CETP expression prolongs mice survival rate in sepsis by increasing leukocyte migration and reducing the concentrations of plasma IL-6 and of hepatic TLR4

Eder C R Quintao¹, Tatiana Martins Venancio¹, Roberta Marcondes Machado¹, Valeria Sutti Nunes¹, Alessandro Salerno¹, Francisco Garcia Soriano², Chin Jia Lin² and Patrícia Miralda Cazita¹

¹State University of Campinas, Brazil
²University of Sao Paulo, Brazil

Cholesteryl ester transfer protein (CETP) transfers neutral lipids among plasma lipoproteins; its inhibition raises plasma HDL. There has been considerable debate on the role of CETP in human atherogenesis. This may in part be explained by the involvement of CETP on the protection against against microbial infection and human sepsis. In order to evaluate the role of CETP in polymicrobial sepsis induced by caecum ligation and puncture (CLP), mice expressing human CETP, and wild-type mice (WT) underwent CLP sepsis. Sham-operated mice were utilized as controls. After CLP, mice survival rates were evaluated over five days. Also, mice were sacrificed at 24 or 48 hours after CLP, and blood, peritoneal cells and liver were collected. After CLP, as compared to wild type mice, CETP mice survived longer, had increased leukocyte migration into the peritoneal cavity, lower plasma IL-6 and TLR4 and acyloxyacyl hydrolase (AOAH) expressions in their liver. CETP mice had reduced liver inflammation and plasma inflammatory factors, and increased leukocyte recruitment to the infectious focus. Thus, CETP is involved in the first line of defense against an exacerbated production of proinflammatory mediators. These results indicate that the regulation of TLR4 in the liver plays a role in the proinflammatory response and pathophysiology of polymicrobial sepsis that helps explaining why CETP pharmacological inhibition has consistently failed to provide protection against atherosclerosis in human investigations.

Biography

Eder C R Quintao, MD, was Research Associate at the Rockefeller University, N. York (1965-1970). After 1970: chief of the Lipid Metabolism Lab (LIM10). He was tenured Head Professor of Endocrinology at Faculty of Medical Sciences, University of São Paulo, Brazil, in 1997. Since 2003, has been Emeritus Professor of Endocrinology. He has published 106 papers, most of them dealing with the control of the metabolism of cholesterol; collaborates with the International Atherosclerosis Society advising on papers dealing with cholesterol metabolism. He is Member of the Brazilian Academy of Sciences.

equintao@terra.com.br