Caveolin-1-mediated apolipoprotein A-I membrane binding sites are not required for cholesterol efflux.

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Caveolin-1 (Cav1), a structural protein required for the formation of invaginated membrane domains known as caveolae, has been implicated in cholesterol trafficking and homeostasis. Here we investigated the contribution of Cav1 to apolipoprotein A-I (apoA-I) cell surface binding and intracellular processing using mouse embryonic fibroblasts (MEFs) derived from wild type (WT) or Cav1-deficient (Cav1(-/-)) animals. We found that cells expressing Cav1 have 2.6-fold more apoA-I binding sites than Cav1(-/-) cells although these additional binding sites are not associated with detergent-free lipid rafts. Further, Cav1-mediated binding targets apoA-I for internalization and degradation and these processes are not correlated to cholesterol efflux. Despite lower apoA-I binding, cholesterol efflux from Cav1(-/-) MEFs is 1.7-fold higher than from WT MEFs. Stimulation of ABCA1 expression with an LXR agonist enhances cholesterol efflux from both WT and Cav1(-/-) cells without increasing apoA-I surface binding or affecting apoA-I processing. Our results indicate that there are at least two independent lipid binding sites for apoA-I; Cav1-mediated apoA-I surface binding and uptake is not linked to cholesterol efflux, indicating that membrane domains other than caveolae regulate ABCA1-mediated cholesterol efflux.

Résumé en anglais

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