Esterase 22 – A Liver Retinylester Hydrolase

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Retinol (vitamin A) is an essential lipid in mammalians required for a variety of physiological functions such as embryogenesis, reproduction, vision, and immunity. The majority of retinol is stored as retinyl-palmitate in lipid droplets of liver stellate cells. Upon demand, retinol is secreted from the liver and transported to peripheral tissues. Retinol is biologically inactive, but is a precursor for active metabolites such as 11-*cis* retinaldehyde in the visual cycle or retinoic acid as ligand for gene regulation.

Circulating retinol levels depend on the balance between retinylester (RE) synthesis and hydrolysis. The release of retinol by the action of RE hydrolases has therefore an important regulatory function in retinoid homeostasis. The synthesis of RE is predominantly catalyzed by acyl CoA:retinol acyltransferase (ARAT) and lecithin:retinol acyltransferase (LRAT). However, the rate-limiting enzymes in RE catabolism are unknown. In this study, we identified Esterase 22 (Es22) as a liver RE hydrolase. COS-7 cell lysates overexpressing Es22 exhibit substantially increased RE hydrolase activities *in vitro*. Moreover, Es22 expression attenuates RE accumulation in COS-7 cells indicating that this protein affects cellular retinoid metabolism. Furthermore, Es22 mRNA is highly expressed in the liver representing the major storage site for RE. Fractionation of liver cells revealed that Es22 is expressed specifically in hepatocytes, but not in hepatic stellate cells even though they contain a large fraction of liver RE stores. Microscopic studies showed that GFP-tagged Es22 is localized exclusively at the ER and does not bind to lipid droplets. Taken together, these findings implicate that Es22 counteracts the esterification of retinol at the ER and thus could affect retinol storage and secretion.