

MEMBRANE PROTEINS INVOLVED IN FLAVONOID TRANSPORT IN ENDOTHELIAL CELLS

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Endothelial cells play a key role in the maintenance of cardiovascular homeostasis. They have multiple functions, such as the preservation of integrity of the vascular wall; moreover they represent a functional barrier between the circulating blood and the surrounding tissues, through which the transport of several substances is regulated. A great deal of epidemiological studies has investigated the correlation between a flavonoid-enriched dietary intake and a reduced risk factor in the development of cardiovascular diseases, such as atherosclerosis. However, the actual mechanism of transport of flavonoids through the endothelium remains unclear. It was demonstrated that flavonoids can interact with a number of membrane transport proteins. One of them is bilitranslocase (BTL), a membrane carrier of various organic anions such as bilirubin and anthocyanins, which was recently shown to mediate the uptake of some dietary flavonoids in liver cells (1). In addition, some ABC transporters, acting as multispecific efflux pumps by an ATP-mediated mechanism, may cause a decrease in the cytoplasmic levels of flavonoids (2).

The aim of this research was to investigate the expression of these proteins in endothelial cells and to study their role in the transport of flavonoids.

The permanent human cell line Ea.hy 926, exhibiting an endothelial phenotype, was used for the purpose. Comparative studies were also carried out in primary endothelial cells isolated from rat aorta. Western blot and immunocytochemistry analysis were carried out, using specific antibodies, to study the expression of BTL and of ABC transporters P-glycoprotein, MRP1 (Multidrug Resistance related Protein 1), MRP2 (Multidrug Resistance related Protein 2) and BCRP (Breast Cancer Resistance related Protein).

Transport studies have shown that quercetin is uptaken in these cells and the intracellular concentration of the flavonoid is reduced in the presence of specific inhibitors of BTL.

These results suggest that the expression and function of BTL in the vascular endothelium could be responsible for the transport of flavonoids and could be involved in the protection of blood vessels from atherosclerosis. Further studies will be addressed to investigate these transport mechanisms in human primary endothelial cells.

1. Passamonti, S., Vanzo, A., Vroshek, U., Terdoslavich, M., Cocolo, A., Decorti, G., Mattivi, F. (2005) *Food Res. Int.* 38:953-960.
2. Morris, M.E., Shuzhong, Z. (2006), *Life Sci.* 78: 2116-2130.