates the uptake and biliary secretion of HDL cholesterol by the liver (4, 5). Therefore, and perhaps also for other reasons, SR-BI is of great importance in the prevention of atherosclerosis (6). SR-BI is most highly expressed in liver and steroidogenic tissues (4), where it mediates selective uptake of cholesterol from HDL, i.e. without concomitant uptake and degradation of HDL apoproteins. The detailed mechanism of this process has not been elucidated yet, including whether it occurs at the cell membrane (7) or during endocytosis and retroendocytosis of HDL (8). SR-BI is known to influence membrane structure (9, 10) and membrane cholesterol distribution (11, 12), both of which may contribute to SR-BI-facilitated selective lipid uptake.

SR-BI is a ~82-kDa protein with two short cytoplasmic termini, two transmembrane domains, and a large, heavily glycosylated extracellular loop (2). In nonpolarized cultured cells, only the extracellular loop of SR-BI is essential for selective uptake (13–15); both the N- and C-terminal cytoplasmic tails can be deleted or exchanged with the corresponding region of the other class B receptor CD36 (14, 15). Cooperation of other proteins with SR-BI seems not to be essential for this process, because mere liposomes containing purified SR-BI can selectively absorb HDL cholesterol (16). However, in polarized hepatocytes, the interaction of the C terminus of SR-BI with a protein called CLAMP, or PDZK1, is required for cell surface expression of the receptor (17, 18). A domain consisting of the three C-terminal amino acids in murine SR-BI, Arg-Lys-Leu, is required for binding PDZK1. Lack of the terminal leucine residue results in decreased surface expression of SR-BI in the mouse hepatocyte and consequently to impaired HDL clearance (18).

Previously, our group discovered an alternative mRNA splicing variant of SR-BI, called SR-BII, which differs from SR-BI by an entirely different C-terminal cytoplasmic tail (19, 20). In liver, adrenal, adipose, and testicular tissue, SR-BII mRNA levels are comparable with the SR-BI isoform, although protein levels are lower (19). Nevertheless, in the liver, SR-BII accounts for some 10–15% of SR-BI/II protein, and in rats treated with 17β-estradiol, SR-BII in liver is substantially up-regulated (21). SR-BII protein was also detected in human retinal epithelial cells (22) and in rat Leydig cells (23). Another indicator for a possible biological function of SR-BII is the high degree of conservation of the C terminus between various species (19).

The presence of an entirely different C terminus in SR-BII is intriguing in light of the reported critical importance of the corresponding domain in the cellular distribution of SR-BI. In the present study we investigated SR-BII expression in more detail, focusing on its cellular distribution and interaction with HDL. Our data show that SR-BII is mainly expressed intracellularly in nonpolarized (CHO) cells, with reduced selective
uptake capacity. In contrast to SR-BI, SR-BII appeared to mediate the rapid internalization of HDL particles and their accumulation in the transferrin-positive endosomal recycling compartment (ERC). Our results suggest that selective lipid uptake by SR-BI does not require receptor/ligand recycling. SR-BII may influence cellular cholesterol trafficking and homeostasis in a manner distinct from SR-BI.

MATERIALS AND METHODS

Cells—CHO-A7 cells (donated by Dr. M. Krieger, M.I.T.) were grown in 250-mL tissue culture flasks in Ham’s F-12 medium (Invitrogen) containing 5% heat-inactivated fetal calf serum (Invitrogen). MDCCK and COS cell lines were grown in American Type Culture Collection (ATCC) Dulbecco’s modified Eagle’s medium (Invitrogen) containing 10% fetal calf serum. Both media were supplemented with 2 mM l-glutamine, 0.1 mM non-essential amino acids, 50 units/liter penicillin G, and 50 μg/liter streptomycin (all Invitrogen). The cells were subcultured until 70% confluency was reached, using a 1:5 split ratio. Stably transfected CHO cells expressing murine SR-BI or SR-BII were generated as described elsewhere (19) and were cultured in medium containing 0.25 g/liter geneticin (Invitrogen). The clones were screened for expression of the scavenger receptors by immunoblotting with a rabbit polyclonal antibody recognizing the common extracellular domain (red-1, for receptor extracellular domain 1) (18); one of each clone was selected based on similar expression levels (CHO-SR-BI and CHO-SR-BII). COS cells were transiently transfected with pCMV5-based expression vectors (24) (1 μg of DNA/ml) using the Lipofectamine transfection reagent (Invitrogen), and the cells were used experimentally 16 h after transfection. For biochemical assays, CHO and COS cells were grown in 12-well clusters (Corning Corp., Corning, NY). For microscopy, CHO and COS cells were grown on glass coverslips, and MDCK cells were grown on Transwell Clear filter membranes (Corning).

Isolation and Labeling of Lipoproteins—Human HDL (ρ = 1.063–1.21 g/ml) fractions were isolated from fresh human plasma by density gradient ultracentrifugation as previously described (25). Human HDL3 (ρ = 1.13–1.18 g/ml) was obtained from total HDL by density gradient ultracentrifugation. All of the isolated fractions were dialyzed against 150 mM NaCl, 2.5 mM EDTA, sterile filtered, and stored under N2 gas at 4 °C.

The lipoproteins were iodinated in presence of 125I (Amersham Biosciences) by the iodine monochloride method (26). HDL-associated cholesteryl ester was traced with nonhydrolyzable 1,2-3Hcholesteryl oleoyl ether (Amersham Biosciences) according to the method of Gwynee and Mahaffee (27), with the following modifications: (1,2α-3H)cholesteryl oleoyl ether was dried in a 12 × 75-mm borosilicate glass tube (20 μCi/mg HDL protein), after which HDL and partially purified cholesteryl ester transfer protein were added. Following 16 h of incubation at 37 °C, HDL was resolated by ultracentrifugation at a density of 1.21 g/ml. The specific activity of the [3H]-HDL ranged from 10–30 dpm/mg protein. Labeled lipoproteins were verified by SDS-PAGE and gradient gel electrophoresis. HDL3 lipid was labeled with 1,1-dioctadecyl-3,3',3'-tetramethylindocarbocyanine perchlorate (DiI; Molecular Probes, Eugene, OR) as described elsewhere (1) and protein with Alexa 488 (Molecular Probes) according to the manufacturer’s instructions and were stored at 4 °C under N2 gas.

HDL Association and Selective Uptake—Cell association assays were performed as previously described (19), in radiolabeled lipoprotein-containing medium with 0.5% bovine serum albumin (BSA) instead of serum. Cell monolayers were seeded on 12-well clusters for 24 h to reach confluency before the experiment. The cells were washed with 0.5% BSA instead of serum, followed by incubation with 0.5% BSA for 2 h at 37 °C for incubation times on 0–6 h. The resulting recombinant expression vector encodes EGFP-SRBI/II fusion proteins with the enhanced EGFP signal at the N terminus of the receptor. The DNA sequence of the coding region was verified, and protein expression and function were studied in transfected COS cells. All EGFP fusion proteins were found to yield SR-BI/II immunoreactive protein bands (Fig. 5). COS cells expressing these constructs showed HDL binding and selective uptake comparable with COS cells expressing non-EGFP SR-BI/II (not shown).
RESULTS

Expression of SR-BII—Stably transfected CHO-A7 clones were screened by immunoblotting for expression of murine SR-BI or SR-BII using the red-1 antibody, which detects the common extracellular domain of the receptors (19). Two lines expressing similar amounts of either SR-BI (CHO-SRBI) or SR-BII (CHO-SRBII) were selected. Surface expression of both isoforms was studied by a biotinylation approach. In CHO-SRBI cells labeled at 4 °C with nonabsorbable biotin, approximately 70% of total scavenger receptor could be precipitated with immobilized streptavidin, indicating that this isoform was mainly expressed at the cell surface (Fig. 1A). In the case of CHO-SRBII cells, only 10–20% of SR-BII protein could be precipitated, indicating that this isoform is much less expressed on the cell surface, with 80–90% being expressed intracellularly. The surface expression of both receptors was unchanged by 5 h of exposure of cells to HDL in the medium, as opposed to cells not exposed to HDL (Fig. 1B), indicating that the presence of the ligand did not induce the redistribution of receptors.

The distinct cellular distribution of SR-BI and SR-BII was confirmed by fluorescence microscopy of CHO cells expressing EGFP fusion constructs of either SR-BI or SR-BII. These fusion proteins were functionally active, as shown by their capacity to mediate selective uptake with an efficiency similar to non-EGFP isoforms in transiently transfected COS cells (not shown). As shown in Fig. 2A, SR-BI is highly expressed on the cell surface, whereas SR-BII is expressed predominantly intracellularly with little enrichment of the cell surface being evident (Fig. 2B). Interestingly, EGFP-SRBII lacking the normal cytoplasmic C terminus showed a cellular distribution (Fig. 2C) similar to that of full-length EGFP-SRBI, suggesting that the presence of the SR-BII C-terminal cytoplasmic tail, and not the absence of the SR-BI C terminus, is responsible for the more intracellular distribution of SR-BII. Fig. 2D shows cells expressing only EGFP protein in a diffuse intracellular manner. The marked difference in the intracellular localization of SR-BI and SR-BII was also observed in stably transfected polarized MDCK cells. EGFP-SRBI is predominantly expressed on the cell surface of these cells (Fig. 2E), mostly on the basal membrane (Fig. 2F). In contrast, EGFP-SRBII is localized mainly intracellularly (Fig. 2, G and H).

HDL Binding and Selective Uptake—The predominantly intracellular expression of SR-BII was in line with the observation that receptor-specific binding of HDL at 4 °C was significantly lower for CHO-SRBII than CHO-SRBI cells (Fig. 3A), whereas receptor levels in the two cell types were similar (data not shown). Receptor-specific cell association of HDL and selective cholesteryl-ester uptake at 37 °C were also measured. Unlike HDL binding at 4 °C, cell association at 37 °C was similar for SR-BI- and SR-BII-expressing cells (Fig. 3B). Both receptors mediated selective uptake, but this was significantly lower for SR-BII (Fig. 3C). For both receptors, HDL protein degradation was low, indicating little delivery of lipid to lysosomes via typical endocytic pathways (Fig. 3D). If the efficiency of selective uptake is expressed as selective uptake relative to cell associated HDL at 37 °C, the efficiency of SR-BII was 2-fold lower than SR-BI. However, when the efficiency of selective uptake is calculated relative to the number of receptors at the cell surface, calculated from HDL binding at 4 °C, the efficiencies of uptake for SR-BI and SR-BII are similar. The relatively greater difference between HDL cell association at 37 and 4 °C in the case of SR-BII, compared with SR-BI, suggests that, at 37 °C, SR-BII may accumulate HDL in an intracellular compartment to a greater extent than SR-BI. Cell association and selective uptake, as a function of time, are shown in Fig. 4. Cell association for both SR-BI and SR-BII reached a plateau after 1–2 h (Fig. 4A), whereas the selective uptake in cells continued over time (Fig. 4B). These results are consistent with the previously described selective uptake process (29).

Intracellular Distribution of HDL Lipids and Proteins—To assess possible HDL particle uptake, CHO cells were first incubated for 2 h at 4 °C with HDL3 labeled with Alexa 488 in the protein moiety and then washed and incubated at 37 °C in medium for 1 h. Confocal laser scanning microscopy showed surface binding of HDL at 4 °C to both SR-BI-expressing (Fig. 5A) and SR-BII-expressing (Fig. 5B) cells. Following incubation at 37 °C, the cell-associated HDL remained largely localized at the cell surface in the case of SR-BI (Fig. 5C). In contrast, significant amounts of surface-bound HDL3 were internalized.
by CHO-SRBII cells (Fig. 5D). No significant cell association of Alexa-labeled HDL was observed in CHO-A7 cells that do not express SR-BI or SR-BII (data not shown).

When cells were continuously exposed to Alexa-labeled HDL3 at 37 °C, for up to 120 min, CHO-SRBI cells accumulated limited amounts of HDL protein intracellularly, with the majority of the ligand after 30 min (Fig. 5E) and 120 min (Fig. 5G) being associated with the cell surface. In the case of CHO-SRBII cells, significant amounts of ligand were rapidly taken up, such that the amount of surface-bound ligand was small compared with intracellular ligand (Fig. 5, F and H), with the latter allowing us to distinguish the apical from the basolateral side.

To study HDL particle uptake in more detail, CHO cells were incubated with a mixture of DiI- and Alexa 488-labeled HDL3. After a 1-h continuous pulse at 37 °C, CHO-SRBI cells appeared to accumulate some HDL protein within the cell, yet most HDL protein remained on or in proximity to the cell membrane (Fig. 6A). There appeared to be some heterogeneity in terms of protein distribution, however, with some cells showing more intracellular accumulation of HDL protein than others. Although most DiI label was clearly enriched in the plasma membrane and co-localized with Alexa, in the case of CHO-SRBI cells, a significant portion of DiI appeared dissociated from the protein fraction and was dispersed throughout the cell (Fig. 6, C and E). This is consistent with selective lipid uptake mediated by SR-BI (1). In CHO-SRBII cells, in contrast, most of the HDL proteins and lipids were accumulated in a perinuclear region, with strong co-localization of both HDL components (Fig. 6, B, D, and F). Although co-localization suggests that the protein and lipid fractions of HDL remain associated, at this resolution it cannot be excluded that at least partial dissociation had occurred. CHO-A7 cells that do not express either scavenger receptor isoform did not accumulate detectable amounts of ligand (not shown). Similar results on the uptake of these tracers by SR-BI and SR-BII were observed in transiently transfected COS cells (data not shown).

The cellular distribution of SRBI/II and acquired HDL was also studied in CHO cells expressing EGFP-SRBI or EGFP-SRBII fusion constructs following a 1-h exposure of cells to...
Alexa 568 (red)-labeled HDL at 37°C. As seen in Fig. 7, SR-BI (Fig. 7A) and SR-BII (Fig. 7B) showed extensive co-localization with HDL proteins, with SR-BI being mainly expressed on the cell surface and SR-BII within the cell.

These observations support the biochemical data, in that SR-BII mediates intracellular accumulation of HDL into a compartment in which selective uptake does not occur or occurs only slowly. In the case of SR-BI, however, lipids seem to dissociate more readily from the HDL particle, in a process that seems to occur mainly at or in proximity of the cell membrane.

SR-BII Accumulates HDL Protein into a Transferrin-positive Endosomal Recycling Compartment—To characterize the intracellular compartment into which SR-BII accumulates ligand, CHO cells were simultaneously incubated for 1 h with Alexa 488 (green)-labeled HDL3 and Alexa 568 (red)-labeled transferrin that is known to recycle to the plasma membrane from the ERC. In the case of SR-BI, little co-localization of HDL3 and transferrin could be observed (Fig. 8, A, C, and E). Strikingly, as shown in panels B, D, and F of Fig. 8, virtually all HDL3 acquired by CHO-SRBII cells co-localized with transferrin. These results indicate that the internalization of HDL by SR-BII into the transferrin-containing ERC occurred at a relatively rapid rate compared with SR-BI.

Internalization of SR-BII—Because SR-BII appeared to accumulate substantial amounts of HDL3 within the ERC, we assessed whether the receptor undergoes endocytosis. COS cells were transiently transfected with either SR-BI or SR-BII. Surface receptors were labeled at 4°C with the red-1 antibody that recognizes the common extracellular domain. The cells were then chased at 37°C with complete medium. Fig. 9 shows that after 45 min, significant amounts of SR-BII antibody were found within the cell, whereas SR-BI remained mainly on the cell surface. These observations indicate a relatively rapid rate of internalization of SR-BII compared with SR-BI and are consistent with the observed rapid SR-BII-mediated endocytosis of HDL.
DISCUSSION

In this study we show that the C-terminal cytoplasmic tail of SR-BII, which is entirely different from that of SR-BI (20), contains a signal that leads to reduced surface expression compared with SR-BI in both polarized and nonpolarized cells. Furthermore, SR-BII, but not SR-BI, undergoes rapid endocytosis and mediates intracellular accumulation of HDL in the ERC. Despite the fact that SR-BII mediates cell association of HDL at 37 °C in similar amounts compared with SR-BI, much of it intracellularly, the selective uptake capacity of SR-BII is less than SR-BI. Indeed, intracellular ligand shows considerable co-localization of HDL lipids and proteins, suggesting that selective uptake from the ERC is not efficient.

Our finding that SR-BII is expressed mainly intracellularly in polarized MDCK cells is not unexpected, because a PDZ domain in the C terminus of SR-BI is essential for surface expression in polarized cells (18), through interaction with the “scaffolding” protein PDZk1 (17). Our finding, however, that SR-BII is mainly expressed intracellularly in CHO cells is surprising, because previous reports suggest that the C termini-
nus of SR-BI is not required for HDL cell association in non-polarized cells (14, 15, 17, 18). Thus, the C terminus of SR-BII contains a signal that confines this isoform to the cell interior. This points to a possible interaction of the C-terminal tail of SR-BII with another cellular protein that serves to regulate its trafficking and intracellular distribution.

Previously, it was reported that SR-BII is capable of mediating selective uptake of HDL lipids, albeit at a lower efficiency (13, 19). Here we used CHO clones that were carefully selected for expression of equal levels of murine SR-BI or SR-BII protein and found that selective uptake by SR-BII was indeed less efficient, despite the fact that SR-BII-expressing cells showed similar amounts of HDL protein association at 37 °C compared with SR-BI-expressing cells. The relatively high level of HDL protein association to SR-BII could not be accounted for by surface-bound material, because biotinylation studies and HDL binding at 4 °C clearly showed that less SR-BII was expressed on the cell surface than SR-BI. We therefore hypoth-
esized that SR-BII mediates the internalization and accumulation of HDL in an intracellular pool from which selective uptake occurs only inefficiently. Our results indeed showed a marked difference in behavior of SR-BI and SR-BII with respect to the rate at which they accumulate intracellular HDL particles. SR-BII was found to rapidly internalize HDL particles as judged by the internalization of HDL protein together with HDL lipid (Fig. 6). In contrast, SR-BI mediated internalization at a markedly slower rate.

Interestingly, selective uptake by SR-BI and SR-BII was shown to correlate closely with the surface expression of SR-BI and SR-BII rather than the rate at which the two receptors accumulate HDL intracellularly. This strongly suggests that the majority of selective uptake occurs at the cell membrane rather than intracellularly during SR-BI/II-mediated recycling of HDL. This finding provides support for the current model of the mechanism of SR-BI-mediated selective lipid uptake. This model suggests that selective uptake occurs exclusively at the cell surface (29–33), in a two-step mechanism involving ligand binding followed by lipid transfer from HDL at the cell surface (14), perhaps through the formation of a hydrophobic channel through which cholesteryl esters subsequently enter the cell (7).

The majority of HDL protein that was internalized in CHO cells by SR-BII appeared in the ERC. HDL protein uptake into this compartment was accompanied by the uptake of HDL lipid, indicating whole particle endocytosis into the ERC. Following exposure of cells to HDL, the amount of internalized protein reached a steady state level within about 2 h (Fig. 4A), indicating that HDL recycles back to the cell surface, with little intracellular degradation of HDL apolipoproteins. Transferrin is a well known protein that recycles through the ERC. Transferrin releases its iron load in early endosomes and recycles back to the cell surface, together with its receptor (34). Interestingly, it was recently suggested that HDL proteins are at least partially recycled through the ERC in hepatocytes (35). Later, these findings were related to recycling of SR-BI through this compartment (8). Silver et al. (8) then proposed an intriguing concept of SR-BI-dependent selective sorting of HDL lipids in hepatocytes, in which basolaterally expressed SR-BI would internalize HDL into a selective-sorting compartment that partially overlaps with the ERC. Apolipoproteins would be secreted basolaterally and cholesterol apically, thus providing an attractive model for SR-BI-dependent biliary cholesterol secretion. This model seems plausible in light of the well documented retroendocytosis of HDL particles in polarized cells (36–38). A potential shortfall of the study by Silver et al. (8) was, however, that the authors could not discriminate between the movement of SR-BI and SR-BII in hepatocytes, because they used an antibody that recognizes the common extracellu-

![Fig. 8. Uptake of HDL protein and transferrin. CHO-SRBI (A, C, and E) or CHO-SRBI (B, D, and F) cells were incubated at 37 °C for 1 h with Alexa 488-labeled HDL3 (green; 10 μg/ml) and Alexa 568-labeled transferrin (red; 20 μg/ml). As seen in E, after 1 h, little HDL was found in the endosomal recycling compartment in the case of SR-BI. In the case of SR-BII, however, extensive co-localization was observed (yellow signal in F).](http://www.jbc.org/)

This model seems plausible in light of the well documented retroendocytosis of HDL particles in polarized cells (36–38). A potential shortfall of the study by Silver et al. (8) was, however, that the authors could not discriminate between the movement of SR-BI and SR-BII in hepatocytes, because they used an antibody that recognizes the common extracellular...
Fig. 9. Endocytosis of SR-BI and SR-BII. COS cells were transiently transfected with either SR-BI (A and C) or SR-BII (B and D) and then incubated with red-1 antiserum at 4 °C for 1 h. The cells were then incubated with complete medium for 45 min at 37 °C (C and D) or remained at 4 °C (A and B). After extensive washing, the cells were fixed, permeabilized, and incubated with fluorescent secondary antibody. Each image contains at least one cell that was not stained with the antibody, showing specificity of the antiserum. Furthermore, untransfected cells showed no fluorescent signal when incubated with red-1 and secondary antibody or secondary antibody alone (not shown).

The physiological relevance of extensive and rapid HDL internalization by SR-BII into the ERC is not yet clear. Protein levels of SR-BII are generally low, compared with SR-BI. In the liver, it is estimated to represent 10–15% of total SR-Bx protein mass (19), even though it has been reported that SR-BII may be strongly up-regulated under certain conditions (21). SR-BII internalization of HDL may play an important role in previously reported cellular trafficking of HDL (8, 35). Internalization of HDL and its retroendocytosis has been demonstrated in macrophages and CaCo-2 cells (36, 40–43). Such HDL recycling has been reported to be important in the process of cholesterol efflux from macrophages (41) and also in the pathway by which apolipoprotein E is recycled in hepatocytes (44). It is possible that SR-BII plays a key role in mediating HDL retro-endocytosis. In the liver, as discussed, SR-BI appears to play a role in biliary cholesterol secretion. Evidence has been presented that this involves HDL internalization by SR-BI and intracellular selective sorting of HDL lipid from HDL protein. In the light of our findings that SR-BII internalizes HDL at a much faster rate SR-BI, it is possible that SR-BII plays an important or major role in this pathway. Thus, SR-BII allows for endocytic uptake of HDL lipid and protein in a manner that is distinct from cell surface selective uptake and that allows for lipid delivery into a different subcellular compartment in which cholesterol may be processed differently.

In conclusion, we have demonstrated that the C terminus of SR-BII, an alternative splicing variant of the important HDL receptor SR-BI, contains a signal that leads to marked alterations in the cellular distribution and cellular trafficking of SR-BII compared with SR-BI. Surface expression of SR-BII and selective uptake capacity are reduced compared with SR-BI. The lack of correlation between the rates of SR-BI and SR-BII mediated HDL internalization and the rates of selective lipid uptake by these receptors provides strong evidence that selective lipid uptake by SR-BI occurs at the cell surface and does not require HDL internalization and recycling. In contrast to SR-BI, SR-BII mediates the rapid uptake of significant amounts of HDL into the ERC by a pathway that is distinct from selective lipid uptake at the cell surface.

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High Density Lipoprotein Uptake by Scavenger Receptor SR-BII
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