Doctoral College
Metabolic & Cardiovascular Disease

Reverse Cholesterol Transport in mice and humans; role of HDL and transintestinal cholesterol excretion (TICE)

GUEST LECTURE by

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Friday, 27.01.2012, 16:00h

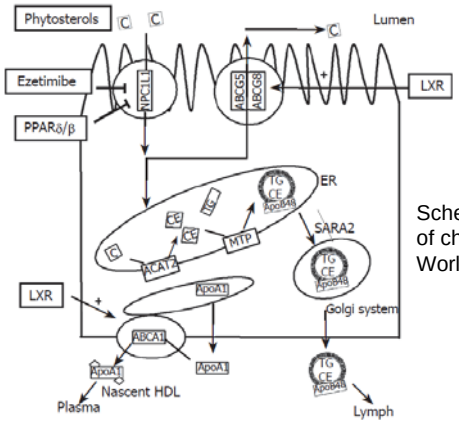
SR 07.11, Preclinics, MUG

Abstract

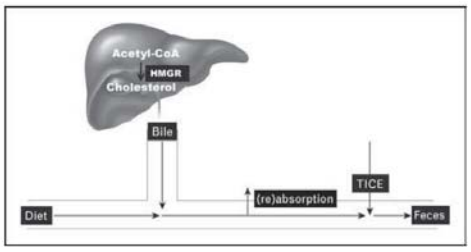
Reverse cholesterol transport (RCT) is defined as the HDL mediated transport of excess cholesterol from the periphery via the liver into the feces. It is generally assumed that defects in RCT play an important role in the etiology of atherosclerosis. The actual importance of this pathway in cholesterol excretion from the body has never been quantified.

Interestingly, animals but also humans with defects in HDL formation do not show defects in cholesterol excretion suggesting that alternative routes exist. We have shown that this is indeed the case; cholesterol can also be excreted via a direct route which we called transintestinal cholesterol excretion. In mouse models the capacity of this transintestinal cholesterol secretory pathway (TICE) is higher than the hepatobiliary route and can be stimulated via diet but also pharmacologically. Surprisingly, HDL does not play an important role as cholesterol donor to this pathway.

We have now demonstrated the presence of TICE in humans where it can be activated as well. In conclusion, next to the traditional RCT pathway, cholesterol can also be excreted via TICE. Both pathways provide attractive targets for therapy aiming at reduction of atherosclerosis.



Schematic overview of the regulation of cholesterol transport in enterocytes.
World J Gastroenterol 2006; 12(40): 6429-6439



Transintestinal cholesterol efflux
Current Opinion in Lipidology 2010, 21:167–171

Host: Dagmar Kratky