

## Publication

ABC-transporters are localized in caveolin-1-positive and reggie-1-negative and reggie-2-negative microdomains of the canalicular membrane in rat hepatocytes

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The canalicular plasma membrane is constantly exposed to bile acids acting as detergents. Bile acids are essential to mediate release of biliary lipids from the canalicular membrane. Membrane microdomains (previously called lipid rafts) are biochemically defined by their resistance to detergent solubilization at cold temperature. We aimed to investigate the canalicular plasma membrane for the presence of microdomains, which could protect this membrane against the detergent action of bile acids. Highly purified rat liver canalicular plasma membrane vesicles were extracted with 1% Triton X-100 or 1% Lubrol WX at 4 degrees C and subjected to flotation through sucrose step gradients. Both detergents yielded detergent-resistant membranes containing the microdomain markers alkaline phosphatase and sphingomyelin. However, cholesterol was resistant to Lubrol WX solubilization, whereas it was only marginally resistant to solubilization by Triton X-100. The microdomain marker caveolin-1 was localized to the canalicular plasma membrane domain and was resistant to Lubrol WX, but to a large extent solubilized by Triton X-100. The two additional microdomain markers, reggie-1 and reggie-2, were localized to the basolateral and canalicular plasma membrane and were partially resistant to Lubrol WX but resistant to Triton X-100. The canalicular transporters bile salt export pump, multidrug resistance protein 2, multidrug resistance-associated protein 2, and Abcg5 were largely resistant to Lubrol WX but were solubilized by Triton X-100. Conclusion: These results indicate the presence of two different types of microdomains in the canalicular plasma membrane: "Lubrol-microdomains" and "Triton-microdomains". "Lubrol-microdomains" contain the machinery for canalicular bile formation and may be the starting place for canalicular lipid secretion.

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