Sphingomyelinase and Ceramidase Activity in Human Plasma

Lars I. Hellgren, Jacob H. Mathiessen, Elizabeth A. Miles & Philip C. Calder
Center for Biological Sequence Analysis, BioCentrum-DTU, Technical University of Denmark &
Institute of Human Nutrition, University of Southampton
lih@biocentrum.dtu.dk

It has been suggested that accumulation of the sphingolipid ceramide in the circulation is an important event in the atherogenic process. Accumulation of ceramide in LDL-particles makes them more prone to aggregation and enhances their uptake by macrophages. Thus ceramide stimulates foam cell formation [1-3]. Furthermore, ceramide accumulates in the atherosclerotic plaque, and it has been suggested that ceramide-induced apoptosis in both smooth-muscle cells and endothelial cells, might destabilize the plaque and hence induce cardiac infarction [4,5]. Therefore, ceramide accumulation can both accelerate the atherogenic process, as well as increase the risk of an acute cardiac infarction. Ceramide can be formed from sphingomyelin in the lipoprotein-particles through the activity of the secretory sphingomyelinase, but ceramide can also be further hydrolyzed to sphingosine and a free fatty acid by a ceramidase activity. Hence, the specific turn-over of ceramide in the circulation is determined by the activity of these two enzymes. Despite the potential importance for human health, very little is known on the presence and regulation of ceramidase activity in the circulation or on the impact of dietary alterations on the activities of either the secretory sphingomyelinase or ceramidases.

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In this paper, we will for the first time present evidence that not only sphingomyelinase, but also ceramidase activity are present in normal human plasma. We will also present results from a human intervention study, in which we have studied how different levels of EPA intake for 12 weeks affects the activity of secretory sphingomyelinase and ceramidase in young (18-42 years old) subjects.

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