



ABCC6 is a basolateral plasma membrane protein

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RÉSUMÉ: ABCC6 plays a crucial role in ectopic calcification; mutations of the gene cause pseudoxanthoma elasticum and general arterial calcification of infancy. To elucidate the role of ABCC6 in cellular physiology and disease, it is crucial to establish the exact subcellular localization of the native ABCC6 protein. OBJECTIVE: In a recent article in Circulation Research, ABCC6 was reported to localize to the mitochondria-associated membrane and not the plasma membrane. As the suggested mitochondrial localization is inconsistent with published data and the presumed role of ABCC6, we performed experiments to determine the cellular localization of ABCC6 in its physiological environment. METHODS AND RESULTS: We performed immunofluorescent labeling of frozen mouse and human liver sections, as well as primary hepatocytes. We used several different antibodies recognizing human and mouse ABCC6. Our results unequivocally show that ABCC6 is in the basolateral membrane of hepatocytes and is not associated with the mitochondria, mitochondria-associated membrane, or the endoplasmic reticulum. CONCLUSIONS: Our findings support the model that ABCC6 is in the basolateral membrane, mediating the sinusoidal efflux of a metabolite from the hepatocytes to systemic circulation.

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